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We dedicate this book to our families:
To my wife, Susan Crisp; my children, Justin and Mary;
my parents, Robert and Sandy; and my brother, Thomas.
(SJB)
To my wife, Sherrie, and my son, Cameron.
(RGS)

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Diseases of the Stomach
Diseases of the Intestines
Diseases of the Liver and Biliary Tract
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Fractures of the Femur

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Surgery of the Urinary Bladder
Surgery of the Ovaries and Uterus
Surgery of the Vagina and Vulva

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Selected Skin Graft and Reconstructive Techniques
Surgery of the External Ear Canal and Pinna

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Electrocardiography
Disorders of the Cardiac Rhythm

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Fractures of the Skull
Neoplasia of the Axial Skeleton

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Diseases of the Lens
Diseases of the Uvea
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Preface

The world of small animal veterinary medicine continues to grow in scope and complexity. Practicing veterinarians and veterinary students are continuously bombarded with new information on the diagnosis and treatment of diseases affecting pet animals. Busy veterinarians have precious little time to keep up with current developments in the profession. We recognize that challenge, and thus we attempt to provide a comprehensive book that covers the commonly encountered disorders seen in small animal practice.

Although difficult to include all the pertinent material in a one-volume text, the semi-outline format used in the Manual allows our authors to be concise, yet thorough. As in the first two editions, we continue to make information user friendly by including many key points, condensing information into tables and bulleted lists, and illustrating procedures and surgical techniques with many simple line drawings. However, it is impossible to provide an exhaustive discussion of all small animal diseases in one book. Pathophysiology of disease, rare conditions, and infrequently used diagnostic and treatment methods are not included. Readers are directed to many well-written veterinary textbooks or journals that cover various subjects in greater detail than what we have space for in the Manual. But the Manual seems to have found a niche. From what countless practitioners and students have told us, it is a text that is not kept on a bookshelf gathering dust, but is open on a counter, desk, or exam table where it is almost constantly being used to update or review important clinical information. This is exactly how we hoped the book would be used.

Although we have stayed true to the book's original style, we have added some new authors, section editors, and chapters. New chapters include Pain Management, Vaccination Guidelines, Disorders of the Claw, Postoperative Physical Rehabilitation, and Syncope. Examples of other new areas covered in the third edition are: new emerging infectious diseases; skin cytology for diagnosis of skin disorders; an overview of current imaging techniques such as digital radiography, computed axial tomography, and magnetic resonance imaging; technique for laser declaw; indications for laparoscopic and thorascopic surgery; and a brief discussion of arthroscopic procedures for certain joint disorders. Additionally, all chapters, even if rewritten by the same author, have been thoroughly and meticulously revised and updated, and several new illustrations have been added. The Appendix of Drug Dosage Guidelines has also been updated and many new drugs included.

We are very grateful to all those who have contributed to the third edition of the Manual. The section editors and chapter authors have done an excellent job organizing and presenting information in their areas of expertise. They have correlated their own clinical experience with information available in the literature and have provided useful and practical information. We also wish to thank the faculty, residents, and students at The Ohio State University College of Veterinary Medicine for their support and advice on the preparation of this edition.

The Manual is the result of a tremendous amount of organizing, copyediting, proofreading, and attending to details. We are indebted to the staff at Elsevier for all their hard work, particularly Ms. Jolynn Gower, Managing Editor. Thanks also to Ms. Joy Moore, Senior Project Manager. We also thank Ms. Sarah Self, Production Editor and the staff at Graphic World Publishing Services. Finally, we appreciate the work of our very talented medical illustrator, Ms. Felecia Paras.

As we have indicated in both of the previous editions of the Manual, we are striving for continued improvement of our work. We welcome any comments or criticisms that will help make future editions an even more valuable part of the small animal clinicians' library.

Stephen J. Birchard, DVM, MS
Robert G. Sherding, DVM

Section 1

Patient Management

Stephen J. Birchard

Chapter 1

History and Physical Examination

Denise Jones

Veterinarians are faced with many diagnostic challenges on a daily basis. By far the most important diagnostic tool that veterinarians possess is their ability to obtain a complete history and perform a thorough physical examination. This information, when accurately interpreted, lays the foundation for a logical diagnostic and therapeutic plan. A systematic and thorough history and physical examination prevents unnecessary diagnostic testing and needless cost to the owner.

GENERAL HISTORY

Obtain both objective and subjective information when collecting the history.

- Objective data consist of the signalment, environment, diet, and medical history. For a patient's first visit, determine the length of ownership and the place of origin.
- Subjective data include a description of the primary complaint and a historical overview of the patient's general health. The owner often may not realize how a seemingly unimportant observation may be related to the primary problem. Tailor specific questions to the individual case.

Signalment

- The signalment consists of the patient's age, species, breed, and gender. Note whether the patient is intact or neutered. The patient's breed will sometimes become a key factor when formulating differential diagnoses. Congenital or hereditary disorders should be considered. For example, familial renal disease should be a primary differential for a young Shih Tzu presenting with polydipsia and polyuria. In other cases the disease process may not be congenital or hereditary, but it may be more prevalent in certain breeds than others. For example, a small-breed dog that presents with lameness that is localized to the hip is more likely to have avascular necrosis of the femoral head (Legg-Perthes disease) than hip dysplasia.
- Verify that previously recorded data are correct and up-to-date. For example, the patient may have been neutered since its last visit or the physical examination may indicate that the recorded age is questionable.

Environment

- Gather environmental information as a routine part of the patient's history. In many circumstances, where the pet is kept provides a vital clue in diagnosis.
- Determine whether the pet is free roaming or confined to a yard or house. If the patient is confined to a yard, ask the owner if the yard is fenced, if the pet is chained, and if an escape has been possible in the recent past. The free-roaming or recently escaped pet may have had access to toxins or have been

subject to trauma, which is less likely for an indoor pet. For example, in a dyspneic patient, diaphragmatic hernia ranks higher on the differential diagnosis list for a free-roaming pet than for a strictly indoor pet.
- Determine the geographic origin of the pet and any record of recent travels. This becomes paramount if the patient has been exposed to diseases endemic to certain regions but not prevalent in the current environment, such as systemic mycoses and vector-borne diseases.
- Determine the pet's water source. This may be important if the pet has access to contaminated outdoor water, toilet-bowl water treated with deodorants or cleansers, or if the pet has limited access to water.
- Question the owner if there has been any potential exposure to toxins such as antifreeze, pesticides, or insecticides if the patient's clinical presentation is indicative of intoxication. Exposure to houseplants or outdoor vegetation may also provide a clue. For a vomiting or anorexic patient, questions should include access to potential ingested foreign bodies.

Dietary History

- Always include dietary information in the routine database. Question the owner about the patient's appetite and noticeable weight gain or loss. Also note whether the owner watches the pet eat.
- Determine the following pertinent facts in the dietary history:
  - Type of diet (e.g., dry, moist, semimoist, or table food)
  - Brand name of food
  - Type of snacks
  - Method of feeding (i.e., free-choice or individual meals)
  - Amount

Preventive Health Care Status

- Evaluate the patient's preventive health care status. Review the patient's prior medical record.
- Record all previous vaccinations received and the dates of each. Avoid simply asking if the patient is current on vaccinations because many clients are unfamiliar with vaccination recommendations. Inform the client about what vaccinations are available as well as the indications and booster intervals for each (see Chapter 7).
- For a feline patient, discuss the subjects of feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV), including the dates and results of previous testing. Exposure to stray cats or cats known to be FeLV-positive or FIV-positive may also be relevant. History of previous cat fight wounds may warrant repeat testing for FIV. However, if the patient has been previously vaccinated for FIV, then further FIV testing will be invalid since the FIV test is an antibody test.
- For a canine patient, record heartworm test dates and results. If the patient is receiving heartworm preventive therapy, note the type, frequency, and dose (see Chapter 152).

Prior Medical History: Previous Illnesses and Surgeries

- Often the patient's prior or ongoing health problems play a role in its presenting ailment; therefore, review the information previously recorded in the medical record and discuss previous problems managed by other veterinarians.
- Record the dates of the previous illness or surgery, followed by a brief description of the problem, how it was managed, and the response to treatment.
- Discern the relevance of prior illnesses before obtaining extensive details; otherwise, the history may become unnecessarily lengthy and confusing.
- Specifically question the owner as to any medications the patient is currently or has recently been given. Over-the-counter products as well as prescription medications should be noted.

Primary Complaint

- Use the history to identify and localize the primary problem. Much of this information is subjective, based mostly on the owner's interpretation of the pet's clinical signs and behavior. Be aware that some owners are extremely observant of their pet and others are not. Prompt owners to describe the pet's behavior and clinical signs in their own words. An astute clinician collects all data and subjectively analyzes this information in context of an owner's perceptivity.
- Encourage the owner to describe the patient's problem from its onset so that a chronologic picture is obtained.
- Avoid leading questions that might result in a deceptive history. For example, ask if there has been any change in frequency of defecation. Do not ask if the patient is defecating more frequently than normal.
- Determine the last period of normalcy or the duration of the clinical signs. This will help determine how acute or chronic the problem may be and will guide the ranking of differential diagnoses. Some differentials are more likely for an acute problem; others are more likely for a chronic problem. For example, intestinal intussusception or an intestinal foreign body are likely differentials for a puppy presenting with an acute episode of persistent vomiting. A gastric foreign body or inflammatory bowel disease are more likely in a similar patient with chronic intermittent vomiting. The onset and severity of the illness influences how rapidly or aggressively the problem should be approached.

- Determine the progression of the clinical signs. Once again, this may help not only in formulating a list of differentials but also in developing a treatment plan. For example, a patient presenting with a history of seizures is managed more aggressively when the seizures are increasing in frequency and length than when they have been the same for months or years.
- Question the owner as to any intervening signs that might provide a clue to the most likely differential diagnosis. For example, a cat with chronic diarrhea and intermittent episodes of fever is considered a more likely candidate for infectious disease than for dietary intolerance.
- Attempt to further define and localize the problem. For example, characterize diarrhea as originating in the small or large bowel before proceeding to a diagnostic or therapeutic plan. Ask questions regarding frequency, appearance (color and consistency), and presence or absence of straining to help localize this problem. Specific questions oriented by body systems follow in the next section.
- Determine treatments and response. For example, a dog presenting with pruritus unresponsive to previous treatment with corticosteroids is a more likely candidate for food allergy dermatitis than for atopy. Record what medication was given, the dose, the duration of treatment, and the level of response observed.

HISTORY ORIENTED BY BODY SYSTEMS

For a complete history, include a system-by-system review of the patient's general health. This can be accomplished by the experienced clinician as the physical examination is performed. The novice may prefer to obtain the entire history before proceeding with the physical examination. Develop a consistent and systematic method. One method is to begin with questions concerning the patient's head and proceed caudally, as demonstrated in the following text. It is left to the clinician's discretion as to how in-depth the client is questioned about systems that do not appear to affect the primary complaint. Apply the general principles described in the previous section in the approach to all body systems (e.g., onset and duration).

Eyes

- Ask if any ocular discharge has been noted. If so, describe the discharge (serous, mucoid, or mucopurulent) and determine if it has been unilateral or bilateral.
- Determine if ocular pain or discomfort is present as indicated by blepharospasm, face rubbing or pawing, or photophobia. These signs may be seen with anterior uveitis, glaucoma, corneal ulcerations, or foreign bodies.
- Ask about ocular redness, swelling, and asymmetry.
- Ask if the owner has noticed a color change in the pet's eye. This change can occur with anterior uveitis and iriditis, in which hyphema may be present or the iridial color may be altered. A localized pigment change in the iris may occur with an iris cyst or melanoma.
- Ask the owner if their pet seems to be experiencing any loss of vision. If there is an apparent problem, does it seem to be affected by daylight or darkness? Also ask if decreased vision appears to be a unilateral or bilateral problem. See also Section 10.

Head, Neck, Ears, Nose, and Oral Cavity

- Record any history of swelling or asymmetry of the head and neck region.
- Inquire about head shaking, ear scratching, and otic discharge or odor that may indicate the possibility of otitis or a foreign body in the ear. Determine if any loss of hearing has been evident.
- Ask if any nasal discharge has been present. Note the character of any nasal discharge (serous, mucoid, mucopurulent, or hemorrhagic) and whether it has been unilateral or bilateral. Note any history of sneezing, nose rubbing, nasal asymmetry, or stridor.
- Request information relating to the oral cavity, such as odor, difficulty eating or drinking, abnormal swellings involving the gingiva or tongue, and changes in gingival pigmentation. Ask if there has been any change in the patient's ability to vocalize. The patient's voice can be affected either by a mass in the laryngeal region or by laryngeal paralysis.

Cardiopulmonary System

- Ask if cough, exercise intolerance, weakness, or fainting have been observed. These may indicate cardiopulmonary disease.

▼ ***Key Point*** Attempt to differentiate syncope from seizures based on the owner's description of the event.

- Syncope is a transient loss of consciousness that may be precipitated by exercise in patients with underlying cardiac disease (see Chapter 148). During a syncopal episode the patient usually demonstrates very little motor movement. The episode typically lasts less than a minute, and usually the patient returns to normal within a short period of time. Seizures vary greatly in severity. They are often preceded by a preictal phase during which the patient may be anxious or disoriented. The actual seizure usually involves a loss of consciousness and active motor activity such as tonic-clonic limb movements and rapid jaw movements. The postictal phase may last from minutes to days. The patient may be either overly agitated or depressed during this time. Seizure disorders are discussed in Chapter 127.

- Characterize coughing as productive or nonproductive, moist or dry, and harsh or honking. Some owners may confuse a productive cough with vomiting; therefore, ask whether abdominal heaving occurs prior to the production of fluid or foam or whether coughing and gagging are more typical. Yellow or green fluid is indicative of vomitus. The circumstances surrounding the cough are often relevant. For example, cough associated with tracheal collapse is often elicited with excitement or pulling on the patient's collar. Coughing secondary to congestive heart failure may be exacerbated with the pet in a sternal position. Is the pet routinely exposed to cigarette smoke? This can play a role in chronic bronchitis or feline asthma.
- Determine if dyspnea has been observed. It may be difficult for an owner to differentiate between heavy panting and true dyspnea. Ask if the pet is breathing the same during the exam as it was at home. Also inquire if the pet seems reluctant to exercise or lie down, as would be expected with most dyspneic animals. Open-mouth breathing for a cat is always considered abnormal except when it is excessively stressed. See also Chapter 142.

Digestive System

Most problems related to the digestive system are clinically manifested as anorexia, regurgitation, vomiting, diarrhea, constipation, weight loss, or a combination of these. Determine which clinical sign is being exhibited, because the owner may incorrectly interpret what is observed. For example, owners often assume that their pet is constipated if it is observed straining to defecate, when diarrhea may be the actual cause. Ask specific questions to differentiate between vomiting and regurgitating. Regurgitation is characterized as a passive ejection of ingested material from the esophagus. It typically occurs soon after a meal is eaten. The regurgitated material is usually undigested and tubular in form. Vomiting frequently involves an abdominal heave movement or retching. Time of vomiting in relation to eating should be noted and is variable depending on the underlying disorder. Vomitus is not tubular in form and may consist of froth, fluid, yellow-green bile, food, or ingested foreign material. Include the following specific information in approaching a digestive system problem:

- Review dietary history, as previously described. Specifically ask about treats or access to garbage.
- Record environmental history, as previously described.
  - Has there been any exposure to toxins, drugs, or plants?
  - Are there any toys or other foreign objects that the pet may have ingested?
- Note vaccination status.
- Ask how the patient's appetite has been and how it compares with its normal appetite.
- Has any vomiting been noted (onset, frequency, progression)?
  - Has the owner actually observed the pet vomiting? In a multi-pet household, verify that it is the presenting patient that is actually vomiting.
  - Does the pet exhibit any retching or abdominal heaving when "vomiting"?
  - How frequently is the pet vomiting?
  - What is the relationship of vomiting to eating, if any?
  - What is produced when the pet vomits? Describe the vomitus—digested or undigested food, fluid, foam, and color. Green or yellow fluid is typical of bile.
- Has the owner witnessed the patient defecating, and are there any abnormalities?
  - How long since the last observed bowel movement?
  - Has any diarrhea been observed (onset, progression)?
  - Has the stool been persistently loose?
  - How frequently does the animal defecate?
  - What volume of stool is typically produced? Small amounts of stool produced frequently are indicative of large bowel disease, and larger amounts of stool produced less frequently are more typical of small bowel disease.
  - What is the color and consistency of the stool (formed but soft, cow patty–like, watery)?
  - What is the consistency of the last stool produced?
  - Is there any blood or mucus present? (These are indicative of large bowel disorders.)
  - Does the animal strain while defecating? Straining is typical of diseases localized to the colon, rectum, or anus.
  - Does the owner witness all eliminations (i.e., is the pet walked on a leash, does it have access to a fenced yard. or does it roam free)? Consider that owners may not be fully aware of what their pet is eliminating.

See also Section 6.

Urinary System

Often, the owner complaint may be that the pet is urinating excessively. The following questions help distinguish whether excessive urination is due to polyuria or pollakiuria:

- Has there been any change in the quantity of water that the pet consumes?
- Are there other pets in the household that have access to the same water source?
- Is the pet urinating inside the house (i.e., having "accidents")?

- Are these urinations observed? (The owner should verify that this is the pet having the accidents versus another pet in the household.)
- Does the owner know if the accidents occur while the animal is awake or asleep? If the owner has not observed the act, there may be other clues to pursue. Where has the owner found the accidents (where the pet sleeps, next to a door, etc.)? A patient that is experiencing urinary incontinence may be dribbling urine while resting in its sleeping area. Dogs that are well house-trained may urinate close to an outside door if they are unable to hold their urine until allowed access to the outside yard. Another clue to urinary incontinence is the presence of urine on the pet's perineal region or rear legs.
- Does the animal seem to be consciously aware of the act, or does the animal dribble urine without seeming to be aware?

- Has there been any change in frequency of urination? If the patient is urinating frequent small amounts (pollakiuria), then differentials should include lower urinary tract disorders such as cystitis, urolithiasis, and neoplasia.
- Does the animal appear to strain while urinating? (This is typical of lower urinary tract disease.)
- What quantity of urine is produced? Larger quantities of urine are indicative of polyuria, which occurs with a large number of underlying metabolic disorders (renal disease, liver disease, diabetes, mellitus, diabetes insipidus, hyperadrenocorticism, hypercalcemia, etc.).
- Has the owner noticed any blood in the urine? If so, is it before, during, or after urination? Bleeding only at the beginning of urination is more likely to be from the urethra. Hematuria present throughout the urination is most typical of bleeding of renal origin. Blood seen at the end of urination usually originates from the urinary bladder. Remember to consider the genital system as a potential source for the blood, as with prostatic disease or vaginal masses.

See also Section 7.

Genital System

Females

- Verify if the patient is intact or spayed.
- Note any vulvar discharge and describe the amount, consistency, color, and odor. This type of discharge may be valid for spayed pets as well as intact ones.
- If the patient is intact, ask the following questions:
  - When did the owner last observe a heat cycle for the patient? Was it a normal cycle? How long did it last?
  - Have the heat cycles been at regular intervals?
  - Has the pet been intentionally bred or is there any possibility of an accidental breeding? Is there any previous history of pregnancy? If so, were there any complications (e.g., dystocia, abortions, mastitis, metritis, etc.)?
  - If there is a history of successful pregnancy, how many puppies were whelped?
  - Has the patient been tested for brucellosis? When? Was the mate previously tested?

Males

- Verify if the patient is intact or neutered.
- Has the patient exhibited any evidence of difficulty urinating or defecating?
- Has any preputial or penile discharge been noted? (Describe the amount, consistency, color, and odor.)
- The following questions apply to intact males:
  - Has the patient been used for breeding? If so, when was he last bred? Was there any difficulty in breeding?
  - Were any litters sired? If so, how many puppies were in each litter?
  - Has the patient been tested for brucellosis? When? Was the mate previously tested?

See also Section 7.

Swelling or Masses

Ask if any abnormal masses or swellings have been observed that have not been previously mentioned. Note the location, how long the mass or swelling has been present, and any change in appearance, character, or size. If the patient has not been examined in your practice before, ask if the mass has been previously sampled by either a fine needle aspirate or a surgical biopsy. Obtain a fine needle aspirate from masses that have not been previously investigated.

▼ ***Key Point*** Perform diagnostics on masses that are changing rapidly since there is a higher incidence of malignancy associated with these.

Skin

An accurate and detailed history is essential for successful management of dermatologic problems. Remember that some systemic disease processes may manifest themselves in cutaneous changes, such as hyperadrenocorticism or systemic lupus erythematosus (SLE). Some clinicians prefer to have the owner fill out a standardized dermatologic history form prior to specific questioning. Include the following questions on such a form, or directly ask the owner:

- Has any hair loss been observed? Did hair loss involve the undercoat or the main coat?
- Is there evidence of pruritus (scratching, biting, or licking)?
- Where does the pet seem to be most pruritic? Many atopic and food-allergic patients may rub their faces

and lick their feet excessively. Flea-allergic patients predominantly chew the dorsal tail-base region.
  - If the pet is pruritic, how severe is it? Have the owner grade the degree of pruritus on a scale of 1 to 10, with 10 being the most severe. This helps subsequent evaluation of treatment response.
  - Is the skin problem continuous or seasonal? If seasonal, then determine when the pet is most severely affected.
  - Has the owner noticed fleas? What flea products have been used? Has the pet been on monthly preventive treatment? If so, which product?
  - What type of bedding does the pet use?
  - Is there any exposure to feathers?
  - What type of carpet is in the house (wool, synthetic, cotton)?
  - What is the diet? What treats are given?
  - Are there any indoor plants?
  - Is the pruritus worse indoors or outdoors?
  - Is there any exposure to tobacco smoke?
  - Has the pet ever had any drug reactions? (describe)
- Describe odors, pigment changes, or texture changes of the skin or hair coat.
- Does the pet have any dandruff? If so, what areas are involved?
- How often is the patient groomed (clipped, brushed, combed)?
- How often is the patient bathed? When was the pet last bathed, and what products were used?
- Are there other pets in the household? Has the pet been exposed to other animals outside of the household? Did any of these animals exhibit signs of skin disease?
- Do any members of the household have skin problems?
- Do any of the pet's close relatives have a history of skin problems?
- Has there been any previous treatment? When was the pet last treated? What was the name of the drug, the dose, the route of administration, and the frequency of treatment? What level of response was noted?

See also Section 5.

Musculoskeletal System

- History relating to the musculoskeletal system generally focuses on lameness or discomfort.
- Remember to correlate the age and breed of the individual to the lameness observed. There are numerous examples in which the signalment may provide a clue to the underlying disorder. Many musculoskeletal disorders occur predominantly in young, large-breed dogs. These include but are not limited to osteochondritis dissecans, ununited anconeal process, panosteitis, and hypertrophic osteodystrophy. Middle-aged to older large-breed patients are more at risk for neoplasia such as osteosarcoma. Small-breed individuals have a higher tendency toward medial patellar luxation and avascular necrosis of the femoral head.
- When lameness has been observed, discern if the patient has been bearing weight on the affected leg. Determine if lameness has been previously observed in this limb or other limbs. For example, panosteitis is often considered a shifting leg lameness. Ask if there are any other signs of illness in addition to the lameness. The lameness may be a manifestation of systemic disease such as SLE or Lyme disease. Has the owner noticed any swelling or masses associated with the affected limb?
- Is the lameness intermittent, progressive, or static? Is the lameness worse before or after exercise? Arthritic patients often "warm out" of their lameness.
- Question owner in regard to routine daily activity such as running, jumping, hunting, jumping on and off furniture, etc. Has the pet engaged in any activities out of the ordinary lately? These patients are more at risk for traumatic injuries such as a cranial cruciate ligament tear or a ruptured intervertebral disc.
- Ascertain any possibility of trauma that could have resulted in a fracture. In some cases, the owner may have witnessed the traumatic incident. In others, the patient may have been unsupervised during the time in question. Specifically ask if the patient was confined to the house or a fenced area. If the animal was free roaming and unobserved, determine how long it was unsupervised to help assess the possibility of a traumatic incident.
- Determine if the owner has observed loss of muscle mass, asymmetry of the limbs, or swollen joints.
- Ask if the patient has demonstrated any difficulty rising, climbing stairs, or descending stairs. These problems are frequently noted in patients with hip dysplasia, intervertebral disc disease, or neurologic diseases such as degenerative myelopathy.
- In regions endemic for Lyme disease, ask if any ticks have been observed on the pet. Check vaccination status regarding Lyme disease. In nonendemic areas, obtain a travel history.

See also Section 8.

Nervous System

Many questions related to the nervous system may have been previously asked while taking the history of the other body systems. Once again, consider the age and breed to help provide clues to the differential diagnoses. Small-breed dogs are more commonly seen with portosystemic shunts and may present with neurologic signs. Hypoglycemia and congenital diseases are prime differentials for seizuring puppies. Epilepsy typically has an onset in young adults. For seizures with an onset during middle age or geriatric years, consider metabolic disease or neoplasia. Diseases of the central nervous

system (CNS) may be reflected by abnormalities in other systems (e.g., blindness, hearing loss, or urinary incontinence). With a presenting complaint of rear limb "weakness," differentiate between disorders of the musculoskeletal system and those of the nervous system with the history and physical examination. Consider the following points in regard to the nervous system:

- Verify vaccination history for distemper and rabies.
- Focus on obtaining a good environmental history, such exposure to toxins or plants. Is there any possibility of a traumatic accident resulting in head trauma or spinal injury?
- Ask if any behavioral changes, such as aggression or dementia, have been observed. If these signs are present, are they intermittent or persistent?
- Is there any evidence of pain when the patient is touched or picked up? Does the pet cry or yelp when it moves? These signs can occur in a patient with intervertebral disc protrusion.
- Record any history of seizures, including their duration and the time interval between them. Obtain a description of the seizure.
- If behavioral changes or seizures have been observed, ask if there is any relationship between when the pet eats and when these signs occur. Neurologic signs may be exacerbated postprandially in patients with a portosystemic shunt.
- Ask if there has been any evidence of weakness in the patient. If present, is the weakness generalized or localized (i.e., to one side of the body, in the forelegs, or to the rear)? Determine if any abnormalities in posture or ambulation have been observed, such as the pet's tendency to fall to one side, to circle to one side, to knuckle over, or to drag its toes. Be sure to note the acuteness of onset and the progression of the neurological signs.

See also Section 9.

PHYSICAL EXAMINATION: GENERAL OBSERVATION

- To begin the physical examination, watch the patient as it enters the room.
- Continue the visual evaluation of the patient while the history is collected. Observe the general body condition and any abnormalities in behavior, attitude, posture, ambulation, and respiratory pattern. During this time, the patient may be placed on the examination table or allowed to roam the examination room.
- During the general observation of the patient, evaluate its body condition. Several body condition scoring systems have been developed to aid in assessing the amount of body fat present in the individual dog or cat. The most commonly used systems utilize either a 5- or 9-point scale. I prefer the 5-point scale, where score 1 correlates to an emaciated body condition and score 5 indicates a grossly obese state. Score 3 is considered an ideal weight for the patient. Those body conditions that fall between two scores are assigned a half score. For example, a patient that is just over its ideal weight would be scored as 3.5. Refer to Tables 1-1 and 1-2 for details of body condition scoring in dogs and cats, respectively. Record the patient's body condition score (BCS) in the patient's record each visit.
- If the collection of the history and the physical exam result in a vague, poorly defined illness, consider hospitalizing the patient for observation. Sometimes owners may find it difficult to accurately describe the pet's behavior or clinical signs. Also, some patient's may mask their depression or pain when they initially arrive in a new environment. A nervous patient should be reevaluated once it has adjusted to the hospital surroundings. Occasionally, animals become more agitated the longer they are away from their owner. Finally, many disease processes become more evident with time, so the physical should be repeated on any undiagnosed or hospitalized patient.

Table 1-1. BODY CONDITION SCORING FOR DOGS

Score	Body Condition	Parameters Evaluated
1	Emaciated	Skeletal in appearance with no obvious body fat and minimal muscle mass. Boney prominences visible.
2	Thin	Ribs slightly visible and easily palpable. Prominent waist and abdominal tuck from side and dorsal views.
3	Ideal	Ribs not visible but palpable with only a slight fat covering. Abdominal tuck present from side view, and waist present from dorsal view. Smooth contour over tail base.
4	Overweight	Difficult to palpate ribs because of moderate fat layer. Loss of abdominal tuck from side view, and wide waist from dorsal view. Thickening over tail base.
5	Obese	Excessive fat cover over entire body. Ribs extremely difficult to palpate. No waist present from dorsal view. Fat skin folds droop from caudal abdomen on side view. Thick fat roll at tail base.

Table 1-2. BODY CONDITION SCORING FOR CATS

Score	Body Condition	Parameters Evaluated
1	Emaciated	Skeletal in appearance in the shorthaired cat. Boney protrusion of the wing of ilia and lumbar vertebra.
2	Thin	Ribs easily palpable with only slight fat covering. Waist prominent caudal to ribs. Minimal abdominal fat present.
3	Ideal	Uniform distribution of body fat. Ribs palpable but not prominent. Slight waist present caudal to ribs. Minimal abdominal fat pad present ventrally.
4	Overweight	Ribs difficult to palpate. Loss of visible waist and some abdominal distention present. Moderate abdominal fat pad present ventrally.
5	Obese	Ribs not palpable. Excessive fat deposits generalized but especially noted in abdominal region.

PHYSICAL EXAMINATION: VITAL SIGNS

Initially, record the vital signs and current body weight of every patient.

Body Temperature

- Obtain the rectal temperature early in the course of the examination to help avoid an elevation of temperature that may result from anxiety or excitement. If you are unsure whether the elevated temperature is the result of environmental factors, then consider hospitalizing the patient to recheck the body temperature in a few hours. In emergency situations, attend to hypothermia or hyperthermia early in the course of the examination.
- Normal rectal temperature for dogs range from 99.5°F to 102.5°F. For cats the range is 100.5°F to 102.5°F.
- Note any blood or melena that is evident on the thermometer.

Pulse and Heart Rate

- Record the pulse rate and evaluate the pulse quality.
- Normal heart rate values (beats per minute) are as follows:
  - Large dogs—60 to 100 bpm
  - Medium-size dogs—80 to 120 bpm
  - Small dogs—90 to 140 bpm
  - Domestic cats—140 to 250 bpm
- Determine if arrhythmias or pulse deficits are present.

Capillary Refill Time

- Lift up the upper lip, press on the buccal mucous membranes, and determine how long it takes for the membranes to resume normal pink color (normal is <2 seconds).

Respiratory Rate

- Evaluate the respiratory pattern as the rate is taken.
- The normal respiratory rate for dogs is 10 to 30 breaths per minute. For domestic cats the normal rate is 20 to 30 breaths per minute.
- If moderate or severe dyspnea is present, observe caution in continuing with the remainder of the examination. The additional stress of restraint and examination may result in life-threatening respiratory compromise. Administer oxygen therapy followed by a rapid oral examination and thoracic auscultation to help determine the source of the dyspnea and the appropriate emergency therapy. After stabilizing respiratory function, continue with the remainder of the physical examination.

Hydration

- Note if the eyes appear sunken or if the third eyelids are protruding bilaterally. This can be seen in a markedly dehydrated patient.
- Note if the mucous membranes are dry or tacky, as is typical of a moderately dehydrated patient.
- Evaluate skin turgor by gently lifting the skin over the dorsal thorax. Geriatric or cachectic patients may appear to be dehydrated based on their skin turgor alone because of the loss of the skin's natural elasticity.

PHYSICAL EXAMINATION: BODY SYSTEMS

The physical examination should follow the same logical pattern as the history. A consistent approach is taken so that no part of the examination is overlooked. For example, analyze one body system at a time, starting with the patient's head and proceeding caudally. Look at each body system as a piece of the puzzle. Attempt to link the results of the entire history and physical exam so that multisystemic disorders will not be overlooked. Additionally, your evaluation of one body system may affect what you recommend for an unrelated problem for another body system. Consider the whole patient when you formulate your diagnostic and therapeutic plans.

Head

- Examine the head carefully for evidence of asymmetry or localized swellings. Palpation is necessary to assess the nature of any swelling or mass (firm or fluctuant, mobile or attached).
- Evaluate the posture of the head and neck. Ventriflexion may be observed in cats with hypokalemia, chronic organophosphate toxicity, thiamine deficiency, and polymyopathies. Reluctance to move the head may be noticed in a dog with cervical intervertebral disc protrusion.

Eyes

The ocular exam often provides information that relates to systemic disorders. Systemic infections may manifest themselves through retinal lesions (FeLV, toxoplasmosis, fungal infections, etc.) or as anterior uveitis (FeLV, feline infectious peritonitis, ehrlichiosis, etc.).

- Determine if abnormalities are present unilaterally or bilaterally. If only one eye is affected, examine the normal eye first.
- Note evidence of pain such as blepharospasm, photophobia, and pawing or rubbing at the eye(s).
- Observe the size and symmetry of the eyes. Congenital microphthalmia or acquired phthisis bulbi results in a smaller-than-normal eye, whereas chronic glaucoma results in a larger-than-normal eye.
- Examine the position of the eyes for evidence of enophthalmos, exophthalmos, or strabismus. Enophthalmos may be secondary to microphthalmia, loss of the orbital fat pad (e.g., cachexia), Horner syndrome, dehydration, or acute ocular pain (e.g., anterior uveitis). Exophthalmos may be due to space-occupying lesions of the orbit (neoplasia, abscess, or cellulitis), buphthalmos (glaucoma), myositis, or breed predisposition.
- Note ocular discharge and characterize it as serous, mucoid, or mucopurulent.
- Note any swelling or masses involving the eyelids. Evaluate the eyelids for entropion and ectropion. Carefully examine the palpebral margins under magnification for evidence of distichiasis. Magnification may be necessary to identify distichia.
- Evaluate the conjunctiva for hyperemia, chemosis, pallor, or jaundice of the underlying sclera. The superior conjunctiva is more reliable for evaluating hyperemia than the inferior conjunctiva, which may normally appear somewhat hyperemic over the surface of the third eyelid. Note any abnormal pigmentation or masses involving the sclera or conjunctiva.
- Protrusion of the third eyelid may be a reflection of enophthalmos or Haw syndrome in cats. Haw syndrome is a bilateral protrusion of the third eyelids that may be seen in feline patients with gastrointestinal disease or parasites. Note any masses associated with the nictitans or prolapse of the gland of the nictitans. Apply gentle pressure to the superior globe to aid in exposing the nictitans. Apply topical anesthesia and grasp the third eyelid gently with forceps so that the posterior surface of the third eyelid can be examined for foreign bodies or follicular hyperplasia.
- Examine the cornea for cloudiness, pigmentation, vascularization, or obvious defects.
- Evaluate the anterior chamber for aqueous flare, hypopyon, hyphema, or abnormal masses. If a slit lamp is not available, use a magnifying lens and a penlight to produce a narrow beam of light so that subtle aqueous flare can be detected when the anterior chamber is viewed from the lateral aspect.
- Evaluate pupil size and symmetry and direct and consensual pupillary light reflexes. A darkened room aids in this examination. Persistent pupillary membranes may also be identified.
- Evaluate the iris for pigmentary changes, hyperemia, roughening, swelling, or synechia. Any of these changes can be seen with anterior uveitis. Tumors or cysts may occasionally occur on the iris. Melanoma of the iris may initially present as patchy pigmentation in the iris. Ask the owner when the color change was first noticed.
- Evaluate the lens via direct or indirect ophthalmoscopy for the presence of lenticular sclerosis, cataracts, or displacement of the lens.
- If a "red eye" is found during the exam, perform a Schirmer tear test, a fluorescein stain, and a measurement of intraocular pressure. Perform the Schirmer tear test prior to the other tests since eye drops used in the subsequent tests can affect results. A Tonopen is a valuable tool for easily measuring intraocular pressure.
- For a complete fundic examination, dilate the pupil with a short-acting topical mydriatic. Evaluate the fundus for vascularity, areas of hemorrhage, pigmentary changes, chorioretinal dysplasia or hypoplasia, and retinal detachment. Evaluate the optic disc for color, size, vascularity, fissures or colobomas, and abnormal masses. Practice and experience are the keys to retinal examinations.
- Evaluate vision by dropping a cotton ball in front of the patient or by rolling a cotton ball across the table or floor. Alternatively, create an obstacle course to discern if the patient has the visual ability to negotiate barriers. Compare the patient's performance in full-light versus low-light settings. Evaluate the menace response. Young puppies and kittens (<6 weeks of age) normally do not respond appropriately to menace.

See also Section 10.

Oral Cavity

- Perform a thorough oral examination if the patient's demeanor allows (Fig. 1-1). If this examination is indicated but the patient is uncooperative or aggressive, sedation (see Chapters 2 and 64) may be necessary. Sedation also allows the clinician to perform a more thorough oral exam in any patient presenting with clinical signs suggestive of oral cavity disease (i.e., ptyalism, halitosis, bleeding, or oral pain).
- Always carefully evaluate the mucous membranes for color, moisture, and capillary refill time to assess the hydration status. Hyperemia, congestion, cyanosis, jaundice, pallor, or petechiae can provide vital diagnostic clues to the underlying disorder.
- Note gingival masses, ulcerations, inflammation, or pigmentary changes.
- Examine the teeth for calculus or exudate at the gingival margin. Digital pressure applied to the gingiva may aid in expressing exudate when a tooth root abscess is suspected. Note any fractured teeth, and look for evidence of pulp exposure. Slab fractures of the upper fourth premolar may be difficult to identify. Be suspicious of a fracture if a significant amount of calculus has accumulated on the surface of this tooth compared to the surrounding teeth and the contralateral carnassial tooth.
- Examine the tongue for evidence of trauma or masses when unexplained oral hemorrhage has been observed.

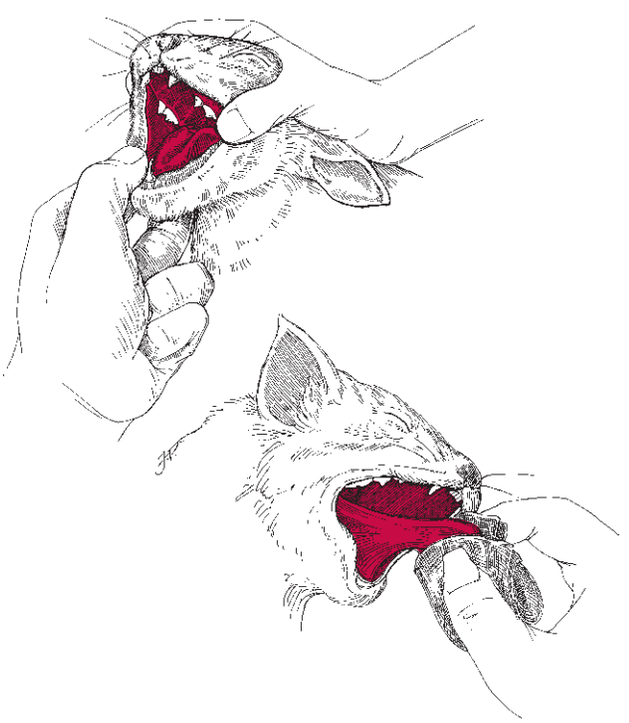

Figure 1-1. Oral examination of the feline mouth and tongue.

▼ ***Key Point*** In the feline patient that presents for vomiting, examine the sublingual area for evidence of a linear foreign body.

- Use one of the following two methods:
  - Open the patient's mouth and, with the middle finger of the hand depressing the mandible, apply pressure between the mandibular rami from the ventral aspect. In this manner, the tongue is elevated so that the sublingual surface can be seen (see Fig. 1-1, *top*).
  - Occasionally, a linear foreign body can be overlooked with the first method. The sublingual tissue can overlap a thin string that has been drawn taut so that it is not seen. In this case, the second method is to grasp the tongue with a gauze sponge and pull the tongue out and laterally so that the string can be seen more completely (see Fig. 1-1, *bottom*). Sedation may be required for this in some patients.
- Examine the hard palate in the neonate for clefts. Evaluate the soft palate (if possible) for defects or masses.
- Examine the pharyngeal region for asymmetry, masses, or foreign bodies or for evidence of inflammation or trauma. Examine the tonsils for enlargement or masses. Depress the caudal aspect of the tongue to see the caudal pharynx. Once again, sedation may be necessary for a thorough exam.
- In the cat, if pharyngeal polyps are a differential diagnosis based on the history, examine the soft palate for evidence of bulging. For a more complete exam, sedate the patient to look under the soft palate.

See also Chapter 64.

Nose

- Examine the nose for asymmetry or swelling. If a mass or swelling is present, palpate it carefully to determine whether it is firm or fluctuant. Evaluate brachycephalic breeds for stenotic nares.
- Note evidence of nasal discharge. Examine the nares closely to determine if the discharge is unilateral or bilateral. Characterize it as serous, mucoid, mucopurulent, or hemorrhagic. It may be beneficial to gently swab the external nares to detect a subtle discharge.
- If either nasal swelling or discharge is present, evaluate the patency of each nostril. Several techniques can be utilized to aid in this evaluation. Occluding one nostril at a time and listening for stertorous breathing may help identify a partially obstructed passageway. Another technique is wiping the examination table with an alcohol swab and positioning the patient's nose close to the table to observe condensation of the patient's breath on the surface. An alternative method is placing a wisp of cotton in

front of each nostril and observing movement from air flow

See also Chapter 160.

Ears

- Inspect both the external and inner surfaces of the pinna for skin lesions, hair loss, erythema, or swelling.
- Examine the external ear canals for erythema, discharge, and odor before an otoscopic examination. Palpate the ear canal cartilages for calcification, masses, pain, or other abnormalities.
- An otoscopic exam is invaluable in assessing an ear-related problem.
- Otoscopic technique requires practice to be successful. Sedation of the pet may be required if the patient is painful or aggressive.
- Lift the pinna and gently place the otoscopic cone in the vertical canal from a dorsal approach and direct it ventrally (Fig. 1-2). As the otoscope is guided deeper into the vertical canal, pull the pinna and otoscope horizontally to bring the horizontal ear canal and tympanic membrane into view.

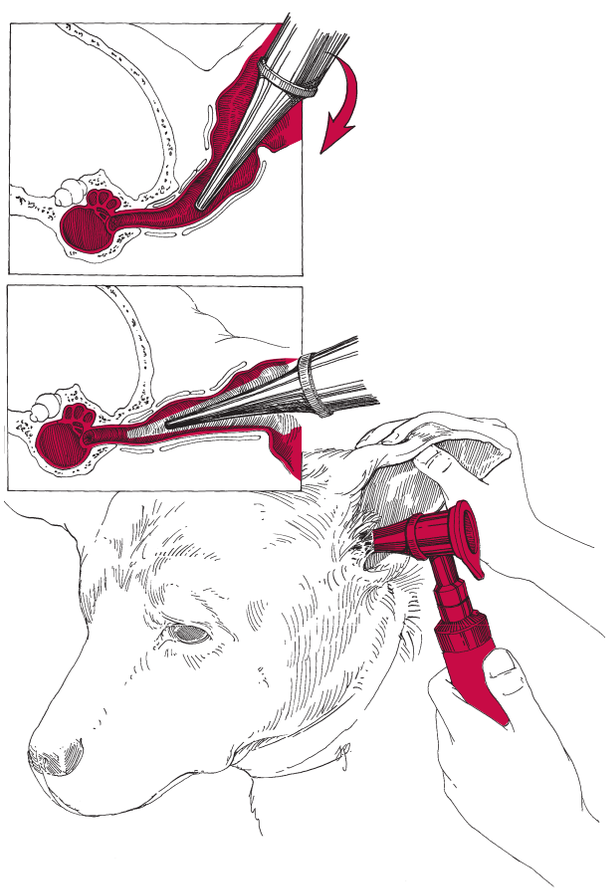

Figure 1-2. Otoscopic examination.

- Examine both the horizontal and vertical canals for stenosis, masses, foreign bodies, discharges, and parasites (ear mites and ticks). Assess the tympanic membrane for rupture or evidence of otitis media (erythema or protrusion).

See also Chapters 58 to 60.

Neck

- Palpate the paratracheal area from the larynx to the thoracic inlet.
  - In middle-aged to older cats, this palpation is especially important because of the high incidence of hyperthyroidism caused by thyroid adenomas. The normal thyroid is not palpable.
  - Stand behind the cat with it standing or sitting, extend the neck, and point the nose upward. Place your thumb and forefinger on each side of the trachea. Starting at the larynx, slide them down the length of the trachea using gentle pressure. The typical thyroid nodule will "pop" as your thumb and forefinger slip over the caudal pole (Fig. 1-3*A*).
  - Alternatively, palpate each side individually. Turn the patient's head slightly to one side and place your forefinger between the trachea and the adjacent muscles on the opposite side (Fig. 1-3*B*). Once again, start at the larynx and slide your finger down to the thoracic inlet. Turn the patient's head to the opposite side and repeat the procedure on the second side. Repeated palpation may be necessary to detect subtle nodules.
  - In dogs, palpation may detect a thyroid tumor.

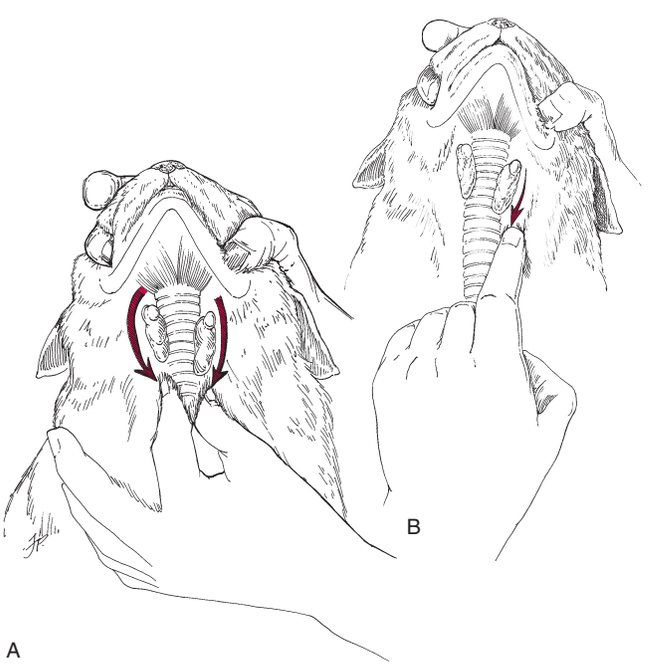

Figure 1-3. *A,* Paratracheal palpation of the thyroid. *B,* The alternative, palpation of each side of the thyroid gland individually.

- Palpate the trachea for collapse, soft cartilage, or flattening.
- Attempt to elicit a cough by gently encircling the trachea with one hand and applying pressure on the tracheal muscle dorsally. If a cough is produced by this method, it suggests tracheal collapse or tracheobronchitis. Conduct this part of the examination after the thorax has been auscultated because it may induce paroxysms of coughing.
- Evaluate the jugular veins for distention. A jugular pulse extending more than one third of the way up the neck is indicative of right-sided heart disease. It may be necessary to moisten this area with alcohol or to clip the hair to aid in visualization of the jugular vein.

Lymph Nodes and Subcutaneous Masses

- Palpate all external lymph nodes (Fig. 1-4). Generalized lymphadenopathy usually indicates a systemic disease (systemic fungal infection, immune-mediated disease, or neoplasia), whereas local lymph node enlargement usually indicates a localized tumor or a regional infection. If enlarged lymph nodes are present, use calipers to measure and record the size of the affected node or nodes. This information is helpful in monitoring the patient's response to treatment (antibiotics or chemotherapy).
- The mandibular lymph nodes are located at the angle of the mandible, slightly cranial and ventral to the parotid and submaxillary salivary glands. The nodes are generally smooth and ovoid in contrast to the irregular texture of the salivary glands. Practice distinguishing these lymph nodes from salivary glands.
- The superficial cervical or prescapular lymph nodes can usually be palpated just in front of the cranial border of the scapula. Grasp them by palpating beneath the scapular border. They may be more difficult to palpate in the obese or heavily muscled patient.
- The axillary lymph nodes are not always palpable because of their disc-like shape and the surrounding musculature.
- The superficial inguinal lymph nodes are located at the junction of the abdominal wall and the medial thigh and may be difficult to palpate in the obese patient.
- The popliteal lymph nodes are usually palpable caudal to the stifle joint. The surrounding subcutaneous fat may make these nodes seem larger than their actual size, especially in cats.
- Palpate the trunk and extremities for abnormal masses or swelling. When a mass is found, note the location, size, and consistency. Use calipers to accurately measure the size of the mass. Determine which tissues are involved (dermal, epidermal, subcutaneous, underlying tissue, etc.). Note whether the mass is freely movable or attached to the underlying muscle, fascia, or bone.

Thorax

- As previously described, evaluate the respiratory rate, rhythm, and effort.

Palpation

- Palpate the thorax for evidence of fractured ribs, congenital malformations (pectus excavatum), subcutaneous emphysema, and masses. Palpate the areas

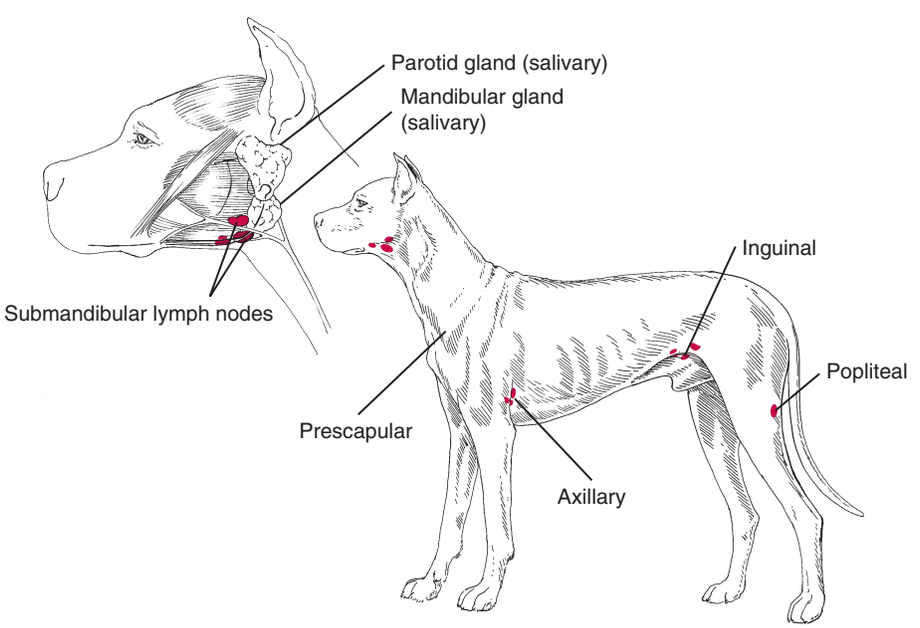

Figure 1-4. Commonly palpated lymph nodes.

between the fourth and sixth intercostal spaces on either side of the thorax for the point of maximum intensity (PMI) of the heartbeat and for cardiac thrills.
- Attempt to compress the cranial thorax in cats to help identify the presence of a mediastinal mass. In a normal feline, the cranial thorax is easily compressible.

Auscultation

- Perform auscultation in a quiet room with a calm patient. Have the patient standing during the examination so that the heart is in its normal position. Evaluate the heart independently from the lungs.
- Disregard sounds that are artifacts. These sounds include rumbles secondary to shivering and crackles created by the stethoscope rubbing against the hair. Close the patient's mouth for short periods of time to reduce upper respiratory noise. An additional technique is to apply moderate pressure on either side of the chest to help decrease motion caused by panting or shivering.
- Auscultate the heart initially over the PMI and identify the first and second heart sounds. Characterize the cardiac rhythm. Sinus arrhythmia is considered normal and is typified by increased cardiac rate during inspiration and decreased rate during expiration. Evaluate the femoral pulses for quality and deficits while auscultating the heart. Note split heart sounds, murmurs, and clicks. Auscultate all cardiac valve areas, because some murmurs are localized, such as the mitral, aortic, and pulmonic on the left hemithorax and the tricuspid on the right (see also Chapter 142).
- Note muffled heart sounds that may be due to obesity, pleural effusion, pericardial effusion, thoracic mass, or diaphragmatic hernia.
- Pulmonary auscultation requires practice and persistence. Normal bronchovesicular sounds may be increased, decreased, or normal. They may be intensified in the nervous or tachypneic patient. These sounds are heard equally on both sides of the chest. Abnormally quiet or dull areas are suggestive of pleural effusion, pneumothorax, thoracic mass, and pulmonary consolidation. Crackles are abnormal discontinuous sounds resulting from popping open of small airways or air moving through airway secretions. Wheezes are abnormal continuous, musical sounds resulting from passage of air through narrowed or partially obstructed airways.

Percussion

- Percussion is a technique for evaluating the resonance (pitch and tone) of sound produced by a series of quick taps of uniform force at various points on the chest wall using a finger or a percussion hammer.
- Increased resonance (tympany) is indicative of pneumothorax, and decreased resonance (dull sounding) suggests pleural effusion, a diaphragmatic hernia, a large pulmonary mass, or an area of consolidation.

See also Chapter 142.

Abdomen

- Examine the external appearance of the abdomen for distention or asymmetry. If distention is apparent, perform percussion to help determine if it is a result of peritoneal effusion, air (gastric dilatation or volvulus), obesity, or a mass.
- Palpate the abdomen systematically proceeding in a cranial-to-caudal direction with the animal standing. Palpate the trunk superficially for evidence of skin masses or hernias. In puppies and kittens, check for evidence of umbilical or inguinal hernias. To palpate abdominal organs, apply firm but gentle pressure. In small animals, use a one-handed technique. With larger patients, two hands are needed, one on each side of the abdomen (Fig. 1-5). If the patient is nervous or tense, try to get the patient to relax by talking reassuringly and stroking its belly or sides just prior to palpation. Start again in a cranial-to-caudal direction just as you did with the superficial palpation. Use a systematic method to attempt to identify each organ.

Stomach

- Palpate the cranial abdomen for evidence of gastric distention (see also Chapter 67). The normal stomach is rarely palpable. Tympany indicates gastric dilatation or volvulus. Diagnosis and treatment should be pursued aggressively. Overeating may result in a doughy or fluid-filled stomach in the left side of the cranial abdomen.

Liver

- The liver may be difficult to palpate in the normal patient (see also Chapter 71). The caudal edges are barely palpable, smooth, and well defined. Hepatomegaly results in a liver that extends past the costal arch. The edges may be rounded rather than sharp. Palpation with the animal in lateral recumbency or standing on its hind legs may be helpful.

Spleen

- The spleen is located in the mid-abdomen and may not always be palpable (see also Chapter 25). If splenomegaly is present, it is usually palpable. Determine if the spleen is irregular or if a palpable mass is present. Use gentle palpation on mid-abdominal masses. It is possible to rupture a splenic or hepatic hematoma or hemangiosarcoma.

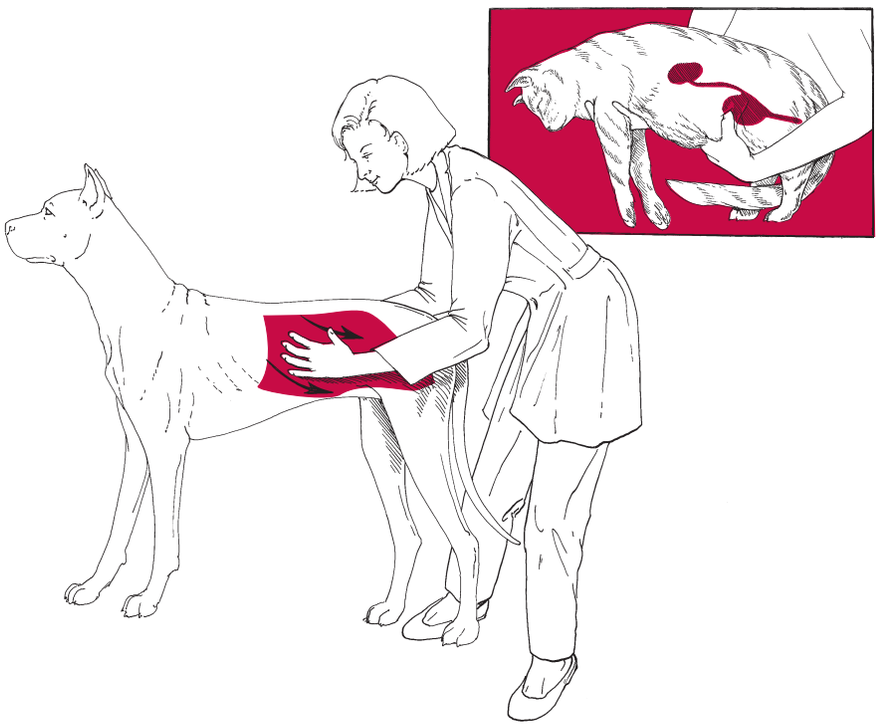

Figure 1-5. Perform abdominal palpation with two hands or with one hand *(inset)*.

Intestines and Mesenteric Lymph Nodes

- Other organs in the mid-abdomen include the mesenteric lymph nodes and intestines. The mesenteric lymph nodes are not usually palpable unless markedly enlarged, as with lymphoma. Occasionally, mesenteric lymph nodes are palpable in cats with inflammatory bowel disease.
- Palpate the thickness of the bowel wall and evaluate for the presence of gas, fluid, foreign bodies, or masses (see also Chapter 69). Plication and clumping of the intestines may sometimes be palpated in patients with a linear intestinal foreign body. Note if palpably abnormal sections of the bowel appear painful. Palpation of an intestinal foreign body frequently produces a painful response.
- Palpate the colon in the dorsal-caudal abdomen, and note the presence of feces. To determine whether the palpable structure is feces or a mass, apply gentle pressure to test for deformability of the stool. Evaluate quantity and consistency of the feces to aid in the diagnosis of constipation.

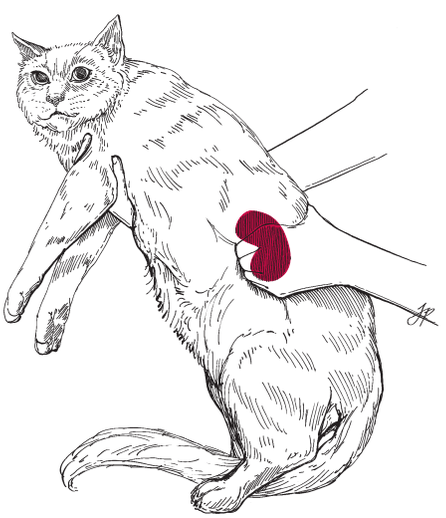

Figure 1-6. Renal palpation in the cat.

Kidneys

- The kidneys can be palpated in the feline patient in the dorsal region of the abdomen. The right kidney tends to be further cranial than the left and may be obscured by the caudal rib cage. Elevate the cat's thorax with one hand while palpating with the other. This maneuver allows the kidneys to fall into a palpable position (Fig. 1-6). Palpate both kidneys and compare them for size, shape, firmness, and surface irregularities. The left kidney is especially movable. Do not mistake it for a mid-abdominal mass. The kidneys are not as readily palpable in the dog unless the patient is young or thin. The caudal and lateral aspects may be palpable in other patients. Kidney palpation will also be discussed in Chapter 77.

Urinary Bladder

- If the urinary bladder is moderately or markedly distended, it can usually be palpated in the ventral-caudal abdomen (see also Chapter 79). The patient does not usually resist palpation of the normal bladder. Assess size, turgidity, and thickness of the bladder wall. The normal urinary bladder is thin walled. Careful palpation may reveal cystic calculi. A painful, firm distended urinary bladder indicates urethral obstruction.

Uterus

- The normal uterus usually cannot be palpated (see also Chapter 90). If it is markedly enlarged, because of pyometra or late pregnancy, the uterus is found in the mid- to-ventral abdomen, often extending from the diaphragm to the pelvic inlet. The uterus often is tubular in shape with pyometra or late pregnancy. In mid-gestation, the individual fetuses may be palpated. In the pregnant cat, these fetuses may feel similar to the urinary bladder but will usually be present in multiple numbers and feel slightly thicker walled than the bladder.

Prostate

- The prostate in intact male dogs can occasionally be palpated in the caudal abdomen ventral to the colon and caudal to the urinary bladder (see also Chapter 84). If found in this location, evaluate the prostate for size, shape, and surface irregularities.

External Genitalia

- In the female patient, palpate the mammary glands carefully for masses. If the history indicates a possibility of pregnancy or pseudopregnancy, gently express the nipples for signs of discharge or milk. In the nursing bitch or queen, examine the mammary glands for abnormal swelling, firmness, or heat, as seen with mastitis or abscessed glands.
- In the female patient, examine the vulva for conformational abnormalities, swelling, or discharge. Determine the color, consistency, and odor of the discharge. Examine the vulvar mucous membranes for evidence of jaundice, cyanosis, petechiae, or ulceration for clues of systemic disease. In dystocia or when a vaginal discharge is present, a vaginal examination is indicated. Vaginoscopy may be required to rule out the presence of vaginal masses.
- In the male canine, examine the prepuce and penis. Retract the preputial sheath caudal to the bulb so that the entire penis can be examined for any signs of trauma or masses. Inspect the penis for jaundice, cyanosis, petechiae, ulceration, or masses. Examine the tip of the feline penis for evidence of obstruction (discoloration or the presence of plug material) if indicated by the history.
- In the male intact patient, palpate both testicles for symmetry, firmness, and irregularity. If both testicles are not present in the scrotum, examine the inguinal region for the presence of a retained testicle and palpate the abdomen for masses.

See also Section 7.

Rectal Examination

- A rectal examination often provides valuable information during a physical examination.
- During a rectal examination, palpate the sublumbar lymph nodes in the dorsal aspect of the pelvic canal. Enlargement is usually suggestive of metastatic neoplasia.
- Note the symmetry of the pelvis and the presence of palpable fractures during the rectal examination. This is always indicated in a trauma victim. Evaluate abnormal masses in the pelvic canal for size, position, and consistency.
- During the rectal examination, evaluate the perineal and perianal regions for hernias or abnormal masses.
- Evaluate the anal sacs for evidence of infection, distention, or masses.
- Examine any fecal material obtained for amount, consistency, color, and presence of blood or mucus. Note the presence of foreign material such as bone fragments, gravel, cloth, or plastic.
- Perform a rectal examination in all mature male dogs to evaluate the prostate. The normal prostate is bilobed (characterized by the presence of the median raphe), symmetric, smooth, and nonpainful. If the prostate is enlarged, it may extend slightly over the brim of the pelvis or fall into the abdomen, as previously described for the palpation of the caudal abdomen.
- In female dogs, abnormal masses associated with the uterus or urethra may occasionally be detected on rectal palpation.

Skin

- Inspect the general appearance of the haircoat for luster, fullness, and areas of hair loss. Note symmetric alopecia as seen with endocrinopathies, such as hyperadrenocorticism, hypothyroidism, or sex hormone imbalances. Inspect areas of alopecia for broken hairs as seen with pruritic or psychogenic conditions. Check for erythema as will be seen in allergic or inflammatory conditions.
- When approaching a pet with a dermatologic problem, examine all areas of the body. Location of skin lesions often aids in the diagnosis. For example, localized demodicosis causes patches of alopecia involving the head and forelegs. Sarcoptic mange typically causes scaling and partial alopecia of the pinnae, elbows, and hocks. Do not overlook the interdigital areas and the foot pads. Examine mucocuta-

neous junctions (lips, anus, vulva, preputial orifice, etc.) for evidence of an immune-mediated disease.
- Identify all skin lesions and categorize them as primary or secondary. Primary lesions include papules, pustules, nodules, wheals, macules, and vesicles. Common secondary lesions are scales, crusts, ulcers, excoriations, lichenifications, hyperpigmentations, and hyperkeratoses.
- Note evidence of external parasites. Large flakes and scales in a pruritic patient may indicate *Cheyletiella* infestation. If fleas are not seen, search the patient for flea dirt, especially in the tail-head region. A flea comb is often helpful in discovering small amounts of flea dirt. Repetitive combing may be necessary to find small amounts of flea dirt in the flea allergy dermatitis patient. While combing the patient, you can educate the owner regarding flea control.

See also Section 5.

Musculoskeletal System

- Initially evaluate the musculoskeletal system by observing for lameness while the patient is in motion both at a walk and at a trot. Observe the patient's posture with special attention to head carriage, head bobbing, arching of the back, or stilted gait. For forelimb lameness, an obvious downward bobbing of the head will be present as the sound leg makes contact with the ground.
- A complete musculoskeletal examination is not necessary unless evidence of lameness or pain is noted in the history or on initial observation of the patient.
- Gently manipulate the patient's head dorsally, ventrally, and to either side to look for evidence of pain or resistance. Palpate the vertebral column for signs of a pain response. Pressure applied to either side of the dorsal spinal process of each vertebra may be necessary to elicit pain (see Chapters 100, 128).
- If lameness is present, examine the affected limb systematically to localize the area involved. First, examine the foot for evidence of traumatized or abnormal toenails or nail beds. Evaluate each interdigital area for erythema, swelling, or draining tracts, which may be indicative of a foreign body. Palpate each toe individually and note swelling or pain.
- Palpation proceeds proximally. Evaluate each long bone for pain, swelling, abnormal masses, or palpable fractures.
- Evaluate each joint for evidence of effusion, soft-tissue swelling, crepitation, or pain with flexion and extension.
- In examining the stifle, note the position of the patella in extension and flexion. If the patella is in its normal location, attempt to luxate it medially and laterally. Extension of the stifle usually aids in mobilizing the patella. Manipulate the stifle for evidence of a cranial drawer sign that indicates an anterior cruciate ligament tear (see Chapter 110).
- Evaluate each coxofemoral joint range of motion and evidence of pain. Test for a positive Ortolani sign to evaluate for hip laxity if the patient's breed is at risk for hip dysplasia (see Chapter 108 for more details).
- If difficulty arises in localizing the lameness, always compare the results of palpation and manipulation of the affected limb with those on the contralateral limb.

Nervous System

As with the musculoskeletal system, a complete neurologic examination is not necessary unless specifically indicated by the history or the general physical examination. The details of the neurologic examination are discussed in Chapter 125. A brief overview of the basic procedures for the localization of lesions is provided here.

- Observe mental status and behavior as previously described.
- Evaluate the gait and posture while the patient is walking and standing. Pay particular attention to strength, symmetry, and coordination.
- Always perform a complete cranial nerve examination when evaluating neurologic problems (see Chapters 125 and 126). This includes checking for a menace response, palpebral reflex, and pupillary light flexes. Note pupillary symmetry and ocular positioning. Facial sensation can be tested by lightly touching the nasal mucosa with a hemostat. The presence of a gag reflex should have been noted during the oral exam.
- Evaluate and compare postural reactions in all limbs, including proprioception, "wheelbarrowing," hopping, extensor postural thrust, and placing reactions.
- Evaluate and compare spinal reflexes with the calm patient in lateral recumbency. Important segmental reflexes include the triceps, biceps, patellar, and cranial tibial reflexes, as well as the flexor (withdrawal) reflexes of the thoracic and pelvic limbs. Evaluate the panniculus reflex by needle stimulation of the thoracic or lumbar skin (see Chapter 125).
- Evaluation of some parts of the neurologic examination is subjective. If you are unsure how the patient responded to a particular test, then repeat the test in question and compare the results. If the patient is hospitalized, the exam will need to be repeated at regular intervals to evaluate progression of the disease and response to treatment.

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Chapter 2

Practical Methods of Anesthesia

John A. E. Hubbell

Anesthesia is an integral part of the practice of companion animal medicine. In addition to surgical applications, some form of anesthesia may be required for a wide variety of procedures, such as radiography, endoscopy, cerebrospinal fluid collection, and bone marrow aspiration.

▼ ***Key Point*** The keys to successful anesthesia include (1) an understanding of what is "normal" in the various species; (2) a working knowledge of the pharmacology of anesthetic drugs; and (3) a systematic evaluation and reevaluation of the patient's status (monitoring) during the period of anesthesia.

The understanding of what is "normal" comes with experience. Several excellent texts describe the pharmacology of anesthetic drugs (see "Supplemental Reading" at the end of this chapter). Monitoring is a matter of establishing a routine and maintaining the discipline to adhere to the routine. This chapter suggests some basic anesthetic techniques and protocols that can be used successfully in small animal practice.

GENERAL PRINCIPLES

Preoperative Assessment (Table 2-1)

- A history of vomiting or a recent meal is an indication for postponing surgery or using techniques that produce rapid induction, allowing rapid endotracheal intubation that minimizes the potential for aspiration of gastric contents.
  - On an elective basis, withhold food 6 to 8 hours before the administration of anesthetic drugs.
  - Do not withhold water.
  - Potential problems discovered from the history include exercise intolerance or cough, as an indicator of cardiorespiratory dysfunction; polyuria or polydipsia, as an indicator of endocrine or renal dysfunction; or any other recent change in the animal's physical status.
- Perform a physical examination with emphasis on the cardiovascular and respiratory systems (Table 2-2 provides normal values).
  - Evaluate traumatized patients more extensively because of the potential for blood loss, cardiac arrhythmias (ventricular tachycardia), and thoracic trauma (pneumothorax).
  - Evaluate abnormalities discovered after auscultation, percussion, palpation, and examination of mucous membranes with ancillary tests, such as thoracic radiography and electrocardiography.
  - The pertinent abnormalities associated with various metabolic diseases are discussed in the appropriate chapters of this text.
- Weigh the animal. Estimate the lean body weight if the animal is obese to more accurately calculate correct anesthetic drug doses.
- Determine packed cell volume and total plasma protein to establish a baseline for reference if hemorrhage occurs. Check renal function with blood urea nitrogen (BUN) or creatinine concentrations in older (>7 years) animals. Increases in BUN or creatinine values may dictate a more careful perianesthetic fluid management to prevent further renal dysfunction (see Table 2-2).

Intravenous Catheterization

Place an IV catheter before induction of anesthesia to provide a convenient pathway for the administration of drugs, to allow fluid or blood administration if required, and to ensure access to the vascular space if an emergency occurs.

Endotracheal Intubation

A patent airway is essential to any anesthetic protocol.

- Place a cuffed endotracheal tube in the trachea soon after induction of anesthesia.
- Alternatively, use drugs that maintain the swallowing reflex (ketamine or tiletamine/zolazepam).
- Clean, thoroughly rinse, and dry endotracheal tubes between uses. Sterilization of endotracheal tubes between uses is not necessary on a routine basis. Use chemical sterilization or discard the tube if a known pathogen is present. Glutaraldehyde is a safe disinfectant if the tubes are thoroughly rinsed following sterilization.
- See Table 2-3 for the suggested range of sizes of endotracheal tubes for dogs and cats.

Table 2-1. PREANESTHETIC CHECKLIST

History and Physical Examination
Age
Body weight
Temperature
Auscultation
Respiratory rate
Pulse rate, rhythm, and strength
Hydration, mucous membrane color, and capillary refill time
Mentation
Current medication history
Cardiopulmonary, renal, and nervous system disease history

Laboratory Data
Packed cell volume
Total plasma protein
Blood urea nitrogen, creatinine, or serum dipstick analysis (Azostick) if less than 7 years
Other tests optional, dependent on primary disease

Drugs
Appropriate anesthetic drugs
Sufficient oxygen supply
Emergency drugs
- Atropine or glycopyrrolate
- Lidocaine
- Epinephrine
- Sodium bicarbonate
- Intravenous fluids
- Dopamine
- Doxapram

Equipment
Syringes, needles, and catheters
Leak-tested anesthetic machine
Cuffed endotracheal tubes
Optional monitoring equipment
- Electrocardiogram
- Blood pressure monitor (pulse detector)
- Stethoscope
- Pulse oximeter

PRODUCING A TRACTABLE ANIMAL

Many procedures, such as radiography and cystocentesis, do not require complete anesthesia. In these instances, the combination of appropriate sedation and physical restraint can facilitate the completion of the procedure with minimal stress to the patient and minimal drug-induced cardiopulmonary depression. The choice of drugs is based on species, the patient's temperament, physical status, the veterinarian's familiarity with the drug, and the intended purpose. The agents that follow are employed as components of many anesthetic protocols.

The doses of drugs alone and in combination are listed in Table 2-4 (dogs) and Table 2-5 (cats).

Tranquilizers

Acepromazine

- A potent phenothiazine tranquilizer that produces sedation in the dog. It also has antiemetic and antiarrhythmic properties.

Table 2-3. APPROXIMATE ENDOTRACHEAL TUBE SIZES

	Weight (kg)	Cuffed Tube Diameter (mm)
Dogs	3–7	3.0–5.0
	7–15	5.0–7.5
	15–30	7.5–9.5
	>30	9.5–12.0
Cats		2.5–4.0

Table 2-2. NORMAL VALUES

	Dogs Awake	Anesthetized (If Different)	Cats Awake	Anesthetized (If Different)
Temperature (°F)	99.5–102.5		100.0–102.5	
Heart rate (bpm)	70–180	60–180	145–200	100–200
Respiratory rate (breaths/minute)	20–40	8–20	20–40	10–30
Capillary refill time (sec)	<1.5		<1.5	
Packed cell volume (%)	35–54		27–46	
Total plasma protein (g/100 ml)	5.7–7.3		6.3–8.3	
Total leukocytes (6,000–17,000/µl)	6–18		6–20	
Albumin (g/100 ml)	2.1–3.6		2.3–3.6	
Sodium (mEq/L)	140–155		149–162	
Potassium (mEq/L)	3.8–5.3		3.6–5.4	
Chloride (mEq/L)	105–121		105–135	
Calcium (mg/100 ml)	8.8–11.3		8.3–11.3	
Creatinine (mg/100 ml)	0.3–1.3		0.8–1.8	
Blood urea nitrogen (mg/100 ml)	8–25		15–35	
Arterial pH	7.30–7.43		7.27–7.40	
Arterial pCO_2 (mm Hg)	30–49		35–49	
Arterial pO_2 (mm Hg)	91–97	90–500 (>50% inspired O_2)	91–97	100–500 (>50% inspired O_2)
Arterial HCO_3 (mEq/L)	18–22		18–25	
Arterial base excess (mEq/L)	–3 to +3		–5 to +1.5	
CO_2 combining power (mEq/L)	15–25		16–30	

Table 2-4. ANESTHETIC DRUGS AND DOSES IN DOGS

Drug	Intravenous Dose (mg/kg)	Intramuscular or Subcutaneous Dose (mg/kg)
Anticholinergic		
Atropine	0.02–0.04	0.02–0.04
Glycopyrrolate	0.005–0.010	0.005–0.010
Tranquilizer/Sedative		
Acepromazine	0.05–0.20	0.1–0.3
Xylazine	0.3–0.8	0.5–1.5
Medetomidine	0.007–0.020	0.01–0.04
Diazepam	0.10–0.25	0.10–0.25
Midazolam	0.05–0.20	0.1–0.2
Analgesic		
Morphine	NR*	0.2–0.5
Oxymorphone	0.05–0.10	0.1–0.3
Fentanyl	0.002–0.005	0.004–0.008
Meperidine	0.4–2.0	1.0–4.0
Butorphanol	0.1–0.2	0.1–0.4
Nalbuphine	0.5–2.0	0.5–2.0
Buprenorphine	0.005	0.005
Hydromorphone	0.05–0.2	0.1–0.4
Anesthetic		
Tiletamine/zolazepam (Telazol)	0.5–4.0	4–10
Thiopental	6–10	NR
Etomidate	1–4	NR
Propofol	2–6	NR
Combination		
Acepromazine/oxymorphone	0.05–0.10/0.01–0.02	0.1–0.2/0.1–0.2
Acepromazine/butorphanol	0.05–0.10/0.1–0.2	0.1–0.2/0.1–0.2
Ketamine/acepromazine	2–5/0.05–0.10	5–10/0.1–0.2
Ketamine/xylazine	1–5/0.1–0.8	5–10/0.3–1.5
Ketamine/diazepam (50:50)	1 ml/10 kg	NR

*NR, not recommended.

- Not an analgesic itself, but it may potentiate other drugs that are analgesics.
- Produces hypotension through an α-adrenergic blockade, particularly in large doses.
- Potentiates hypothermia.
- Epinephrine reversal (i.e., hypotension after epinephrine administration) can occur.
- Calms excitable dogs. Aggressive dogs or cats may not become tractable. Combine with opioids or cycloheximides to produce the desired effect (see Tables 2-4 and 2-5).
- Avoid in animals with epilepsy, shock, bleeding disorders (inhibition of platelet function), or liver disease.
- Reduce the dose or choose another agent in stressed or older animals because effects may be exaggerated. Cats are calmed but usually still resist restraint.

Xylazine

- An α_2-adrenergic agonist that produces sedation with muscle relaxation and analgesia.
- Produces an obtunded state from which the patient is difficult to arouse.
- Produces analgesia for minor procedures. Is not usually sufficient for surgery.
- Produces profound cardiopulmonary depression, including bradycardia, first- and second-degree atrioventricular blockade, catecholamine sensitization, and decreased respiratory rate.
- Combine with an anticholinergic (atropine or glycopyrrolate), particularly if large doses are administered.
- Do not use in patients with preexisting cardiac, liver, or kidney disease or with shock.
- Reverse effects with yohimbine, tolazoline, or atipamezole (see "Recovery and Reversal" for doses).
- Vomiting occurs in approximately 25% of dogs and 50% of cats.
- See Tables 2-4 and 2-5 for doses.

Medetomidine

- An α_2-adrenergic agonist that produces sedation with muscle relaxation and analgesia (see Tables 2-4 and 2-5 for doses).
- Similar to but approximately 100 times more potent than xylazine with a longer duration of action.
- Produces analgesia for minor procedures. Combine with ketamine or opioids to enhance analgesia.
- Produces dose-dependent cardiopulmonary depression including bradycardia, decreased arterial blood pressure, and slowing of respiratory rate.

Table 2-5. ANESTHETIC DRUGS AND DOSES IN CATS

Drug	Intravenous Dose (mg/kg)	Intramuscular or Subcutaneous Dose (mg/kg)
Anticholinergic		
Atropine	0.02–0.04	0.02–0.04
Glycopyrrolate	0.005–0.010	0.005–0.010
Tranquilizer/Sedative		
Acepromazine	0.05–0.20	0.1–0.3
Xylazine	0.4–1.0	0.8–1.8
Medetomidine	0.01–0.03	0.03–0.08
Diazepam	0.10–0.25	0.10–0.25
Midazolam	0.05–0.20	0.1–0.2
Analgesic*		
Oxymorphone	0.01–0.04	0.05–0.10
Butorphanol	0.05–0.20	0.1–0.3
Nalbuphine	0.5–1.5	0.5–1.5
Buprenorphine	0.005	0.005
Hydromorphone	0.05–0.1	0.1–0.3
Anesthetics		
Ketamine	4–10	10–20
Tiletamine/zolazepam (Telazol)	0.5–4.0	4–12
Thiopental	6–10	NR†
Etomidate	1.0–4.0	NR
Propofol	2–6	NR
Combination		
Acepromazine/oxymorphone	0.05–0.07/0.01–0.04	0.1–0.2/0.05–0.20
Acepromazine/butorphanol	0.05–0.07/0.07–0.15	0.1–0.2/0.1–0.2
Ketamine/acepromazine	4–8/0.05–0.10	7–15/0.1–0.2
Ketamine/xylazine	4–8/0.1–0.8	7–15/0.3–1.5
Ketamine/diazepam (50:50)	1 ml/10 kg	NR

*Higher doses can be associated with nervousness and excitement.
†NR, not recommended.

- Combine with an anticholinergic (atropine or glycopyrrolate), particularly if large doses are administered.
- Do not use in patients with preexisting cardiac or kidney disease or with shock.
- Reverse effects with yohimbine, tolazoline, or atipamezole (see "Recovery and Reversal" for doses).
- Vomiting, diuresis, and muscle jerking may occur.

Diazepam and Midazolam

- Benzodiazepine derivatives that produce mild sedation in dogs and cats. Neither is effective in calming an excited patient when used alone. Both are anticonvulsants.
- Use to enhance tractability in depressed patients or in combination with other agents (primarily opioids).
- Administer diazepam IM or slowly IV with caution. The drug is solubilized in a propylene glycol base that can produce bradycardia and hypotension.
- Administer water-soluble midazolam IV, SC, or IM.
- Use in patients with cardiorespiratory compromise or another metabolic disease. Both agents produce minimal cardiopulmonary side effects and provide muscle relaxation.
- Use both drugs as premedicants to parenteral or inhalation anesthesia.
- Occasionally, paradoxical responses occur, including disorientation and aggression.
- Diazepam can be given as an appetite stimulant in cats.
- See Tables 2-4 and 2-5 for doses and suggested combinations.

Analgesic Drugs (see also Chapter 6)

Nonsteroidal Anti-inflammatory Drugs

- Use nonsteroidal anti-inflammatory drugs (NSAIDs) for acute and chronic pain associated with inflammation. They reduce pain by inhibiting prostaglandin formation and through central effects.
- Potentiate the action of other analgesics.
- Use NSAIDs orally or by injection to provide analgesia, antipyresis, and as an anti-inflammatory in the perioperative period and for chronic pain. Analgesia produced is equivalent to opioids for some types of pain.
- NSAIDs can cause gastrointestinal injury and renal damage.
- See Table 2-6 for doses.

Table 2-6. NONSTEROIDAL ANTI-INFLAMMATORY DRUG USE IN DOGS

Nonsteroidal Anti-inflammatory Drug	Dosage
Carprofen	2 mg/kg twice daily or 4 mg/kg once daily orally (injectable 4 mg/kg SC once daily)
Deracoxib	3–4 mg/kg once daily orally for 7 days
Etodolac	10–15 mg/kg once daily orally
Ketoprofen	2.2 mg/kg IV, SC, or IM for dogs and cats, single dose
Meloxicam	0.1 mg/kg (0.2 mg/kg loading dose) once daily, SC, PO (cats: if given SC, dose of 0.3 mg/kg is used one time only)
Phenylbutazone	40 mg/kg daily in three divided doses for 2 days then reduce
Tepoxalin	10 mg/kg once daily orally

Opioids

- Use in dogs and cats to augment the effects of sedatives and tranquilizers and to provide analgesia.
- Minimal or no sedation is produced when administered alone, except for morphine and meperidine. Use in combination with tranquilizers or sedatives.
- Use lower doses in cats compared with dogs (see Tables 2-4 and 2-5), because higher doses have the potential to cause excitement and disorientation.
- Morphine, oxymorphone, fentanyl, hydromorphone, and meperidine are opioid agonist drugs frequently used in small animal practice. Regulations require rigorous recordkeeping and security.
- Vagal tone is increased (bradycardia), and respiration is depressed.
- Sensations of touch or vision are not diminished. Sensitivity to sound may be increased.
- May cause vomiting and defecation.
- Reverse agonists and agonist-antagonists with naloxone. Partial reversal of the respiratory and central nervous system (CNS) depressant effects of agonists can be accomplished with agonist-antagonists (e.g., butorphanol), which reverse the deleterious effects of the agonists and provide the animal with some analgesia.

Fentanyl

- Fentanyl can be administered transdermally using a patch developed for human use. Time from patch application until full effect is 2 to 6 hours in cats and 12 to 24 hours in dogs.
- The skin must be clipped (or shaved) to facilitate absorption, but absorption varies considerably. Duration of action may be as long as 5 days. Prevent ingestion by the animal or humans.

Other Opioids

- Butorphanol, nalbuphine, and buprenorphine are opioid agonist-antagonist or partial agonist drugs. This classification means that these compounds produce analgesia but have less addictive potential.
- Degree of analgesia may be sufficient for mild to moderate pain but not for severe pain.

Dissociative Anesthetics

Ketamine and Tiletamine/Zolazepam

- Ketamine and tiletamine/zolazepam (Telazol, Ft. Dodge Animal Health, Ft. Dodge, Iowa) produce a unique form of sedation or anesthesia that has been called dissociative anesthesia.
- These maintain swallowing and ocular reflexes, increase muscle tone, and produce amnesia, superficial analgesia, and catatonia.
- They stimulate the cardiovascular system, resulting in increased heart rate and arterial blood pressure.
- They produce an apneustic (breath-holding) respiratory pattern. The intensity is dose related.
- Use low doses of ketamine (up to 6 mg/kg IM) in the cat to produce an obtunded state with malleable rigidity of the limbs, dilated pupils, and hypersalivation. Higher doses (14–20 mg/kg IM) have been used, but analgesia is not an appropriate level for visceral surgery. Using ketamine with other drugs (xylazine, medetomidine, diazepam, or midazolam) is a better approach in both dogs and cats. Do not give ketamine alone in the dog because of resultant muscle rigidity and seizure activity. See Tables 2-4 and 2-5 for doses.
- Use tiletamine/zolazepam (Telazol) to produce a state similar to that of ketamine with the addition of muscle relaxation. The drug is approved for IM use in both the dog and the cat. At low doses (2–4 mg/kg IM) it provides helpful restraint in both the dog and the cat. It is also used in small doses IV (0.5–1.5 mg/kg) in a manner similar to ketamine/diazepam for induction and short-duration restraint (see Tables 2-4 and 2-5 for doses).

INJECTABLE DRUGS FOR SHORT-TERM ANESTHESIA

A variety of injectable drugs and drug combinations can be used for short-term anesthesia or restraint in dogs (Table 2-7) and cats (Table 2-8). Many of these combinations employ the drugs previously described. Prior administration or coadministration of sedatives or

Table 2-7. SUGGESTED ANESTHETIC PROTOCOLS FOR DOGS

Patient (Agent)	Dose	Comments
Healthy (Elective Procedure)		
Acepromazine	0.02 mg/kg SC or IM	Total dose not to exceed 4 mg
Thiopental	6–10 mg/kg IV	Give 6 mg/kg initially, increase in 2 mg/kg increments
Isoflurane* (or)	0.5%–3.5%, inhaled	Adjust to anesthetic depth
Sevoflurane*	2.0%–4.5%, inhaled	Adjust to anesthetic depth
Aged Patient		
Intravenous fluids		
Ketamine/diazepam (50:50) (or)	1 ml/10 kg IV	Short duration of action
Propofol	2–4 mg/kg IV	
Isoflurane* (or)	0.5%–3.5%, inhaled	
Sevoflurane*	2.0%–4.5%, inhaled	
Patient in Pain		
Intravenous fluids		
Acepromazine	0.01–0.02 mg/kg IM	Can be mixed with oxymorphone
Oxymorphone	0.05–0.02 mg/kg IM	Watch for bradycardia
Thiopental	4–8 mg/kg IV	Dose is reduced after premedicant; start with 4 mg/kg
Isoflurane* (or)	0.5%–3.5%, inhaled	
Sevoflurane*	2.0%–4.5%, inhaled	
Critical Patient		
Intravenous fluids		
Diazepam and	0.02 mg/kg IV	Give slowly
Propofol (or)	2–4 mg/kg IV	Give to effect
Ketamine/diazepam (50:50)	1 ml/10 kg IV	
Isoflurane* (or)	0.5%–3.5%, inhaled	
Sevoflurane*	2.0%–4.5%, inhaled	

*Concentration required depends on fresh gas flow rate. The lower the flow rate, the higher the concentration required.

Table 2-8. SUGGESTED ANESTHETIC PROTOCOLS FOR CATS

Patient (Agent)	Dose	Comments
Healthy (Elective Procedure)		
Acepromazine (with)	0.01–0.02 mg/kg SC or IM	Mix acepromazine with ketamine; add opioid for analgesia
Ketamine (and)	4–8 mg/kg IM	
Thiopental (or)	5–10 mg/kg IV	Give to effect
Tiletamine/zolazepam (with)	3–5 mg/kg IM	Tiletamine/zolazepam may be sufficient for intubation
Thiopental	3–7 mg/kg IV	
Isoflurane* (or)	0.5%–3.5%, inhaled	
Sevoflurane*	2.0%–4.5%, inhaled	
Aged or Renally Compromised Patient		
Intravenous fluids	0.05 mg/kg IM	
Midazolam with oxymorphone	0.1–0.2 mg/kg IM	Drugs can be mixed
Ketamine (or)	1–2 mg/kg IV	
Thiopental (or)	3–7 mg/kg IV	
Propofol	2–4 mg/kg	Give slowly to effect
Isoflurane* (or)	0.5%–3.5%, inhaled	
Sevoflurane*	2.0%–4.5%, inhaled	
Critical Patient		
Intravenous fluids		
Ketamine/diazepam (50:50)	0.5 ml/5 kg IV	Administer slowly
Isoflurane* (or)	0.5%–3.5%, inhaled	
Sevoflurane*	2.0%–4.5%, inhaled	

*Use a non-rebreathing anesthetic system (Bain or Ayres T-piece).

tranquilizers with drugs that produce anesthesia allows a reduction in the dose of the anesthetic drug. Anesthetic drugs tend to produce more depression of cardiopulmonary function than do sedatives or tranquilizers; thus the patient benefits from the decreased dose. Thiobarbiturates are the primary addition to the list of drugs already discussed. Other drugs, such as etomidate and propofol, offer potential advantages, such as fewer cardiopulmonary effects and lack of cumulative effects, but are expensive. Although endotracheal intubation is not required for the delivery of injectable anesthetic drugs, patients can benefit from intubation for protection of the airway and for oxygen supplementation.

Thiobarbiturates (Thiopental)

- Sedative or hypnotic agents that produce short-term IV anesthesia.
- Barbiturates produce CNS depression that ranges from drowsiness to coma.
- Not good analgesics at subhypnotic doses. When doses are increased to produce unconsciousness, anesthesia is produced.
- Cause respiratory depression and some arterial blood pressure depression.
- Sensitize the heart to catecholamine-induced arrhythmias. Ventricular bigeminy is often noted but resolves without treatment.
- Duration of effect is primarily determined by redistribution away from the brain into muscle and lean body tissues. Level and duration of anesthesia produced by a given dose depends on what other drugs have been administered, the rate of administration, and the level of awareness of the animal at the time of administration.
- Use with caution in patients with preexisting cardiovascular disease, hypotension, or shock.

▼ ***Key Point*** Do not use thiobarbiturates in greyhounds or other sighthounds because of prolonged elimination.

- Administer to effect, beginning with doses in the range of 4 to 6 mg/kg, increasing in 2 mg/kg increments. Onset of action is within 30 seconds.
- Can be mixed 50:50 (volume to volume) with propofol to allow a reduction in the dose of both drugs as a way to reduce cost. Can cause sloughing of tissues if administered perivascularly.
- Use for induction to inhalation anesthesia. Compatible with all agents previously described. Reduce the dose by approximately half if sedatives or tranquilizers are given prior to administration.
- Duration of action is prolonged by hypoproteinemia and acidosis. Administer IV fluids to shorten duration by promoting diuresis, and administer $NaHCO_3$ (2 mEq/kg) to shorten duration by alkalinizing the urine.

Propofol

- A phenolic compound that produces hypnosis similar to thiopental.
- Depresses hemodynamics comparable to thiobarbiturates, but does not sensitize the myocardium to epinephrine-induced arrhythmias.
- Depresses respiration. Administer slowly IV over a 30- to 60-second period to minimize the potential for apnea.
- Use with analgesics for painful procedures. Anesthesia can be maintained using propofol as a continuous IV infusion (0.4–0.8 mg/kg/min).
- Noncumulative, so recovery following multiple doses or an infusion occurs within the same time frame as that following a single dose.
- Relatively insoluble. Supports microbial growth if contaminated. Discard unused drug.
- Useful for induction of anesthesia in sighthounds and patients requiring cesarean section. Useful in compromised patients because of the lack of residual effects.

Ketamine Mixtures

Use ketamine in combination with sedatives and tranquilizers to provide short-term injectable anesthesia.

Ketamine/Diazepam

- Administer ketamine with diazepam in a 50:50 (volume-to-volume) mixture at a dose of 1 ml/10 kg IV. Give for brief periods (5–10 minutes) of restraint. Provides enough analgesia for minor surgical procedures. Readminister as needed to effect.
- Works well in depressed or geriatric patients. May not be effective in young, excited, or aggressive animals. Produces moderate muscle relaxation, cardiopulmonary support, and increased salivation. Ocular and swallowing reflexes are maintained, but orotracheal intubation can be accomplished.

Ketamine/Acepromazine

- Use ketamine with acepromazine to produce a quieter recovery than that with ketamine/diazepam but less muscle relaxation. Usually produces enough anesthesia for minor peripheral surgery, but visceral analgesia is not sufficient for abdominal surgery.

Ketamine/Xylazine and Ketamine/Medetomidine

- These combinations produce muscle relaxation, sedation, and analgesia that are improved over other combinations.
- Bradycardia and depression of cardiac contractility and respiration occur. Coadminister an anticholinergic. Use in young animals with good cardiopulmonary reserve. Avoid in animals with preexisting

cardiovascular disease, particularly those with cardiac conduction abnormalities.
- The combination of medetomidine (60–80 μg/kg), butorphanol (0.2 mg/kg), and ketamine (5 mg/kg) administered IM is a useful preanesthetic in cats that is sufficient for some surgery and is easily augmented with inhalants.

Tiletamine/Zolazepam

- Use IV or IM to produce anesthesia.
- Produces muscle relaxation and support of hemodynamics, but also produces respiratory depression.
- Maintains oropharyngeal reflexes. Recovery is prolonged with increasing doses. Recovery is usually uneventful in the cat but may be stormy in the dog.
- Administer low doses of acepromazine to quiet a difficult recovery.

Etomidate

- A nonbarbiturate hypnotic that can be used for short-term IV anesthesia.
- Produces a hypnotic state with little cardiovascular effect.
- Etomidate is expensive. Limit to patients with significant cardiovascular and respiratory disease.
- Recovery can be stormy, with vomiting and muscle tremors. Premedicate the animal with sedatives or tranquilizers to minimize these effects.

Anticholinergics

- Used to reduce salivation, block vagal inhibition of the heart, and quiet the digestive tract if indicated.
- Not innocuous. Respiratory dead space is increased (bronchodilation). Ventricular arrhythmias are more likely to occur.
- Use if bradycardia occurs or is likely to occur.
- Not routinely indicated in anesthesia. Myocardial oxygen consumption is increased owing to tachycardia. Secretions become more viscous.
- Glycopyrrolate is more potent and has a longer duration of action than atropine. It does not cross the placental or blood-brain barrier.
- Give IM, SC, or IV when expediency is important. Atropine dose is 0.02 to 0.04 mg/kg. Glycopyrrolate dose is 0.01 mg/kg.

ANESTHESIA FOR MAJOR PROCEDURES

Anesthesia for major procedures, requiring optimal hypnosis, analgesia, and muscle relaxation for relatively long periods, usually incorporates the inhalant anesthetics (see Tables 2-7 and 2-8). Although inhalant drugs can be given as the sole source of anesthesia, injectable drugs are usually given to facilitate induction and endotracheal intubation. The injectable drugs and drug combinations previously described, with the possible exception of ketamine/xylazine combinations, can be used to induce anesthesia. Ketamine/xylazine combinations produce significant cardiopulmonary depression that can be extreme when inhalant anesthetic drugs are added.

Inhalant Anesthetics

- Inhalant anesthetics have several advantages, including the coadministration of oxygen, the ease with which anesthesia depth is changed, and the fact that recovery does not depend on metabolism. The agents are primarily eliminated by exhalation. Administer via breathing circuits, with circle anesthetic systems being the most common.

Equipment

Circle Anesthetic Systems

- A carbon dioxide absorber removes carbon dioxide from the exhaled gas.
- Exhaled gas is rebreathed, making the system an economic one.
- Use 4 to 7 ml/kg/min as the minimum fresh gas flow rate for oxygen. This rate matches the animal's metabolic need for oxygen. Increase the fresh gas flow rate for oxygen to 10 to 20 ml/kg/min if nitrous oxide is given. Add the nitrous oxide flow to the oxygen flow rate. The pop-off valve in the circle system needs to be open to vent the excess gas at this flow rate.

Non-rebreathing Anesthetic Systems

- Bain and Modified Jackson Rees (Hudson RCI; Temecula, California) (SurgiVet; Waukesha, Wisconsin).
- Use for patients less than 2 to 4 kg, because less resistance to respiration is produced.
- Use a fresh gas flow of 1.5 times the minute ventilation (approximately 150 ml/kg/min). Fresh gas flow rates are higher because the fresh gas removes carbon dioxide from the system.

Scavenging Equipment

▼ ***Key Point*** Use of inhalation anesthetics mandates the removal of expired and waste gases from the operating room environment.

- Exhaust waste gases using suction systems or vent them to the outside via a hole in an exterior wall.
- Directing gases to the floor is insufficient.
- Use activated charcoal canisters as alternatives to absorb halogenated compounds. This is not effective for nitrous oxide.

Isoflurane

- Halogenated ether that produces anesthesia when inhaled in concentrations of 1.0% to 3.0%.
- Produces very rapid induction and recovery; relatively insoluble in blood.
- Maximal attainable concentration at room temperature is 30%.
- Use in precision out-of-the-circle vaporizers.
- Produces dose-dependent cardiopulmonary depression. Adequate ventilation is usually maintained. Ventricular arrhythmias are not enhanced.
- Use in patients with metabolic disease, in geriatric patients, and in patients prone to cardiac arrhythmias.
- Is minimally metabolized (<1%).

Sevoflurane

- Newest inhalant anesthetic approved for use in animals.
- Cardiopulmonary effects similar to isoflurane.
- Very insoluble in blood, and similar to nitrous oxide in speed of induction and recovery.
- Inoffensive odor is useful for masking.
- Administer at concentrations of 5% of induction followed by maintenance at 2.5% to 3.5%.
- Use in a precision out-of-the-circle vaporizer.
- Is minimally metabolized (3%). Do not used with desiccated carbon dioxide absorbent because of fire hazard.

Nitrous Oxide

- A nonirritant gas that produces some analgesia when inhaled in concentrations of 50% to 70%.
- Cannot produce anesthesia when administered alone. Can reduce the required concentration of the other, more potent, gases (e.g., isoflurane) by approximately one third when coadministered.
- Recovery can be complicated by diffusion hypoxia. Oxygen should be supplemented for 3 to 5 minutes after cessation of nitrous oxide administration.
- Total fresh gas flow rate must be increased if nitrous oxide is given.
- Not employed widely in veterinary practice because of its limited potency and potential problems with hypoxia.

▼ ***Key Point*** Do not use nitrous oxide in patients with pneumothorax, gastric torsion, or intestinal obstruction because it will diffuse into closed gas spaces and enlarge them.

Adjuncts to Inhalant Anesthesia

- Inhalant anesthetics may be too depressant for some patients.
- Intravenous opioids such as fentanyl (0.002–0.006 mg/kg IV) can be administered to augment analgesia with little cardiopulmonary effect.
- The combination of morphine, lidocaine, and ketamine can be used to supplement analgesia and reduce the requirement for inhalant anesthetics. Add 15 ml of 2% lidocaine (300 mg), 0.6 ml ketamine (60 mg), and 1.6 ml morphine (24 mg) to 1 L balanced electrolyte solution. Administer the combination at the standard rate (10 ml/kg/hour IV).

LOCAL ANESTHESIA AND ANALGESIA

- Local anesthetics (lidocaine, mepivacaine, bupivacaine, ropivacaine, etc.) produce complete analgesia with few cardiopulmonary effects.
- Local anesthesia can be used alone for some minor surgery, such as skin mass removal.
- Use local anesthetics in combination with other techniques prior to surgery to prevent pain "wind-up," allowing for better postoperative pain relief.
- Block the digital nerves at the level of the carpus prior to performing surgery of the paw, such as declawing cats.
- Epidural injection of local anesthetics or opioids (morphine) is used to produce analgesia for surgery of the rear limbs and caudal abdomen.

MONITORING THE ANESTHETIZED PATIENT

Monitoring is the cornerstone of safe anesthetic practice. Because irreversible CNS changes can occur within 4 or 5 minutes of cardiac arrest, a convenient monitoring interval of 5 minutes is appropriate. The skills needed in basic monitoring of anesthetized patients parallel those needed for performing a physical examination.

Anesthetic Record

- Prompts the anesthetist to evaluate the patient at regular intervals. Serves as a legal document.
- Contains the following information, at minimum:
  - Summary of preoperative physical examination
  - Purpose of anesthesia
  - Drugs administered, including dose, route, and time
  - Regular recording of heart or pulse rate and respiratory rate

Heart Rate

- Measured by auscultation using an esophageal stethoscope (Mallinckrodt), precordial stethoscope, or Doppler flow probe.
- Palpate a peripheral pulse to determine heart rate and provide additional subjective information concerning the strength of cardiac contraction. Feel the pulse on the ventral side of the tongue (lingual

pulse). Alternatively, use the femoral pulse if the animal's head is covered.
- Administer anticholinergics (atropine or glycopyrrolate) if the heart rate falls to less than 60 bpm in dogs and 90 bpm in cats.
- Evaluate the patient for hypotension or anesthetic plane that is too light if the heart rate is greater than 150 bpm in dogs or greater than 180 bpm in cats.
- Evaluate patients with irregular heartbeats or heartbeats of variable intensity with an electrocardiogram for abnormal cardiac rhythms.

Respiratory Rate

- Measure respiratory rate by watching the movements of the thoracic wall or the rebreathing bag of the anesthetic machine.
  - Most anesthetics are respiratory depressants.
  - Increases in rate or depth of respirations or panting usually indicate a plane of anesthesia that is too light.
  - Check the anesthetic depth in patients with irregular respirations; this can be a sign of excessive medullary depression. An apneustic pattern is expected after ketamine or tiletamine administration.

Capillary Refill Time and Mucous Membrane Color

- Gives further information on homeostasis.
- Capillary refill time should be less than 1.5 to 2 seconds.
- May be altered by the anesthetic agent chosen.

Other Monitoring Parameters

- Assess jaw tone to determine the degree of muscle relaxation present. This is an index of anesthetic depth.
  - Gently push the jaws apart and note the resistance to movement.
  - Dissociative agents do not produce muscle relaxation.
- Pinch a toe and look for a withdrawal response to check the depth of anesthesia prior to incision.

Monitoring Equipment

A wide variety of instruments are available to aid in monitoring patients.

Stethoscope

- Use esophageal stethoscopes (Mallinckrodt) to hear heart and respiratory sounds. Amplified stethoscopes are also available.

Electrocardiogram

- Use an electrocardiogram (ECG) to measure heart rate and to determine if cardiac arrhythmias are present.
- The ECG does not always ensure that the heart is beating or producing effective cardiac output.

Pulse and Blood Pressure Monitors

- Use Doppler flow probes (Parks Electronics; Aloha, Oregon) to detect peripheral pulses. Place the probe over a peripheral artery. An audible signal is created as pulses of blood pass under the probe and the sound waves emitted by the Doppler probe are altered. Place an occlusive cuff proximal to the Doppler probe to obtain an estimate of systolic arterial blood pressure. This monitor is reliable as a pulse detector but unreliable as an estimator of blood pressure. It can be used to follow trends. Use cuff widths approximately 30% of the circumferences of the extremity.
- Oscillometric units (Dinamap, Critikon; Tampa Bay, Florida) can record heart rate and estimate systolic, mean, and diastolic blood pressures. The units inflate an occlusive cuff and slowly release pressure. Characteristic pressure fluctuations during deflation are used to estimate blood pressure. These monitors are expensive and tend to lose accuracy as blood pressure falls. Use cuff widths approximately 30% of the circumference of the extremity.
- Dorsal pedal artery can be catheterized with an over-the-needle catheter to directly measure arterial blood pressures. Connect an aneroid manometer to the catheter as a simple way to determine the mean arterial blood pressure. Use a pressure transducer to make more definitive measurements.

Pulse Oximetry

- Detects pulses and uses reflectance or absorbance of light to estimate hemoglobin saturation.
- Pulse oximeters do not assure adequacy of ventilation, only adequacy of oxygenation.
- Most units also display pulse rate.
- Values should be in excess of 90%.
- Probes are usually placed on the tongue.
- Reposition the probe periodically as needed to maintain signal.

Blood Gas Analysis

- More definitive monitoring of respiratory and metabolic integrity is accomplished by measuring arterial pH and blood gas values.

See Chapter 5 for the characterization and treatment of acid-base disorders.

Table 2-9. ANTAGONISTS USED TO REVERSE ANESTHESIA

Benzodiazepine (Diazepam, Midazolam, Lorazepam) Antagonists	
Flumazenil	0.01–0.02 mg/kg IV
α_2-Adrenergic (Xylazine, Medetomidine) Antagonists	
Yohimbine	0.1–0.4 mg/kg IV
Tolazoline	0.5–2.0 mg/kg IV
Atipamezole	0.2–0.4 mg/kg IV
Narcotic Analgesic (Opioid) Antagonist	
Naloxone	0.003–0.010 mg/kg IV or IM

RECOVERY AND REVERSAL

Watch the patient after anesthesia until it can remain in sternal recumbency without being assisted.

- If reversible drugs have been given, the administration of antagonists speeds recovery (Table 2-9). Do not administer an antagonist indiscriminately.
- Doxapram (1–5 mg/kg) is a nonspecific stimulant of respiration and the CNS. Doxapram can be given to cause arousal in an emergency, but it can also produce undesirable excitement.
- Animals recovering from anesthesia may go through a period of emergence delirium. This period apparently results from a rapid return to consciousness with disorientation. The animal may or may not be in pain. Many animals respond to a reassuring voice and petting. Provide analgesia, sedation, or both for animals that do not respond to these actions.
- Check the animal's temperature. Most animals lose body heat during anesthesia.
- Some animals do not return to consciousness until body temperature is restored to 95°F to 97°F (35°C to 36.1°C).
- Warm animals by placing them on recirculating, warm-water heating pad; by providing radiant heat from a lamp; or by using a forced-air blanket.
- Take care to not burn the patient, particularly when heating lamps are used.
- Oxygen use increases dramatically with shivering. Monitor the patient, and provide oxygen if necessary.
- Leave the endotracheal tube in place until the animal regains the oropharyngeal reflexes (i.e., begins to swallow). Give oxygen if necessary.
- Remove IV catheters, if no longer necessary, after the patient is rewarmed and conscious. Postoperative hypotension can occur, particularly if the patient does not rapidly return to consciousness.
- Monitor the patient periodically until it can stand unassisted.

SUPPLEMENTAL READING

Gaynor JS, Muir WW: Handbook of Veterinary Pain Management. St. Louis: CV Mosby, 2002.

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Thurmon JC, Tranquilli WJ, Benson GJ: Essentials of Small Animal Anesthesia and Analgesia. Philadelphia: Lippincott Williams & Wilkins, 1999.

Chapter 3

Emergency and Critical Care Techniques and Nutrition

Shane W. Bateman / C. Anthony Buffington / Cheryl Holloway

This chapter describes commonly used techniques in emergency and critical care medicine. See appropriate chapters for information about diseases that require critical care.

INTRAVENOUS CATHETERIZATION BY CUTDOWN

Indications

▼ ***Key Point*** Venous access is required in every emergency situation.

Perform venous cutdown when percutaneous venous catheterization has been unsuccessful after one or two attempts (depending on the urgency with which access is required). Nonurgent venous cutdown can also be performed when numerous percutaneous catheterization attempts have resulted in severe peripheral hematoma formation or thrombophlebitis.

Contraindications

Relative contraindications include severe hemostatic dysfunction. However, occasionally such patients require IV catheterization, necessitating an easily compressible location as the best choice for a cutdown procedure.

Objective

Obtain vascular access for administration of fluid and drugs.

Equipment

- Local anesthetic
- Scalpel handle and #10 or #15 blade
- Iris scissors (very small sharp/sharp)
- Thumb forceps
- Curved mosquito hemostat
- Suitable size IV catheter (e.g., Surflo catheter, Terumo Medical Corp.)
- Needle holders, tissue forceps
- Monofilament skin suture appropriate to patient
- Skin staples (optional)

Technique

1. When the patient is semicomatose or moribund, local anesthesia is not required. Otherwise, infiltrate small amounts of local anesthetic into the aseptically prepared skin site.
2. In general, the lateral saphenous (canine) or medial saphenous (feline) are easier to approach than the cephalic veins. Jugular cutdown can also be performed with the same technique, but the vein is deeper and may be more troublesome for inexperienced surgeons to find.
3. After aseptic skin preparation and use of aseptic technique, identify the vessel. In many situations the vessel may not be visible even when occluded, so the anatomy of the vessel is important to understand.
4. Place the scalpel blade gently on the skin over the vessel and, without cutting the skin but maintaining skin contact with the blade, pull the skin laterally to the vessel (Fig. 3-1).
5. Incise approximately 1 to 1.5 inches parallel to the vessel.
6. Allow the skin to retract back into place over the vessel.
7. The bluish hue of the vessel should be obvious if the incision was made in a correct location. Move the skin to attempt to identify the vessel if it is not immediately obvious. To differentiate the vessel from underlying muscle bellies, the vessel should blanch with minimal digital pressure; muscle bellies will not.
8. Hold the iris scissors with the thumb and index finger in the finger rings with the tips of the scissors pointing across the palm of your hand, not extending out from the fingers. This allows the shaft of the scissors to be perpendicular to the patient and the vessel.
9. Place the tips of the scissors as close to the vessel wall as possible, apply gentle pressure to the tissue,

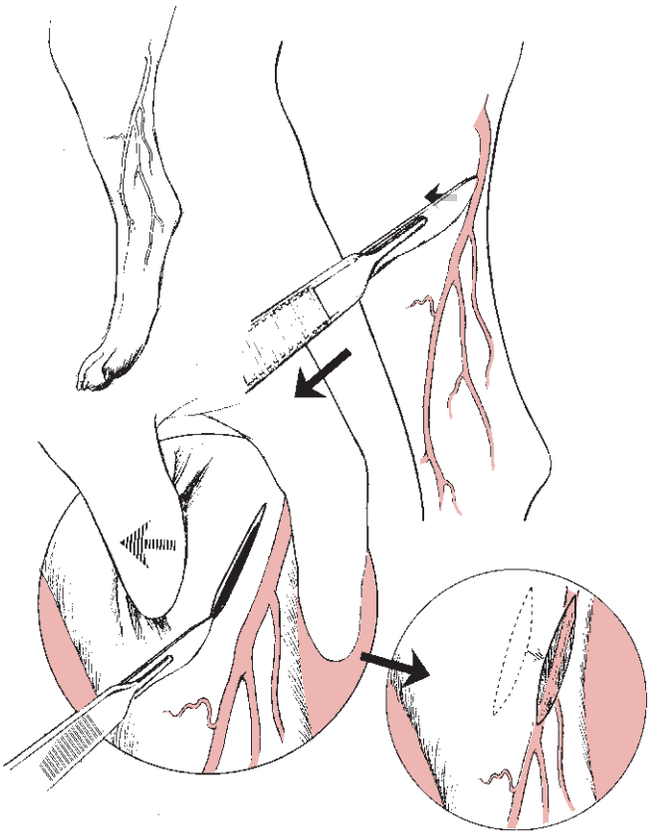

Figure 3-1. Position of scalpel and skin for skin incision.

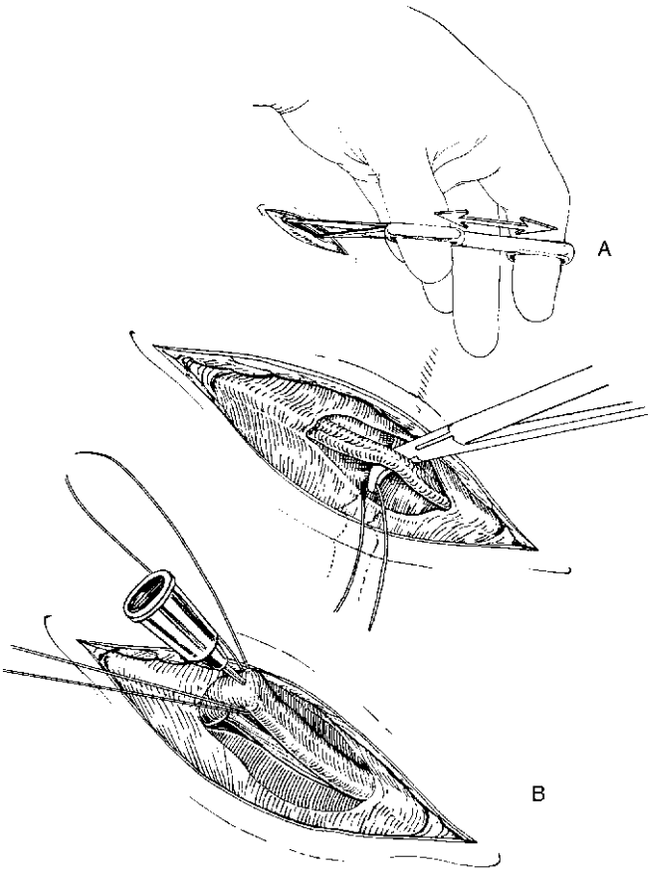

Figure 3-2. *A,* Blunt dissection of the vessel using sharp/sharp scissors. *B,* Catheterization of vessel using stay sutrue.

and extend the blades maximally, bluntly dissecting the fascia from the vessel wall (Fig. 3-2*A*).

10. Repeat this procedure on both sides of the vessel wall until the vessel is freed from its fascial attachments and the mosquito hemostat can be placed under the vessel. Take care not to place the tips of the blades on the vessel itself. In addition, if small side branches of the vessel are present, choose a more proximal or distal location.
11. Pull a loop of suture ventrally underneath the vessel to exteriorize and serve as a manipulator to allow positioning of the vessel for catheterization.
12. Examine the vessel for remnants of fascia. It is easy to catheterize one of these fascial planes by mistake and think that you are in the vessel lumen. Strip the vessel of any remaining fascia by gently using one arm of the Adson thumb forceps.
13. Catheterize the vessel using the suture as a handle to manipulate the vessel into an appropriate position (Fig. 3-2*B*).
14. It is easy to puncture both sides of the vessel wall, so prior to advancing the catheter, verify that the metal of the stylet cannot be seen underneath or beside the vessel wall by gently moving the catheter.
15. Flush the IV catheter to confirm successful catheterization.
16. Remove the loop of suture, connect IV fluids to the catheter, suture or staple the skin with the catheter exiting from the suture line, and secure the catheter to the skin with the normal taping method.

INTRAOSSEOUS ACCESS FOR FLUID ADMINISTRATION

Indications

Intraosseous access is typically utilized only in neonatal or pediatric patients because of the small size of their peripheral vessels.

Contraindications

▼ ***Key Point*** Do not use intraosseous access where severe tissue trauma exists or in areas of potentially infectious dermatitis.

Equipment

- Local anesthetic
- 22- to 20-gauge, 1- to 1.5-inch spinal needle (with stylet)
- Commercial intraosseous catheter (optional)

Technique

1. Aseptically prepare the skin over the appropriate site. In general, the intertrochanteric fossa or the tibial crest is the easiest site to gain access (Fig. 3-3).
2. Infuse a small quantity of local anesthetic into the periosteum and the skin surrounding the site. Be cautious that the volume administered is not in the toxic range for the size of the animal. Lidocaine can be diluted to 1% to prevent toxicity if necessary.
3. Using aseptic technique, identify the site of needle insertion into the appropriate long bone (femur or tibia) and palpate firmly to identify the appropriate direction and angle of needle advancement. Direct the needle as straight as possible down the marrow cavity of the shaft of the long bone.
4. Advance the needle using gentle but steady forward pressure as you slowly twirl the shaft of the needle back and forth.
5. Once the needle is firmly seated into the bone, remove the stylet and attempt to aspirate through the needle. Ability to aspirate bloody fluid (bone marrow) generally indicates successful placement. If awake, animals will often object to aspiration as they would for bone marrow aspiration.
6. Gently flush the needle with isotonic fluid and gently palpate around the long bone for accumulation of fluid. If fluid accumulates outside the bone, then the needle has penetrated the cortex and must be repositioned into the marrow cavity.
7. If successfully placed, attach the IV line to the needle (a luer lock tip assists in prevention of accidental disconnection). Carefully bandage the limb and exposed needle to minimize movement.

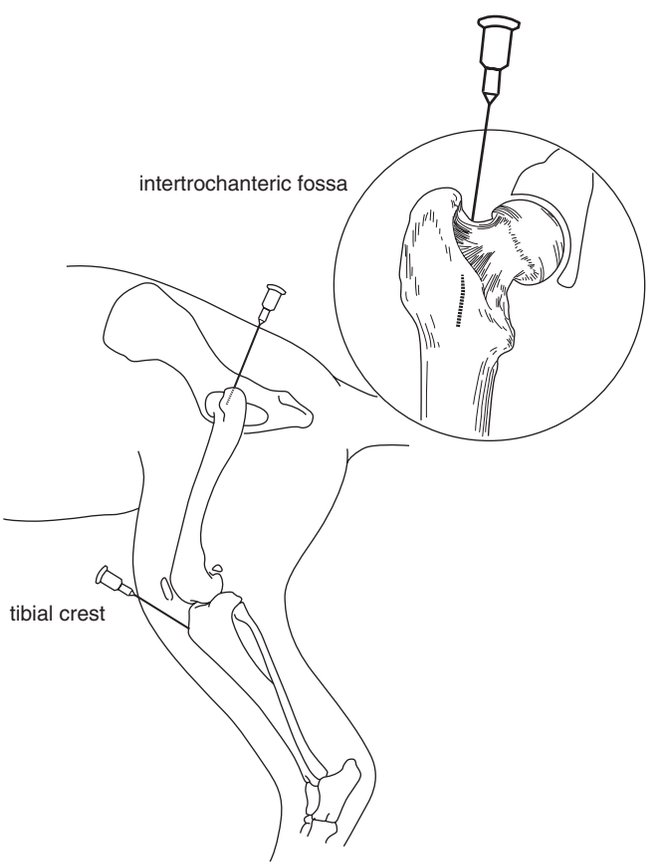

Figure 3-3. Anatomic locations for intraosseous access.

Complications

Poor needle placement can result in inappropriate needle tip placement into the cortex or outside the cortex. Repositioning of the needle usually results in success. Patients that are moving vigorously or traumatizing the needle may shift the tip to an inappropriate location, allowing fluid accumulation in the subcutaneous tissue. Regular monitoring of the limb and needle are warranted to detect this complication.

ARTERIAL SAMPLING FOR BLOOD GAS ANALYSIS

Indications

Collection of an arterial blood sample is often helpful in assessing respiratory function and effective gas exchange. Analysis of a blood gas for acid-base status is more meaningful when venous blood is utilized.

Contraindications

Presence of a severe coagulopathy is a relative contraindication. In general, with firm direct pressure for prolonged periods, significant blood loss is not a concern. The sample is most easily obtained when the patient is in lateral recumbency; thus observe patients with respiratory compromise carefully for worsening of respiratory distress during the procedure and give supplemental oxygen as required.

Objectives

- Obtain arterial blood for blood gas analysis
- Prevent hemorrhage

Equipment

Use either of the following:

- Dry heparin blood gas syringe
- A heparinized regular syringe

Technique

1. If no commercially available dry heparin blood gas syringes are available, heparinize a regular syringe by withdrawing liquid heparin into the syringe so that the insides of the syringe barrel are in contact with the heparin. Depress the syringe plunger to extrude the liquid heparin out of the needle. A small quantity of liquid heparin should remain in the syringe hub. Place a new needle onto the syringe prior to puncturing the skin.
2. The two most commonly utilized sites for arterial sampling are the femoral artery medial to the femur in the inguinal region (Fig. 3-4*A*) and the dorsal metatarsal artery medial to midline and distal to the tarsus joint (Fig. 3-4*B*).
3. Hold the tips of the index and middle fingers of the nondominant hand perpendicular to the artery but parallel to the long axis of the patient and gently palpate the region until the pulsation of the artery can be felt underneath both finger tips. Excessive pressure will often occlude the artery and prevent successful palpation of the pulsation.
4. Gently stabilize the artery and skin between the fingers of the nondominant hand.

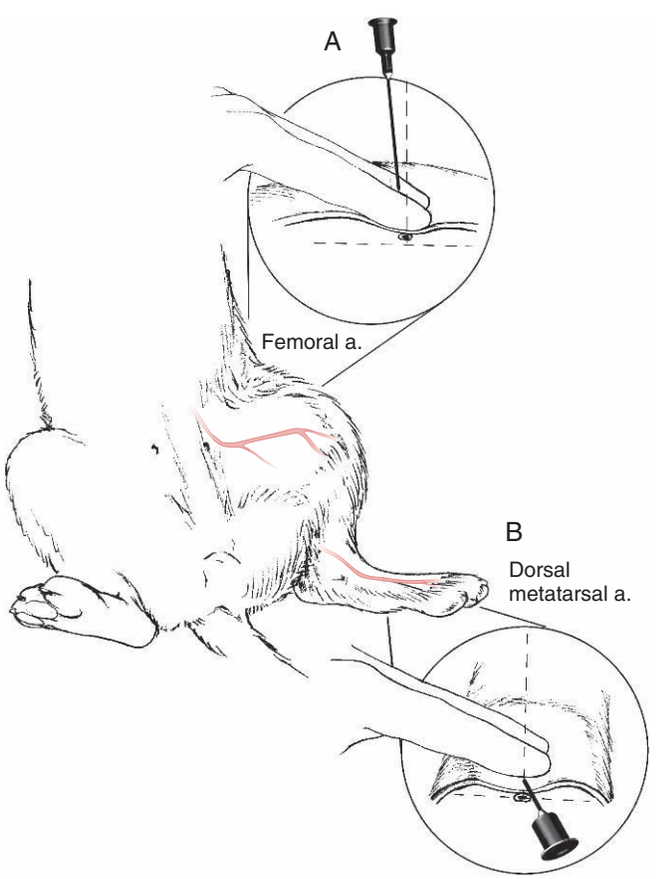

Figure 3-4. *A,* Femoral artery puncture. *B,* Dorsal metatarsal artery puncture.

5. Hold the sampling syringe with the dominant hand. Place the needle between the fingers over the artery and advance slowly at an acute angle (45 degrees or greater for the dorsal metatarsal artery, slightly less than 90 degrees for the femoral artery).
6. Observe the hub of the needle carefully for a blood flashback to "jump" into the hub. Frequently, pulsations can be observed if the patient's blood pressure is high enough. Self-filling blood gas syringes should fill rapidly if the pressure is normal. Withdraw the sample volume if a conventional syringe is being utilized. Slow flashbacks, lack of observable pulsations, color of the blood sample, slow filling of self-filling syringes, and the blood gas results may all indicate that the sample is venous or mixed rather than a pure arterial sample.
7. Place gentle but firm pressure over the sampling site for 3 to 5 minutes, then observe for an additional 30 to 60 seconds to ensure that the puncture site has sealed to prevent hematoma formation.

Complications

Hematoma formation is infrequent and can be prevented by applying pressure for an appropriate duration. Avoid accidental puncture of the nerve that courses parallel to the artery; puncture can cause a painful reaction.

NASAL CATHETER PLACEMENT

Indications

Patients require supplemental oxygen or enteral feeding.

Contraindications

- Patients with severe deforming facial trauma
- Brachycephalic breeds with respiratory distress
- Severe thrombocytopenia or other coagulopathy
- Severe or protracted vomiting (if placing a feeding tube)

Objectives

- Provide oxygen therapy using a nasal catheter
- Provide nutritional supplementation using a nasogastric tube

Equipment

- Nasal oxygen cannula or nasoesophageal or nasogastric feeding tubes
- Topical ophthalmic local anesthetic
- Tape
- Needle holders and tissue forceps
- Monofilament skin suture appropriate to the patient
- Skin staples

Technique

1. Install several drops of local anesthetic into the nostril with the patient's head tipped up slightly; allow several minutes to reach peak effect.
2. Premeasure the catheter to (a) the last rib for nasogastric tube, (b) the base of the heart for nasoesophageal tube, or (c) the junction of the zygomatic arch and the cranial edge of the ramus of the mandible for nasal oxygen.
3. Restrain the patient with the head tipped slightly up and place the tip of the catheter gently into the nostril.
4. Use the thumb of the nondominant hand to push gently up on the nasal philtrum. With the index finger of the same hand, gently squeeze against the thumb from the top of the nasal planum (Fig. 3-5).
5. Advance the catheter quickly and gently, forcing the tube in a ventral and medial direction into the ventral meatus. The patient will often retract away from you, so release your advancing fingers immediately after you have advanced the tube. This is a similar motion to holding and throwing a dart.
6. Advance the catheter with repetitive motions until the premeasured catheter length has been inserted. If placing a nasal oxygen cannula, advance the tube past the nasopharynx if possible to confirm placement into the ventral meatus, then pull back to the premeasured length. Tubes that will not advance past the nasopharynx may be in the dorsal meatus and should be repositioned.
7. Place a small length of tape to the dry tube where it exits the nostril.
8. Place a simple interrupted suture at the ventromedial corner of the nostril. Place a finger trap suture pattern over the tape on the tube to secure the tube to the nostril (Fig. 3-6*A–D*). Tie multiple knots to complete the finger trap.
9. Place a second simple interrupted suture to the ventrolateral corner of the nostril at the mucocutaneous junction using the remaining ends of the suture to further secure the tube from accidental removal (Fig. 3-6*C*).
10. Use skin staples to attach the end of the tube to the patient's face, generally either on the side of the face or up the center of the face between the eyes and to the top of the head (Fig. 3-6*D*).
11. Verify feeding tube placement with radiographs or capnographic confirmation.

Complications

Occasionally the tube will not advance past the nasopharynx (even through the ventral meatus) because of anatomical conformation in individual animals. In such patients, pass the tube through the opposite nasal passage. In addition, feeding tubes may be inadvertently passed into the trachea and airway, especially in sedated, anesthetized, or obtunded patients. Confirm placement using radiography or capnography. Feeding tubes can also be vomited back up the esophagus and chewed off by the patient, so closely observe patients with nasal feeding tubes.

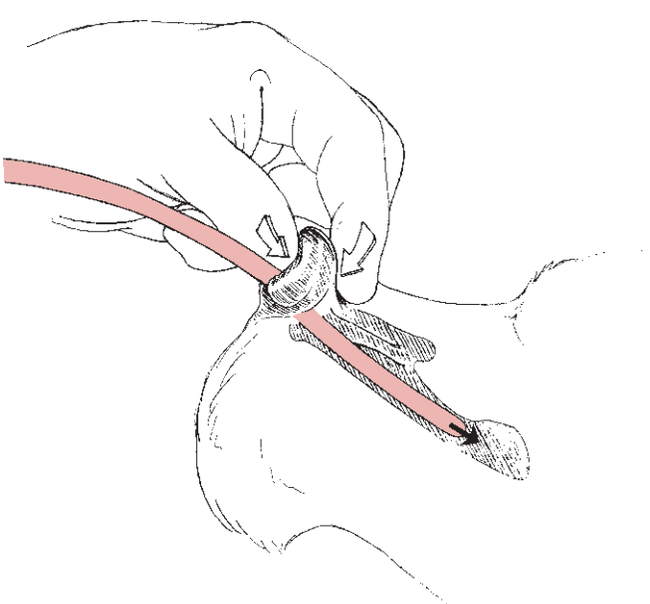

Figure 3-5. Positioning for placement of nasal catheter.

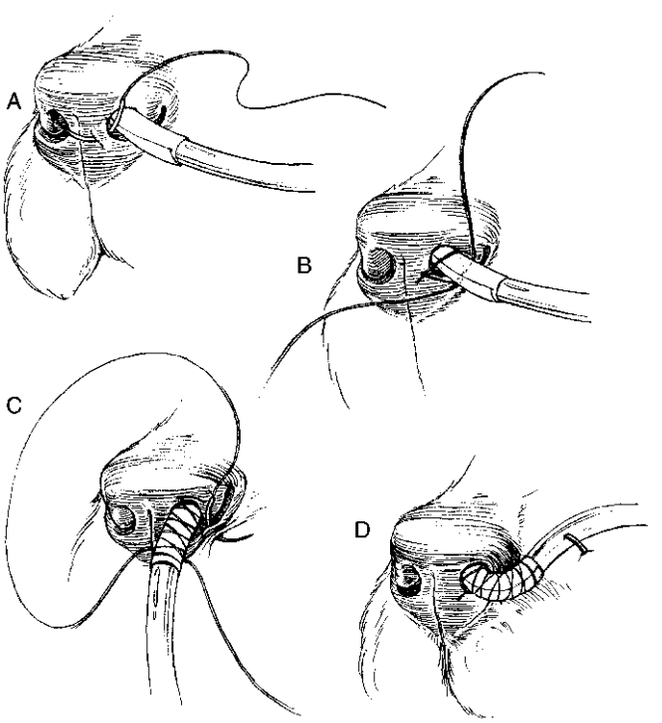

Figure 3-6. Finger trap suture pattern.

EMERGENCY TEMPORARY TRACHEOSTOMY

Indications

Patient has life-threatening upper airway obstruction (proximal to the cervical trachea) and cannot be intubated with an endotracheal tube.

Contraindications

Airway obstruction distal to the site of tracheostomy. Severe coagulopathy is a relative contraindication, but this can be treated with transfusion component support and direct pressure.

Objectives

- Establish a patent airway
- Maintain the patent airway by frequently cleaning or replacing the tracheostomy tube

Equipment

- Scalpel handle and #10 or #15 blade
- Mayo scissors
- Large, curved Kelly or Carmalt hemostat
- Tracheostomy tube
- Monofilament suture material appropriate to patient

Technique

1. Position the patient in dorsal recumbency with the head extended slightly off and over the edge of the table or with the neck over a rolled towel or sandbag.
2. Make one attempt to insert a large over-the-needle peripheral IV catheter into the trachea at the base of the neck close to the thoracic inlet to provide oxygen to the patient while final preparations are made.
3. Rapidly clip and aseptically prepared the skin.
4. The patient will need rapid IV anesthesia for the procedure unless it is moribund.
5. Incise the skin from the larynx to the thoracic inlet.
6. Bluntly force the closed tips of Mayo scissors into the first tissue plane, open and insert one tip into the tissue plane created, then incise the tissue plane to each end of the incision. Attempt to use the sharp edges of the scissors to cut by advancing with the blades open rather than "scissoring" through the tissue.
7. Incise the sternohyoideus muscles (strap muscles) in a similar way, exposing the trachea.
8. Identify the neurovascular bundle on each side and bluntly insert a hemostat through the fascia dorsal to the trachea, allowing it to be elevated into the surgical incision.
9. Do not damage the vessels overlying the trachea.
10. Depending on the experience and skill of the surgeon, two approaches to incising the trachea are possible:
    a. If the surgeon feels comfortable and excellent surgical precision is possible, incise the trachea transversely "between" two rings in the mid cervical trachea (Fig. 3-7). Extend the incision over the ventral two thirds of the circumference of the trachea. Do not incise into the dorsal tracheal membrane.
    b. Alternatively, if the surgeon is less comfortable and a lesser degree of surgical precision is likely, incise longitudinally "through" several rings (Fig. 3-8). Holding the scalpel upside down and gripping the blade carefully to allow only 10 to 15 mm of blade to be exposed, incise approximately four tracheal rings beginning with ring 3 and continuing through ring 6 distal to the larynx.
11. Direct oxygen toward the incision.

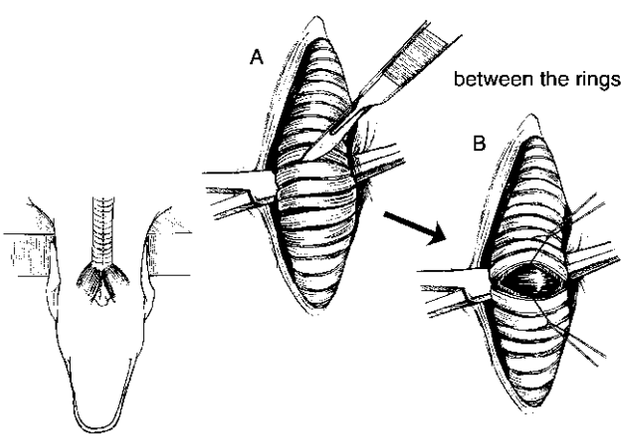

Figure 3-7. Between-the-rings tracheostomy with stay suture placement.

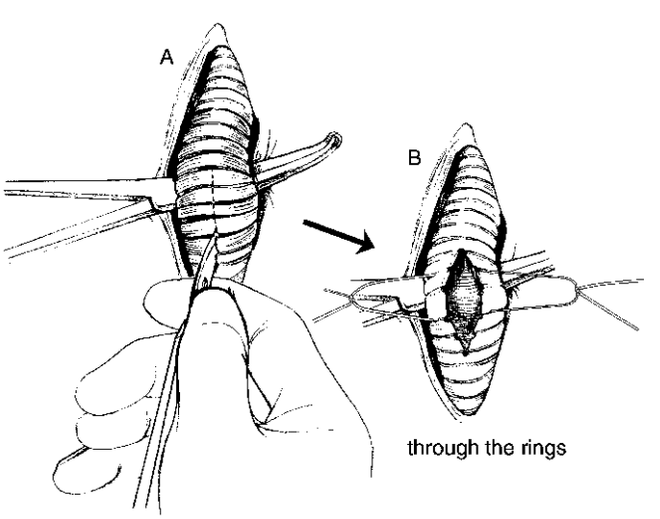

Figure 3-8. Through-the-rings tracheostomy with stay suture placement.

12. Place stay sutures (3-0 or 4-0 silk) in the edges of the tracheal incision. If a transverse incision was made, place stay sutures in the ventral-most aspect of the trachea and around the first proximal and first distal ring. If a longitudinal incision was made, place stay sutures around two adjacent rings, approximately 3 to 5 mm from the tracheal incision and encompassing 2 tracheal rings on both sides of the incision. Leave the suture ends long.
13. Insert the tracheostomy tube into the trachea. Several types of specialized tracheostomy tubes are commercially available. Each has advantages and disadvantages. A simple tracheostomy tube can also be easily constructed from an endotracheal tube (Fig. 3-9).
14. The most critical aspect of tube placement is the size and fit of the tube. If the tube exerts circumferential pressure on the tracheal mucosal, then significant pressure necrosis, scarring, or fibrotic web formation are more likely to occur as a complications. Choose a tube that fits loosely in the trachea with no major points of mucosal pressure. Do not inflate the cuff unless positive pressure ventilation is required.
15. Suture the skin edges to allow easy access to the tracheal incision when the tube needs to be changed.

Postoperative Care and Complications

- Clean or replace the tube as necessary to maintain patency.
- Clean the "dirty tube" and allow it to soak in an appropriate and safe antimicrobial solution, then rinse carefully with sterile saline prior to the next tube exchange.
- Do not apply suction to the tube.
- Keep the animal well hydrated.
- Protect the skin around the tube with petrolatum (Vaseline).

If possible, use tracheostomy heat and moisture exchange devices (HME) to maintain airway humidification and thus decrease viscosity of secretions. These devices add a small amount of increased resistance that contributes to the work of breathing. In patients with marginal muscle strength, this may be significant and lead to a vicious cycle of hyperthermia and increased work of breathing.

Monitor the patient's temperature regularly. Routine administration of saline into the tracheostomy site is not recommended. A poorly fitting tube and inappropriate inflation of the cuff are the most common cause of fibrosis and web formation as a long-term complication.

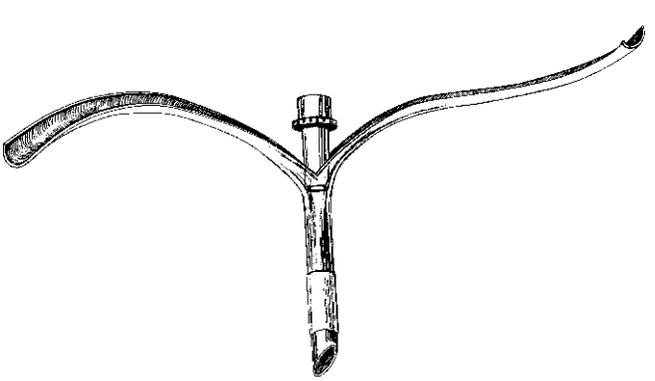

Figure 3-9. Tracheostomy tube construction from endotracheal tube.

ABDOMINOCENTESIS

Indications

Physical examination or radiographic evaluation indicates moderate quantities of peritoneal effusion, and cytological or chemical analysis of the fluid will assist in the diagnostic process.

Contraindications

Severe coagulopathy is a relative contraindication depending on the value or benefit of obtaining a fluid sample. Relative contraindications to use of a blind technique include a large abdominal mass; significant organomegaly, particularly of a vascular organ such as the spleen, liver, or kidney; or distension of a hollow viscus such as bowel or uterus. Consider ultrasonographic guidance if available.

Objectives

- Aseptically obtain fluid from the abdominal cavity for analysis and culture
- Avoid trauma to abdominal organs

Equipment

- 22- to 20-gauge, 1- to 1.5-inch needle and syringe appropriate to patient size (e.g., 3- to 12-ml syringe)

Technique

1. If possible, allow the patient to stand or be positioned in sternal recumbency to allow access to the most dependent site on the abdomen. Alternatively, place the patient in left lateral or dorsal recumbency.
2. The goal of the patient position and of the location and direction of the abdominocentesis attempt is to avoid the spleen, thus preventing hemorrhage that will contaminate the sample.
3. Clip and aseptically prepare the skin. Local anesthetic can be infiltrated if desired.
4. Advance the needle and syringe through the skin and withdraw the plunger of the syringe to create a small amount of negative pressure in the syringe prior to advancing the needle into the peritoneal cavity and away from the presumed location of the spleen.

5. In sternally recumbent or standing patients, frequently productive sites are caudal to the spleen, on or slightly to the right side of midline, with the needle directed toward the cranial aspect of the bladder. In left laterally recumbent patients, frequently productive sites are slightly caudal to the umbilicus, on or slightly to the right of midline, with the needle directed toward the cranial aspect of the bladder and slightly toward the dependent or left side of the patient. If these areas are unproductive, attempt a second site just cranial to the umbilicus, on or slightly to the right of midline, with the needle directed perpendicular to the long axis of the patient or at a 20° to 30° angle (needle tip toward the cranial aspect of the patient). In dorsal recumbency, frequently productive sites are caudal to the umbilicus, on or slightly to the right of midline, with the needle directed toward the cranial aspect of the bladder. If this attempt is unproductive, attempt a second site just cranial to the umbilicus, to the right of midline, with the needle directed perpendicular to the spine.
6. In general, extremely gentle aspiration of the syringe may yield a larger sample size and prevent clogging of the needle with omentum.

Complications

Complications are minimal. Inadvertent splenic aspiration may occur, but unless the patient has a bleeding tendency, this is unlikely to create a problem except for contamination of the sample with blood or potential contribution to an erroneous diagnosis of hemoabdomen.

TENCKHOFF PERITONEAL DIALYSIS CATHETER PLACEMENT

Indications

Tenckhoff peritoneal dialysis catheter placement is ideal for short-term (24 to 48 hours) access to the peritoneal cavity. This may be useful for treating patients with acute intoxication with drugs or chemicals that can be effectively removed by peritoneal dialysis; for core warming or cooling of patients with severe hypothermia or hyperthermia, respectively; for short-term management of uremia in unstable uroabdomen patients; or for performing diagnostic peritoneal lavage (DPL).

Contraindications

Relative contraindications to use of the blind technique for placement include large abdominal masses; significant organomegaly, particularly of a vascular organ such as the spleen, liver, or kidney; or distension of a hollow viscus such as bowel or uterus.

Objectives

- Obtain abdominal fluid or perform DPL
- Perform peritoneal dialysis
- Avoid organ damage
- Avoid subcutaneous leakage of fluid

Equipment

- Local anesthetic
- Scalpel blade (#11 or #15)
- Needle holders and thumb tissue forceps
- Monofilament skin suture appropriate to the size of the patient
- Tenckhoff peritoneal catheter (numerous commercially available kits, e.g., Sherwood Davis & Geck)
- Connecting adapters and fluid lines to maintain a closed ingress-egress system

Technique

1. Place the patient in left lateral recumbency and aseptically prepare a wide area around the abdominal entry site. Infiltrate the site with local anesthetic. Drape the area appropriately and perform the procedure aseptically.
2. The site of entry is just cranial to the umbilicus and slightly to the right of midline.
3. Make a small stab incision through the skin and the external fascial plane of the external rectus abdominus muscle large enough to just accommodate the diameter of the catheter.
4. Several types of catheter kits are available for purchase with differing methods and equipment for actual placement of the catheter through the abdominal wall. Follow the instructions with the kit or modify them to allow placement of the catheter into the peritoneal cavity. Kits using the peel-away introducer or Seldinger (over the wire) technique generally have a lower risk of injury to internal organs.
5. Position the catheter tip near the pelvic canal. Secure the catheter to the patient using the finger trap suture method (see Fig. 3-8).

▼ ***Key Point*** Use aseptic technique and ensure that the system remains closed.

Complications

Minor hemorrhage may be expected for a short time after placement. Ongoing evidence of hemorrhage into the draining fluid indicates more significant hemorrhage. Frequently, the omentum may occlude the openings of the catheter and prevent appropriate drainage. In patients with a thin or compliant body wall or poor body condition, gently palpate the catheter inside the peritoneal cavity and gently strip the omentum from the catheter tip if necessary. Introduction of infection into the peritoneal cavity may have devastating conse-

quences and requires vigilant attention to the care and maintenance of the drainage system.

THORACOCENTESIS

Indications

Perform diagnostic thoracocentesis on all patients that present with symptoms of pleural space disease (rapid shallow breathing, respiratory distress, symmetrical or asymmetrical dullness, or absence of lung sounds on auscultation) as described in Chapter 142. Patients with significant respiratory distress that are unsuitable candidates for radiographic evaluation may also benefit from diagnostic thoracocentesis.

Contraindications

Patients with long-standing chronic effusions (particularly cats with chylous effusion) may be at a higher risk for development of fibrosing (restrictive) pleuritis. Inadvertent needle contact with, and subsequent laceration of, the diseased pleura in this syndrome can produce significant and life-threatening pneumothorax. Exercise extreme caution in using sharp instruments to drain thoracic fluid in such patients.

Objectives

- Evacuate fluid or air from the pleural space
- Avoid iatrogenic pneumothorax or trauma to the lungs, heart, and intercostal blood vessels

Equipment

- 19- or 22-gauge butterfly catheter, 18- to 22-gauge over-the-needle intravenous catheter, 18- to 22-gauge, 1- to 1.5-inch needle, or metal stylet from 18- to 22-gauge over-the-needle catheter with catheter removed
- IV extension set
- Three-way stopcock
- Syringe

Technique

1. Clip hair from the site and aseptically prepare the skin. Many patients will tolerate the procedure without instillation of local anesthetic and often resent the injection of local anesthetic more than the procedure.
2. The site of thoracocentesis will depend on whether air or fluid is suspected to be causing respiratory distress. If fluid is suspected, select a ventral location in intercostal spaces 3 to 7 approximately one third of the distance between the costochondral junction and the sternum. If air is suspected, select a dorsal location in intercostal spaces 5 to 9 at the junction of the dorsal one third and ventral two thirds of the chest wall.
3. Choose a needle or catheter of sufficient size and length appropriate to the situation and patient. Ensure that the three-way stopcock is closed to the atmosphere.
4. Advance the sharp point of the needle or stylet through the skin, then place a small amount of negative pressure on the syringe. Advance the needle tip cautiously until a slight "pop" through the parietal pleura is felt, which ideally is accompanied by productive aspiration of air or fluid from the pleural space.
5. Use one of the following methods:
   a. If using a rigid metal device, attempt to reposition the needle or stylet tip into the intercostal space (parallel to the ribs with the bevel facing into the chest) so that as the pleural cavity is drained and the lung expands closer to the chest wall, there is less likelihood that the lung will be lacerated by the needle tip (Fig. 3-10*A*).
   b. Alternatively, advance the needle under the cranial rib and flatten the needle against the caudal rib (perpendicular to the ribs with the bevel facing into the chest). This method should cause the cranial rib to be pushed gently from the chest, again protecting the tip of the needle and preventing laceration of the lung parenchyma (Fig. 3-10*B*).
   c. In a third method, grasp the rigid shaft of the needle or stylet between the index finger and the thumb such that only the tip of the needle or stylet is within the pleural cavity. Guard the needle or stylet firmly to prevent inadvertent advancement into the thoracic cavity. As soon as a "scratching" or "scraping" sensation is detected on the needle, immediately withdraw it to prevent inadvertent laceration of the lung (Fig. 3-10*C*).
6. Gently reposition the needle or stylet or withdraw it if there is lack of continuing production of fluid or air from further attempts at aspiration.
7. Drain as much as possible from the pleural cavity using the three-way stopcock, syringe, and collection basin (a second thoracocentesis may be required on the contralateral chest wall in some cases).

Complications

Patients with chronic fluid accumulations, especially with significant quantities of fibrin, may have significant compartmentalization of fluid that is difficult to remove with routine thoracocentesis. Ultrasound-guided attempts may be more successful in collecting fluid from such patients; alternatively, consider a chest drain (see the next section). Inadvertent laceration of lung parenchyma resulting in pneumothorax is rare (except in fibrosing pleuritis patients) and can be managed with chest drain placement and intermittent or continuous suction. Laceration of a coronary artery is an extremely rare complication and likely only if the position of

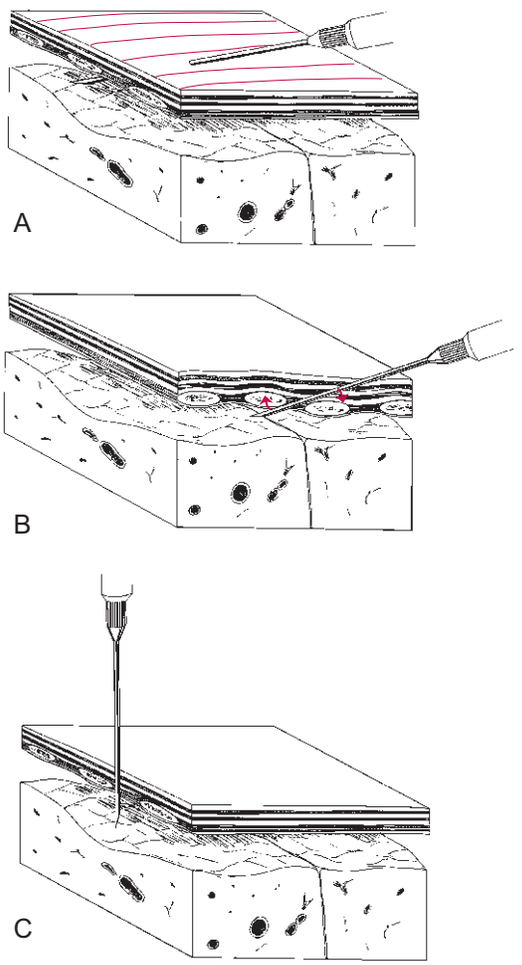

Figure 3-10. *A,* Needle position for parallel intercostal approach to thoracocentesis. *B,* Needle position for perpendicular intercostal approach to thoracocentesis. *C,* Needle position for subpleural approach to thoracocentesis.

the heart is significantly deviated within the thoracic cavity.

THORACIC CATHETER OR TUBE PLACEMENT

Indications

Consider placing a thoracic catheter or tube in patients with large volumes of air or fluid production that are not reasonably and effectively drained with intermittent thoracocentesis.

Contraindications

Significant coagulopathy is a relative contraindication for this procedure. Severe trauma or instability of the chest wall at the proposed site is a contraindication to nonsurgical placement of the catheter or tube.

Objectives

- Aseptically place an indwelling thoracic drain tube without causing iatrogenic trauma to thoracic viscera
- Minimize iatrogenic pneumothorax
- Place the tube so that it effectively drains pleural air or fluid

Equipment

- Scalpel handle with #10 or #15 blade
- Adson Thumb forceps
- Mayo scissors
- Needle holders
- Curved Kelly or Carmalt hemostat appropriate to the size of the patient and tube
- Chest catheter or tube of appropriate size (two thirds of the intercostal space) (Argyle trocar catheter or red rubber feeding tube)
- Monofilament skin suture material appropriate to patient (i.e., 3-0 to 0)

Technique

1. Use either general anesthesia or heavy sedation with local anesthesia and intercostal nerve blocks.
2. Pull the patient's lateral chest wall skin cranially as far as comfortably possible.
3. Clip the hair and aseptically prepare the skin from the 5th to the 12th intercostal space. Use local anesthetic to infiltrate into the 7th or 8th intercostal space at the junction of the dorsal one third and ventral two thirds of the lateral body wall.
4. Incise the skin at the 10th intercostal space. Make the incision approximately 5 mm longer than the diameter of the tube being placed.
5. Using thumb forceps and sharply incise the subcutaneous and latissimus dorsi muscle tissue. Do not use excessive blunt dissection so that you have a tight seal around the tube.
6. Clamp the thoracostomy tube tip 3 to 5 mm behind the tips of the Kelly or Carmalt hemostat (Fig. 3-11*A*). Ensure that the open end of the tube is clamped or plugged with a collection device. Alternatively, use an Argyle trocar catheter.
7. Premeasure the tube from the intercostal entry site (seventh or eighth intercostal space) to the point where the elbow naturally overlies the sternum.
8. Place the clamped tube into the deepest part of the incision, ensuring that the hemostat is curved toward the elbow and the tips are in the intercostal space and not over a rib.
9. Stand at the patient's back and grasp the shaft of the tube or hemostat with the nondominant hand, allowing one finger's width between the patient and the bottom of the nondominant hand. Form a fist over the finger rings of the hemostat (or trocar catheter) with the dominant hand (Fig. 3-11*B*).

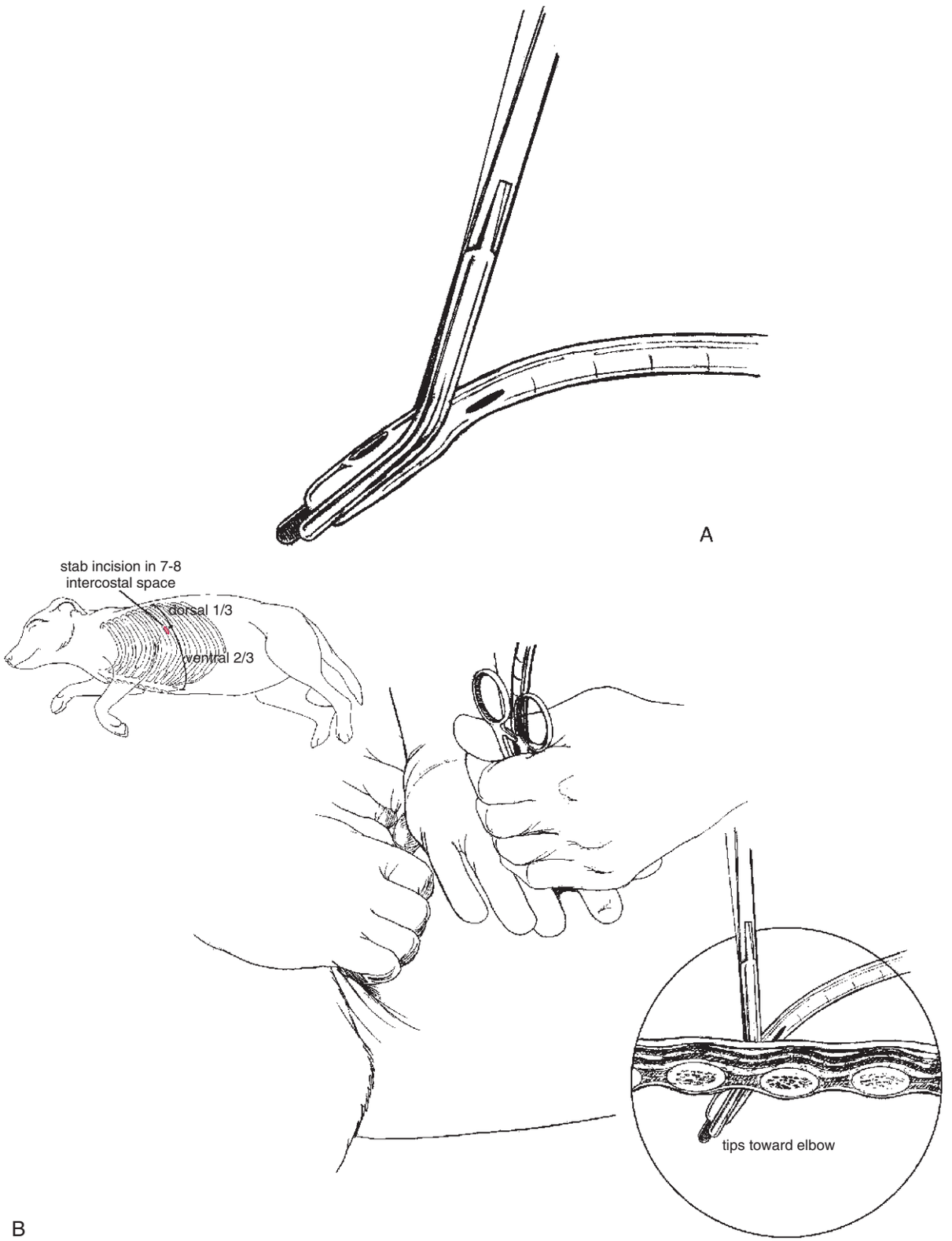

Figure 3-11. *A,* Position of thoracic tube in Kelly or Carmalt forceps. *B,* Technique for placement of thoracic tube.

10. Place the tube into the chest cavity at the seventh or eighth intercostal space with a sharp, quick, and forceful motion.
11. Open the hemostat and slide the tube gently into the chest cavity while the hemostat is removed.
12. After inserting the tube to the premeasured length, release the skin to slide caudally, forming a "tunnel" over the tube as it exits the chest wall.
13. Place a purse-string suture in the skin around the tube. Leave both suture ends of approximately equal length.
14. Place a finger trap suture pattern to secure the tube to the skin (see Fig. 3-6). Also, if desired to prevent leakage around the subcutaneous portion of the tube, place a simple interrupted suture around the tube between its entry site in the skin and where it enters the thorax.
15. Cover the skin-tube interface with copious amounts of antibiotic ointment and bandage it into place.

Postoperative Care and Complications

- Use an Elizabethan collar if necessary to prevent tube damage.
- Change the chest bandage every other day or more often if necessary. Check tube position during bandage changes.
- Frequently check tube connection devices for leaks.
- A small amount of subcutaneous air or fluid ventral to the tube entry site may occur. However, consider replacing the tube in a new site if large amounts of fluid or air drain to the subcutaneous space.
- Obtain thoracic radiographs if necessary to check tube position. Reposition the tube if necessary.
- Pull the chest tube when minimal fluid or air is drained. The chest tube can create 1 to 2 ml/kg/24 hours of pleural fluid.
- Remove sutures and pull the tube quickly and smoothly from the chest. Submit the tube tip for culture if indicated.
- Apply antibiotic ointment and bandage the incision.

FEEDING TUBE PLACEMENT

Nasal Feeding Tubes (Nasoesophageal, Nasogastric)

See "Nasal Catheter Placement" in this chapter.

Esophagostomy Tube Placement

Indications

Enteral tube feeding is required for long-term home feeding in patients with good gastric motility and when longer anesthetic periods or expense precludes the use of a percutaneous endoscopically placed gastrostomy tube (PEG tube).

Contraindications

Contraindications for esophagostomy tube placement include megaesophagus or localized infection at the desired tube insertion site. Coagulopathy is a relative contraindication. Consider severity of the hemostatic dysfunction and the urgency of nutritional support.

Objectives

- Provide nutritional supplementation using an esophageal catheter
- Avoid excessive trauma to the esophagus

Equipment

- Scalpel handle with #15 or #11 blade
- Large curved Kelly or Carmalt hemostat
- Appropriate red rubber feeding tube (size 14 Fr or larger)
- Monofilament skin suture appropriate to the patient

Technique

1. Commercially available customized esophagostomy kits are available. If using a kit, follow the instructions for placement that accompany the kit.
2. Anesthetize the patient and place in right lateral recumbency with an endotracheal tube in place.
3. Premeasure the tube to ensure that the tip of the tube is in the distal esophagus (from the entry site to the eighth rib).
4. Clip and aseptically prepare the skin over the left neck caudal to the ramus of the mandible.
5. Insert a curved hemostat into the mouth with the curve pointed laterally. Use a mouth gag to facilitate hemostat placement if necessary. Advance the hemostat into the esophagus and palpate the tips of the hemostat on the left lateral neck.
6. Place the tips of the hemostats to the level of the second to third cervical vertebral body and as far dorsal from the jugular vein (furrow) as possible. Push outward or upward to "tent" the skin of the neck.
7. Have an assistant's index finger and thumb grasp the tips of the hemostat and gently push down to stretch the skin over the tips of the hemostat to hold it firmly in place and prevent it from moving (Fig. 3-12).
8. Have the assistant make a stab incision directly over the tips of the forceps, making contact with the metal tips with the scalpel blade. Do not remove the blade until the tips of the hemostat penetrate the incision. The goal is to gently use the scalpel to enlarge the incision only until it permits exit

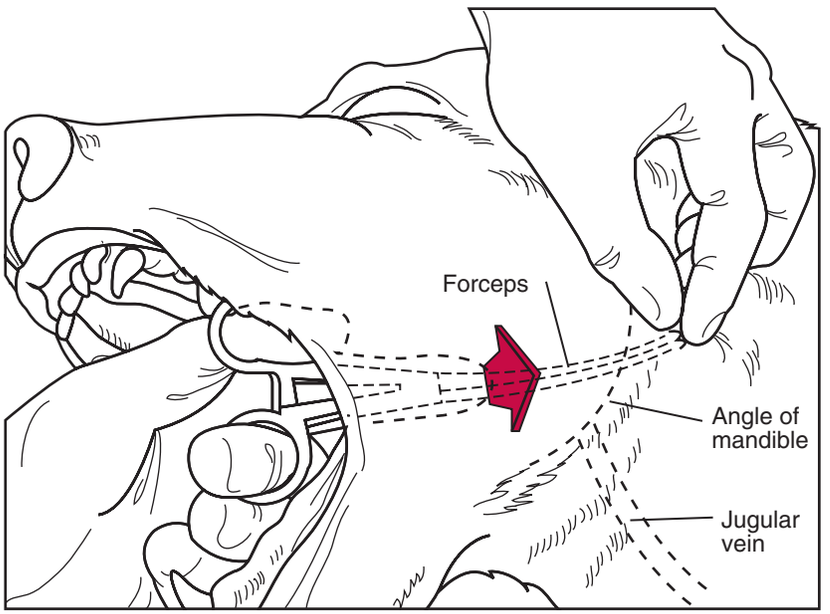

Figure 3-12. Technique for esophagostomy tube placement.

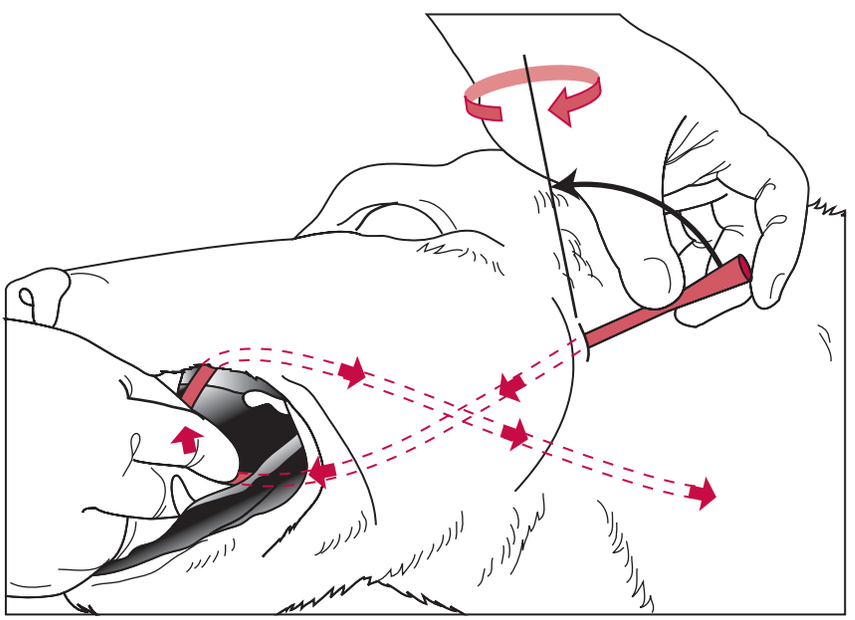

Figure 3-13. Positioning of tube after placement of esophagostomy tube.

of the hemostat. A large or ragged incision is not desirable.

9. Push the hemostat tips outward through the stab incision. If resistance is felt, the blade of the scalpel can be "wiggled" slightly to allow the hemostat to penetrate.
10. Open the jaws of the hemostat, place the distal tip of the feeding tube parallel to the tips, and clamp it into place.
11. Pull the tube through the mouth to the appropriate length and remove the clamp.
12. Direct the end of the tube down the esophagus and advance the tube as far as possible (Fig. 3-13).
13. Gently pull out the tube exiting the neck, and twist while attempting to advance the tube in place into the patient's pharynx. The tube should straighten and "unkink." If correct and unkinked placement has been achieved, the tube can be advanced and withdrawn smoothly from the esophageal incision with little resistance.
14. Suture the tube to the skin using the finger trap suture pattern (see Fig. 3-6).

15. Verify correct tube placement using a portable capnograph (no visible waveform and end-tidal carbon dioxide measured at 0 mmHg) or with lateral and ventrodorsal radiographic views of the thorax before feeding.

Postoperative Care and Complications

- Keep the incision clean and covered with a light bandage or stockinette.
- See the nutrition section of this chapter for supplementation guidelines.
- If the tips of the hemostats remain slightly open during creation of the stab incision, a strip of esophageal mucosa may get trapped between the jaws of the hemostats. When the tube is being pulled into the esophagus from the skin, the strip of tissue will make it difficult to pull the tube back into the esophagus until the tissue breaks or the tube dislodges from the hemostats.
  - Ensure that the hemostat tips are not opened until they are completely free from the skin-esophageal incision.
- If the tube will not straighten or unkink during insertion of the tube down the esophagus, do the following:
  - Ensure that the tube tip is in the esophagus and not the trachea.
  - Gently withdraw the tube from the neck incision and continue twisting.
  - Realize that the tube is not large enough, so it has insufficient tensile strength or memory to straighten or unkink (ensure that the tube is at least 14 Fr).
- If the jugular vein is lacerated, take the following steps:
  - Apply direct pressure to the wound for several minutes to prevent blood loss.
  - Extend the incision and isolate the jugular vein, then ligate it above and below the laceration, sacrificing the vessel.

Percutaneous Endoscopically Placed Gastrostomy Tube

Indications

- Consider a PEG tube for any patient for which long-term (weeks to months) nutritional support is warranted. It is generally the feeding tube of choice for long-term nutritional support when an endoscope is available to assist in placement.
- Use a PEG tube to bypass the oral cavity and esophagus.

Contraindications

Infection at the site of insertion is a contraindication. Coagulopathy is a relative contraindication. Consider the severity of the hemostatic dysfunction and the urgency of nutritional support in the decision. Placement of the tube described later in this section is also a relative contraindication in large-breed (especially deep-chested) dogs because of the increased risk of inadvertent tube removal from the stomach, resulting from excessive tension between the paracostal placement site and the stomach wall. Consider placement of a customized tube with a large, nonremovable inner flange for these patients. Removal of such tubes must also occur using an endoscope and cannot be accomplished percutaneously. The presence of neoplasia or severe disease of the stomach wall increases the risk of leakage and peritonitis and is a relative contraindication.

Objectives

- Allow nutritional supplementation bypassing the oral cavity and esophagus
- Provide a leakage-free, chronic, indwelling gastric tube

Equipment

- Gastrointestinal (GI) endoscope
- Endoscopic grasping forceps
- Bard urologic catheter (18- to 24-Fr Pezzer mushroom-tip model)
- Sovereign over-the-needle IV catheter (14 gauge)
- Three-way stopcock and adapters
- Vetafil suture, size 2-0 (3–5 feet depending on patient size)
- #11 blade
- 20-gauge, 1-inch needle
- Scissors
- Hemostats
- Stockinette (cut to fit for “sweater”)

Technique

1. Prepare the Pezzer catheter by removing the flared end and cutting the flared end into two pieces of approximately equal length. Make a long axis stab incision in the center of each piece large enough to accommodate the diameter of the Pezzer catheter. Advance the hemostats through the stab incision of one piece and pull the catheter through. Advance this “inner flange” piece down to the mushroom tip. Some clinicians prefer to snip off the nipple-shaped tip of the Pezzer catheter to reduce occlusion of the tube with food particles. Cut the shaft of the opposite end of the catheter at an approximately 60 degree angle to leave a tapered tip.
2. Place the anesthetized animal in right lateral recumbency, and clip and aseptically prepare a 10- to 14-cm^2 area of the skin just caudal to the costal arch.
3. Insert an endoscope and distend the stomach with air. Gently palpate the distended stomach from the abdominal wall just caudal to the last rib using an extended finger. Observe using the endoscope to

ensure that the proposed exit site is positioned in the body of the stomach away from the pylorus.
4. Quickly and forcefully insert the Sovereign IV catheter percutaneously into the distended stomach and observe using the endoscope. Withdraw the needle, leaving the catheter in place (Fig. 3-14*A*).
5. Thread Vetafil suture material through the catheter into the stomach.
6. Using endoscopic grasping forceps, grasp the Vetafil suture and withdraw the entire endoscope, along with the luminal end of the suture, out through the mouth. Ensure the end of the suture exiting the body wall does not enter the stomach accidentally (Fig. 3-14*B*).
7. Withdraw the Sovereign IV catheter from the body wall. Place a hemostat on the body wall end of the suture to prevent inadvertent pull-through into the stomach (Fig. 3-14*C*).
8. Insert the luminal end of the suture through the narrow end of the Sovereign IV catheter and advance the catheter toward the patient's mouth (Fig. 3-14*D*).
9. Secure the pointed tip of the Pezzer catheter to the luminal suture end using a horizontal mattress suture.

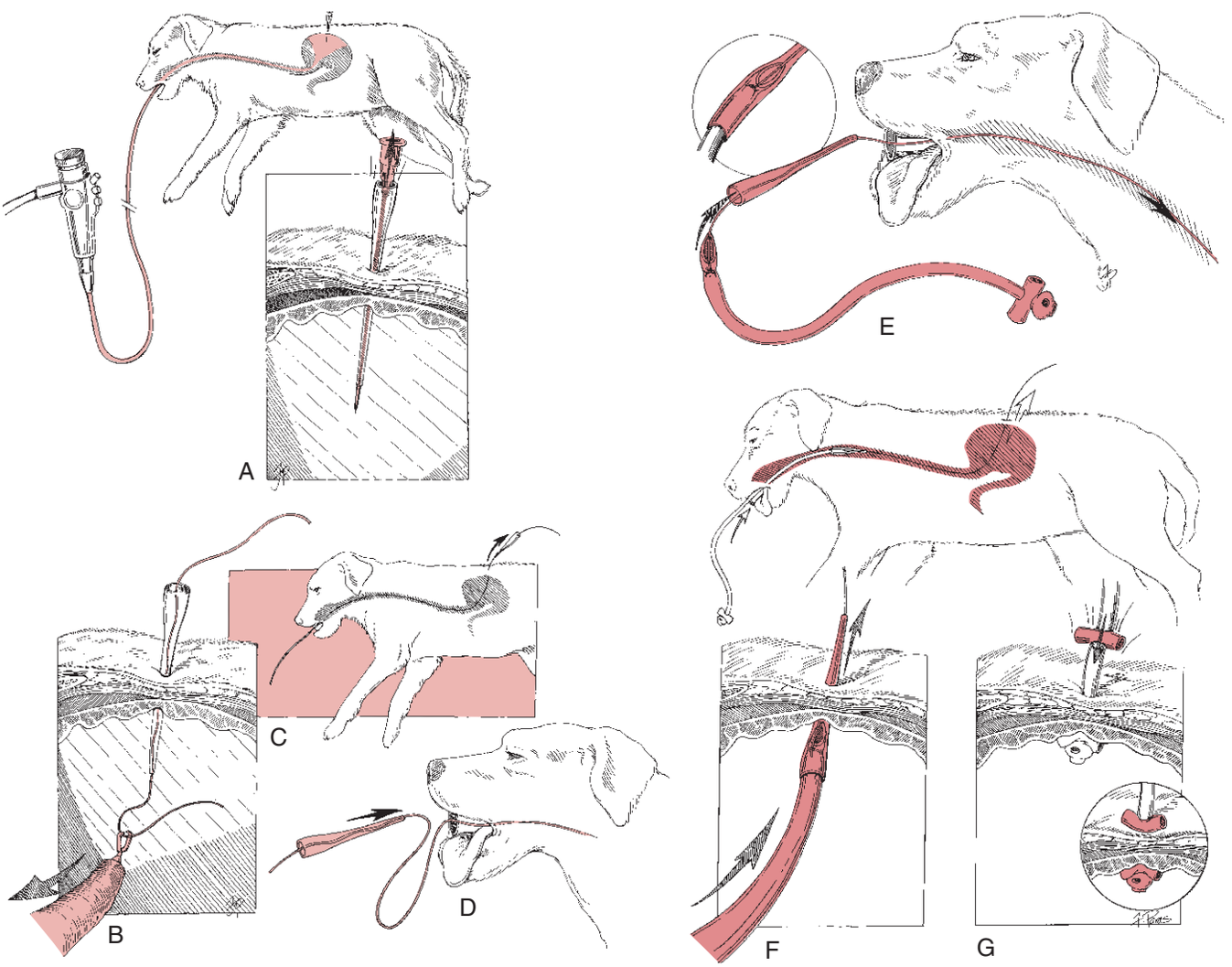

Figure 3-14. Placement of percutaneous endoscopic gastrostomy (PEG) tube. *A,* Over-the-needle catheter is placed through the skin and into the air-distended stomach; *B,* suture threaded through the catheter is grasped by endoscopic forceps and pulled out through the mouth *(C); D,* over-the-needle catheter is threaded onto the suture, which is tied to the gastrostomy tube. (*E*) and subsequently pulled into the stomach and out the gastric and body wall. The flange at the end of the gastrostomy tube should press snugly against the gastric mucosa. See text for *F* and *G.*

10. Slide the Sovereign IV catheter back down the suture toward the Pezzer catheter and firmly seat the pointed tip and suture knot (if possible) into the large flared end of the catheter (Fig. 3-14*E*).
11. Lubricate the IV catheter and the gastrostomy tube.
12. Pull the percutaneous end of the suture until the IV catheter tip is through the skin surface. Frequently, the skin will need to be incised a few millimeters (cautiously using a #11 blade). Place firm downward pressure around the exit site and pull the gastrostomy tube out through the body wall until the mushroom tip and inner flange are positioned against the gastric mucosa and the stomach is pulled up against the body wall. Pull the tube out gently and observe the position of the mushroom tip using the endoscope to ensure correct placement (Fig. 3-14*F*).
13. Slide the "outer flange" over the external end of the Pezzer catheter to ensure a snug fit to the patient's body wall. Secure the tube into place (Fig. 3-14*G*).
14. Wrap a small piece of tape circumferentially around the tube at the junction of the tube and the outer edge of the outer flange to identify ideal positioning and serve as a method for detecting inadvertent flange movement or slippage.
15. Remove the pointed tip of the catheter and the suture material with scissors and place the three-way stopcock into the tube tip. Alternatively, place a small, graduated Christmas tree adapter in the tube tip. Place a cap on all openings of the stopcock or Christmas tree adapter.
16. Cut a 4 × 4 gauze sponge on the folded edge and tuck around the feeding tube-skin interface.
17. Cut a sufficient length of stockinette and pull one end through so that both cut ends are together. Cut holes near the folded end of the stockinette for the patient's front legs and place the stockinette to protect the tube site. Tuck the free end of the tube under the stockinette to prevent inadvertent removal.
18. Small amounts of water can generally be administered through the tube immediately, but delay feeding 12 to 24 hours to allow an appropriate fibrin seal to form around the insertion site.

Postoperative Care and Tube Removal

- Cleanse the skin-tube interface using saline- or water-moistened gauzes once daily.
- Prevent damage to the tube by covering it with a light bandage or stockinette.
- When the tube is no longer required, it can be removed in one of two ways:
  - Cut the tube close to the patient's body wall and push the mushroom tip gently into the stomach using the wooden end of a cotton-tip applicator. Let the mushroom tip pass through the GI tract; if there is concern regarding obstruction because of the tip, retrieve it endoscopically.
  - Alternatively, remove the tube percutaneously by grasping and pulling the mushroom tip through the body wall while applying firm downward pressure to stabilize the body wall. A blunt stylet (e.g., cotton-tip applicator) can be placed inside the tube against the nipple tip to stretch the mushroom tip, making it easier to remove. The inner flange slides off the mushroom tip and passes out the GI tract.
  - Once a strong seal has developed between the stomach and the body wall (at least 2–3 weeks), the Pezzer mushroom catheter can be replaced by any of a variety of low-profile or "button" gastrostomy tubes. These are placed percutaneously into the stoma immediately following extraction of the original Pezzer tube.

Complications

- The opening in the inner or outer flange may be too small and may cause severe constriction of the tube and obstruction to feeding. Observe the tension on the catheter walls when the inner and outer flanges are placed to prevent this complication.
- Inadvertent tube removal from the stomach wall can result in leakage and peritonitis. Stomach wall integrity because of disease and excessive tension on the stomach wall in large-breed dogs because of deep-chested conformation may contribute to this complication. Use caution when placing a tube in a gastric site suspected to have infiltrative disease. Consider alternative tubes for large-breed deep-chested dogs. Inadvertent removal of the tube from the body wall by the patient or by snagging on another object is not a concern if the tube has been in place 10 to 14 days or more to allow fibrous seal or stoma formation. Tube replacement can occur through the same stoma if it is still patent, or a low profile tube (button tube) can be considered.
- Tube obstruction with food can also be a complication. In general, mechanical removal or an attempt to advance the obstruction forward with a narrow diameter stylet is preferable to the use of chemical dissolution methods.

NUTRITIONAL MANAGEMENT OF THE CRITICAL CARE PATIENT

The goal of nutritional support of critical care patients is to get them from the intensive care unit to the ward and then out of the ward to eating their own food at home as efficiently as possible. Until this goal can be achieved, the next best thing is for the patient to eat its own food in the hospital. Encourage feeding of usual and favorite foods whenever possible. Animals, particularly cats, offered novel foods may not eat them and may

develop learned aversions if the food is associated with illness-related nausea or other negative sensations. Encourage owners of hospitalized patients to provide whatever food is typically offered at home and to feed the pet during hospitalization (many pets eat more willingly for their owners than for strangers) when possible. In some cases, however, patients cannot eat by themselves and need more invasive approaches to nutrition support.

Nutritional Assessment

- If malnutrition is not present initially, reevaluate the patient periodically during hospitalization to ensure that malnutrition does not develop secondary to an ongoing disease process, administered drugs or treatments, persistent inability to eat, or inadvertent food deprivation.
- Nutritional support is part of the primary therapy for malnourished patients and when voluntary food intake is impossible for prolonged periods.

▼ ***Key Point*** Do not begin nutritional support until the initial goals of fluid therapy—rehydration, electrolyte replacement, and normalization of acid-base status—have been achieved.

- The steps of nutritional assessment include a history (including a complete diet history), a physical examination, and an evaluation of any supporting laboratory data. Increased risk for malnutrition is suggested by a recent history of one or more of the following clinical situations:
  - Greater than 10% weight loss
  - Decreased food intake
  - Increased nutrient needs because of trauma or surgery
  - Increased nutrient losses resulting from vomiting, diarrhea, or burns
  - Acute exacerbation of a chronic disease problem
- Obtain a diet history to determine the quality and appropriateness of the diet fed and the total daily intake of food. Ask if corticosteroids, cancer chemotherapeutic agents, antibiotics, diuretics, or other drugs that may adversely affect nutritional homeostasis have been administered recently.
- Perform a thorough physical examination, including assigning a body condition score (BCS) (Fig. 3-15).
- Underweight animals lose subcutaneous fat and experience muscle wasting. Patients in a moderate or overweight body condition also may be tissue depleted but may not appear so because of an "overcoat" of fat. This situation occurs when muscle tissue is broken down more quickly than is adipose tissue. Affected patients usually can be recognized by a poor haircoat; easily pluckable hair; thin, dry skin; and abnormal prominence of the bones of the head.
- Use a muscle condition score (MCS) (Fig. 3-16) to quantify the assessment. Structural impediments to eating also may be identified during the examination.
- Hypoalbuminemia, lymphopenia, and anemia are nonspecific laboratory findings that can be associated with severe malnutrition. Decreased resistance to the passage of a needle for blood collection because of loss of skin collagen also is a reasonably sensitive indicator of peripheral protein depletion.
- Assess a serum biochemical profile to provide important information regarding visceral organ function, which may influence the composition of the diet or the route of administration. For example, evidence of significant abnormalities of liver or kidney function could indicate the need for protein restriction, and severe pancreatitis could necessitate parenteral administration of nutrients.

Routes of Nutrient Delivery

Oral Feeding

- Oral feeding is the safest, least expensive, most beneficial physiologically, and most convenient method of feeding; thus, use oral feeding whenever possible.
- Try nursing techniques to improve food intake (often referred to as "coax-feeding") before proceeding to more invasive methods.
- Attempt hand-feeding, petting or stroking, vocally reassuring the animal, offering food when the animal is outside of the cage (during a walk outside or in a quiet area of the hospital), warming the food to body temperature to enhance aroma, or offering a favorite food.
- When new diets must be introduced to hospitalized patients, offer 15 to 30 g of the food initially. If resistance is observed, remove all food and attempt again in 1 to 2 hours. If no intake is observed within another 1 to 2 hours, or if the food hardens, remove it immediately and offer a different food.
- If the diet is intended for long-term patient management, offering it after the patient is home and feels better improves the probability of long-term acceptance and success.
- If attempts to restore food consumption fail, try force-feeding using a syringe for 1 to 2 days. Force-feeding provides some nutrition, but the inconvenience and the stress imposed on the patient during feeding limit its usefulness.
- A feeding tube also may be passed through the mouth into the stomach for each feeding. Passing an orogastric tube is relatively simple; limited restraint and the opening of the animal's mouth just enough to introduce the tube minimize the patient's opposition to this procedure.

Enteral Routes

- If the patient is too debilitated to tolerate repeated tube feedings, or if nutritional support is required for

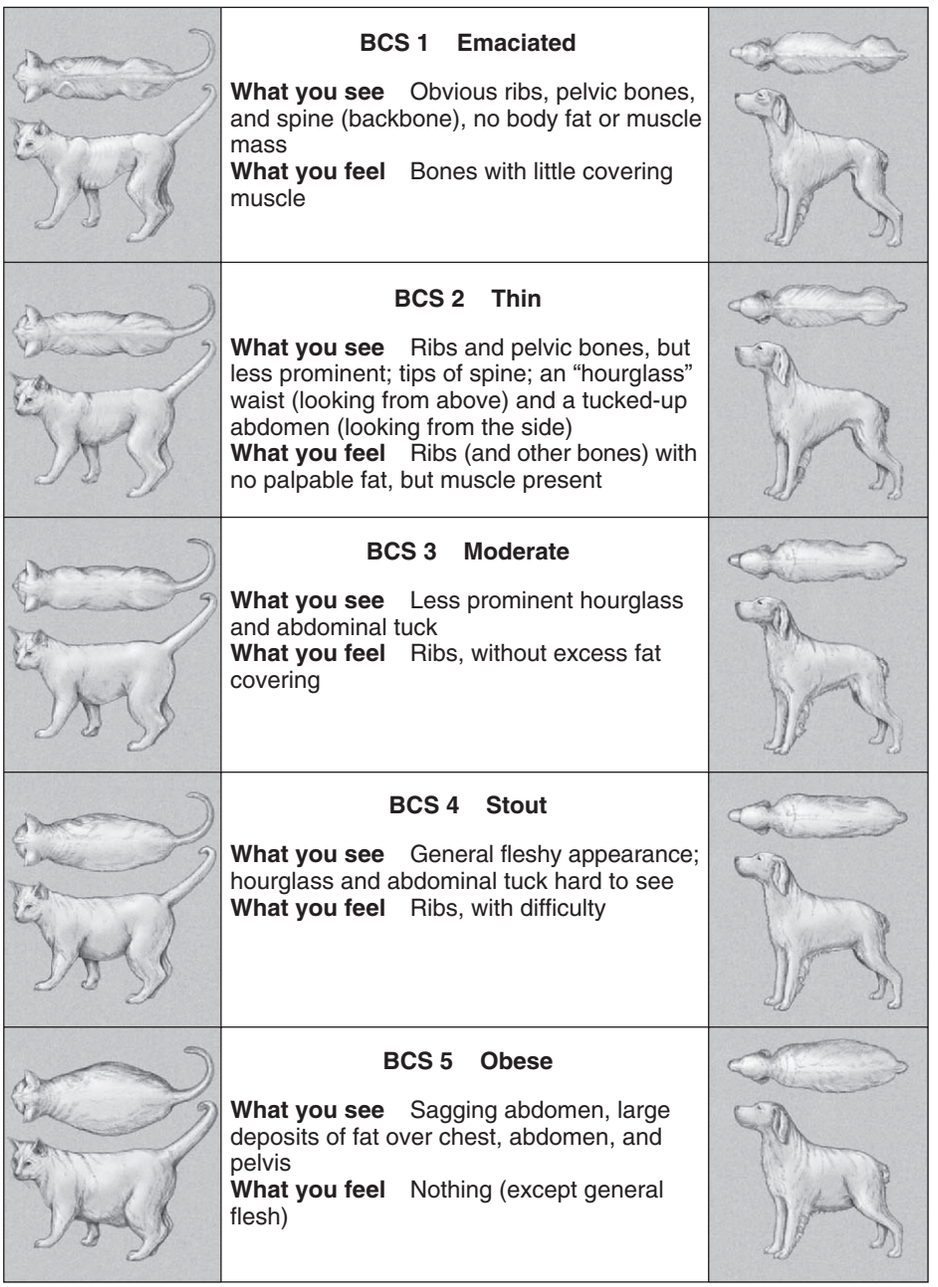

Figure 3-15. Body condition scoring. (Buffington CAT, et al: Manual of Veterinary Dietetics. St. Louis: WB Saunders, 2004.)

more than 2 days, place either a nasogastric or a nasoesophageal tube (see the technique described in "Nasal Catheter Placement"). Tube placement is simple, does not require anesthesia or sedation, and allows provision of fluid and nutrients for days to weeks.

- If a nasal tube cannot be placed, or if a prolonged course of feeding is anticipated, place an esophagostomy tube in patients that have a functional GI tract and no history of vomiting or regurgitation (see "Esophagostomy Tube Placement").
- When access proximal to the stomach is not available in patients with normal GI function, place a gastrostomy feeding tube. Surgical gastrostomies are the safest but the most expensive and difficult to place. Alternatively, a feeding tube can be placed using an endoscope or a blind placement device (see "Percutaneous Endoscopically Placed Gastrostomy Tube"). Gastrostomy tubes can be maintained in patients for months with good nursing care.
- Rarely, a needle catheter jejunostomy or gastrojejunostomy may be necessary when gastric atony, gas-

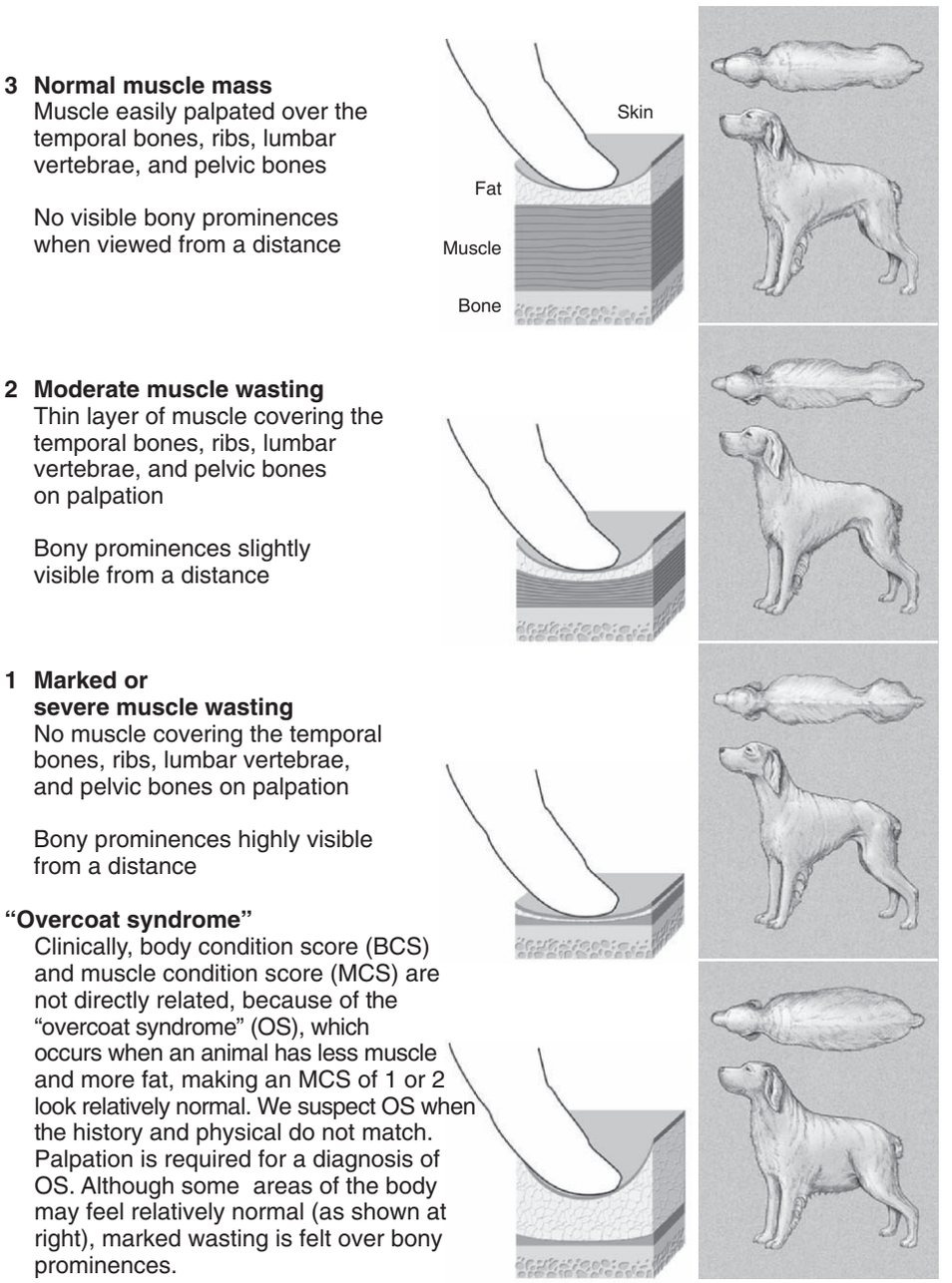

Figure 3-16. Muscle condition scoring. (Buffington CAT, et al: Manual of Veterinary Dietetics. St. Louis: WB Saunders, 2004.)

troduodenal obstruction, neoplasia, regurgitation, or vomiting prevent feeding using more proximal sites. Jejunostomy tubes are typically placed at surgery. Patients requiring extensive surgical procedures of the stomach, duodenum, pancreas, or hepatobiliary system also can be fed in the immediate postoperative period through these tubes.

- Small feeding tubes also can be threaded into the jejunum through a surgically placed gastrostomy tube at the time of surgery if the patient is not expected to eat orally for a prolonged period. Patients can be fed immediately postoperatively using the jejunal tube, which can be removed from the gastrostomy tube to permit gastrostomy feeding once motility returns to the stomach.

Nutrient Needs

Calories

Provide hospitalized patients with their basal energy needs. Graphs of the basal energy needs of dogs and cats over a range of body weights are presented in

Figure 3-17. These graphs were constructed using the following equation: *97 kcal × kg of body weight$^{0.655}$ per day.* Use the exponential equation for patients weighing less than 2 kg or more than 50 kg. For animals weighing between 2 and 50 kg, a linear equation such as *(30 × kg body weight) + 70 = kcal/day* can be used.

These estimates are conservative and may be lower than the energy needs of some patients during the course of their disease. They are only initial guidelines, also intended to avoid adverse consequences of overfeeding. Provide slightly less food than needed to avoid the potential for overfeeding. The estimated energy needs of a patient can be converted to food needs by assuming that many canned foods contain approximately 1 kcal/g and that many dry foods contain approximately 350 kcal/8 oz. If more accurate values are needed, consult the pet food's manufacturer.

Protein

- In patients with no disease-related limitations on protein intake, 7 to 10 g of protein per 100 kcal of energy is usually adequate.
- Patients with advanced liver and kidney disease require careful use of limited amounts of high-quality protein, probably in the range of 2 g (in dogs) to 3 g (in cats) of a high-quality protein per kilogram of body weight per day.
- Monitor animals consuming these amounts or less for signs of protein depletion.

Minerals and Vitamins

In addition to energy and protein, provide vitamin and mineral intake near the National Research Council requirements for growth in the absence of a specific contraindication.

Diet Selection

- Choose an appropriate diet for the disease-related nutrient modifications required.
- Secondary factors include both size and location of the feeding tube.
- Liquid diets specifically formulated for veterinary use (e.g., CliniCare; Abbott Laboratories) are available and may be fed through a tube of any size. To maximize success and minimize the risk of clogged tubes, feed only liquid diets through tubes smaller than 12 Fr. Feed veterinary or commercial canned pet foods that have been processed in a blender (with water added as needed) through tubes larger than 12 Fr. Tables of veterinary foods are available in the *Manual of Veterinary Dietetics* (see "Supplemental Reading") and at www.nssvet.org.

Feeding

- Provide food or water soon after the patient recovers from anesthesia.
- Estimate and deliver fluids and nutrients in four to six feedings over a 24-hour period.
- Give small volumes distributed over several meals during the first 24 to 48 hours of feeding to avoid overdistention of the stomach, vomiting, or regurgitation.
- In severely ill patients, use slow, constant administration rates to help minimize incidents of diarrhea and cramping and to maximize absorption of the nutrients. Hang small volumes of liquid diet (approximately a 12-hour supply) in fluid therapy bags or burettes for gravity-assisted constant-rate infusion to minimize the possibility of "overdosing" patients with the feeding solution during continuous feeding.

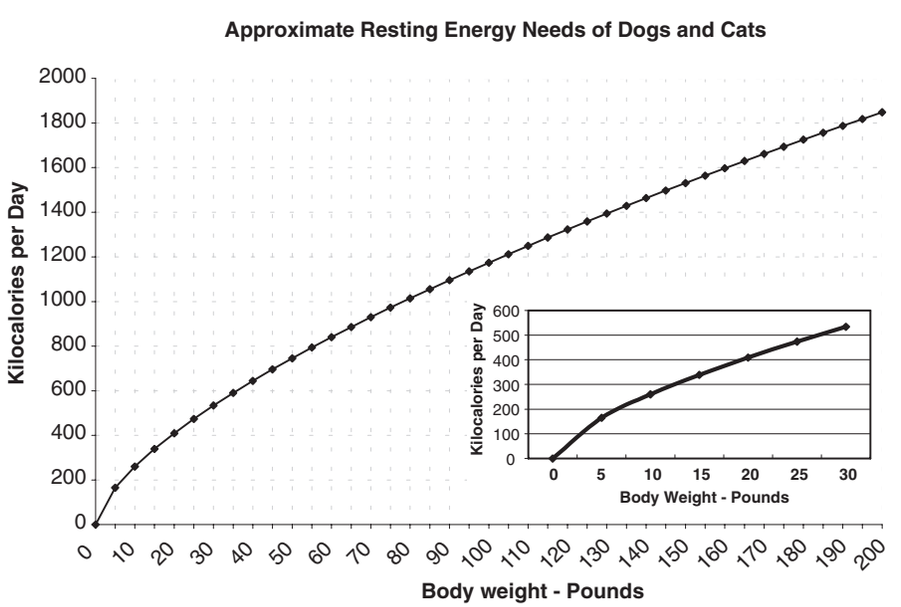

Figure 3-17. Basal energy requirements of dogs and cats.

- Flush tubes with water before and after each feeding to avoid occlusion with food or mucus.
- Diarrhea (usually small amounts of soft, pasty feces) can occur in enterally fed patients. It is generally more of a nuisance than a threat to the patient and usually results from rapid gastric emptying caused by overly rapid administration of a bolus meal. Reduce the feeding rate and feed diets that contain fiber or higher concentrations of fat (>50% of total kcal) to delay gastric emptying.

Parenteral Nutrition

- Parenteral nutrition (PN), or intravenous feeding, allows the provision of short-term metabolic and immune system support to animals with severe GI disease or pancreatitis. Because PN therapy is relatively expensive and is associated with more complications than feeding through the GI tract, use enteral feeding whenever the GI tract can tolerate it. PN is also not indicated when the patient's prognosis is hopeless.
- The high osmolality of PN solutions requires the use of a central venous catheter inserted in the external jugular vein or placed in a peripheral catheter and advanced into a central vein. Proper insertion and maintenance of the PN catheter is one of the keys to successful PN therapy. Use aseptic technique when placing the intravenous catheter. If well cared for, central vein catheters may be used for prolonged periods. Do not remove the catheter unless a specific indication for removal exists.

▼ ***Key Point*** Once a catheter is placed and designated for PN therapy, do not use it for other purposes, such as drawing blood samples, administering medications, or measuring central venous pressure.

Adverse drug-nutrient reactions and clogged catheters are serious potential complications of these practices.

Glucose Content

- Formulate glucose-based PN solutions based on the patient's estimated nutrient needs. The most commonly used PN solution for patients at Ohio State University contains 17.5% glucose. Glucose-based PN solutions are filterable, bacteriostatic because of the high osmolality, relatively easy to prepare, and relatively inexpensive. On the other hand, their hyperosmolality necessitates central venous access, and thrombophlebitis may result if solutions are infused at high rates into small veins.
- Hyperglycemia, usually less than 600 mg/dl, is also more common with glucose-based solutions than with lipid-based solutions. This has minimal pathophysiologic significance but needs to be monitored and controlled with insulin therapy as needed (see "Glucose Monitoring").

Calorie and Protein Content

Estimate energy needs of PN patients as previously described. Attempt administration of nutrients at rates exceeding resting energy needs only after the initial goal has proved tolerable for the animal. Provide 2.5 g of protein per kilogram of body weight. Restrict protein intake to approximately 2 g/kg/day in animals with severely compromised liver or kidney function.

Minerals and Vitamin Content

The macromineral portion of the solution is provided by an amino acid-electrolyte solution. Zinc, copper, manganese, and chromium, as well as water-soluble vitamins, are routinely added to PN solutions. The essential fatty acids, fat-soluble vitamins, and minerals necessary for prolonged PN therapy do not appear to be necessary for the short-term PN more typically provided to veterinary patients.

Apparatus and Delivery

- The apparatus required for PN administration includes the solution, the solution container, an administration set, a 0.22-µm filter, a dedicated central venous catheter, and, preferably, an infusion pump.
- Provide PN at a rate intended to meet resting energy needs by the end of the first 24 hours, then advance to slightly higher rates of intake, if necessary, over the next 24 to 48 hours as patient tolerance allows.

Glucose Monitoring

- During the initiation phase, measure blood glucose every 4 to 6 hours until stable. Once goals are reached, monitor the patient as described subsequently. At the end of therapy, wean the patient from the solution over 4 to 24 hours as tolerance permits by progressively halving of the infusion rate to avoid hypoglycemia, particularly if insulin has been infused. If the patient is able to eat, offer food and record the food intake. As soon as signs of appetite are observed, decrease the PN administration rate to approximately half the previous rate to encourage the animal to begin eating on its own.

▼ ***Key Point*** The most important monitoring parameter for patients receiving glucose-based PN is blood glucose, which is monitored closely during initiation of therapy.

- Treat patients when blood glucose concentrations exceed 250 mg/dl with intramuscular administration of 0.25 U of regular insulin per kilogram of body weight every 4 to 6 hours as necessary. Insulin therapy

is not commonly required for dogs, although consider it for cats during the first 36 hours to control hyperglycemia. Diabetic animals placed on PN often require continuous infusions of higher-than-expected quantities of insulin to control their blood glucose concentration effectively. When insulin is used, caution must be exercised with regard to the central venous catheter, which is presumed to be in place continually. If insulin is given and then vascular access is lost, give a 5% glucose infusion through a peripheral vein immediately to prevent severe rebound hypoglycemia.

Complications of PN

The most common PN-related complications are mechanical, technical, and related to glucose abnormalities. Use a strict protocol for prevention, diagnosis, and treatment of sepsis. PN-related infections occur only rarely.

Returning to Normal Food Intake

- In general, discontinue assisted feeding when patients begin eating a quantity of food that contains at least half of their calculated daily energy needs. Ideally, the weaning process should take place gradually over at least a day or two before the feeding tube is removed or PN administration stopped.

SUPPLEMENTAL READING

Buffington CAT, Holloway C, Abood SK: Manual of Veterinary Dietetics. St. Louis: WB Saunders, 2004.

Chapter 4

Radiographic and Ultrasonographic Techniques

David S. Biller / Laura J. Armbrust

The purpose of the radiograph is to provide a lasting record of maximum information. The sequence of the major operations involved in transforming the altered morphology and tissue density within a diseased animal into a two-dimensional, black-and-white radiograph and then reaching a diagnosis is complex and includes the following steps: (1) making a properly exposed and positioned radiograph; (2) recording the x-ray picture with the assistance of accessory equipment; (3) reviewing radiographs in proper conditions and in a systematic and detailed manner; (4) recognizing lesions—therefore [requiring] a knowledge of normal radiographic anatomy and its variation by age, species, and breed and the ability to recognize and understand artifacts; and (5) evaluating radiographic abnormalities with respect to clinical and laboratory findings.

Dr. Peter Suter

X-RAY MACHINE

Milliampere-Second and Kilovolt Peak

- *mA (milliampere) × seconds (time) = mAs (milliampere-second),* which affects the degree of blackness (density) of the radiograph with no effect on contrast. A direct relationship exists between mA and radiographic density. Time and mA both influence the number of x-rays produced but have no effect on the penetrating ability of the beam. To quickly check the adequacy of the mAs on a film, hold the film up to room light and place a white sheet of paper about 1 inch behind the film. Place a finger between the film and the paper. If the finger can be readily seen through the film in the black area (the most exposed), increase the mAs.
- *kVp (kilovolt peak)* is the only machine factor that influences radiographic contrast and has some control over the amount of radiographic density (blackness). The contrast can be expressed as being low, which means that there are many shades of gray (long scale) between the extremes of black and white. The term *high contrast* means that there are few shades of gray (short scale). Lowering the kVp increases the contrast, and raising the kVp reduces the contrast.
- To adjust the technique to alter film contrast while maintaining the same radiographic density, consider the following:
  - The mAs and the kVp have to be in balance.
  - As the mAs increases, the kVp must decrease.
  - As the kVp increases, the mAs must decrease.
  - Doubling radiographic density requires doubling the mAs or increasing the kVp by 10% in the 40- to 100-kVp range or 15% in the 100-kVp or greater range.

Recommendations

- The *300-mA machine* may have adjustable mA stations of 25, 50, 100, 200, and 300 and two (1 and 2 mm or smaller) focal spots.
- An ideal kVp range is 40 to 120 and is adjustable in 1 or 2 kVp per step.
- A *timing device* is necessary to control the duration of an x-ray exposure. Modern x-ray machines have electronic timers with ranges that can control motion in the patient and prevent blurring. With a timed exposure of $^{1}/_{120}$ second, all significant motion is stopped.
- The *line voltage compensator* is automatic or manual.
- The *tube stand* moves along the full length of the table and has an adjustable height from 0 to 60 inches (152 cm). The tube is able to rotate 90 degrees around the vertical axis and 180 degrees around the horizontal axis.
- The *table* is 5 to 6 feet in length with a top that has floating motion in four directions.
- The *collimator* decreases scatter radiation and human and patient exposure as it increases film quality. Always leave a clear margin of collimation on every film. The collimator is lighted and has a centering mark. A high-quality, dial-adjustable, multileaf lead shutter collimator is highly recommended.
- *Filters* have the primary function of reducing patient radiation dose by removing scatter radiation and increasing (mean beam energy) quality. Most x-ray equipment has inherent filtration equal to 1.5- to

2.0-mm aluminum. Increased film quality can be obtained by adding an additional 2.0-mm aluminum filtration. Total filtration must be at least 2.5-mm aluminum.

- *Grids* consist of a flat plate with a series of lead foil strips separated by transparent spacers. They are made in various sizes and improve the diagnostic quality of radiographs by absorbing the greater part of the scatter radiation. Position grids between the patient and the cassette, usually under the table. Use only for body parts thicker than 10 cm. The reciprocating grid (Potter-Bucky diaphragm) includes a mechanism that moves the grid during exposure to eliminate grid lines from the radiograph. This grid is optional equipment but recommended for the best-quality radiographs.
  - Grids can be classified in three ways: the lead content (g/cm^2), the number of lines per inch, and the ratio of lead strip height to the space between the lead strips. In general, high-ratio grids absorb scatter better but are more expensive. More lines per inch give better quality, because the lead strips are narrower and therefore lines become less prominent; however, they cost more. The most common grid is an 8:1 with 103 lines per inch.
  - The higher the grid ratio, the more critical the x-ray tube alignment. Always stay within the focal zone of the grid. This is usually written on the grid and is 36 to 42 inches (90–105 cm) in most instances.
- *Exposure switches* include the two-position exposure switch on the console and the two-position exposure foot switch, with a cord of sufficient length.
- *High-frequency x-ray machines* have a few advantages over single-phase x-ray machines. A 150-mA high-frequency generator can produce a quantity of x-rays equal to that of a 300-mA, single-phase x-ray machine. Many of the units use 110 volts. They are reliable, with less downtime than single-phase machines. Their cost, at present, is greater than that of single-phase machines but most likely will decrease in the future.
- For a list of x-ray machine manufacturers, see Table 4-1.

ACCESSORY RADIOGRAPHIC EQUIPMENT

Intensifying Screens

The screen is a suspension of phosphor crystals in a binder. The phosphor in the screen converts x-ray photons into visible light, to which the film is more sensitive. A latent image is created by exposure of the film to this light. This technique reduces x-ray exposure to the patient by at least 10 times and the time of x-ray exposure, thus decreasing the chance of blurring.

- Screen speed depends on the thickness of the phosphor layer, the size of phosphor crystals, and the efficiency of phosphor crystals at absorbing x-rays and converting them to light.
- Screen classification varies because each company has a slightly different system for labeling screen speed. Resolution ability of the screen is inversely related to speed. Increased speed gives decreased resolution. Have a technique chart available for each screen speed. Par speed is the starting point for comparison of screens. High speed has a speed 2 times that of par speed. Ultraspeed is 4 times par speed. High detail speed is half that of par speed.
- Types of Screens
  - Calcium tungstate screens reduce the amount of radiation necessary to expose film by 10 times com-

Table 4-1. X-RAY MACHINE MANUFACTURERS

Company	Address	Phone Number	Website
Bennett X-Ray Technologies	445 Oak St. Copiague, NY 11726-2719	800-922-9399	
Continental X-ray	2000 S. 25th Ave. Broadview, IL 60153	708-345-3050	
Control-X Medical	West Pointe Business Park 2289 W. Brooke Dr. Columbus, OH 43228	800-777-9729	www.cxmed.com
Fischer Imaging Corp.	12300 North Grant St. Denver, CO 80241-3120	800-825-8257	www.fischerimaging.com
MinXray	3611 Commercial Ave. Northbrook, IL 60062-1822	847-564-0323	www.minxray.com
Summit Industries	2901 W. Lawrence Ave. Chicago, IL 60625	800-729-9729	www.summitindustries.net
Universal (Del Medical Systems)	11550 W. King St. Franklin Park, IL 60131	800-800-6006	www.delmedical.com

pared with film exposed without a screen. They are also less expensive than rare-earth screens. Calcium tungstate emits a broad spectrum of light in the ultraviolet and blue range.
  - Rare-earth screens are more expensive than calcium tungstate screens. The light emitted is in the ultraviolet, green, or blue range. The major advantage of rare-earth over calcium tungstate screens is that rare-earth screens are fast, because of a more efficient production of light. Therefore, they decrease the production of scatter, the exposure time, the radiation dose, the chance of motion and subsequent blurring, and the wear and tear on the x-ray tube.
- System speed is the speed of film and screen in combination. It is not an additive system. A very low system speed results when screens and films with different color spectrum sensitivities are put together. Ask the film dealer what system speed you have with your particular screens and film. The higher the system speed number, the more sensitive the system and the less radiation necessary to make an exposure. System speeds can vary from 50 to 3200 and higher. The higher the system speed number, the less radiation to the patient and to personnel within the room; however, the lower the system speed number, the better the resolution qualities. When you know the system speed, changing the technique chart is simpler. If the system speed doubles, change the mAs on the technique chart by half. If the system speed decreases by 50%, double the mAs on the technique chart.
- Exposure time

▼ ***Key Point*** Always use the shortest exposure times possible to eliminate blurring.

  - For thoracic radiographs, exposure times of $\frac{1}{60}$ second or shorter stop the effects of respiratory and heart motion.
  - For abdominal radiographs, employ exposure times of $\frac{1}{40}$ second or shorter to eliminate gastrointestinal motion.
  - For extremity radiographs, exposure times of $\frac{1}{20}$ second or shorter eliminate the effects of patient motion.
- Rare-earth screens have a system speed that allows the shortest exposure times possible to eliminate motion problems and to lower radiation exposure to patient and personnel. In general, when using a 300-mA machine and a 400 to 800 speed system, with an 8:1 grid, good-quality radiographs are attainable even for large-breed dogs. In a feline practice, a slower system, such as a 100 to 250 speed system, provides excellent quality. As the crystal size gets larger, the system gets faster but resolution is reduced.
- Clean screens with the product recommended by the manufacturer on a regular schedule (monthly) and whenever debris is noted on the radiographs.

Film

Radiographic film provides a permanent record containing the maximum amount of diagnostic information.

- Film is made of a light-sensitive emulsion, composed of gelatin and silver halide with other ingredients attached to a plastic (polyester) base. The silver halides are sensitive to light and change when exposed to light to produce a latent image. The process of developing changes silver ions into black silver, thus producing the radiographic image. Fixer removes all unexposed silver from the film. The emulsion may be attached to one or both sides of the base. X-ray film may be most sensitive to direct x-ray exposure (nonscreen film) or to blue, green, or ultraviolet light.
- Films vary in their contrast. Some films appear more black and white after exposure and development. Use the film that is recommended by your screen manufacturer to match the spectrum of light produced by your screens. Choose a film that results in the contrast range most pleasing to you. Use a film that gives you a system speed that results in quality radiographs. Make sure to match film, screens, and processing chemicals.
- Film must be sensitive to the type of light emitted by the screens in use. Film speed determines the amount of light required to produce an image on the radiograph. Fast film has large crystals (silver halide), requires less exposure, and produces a grainy image. Slow film has small crystals, requires greater exposure, and produces a sharper image.
- Screen film is manufactured with crystals that are sensitive to fluorescent light. Nonscreen film is a direct exposure–type film and is manufactured to be sensitive to x-rays. Nonscreen film requires 10 to 25 times more radiation than screen film.
- Film is available in both metric and nonmetric measurements. The most common sizes used in small animal practice are 8×10 inches, 10×12 inches, and 14×17 inches.
- X-ray film is sensitive not only to light and x-ray photons but also to humidity, chemicals, and physical stress. Film is stored on end to reduce pressure on the face of the film. High humidity causes film fogging, and low humidity causes film static; therefore, between 30% and 40% humidity is appropriate for film storage. Storage temperature should not exceed 50°F to 70°F (10°C to 21.1°C). Store the film away from developing chemicals and ionizing radiation. Do not put pressure on the film when loading or unloading film.
- Film and screen companies are provided in Table 4-2.

Table 4-2. FILM AND SCREEN COMPANIES

Company	Address	Phone Number	Website
AGFA	100 Challenger Rd. Ridgefield Park, NJ 07660	877-777-2432	www.agfa.com
Eastman Kodak Co.	Health Sciences Division Rochester, NY 14650	800-926-1519	www.kodak.com
Fuji Medical Systems	90 Viaduct Rd. Stamford, CT 06907	800-431-1850	www.fujimed.com
Konica Minolta Medical Imaging	411 Newark Pompton Turnpike Wayne, NJ 07470	800-934-1034	www.medical.konicaminolta.us
Picker International	595 Miner Rd. Highland Heights, OH 44143	800-635-972	
3M Medical Imaging System	3M Center St. Paul, MN 55144-1000	888-364-3577	www.3m.com

Cassettes

Cassettes are used primarily to contain and protect film. Two basic types are available: rigid cassettes that contain both the film and the screen and cardboard cassettes that hold nonscreen film.

- Rigid cassettes protect both screens and film from physical damage and film from exposure to light. The cassette provides snug contact between the film and the screens. The front of the cassette is usually a rigid plastic, aluminum, or other substance that absorbs relatively few x-ray photons. Usually, a small rectangle in the corner of the cassette shields the film from x-rays to allow an unexposed area for film identification. The back of the cassette is lined with lead to absorb backscatter radiation. The back of the cassette is also equipped with latches to provide a lightproof seal.
- Cassettes for a nonscreen film only protect the film from light exposure. They are usually made from cardboard.
- Cassettes are numbered. When defects are noted on a radiograph, they can be traced to the correct cassette. Dropping a cassette causes warping and results in poor film-screen contact and a distorted radiographic image.

Miscellaneous Accessories

- Use the screen cleaner that is recommended by your screen manufacturer.
- Use safety devices (lead aprons, lead gloves, glasses, and lead thyroid shield) when personnel are required in the x-ray room for patient positioning.
- Film markers consist of right and left lead film markers, Mitchell markers (for horizontal radiographs), and time markers (for upper gastrointestinal and intravenous urography radiographs).
- A device capable of measuring body-part thickness and determining the kVp for exposure is needed.
- Positioning devices include sponge wedges, sandbags, Plexiglas or foam trough, rope, tape, and agents for chemical restraint to avoid human exposure associated with hand-holding whenever possible.
- Film filing envelopes are needed.
- Contrast media are required (see "Contrast Studies" and Table 4-6).
- Monitoring devices (film badges) for employees and room monitoring, a film viewer (at least one double bank), and a hot light (high-intensity light) are needed.
- Radiographic accessory companies are listed in Table 4-3.

CHECKING X-RAY MACHINE ACCURACY

Milliampere Station Check

- Use an aluminum step wedge to check mA station (setting) accuracy. Use the step wedge to determine if your mA stations are linear. It cannot determine if all your mA stations are off by the same amount. A step wedge (see Table 4-3 for sources) gives a general idea about the mA stations. A step wedge is inexpensive ($100) and easy to use. Place the step wedge on a loaded cassette; make many separate exposures of the step wedge, changing the mA but always having the same mAs and kVp. If you cannot keep the same mAs throughout all mA stations, do as many as possible at one mAs setting then go back and check the rest at another mAs.

Example

25 mA	$^1/_{10}$ second	2.5 mAs	70 kVp
50 mA	$^1/_{20}$ second	2.5 mAs	70 kVp
100 mA	$^1/_{40}$ second	2.5 mAs	70 kVp
300 mA	$^1/_{120}$ second	2.5 mAs	70 kVp
100 mA	$^1/_{60}$ second	1.7 mAs	70 kVp
200 mA	$^1/_{120}$ second	1.7 mAs	70 kVp

Compare the densities of all exposures. They should be the same for all mA stations taken at the same mAs. An exposure that varies from the average shows that there is a problem with that mA station. This test

Table 4-3. RADIOGRAPHIC ACCESSORY COMPANIES

Company	Address	Phone Number	Website
Bar-ray Products	P.O. Box 36 Monarch St. Littlestown, PA 17340	888-422-7729	www.bar-ray.com
Burkhart	5201 8th Ave. South St. Petersburg, FL 33707	800-872-9729	www.usaxray.com
Cone Instruments	5201 Naimen Parkway Solon, OH 44139	800-321-6964	www.coneinstruments.com
Fischer Industries	P.O. Box 570 2630 Kaneville Ct. Geneva, IL 60134	800-356-5911	www.fischerind.com
Medical I.D. Systems	3954 SE 44th St. Grand Rapids, MI 49512	800-262-2399	www.medid.com
Picker International	595 Miner Rd. Highland Heights, OH 44143	800-635-9729	
Pulse Medical (Radiation Concepts)	4131 S.W. 47th Ave., Ste. 1404 Davie, FL 33314	800-342-5973	www.rci-pulsemed.com
S&S Technology	10625 Telge Rd. Houston, TX 77095	800-231-1747	www.ssxray.com
Shielding International	182 NW Earl St. Madras, OR 97741-0069	800-292-2247	www.shieldingintl.com
3M Animal Care Products	3M Center St. Paul, MN 55144-1000	888-364-3577	www.3m.com
Wolf X-ray Corp.	420 Hempstead Turnpike West Hempstead, NY 11552	800-356-9729	www.wolfxray.com

does not tell you if all mA stations are accurate, but it does tell you if a particular station has a problem.

- A digital, electronic mA-checking device is the most accurate way to compare your mA stations.

Kilovolt Peak Check

▼ ***Key Point*** The only accurate way to check the kVp is the Wisconsin test cassette ($1300; see Table 4-3 for sources).

- The Wisconsin test cassette has many kVp settings listed on the front of the cassette. Under each of these settings is a certain amount of material to attenuate the beam. After exposure and processing, this film provides information to determine if the kVp settings are accurate.
- Another less accurate way to obtain a general check of kVp accuracy is to vary mAs and kVp. Go through all kVp settings, employing density-changing factors to keep the densities the same throughout all these exposures.

Example

100 mAs at 50 kVp	3.1 mAs at 81 kVp
50 mAs at 55 kVp	1.5 mAs at 90 kVp
25 mAs at 61 kVp	0.8 mAs at 99 kVp
12.5 mAs at 67 kVp	0.4 mAs at 108 kVp
6.2 mAs at 74 kVp	0.2 mAs at 124 kVp

If your mA stations and kVp settings are working correctly, each exposure has the same density but a different contrast range. Remember to employ density-changing factors when necessary.

Exposure Timer Check (Single-Phase Machine)

Use a spinning-top test tool. It can be purchased from the same company as the machine (see Table 4-1) or from an accessory company (see Table 4-3). This tool is inexpensive ($50) and easy to use. It is a flat metal spinning top with a hole in one side. The top is set on a loaded cassette and spun. Take an exposure at $^1/_{120}$ second. Move the top to another corner of the film, spin again, and expose at $^1/_{60}$ second. This maneuver is repeated at $^1/_{40}$ and $^1/_{30}$ second. At $^1/_{120}$ second, only one dot should be seen; at $^1/_{60}$, two dots; at $^1/_{40}$, three dots; and at $^1/_{30}$, four dots. If more or less dots are on the film than expected, the timer is not accurate.

Line Voltage

Line voltage is the amount of current coming into the machine. The amount of current may vary, depending on electrical wiring, consistency of voltage in the area, and usage of current on the same circuit in the particular practice. Almost all machines used for small animals have a line voltage-check device. Some have a meter and a dial to adjust line voltage and do not permit exposure until the voltage is manually adjusted. Other machines have an automatic line voltage adjustment.

Almost all equipment in small animal practice uses 120 volts (i.e., right out of the socket).

FILM PROCESSING

Manual Processing

Film developing is a chemical process and therefore depends on both time and temperature.

Advantages and Disadvantages

- Advantages
  - Less expensive setup costs than those of an automatic processor.
  - No special electrical or structural changes are necessary for the darkroom.
- Disadvantages
  - Valuable technician time to develop films and maintain chemical baths (i.e., increased labor costs).
  - Quality is not consistent, due to human error, compared with automatic processors.
  - Longer time to prepare diagnostic films compared with automatic processors.

Accessories

- Developing tanks
- Two stirring paddles
- Two thermometers
- Film developing hangers of different sizes
- Chemicals
- Adjustable mixing valve for measuring water temperature
- Timer
- Dust-free drying cabinet or area

Darkroom Safelight

Darkroom safelights must produce enough illumination in the darkroom so that a person can see to process radiographic film (load and unload cassettes) without unwanted density (fog) to the film. Safelights utilize a wavelength of light different from that to which the film is sensitive. A Wratten 6B filter is adequate for blue-sensitive film. A GBX-2 filter is employed with green-sensitive or both green- and blue-sensitive films. Usually, 15-watt bulbs are used with safelights. The safelight is about 4 feet from the film-handling area. No system is 100% safe; therefore, expose the film no longer than necessary.

Radiograph Labeling

- A radiograph is a legal document and must therefore have permanent labeling. On the label, include the hospital or veterinarian's name, the date the radiograph was taken, and the owner's name or the animal's file number. Label the radiograph with right or left, dorsoventral or ventrodorsal (DV/VD), a time marker on contrast studies, and a Mitchell marker when a horizontal beam is used. Basic types of permanent marking systems are available:
  - Lead letters and numbers in a holder with the hospital or veterinarian's name, placed on the cassette during exposure.
  - Radiopaque marking tape (lead-impregnated tape). Information may be written on the tape, and the tape is placed on the cassette before exposure.
  - A darkroom printer transfers data from a card to the corner of the x-ray film that was shielded from radiation during exposure. This system requires cassettes with special windows. The film is removed from the cassette, and the corner of the film where it was blocked from light exposure is imprinted by exposing the patient information on a 5 × 7-inch card onto the film.

Silver Recovery

Recover silver from fixer solutions by either manual or automatic systems. Fixer solutions may be sold to companies for silver recovery. Alternatively, you may purchase a system (metallic replacement process, electrolytic recovery, or chemical precipitation) for silver recovery in your practice. Exposed developed and undeveloped film may also be sold for silver recovery. Usually, the supplier of the x-ray films or processing solutions can be consulted to determine if silver recovery is feasible and who to contact.

Procedure for Manual Film Processing

- Check temperatures, turn off room lights, use safelights, and agitate (mix) solutions well.
- Place the film on development hangers, making sure all four corners are attached.
- Set and start time depending on the temperature in the developing tank.
- Place the hanger with the film into the developing tank. Rap hard against the tank wall to dislodge air bubbles. Agitate by pulling film out of the developer, and let the developer drain to one lower corner. Return film to the developer. Repeat agitation every minute. Manufacturers recommend a specific temperature for the developed solution that they produce, usually 68°F (20°C). Adjust for change in temperature (increased temperature, decreased time, and vice versa). The chemical manufacturer can provide a time-temperature development chart.

Example

60°F (15.5°C) 8.5 minutes
65°F (18.3°C) 6.0 minutes
68°F (20.0°C) 5.0 minutes
70°F (21.1°C) 4.5 minutes
75°F (23.8°C) 3.5 minutes

- At the end of the developing time, remove the hanger from the developer and drain over the rinse tank. Agitate film in rinse water for 30 seconds.
- Place the hanger with film in fixer at the end of the developing time.
- Set the timer. Fixer time equals twice the development time.
- Agitate film every 2 to 3 minutes while in the fixer.
- At the end of fixation time, remove film from fixer and drain.
- Place the hanger in wash water at the end of fixer time.
- Agitate after 2 to 3 minutes.
- Wash for 15 to 30 minutes, depending on water flow and temperature in wash tank.
- Provide no less than four water changes per hour in the wash tank.
- At the end of the wash, remove from water and drain.
- Place film in a drier cabinet or hang up to dry.

Automatic Processing

- Processors are a good investment for most veterinary practices. New, small, tabletop models are priced from $3500. Most of these processors develop an excellent quality film in 90 to 210 seconds. They can use cold water for processing; therefore, no special needs exist for plumbing. They are also easy to maintain.

▼ ***Key Point*** If your small animal practice is processing 7 to 10 films a day, consider an automatic processor.

- Advantages
  - Highly repeatable results
  - Short waiting time for diagnostic films
  - Ability to process large quantity of films quickly and accurately
  - Good quality control
  - Smaller darkroom necessary
- Disadvantages
  - Machine is expensive.
  - Darkroom structural changes are expensive.
  - Needs daily and weekly maintenance.
  - Repairs can be expensive.
- Equipment includes processor, safelight, water for processing, chemicals, sponges to clean rollers of processor, and processor cleaning solution.
- Tabletop film processors are easy to install (no special plumbing or wiring). Different models process films as fast as 90 seconds or as long as $3\frac{1}{2}$ minutes. Most are made for easy care and cleaning. They are relatively inexpensive (from $3000 to $7000).
- Large, hard-wired, 90-second film processors need special plumbing and electrical wiring, but they are able to process many films. They need special cleaning and repairs and are expensive ($15,000–$25,000).
- The more a processor is used, the fewer problems it will have. It is made to be used on a 24-hour basis. Chemical buildup on rollers can cause film artifacts. Rollers age and crack if oxidized chemicals are left on them.
- Clean processors often.
  - All processors need cleaning daily when not in use. Take out the rollers and wash them down with a sponge and water. Dry and replace the rollers. Clean the chemical tanks. Once a month, clean with processor cleaning solution. Cleaning a processor takes about 15 minutes a day but saves in wasted film and time.
- Consider purchasing a processor with a standby mechanism. This function helps conserve water, energy, and chemicals.
- Automatic processor companies are listed in Table 4-4.

Table 4-4. AUTOMATIC PROCESSOR COMPANIES

Company	Address	Phone Number	Website
AFP Imaging Corp.	250 Clearbrook Rd. Elmsford, NY 10523	914-592-6100	www.afpimaging.com
AGFA	100 Challenger Rd. Ridgefield Park, NJ 07660	877-777-2432	www.agfa.com
All Pro Imaging Corp.	70 Cantiague Rock Rd. P.O. Box 870 Hicksville, NY 11801-1127	800-247-8324	www.allproimaging.com
Eastman Kodak Co.	Health Sciences Division Rochester, NY 14650	800-926-1519	www.kodak.com
Fischer Industries	P.O. Box 570 2630 Kaneville Ct. Geneva, IL 60134	800-356-5911	www.fischerind.com
Konica Minolta Medical Imaging	411 Newark Pompton Turnpike Wayne, NJ 07470	800-934-1034	www.medical.konicaminolta.us
Picker International	595 Miner Rd. Highland Heights, OH 44143	800-635-9729	

Darkroom

Recommendations

- Darkroom location: Locate the darkroom close to water and drains for plumbing purposes, and close to radiographic area to reduce unnecessary walking and to increase efficiency.
- Darkroom layout (Figs. 4-1 and 4-2): Darkrooms do not have to take up much room but are at least 6 × 8 feet. Many darkrooms are located where a bathroom might have been. This eliminates the process of bringing in new plumbing and electrical outlets. Try to include a sink for cleanup and processor maintenance. Keep wet and dry areas separate to eliminate contamination of screens and unexposed film by chemicals. Always have good ventilation to keep heat, humidity, and chemical fumes from destroying film and to reduce exposure of personnel to chemical fumes. Paint all walls white to reflect light from the safelights and for a brighter working environment. Use an adequate number and type of safelights. Make sure all safelights are 40 inches from the working area to prevent film fogging.

TECHNIQUE CHARTS

- Have a working knowledge of equipment (tube rating charts and anode cooling curves). A constant focal film distance is recommended. The same film, screens, and darkroom technique are used, as described previously.
- The technique chart is set up to take radiographs of normal animals. Different animals may have the same lateral thoracic measurement but different body types (obese, emaciated, etc.). The emaciated animal may be overexposed with the technique from the chart; therefore, you will need to decrease the exposure (kVp). The obese animal may be underexposed following the chart technique; therefore, you will have to increase the exposure (kVp).
  - The technique may need to be increased (2–30%) for numerous reasons (e.g., obesity, pregnancy, ascites, pleural effusion, or disease processes that increase lung opacity, such as pneumonia and atelectasis) and for positive-contrast studies.
  - The technique may need to be decreased (2–30%) for numerous reasons, including emaciation, pneumothorax, emphysema, gastric dilatation, and volvulus.

▼ ***Key Point*** Always select the shortest possible exposure times. This entails choosing the highest mA value to achieve the shortest exposure times.

Technique Chart (with Grid) (Fig. 4-3)

Thorax with Grid

1. Use a dog of average size and body condition for all measurements.
2 Take a lateral measurement across the chest at the widest point.
3. Find that measurement on your technique chart.
4. Underneath this lateral measurement, set your kVp at 95—a value in the middle of the ideal kVp parameters for a thorax.
5. Fill out your chart according to the kVp per centimeter increments.
6. Once the kVp values have been assigned, take three chest films at different mAs values. You may begin with 0.8, 1.6, and 3.2 mAs for a rare-earth system and 5, 10, and 20 mAs for calcium tungstate, for example. Select the mAs value at 95 kVp that provides you with the best technique.

Abdomen with Grid

1. Follow the first three steps under "Thorax with Grid."
2. Set your kVp at 85.
3. Fill out the chart according to the kVp per cm increments.
4. Double the mAs value used in the thorax technique.

Spine with Grid

1. Follow the first three steps under "Thorax with Grid."
2. Set your kVp at 65.
3. Fill out the chart according to the kVp per cm increments.
4. Set the mAs value 4 times that used for the abdomen. This setting also works for femur, humerus, shoulder, and pelvis.

Technique Chart (Tabletop without Grid) (Fig. 4-4)

Thorax, Abdomen, and Spine

1. On the grid chart for thorax, abdomen, and spine, find the last kVp setting for 11 cm.
2. Decrease the kVp as the thickness decreases. For example, if 74 kVp is at 11 cm, use 72 kVp at 10 cm, 70 kVp at 9 cm, and so forth.
3. Adjust the mAs by reducing to half (possibly more depending on the type of grid) the mAs value for the base techniques for the thorax, abdomen, and spine. If films are still overexposed, reduce the mAs by half again.

Extremity

1. Measure a normal dog carpus. The average is 4 to 5 cm.
2. Underneath that measurement, set your kVp at 60 (a value in the middle of your ideal kVp parameters for extremities).

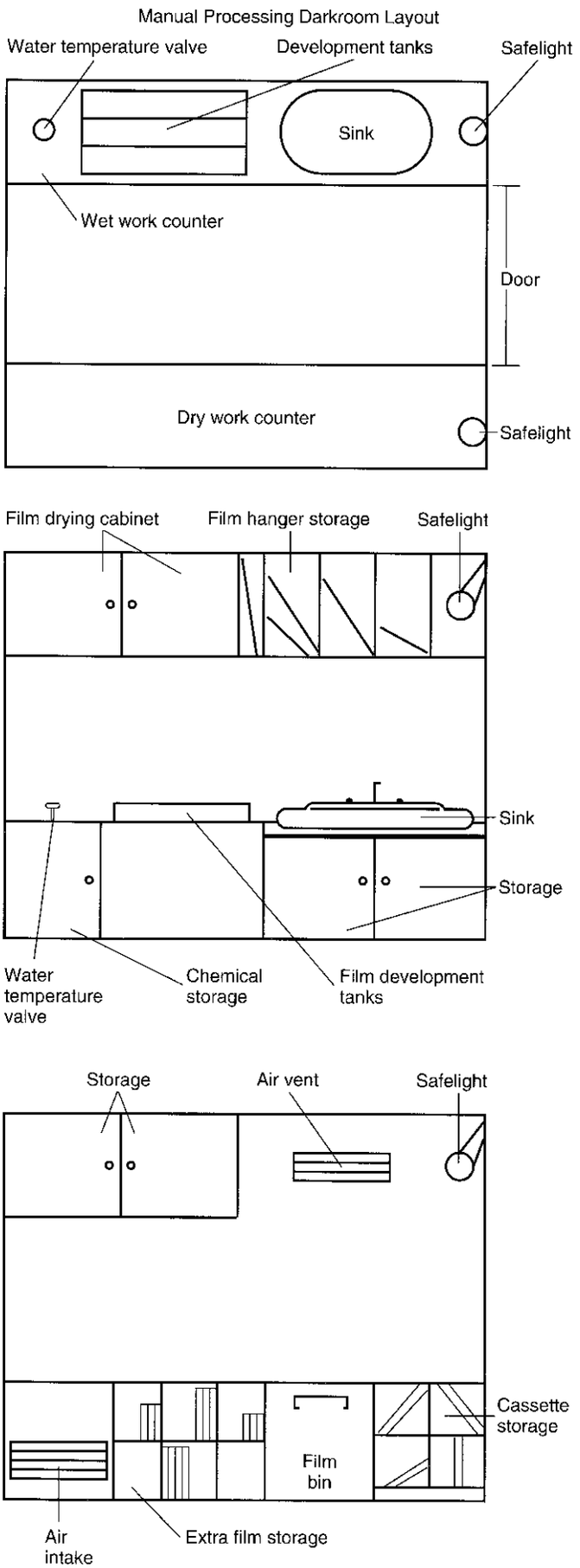

Figure 4-1. Floor plan for a darkroom using manual (wet tank) processing.

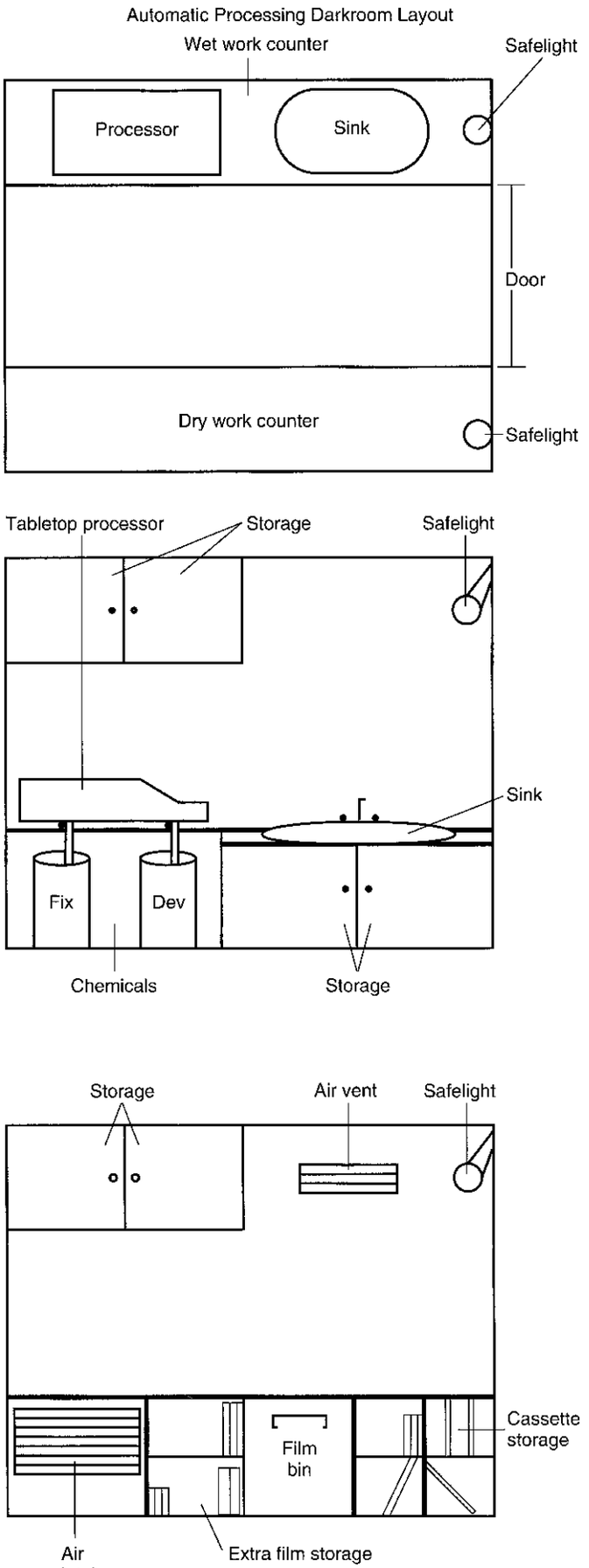

Figure 4-2. Floor plan for a darkroom using automatic processing.

Making a Technique Chart (Grid)

Ideal Parameters	kVp per cm Increments	Appreciable Difference
Thorax — 90 to 100 kVP Abdomen — 80 to 90 kVp Spine Skull — 60 to 80 kVp Pelvis Extremities — 50 to 70 kVp	40 to 80 range = 2 kVp per cm 80 to 100 kVp range = 3 kVp per cm ≥100 kVp = 4 kVp per cm **Chart Factors** Thorax ___ mAs ___ kVp base technique Abdomen - 2 X thoracic mAs, minus 10 kVp Spine - 4X abdomen mAs, minus 20 kVp	Amount of kVp change necessary to see a change in technique per kVp range 40 - 60 kVp = 2 - 4 kVp 60 - 80 kVp = 4 - 6 kVp 80 - 100 kVp = 6 - 8 kVp ≥100 kVp = 10 - 12 kVp

	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	cm
Thorax																					kVp
																					mAs

	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	cm
Abdomen																					kVp
																					mAs

	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	cm
Spine, Skull, Pelvis																					kVp
																					mAs

Figure 4-3. Technique chart to use with a grid.

Table Top Technique Chart
(Without Grid)

	1	2	3	4	5	6	7	8	9	10	cm
Thorax ___ mAs											kVp

	1	2	3	4	5	6	7	8	9	10	cm
Abdomen ___ mAs											kVp

	1	2	3	4	5	6	7	8	9	10	cm
Spine, Skull, Pelvis ___ mAs											kVp

	1	2	3	4	5	6	7	8	9	10	cm
Extremities ___ mAs											kVp

Figure 4-4. Technique chart. For tabletop exposures, take the Buckey grid technique and reduce the mAs by 50% to 75%. Continue kVp down from Buckey chart.

3. Fill out the chart, according to the kVp per cm increments.
4. Take films at three different mAs values (0.8, 1.6, and 3.2 with rare earth; 5, 10, and 20 with calcium tungstate). Continue selecting the mAs values until an appropriate exposure has been made. Your tabletop extremity chart is now complete. Employ this chart for all extremities distal to and including the elbow and stifle.

Nonscreen Film Technique Chart

- For the nonscreen film technique chart, the mAs in your technique chart may vary up or down from the example shown in Figure 4-5.

COMPUTED RADIOGRAPHY

Computed radiography (CR) is an indirect digital imaging technology in which a plate (which looks similar to a cassette but is filmless) is used to record the image. A reader is required to extract the data, which is converted to a digital image and viewed on a computer screen. CR utilizes standard x-ray machines. Components of CR include both the hardware described previously and the software (for display, storage, and archiving). New technique charts must be developed when switching from a traditional film-screen system to CR. CR software allows image manipulation that can adjust for exposure and contrast. Images can also be drawn, and measurements can be taken.

▼ ***Key Point*** The ability of the viewer to appreciate the image quality provided by CR depends on the quality of the computer monitor.

Advantages

- A digital image is generated (these can easily be sent to specialists if needed).
- Existing radiography equipment can be used.
- Excellent image quality.
- Initially less expensive than digital radiography.
- Film, processor, and darkroom can be eliminated.

Disadvantages

- Still have to use an imaging plate
- Need to purchase new plates and a reader
- Need to have computers and a software package to integrate with medical records

DIGITAL RADIOGRAPHY

Direct digital radiography (DR) uses specialized x-ray equipment that has a digital imaging sensor. Once the image is transferred to the computer system, image analysis and storage are similar to those previously listed for CR.

Advantages

- A digital image is generated (these can easily be sent to specialists if needed).
- Excellent image quality.
- Film, processor, and darkroom can be eliminated.

Disadvantages

- Currently more expensive than CR systems (cannot be used with existing x-ray equipment).
- Few current systems allow horizontal beam radiography.
- Need to have computers and a software package to integrate with medical records.

POSITIONING AND TECHNIQUE

Measuring for Radiographic Studies

- Measure all animals standing.
- Measurements for the thorax, abdomen, and thoracolumbar spine are all taken at the same location on the animal. Observe the animal from above, taking the lateral measurement from the widest point across the ribs. The DV/VD measurement is made at the same point. The widest point is usually at the thoracolumbar junction.
- Measure the pelvis across the wings of the ilium. This is a very accessible area to measure, giving highly repeatable results. The same measurement is used for both the lateral and the VD.
- Measure extremities at the widest point.
- Make sure all personnel measure all areas at the same point; otherwise, the technique will vary from one study to the next.

Nasal, Dental, and High Detail Studies

1	2	3	4	5	6	7	8	9	10	11	cm
50	100	125	150	200	250	300	350	400	450	500	mAs

Figure 4-5. Technique chart to use with nonscreen film. Use a lateral measurement across the skull to set technique. Always use 50 kVp for the best contrast.

Thorax

Obtain thoracic films at full inspiration. Include from the thoracic inlet to behind the diaphragm. In a large dog, this may take two radiographs for both lateral and DV/VD views. Short exposure times of $^1/_{60}$ second or less decrease motion artifact from cardiac and respiratory motion. A high-kVp, low-mAs technique increases latitude (increased shades of gray).

- For the lateral (right or left) measurement, elevate the sternum to the same plane as the spine. Pull the animal's legs cranially to reduce soft tissue over the cranial thorax. Include the sternum, and take the radiograph during peak inspiration (Fig. 4-6).
- For the DV/VD view, the sternum is superimposed over the spine. Center the beam at the caudal border of the scapula; center the beam on the spine. Take the radiograph during peak inspiration. VD radiographs are preferable to DV for evaluation of the accessory lung lobe and the caudal mediastinum. DV radiographs are preferred if evaluation of the caudal pulmonary vessels is important. The dog's disposition, clinical status (e.g., heart failure, pulmonary edema, or pleural effusion), or position of previous radiographs help choose between VD and DV thoracic radiographs (Fig. 4-7). A Plexiglas or foam trough is useful for positioning for the VD view (add 10% kVp to your technique when using a trough).
- Take both right and left lateral views of the thorax with a DV/VD view to evaluate for pulmonary metastases or focal disease.

Abdomen

Withhold food for at least 12 hours for optimal abdominal radiographs. Encourage the animal to defecate and urinate before being radiographed. Radiographs include the diaphragm to the coxofemoral joints. For large-breed dogs, this may require two 14 × 17-inch films for both the lateral and DV/VD views. Use a $^1/_{40}$-second or less exposure time to reduce motion; use a kVp in the 70 to 90 range for maximum latitude.

- For a lateral (right or left) radiograph, pull the legs caudally but not enough to stretch the abdominal musculature taut. Place the edge of the cassette 1 to 2 inches cranial to the xiphoid and at the coxofemoral joint (palpate for the greater trochanter). Take the radiograph at peak expiration (Fig. 4-8).
- The DV/VD is the same as that for the lateral abdomen (Fig. 4-9). A Plexiglas or foam trough is useful for positioning for the VD view (add 10% kVp to your technique when using a trough).
- A horizontal beam radiograph can be used to check for free abdominal air. Place the animal in left lateral recumbency for 10 minutes before radiography. Air is demonstrated around the right liver lobes. The technique is similar to the vertical beam technique in that distance remains at 40 inches. Remember to reduce the mAs if a grid is not used.
- In compression radiography, a wooden spoon can be used to compress the abdomen for separation of

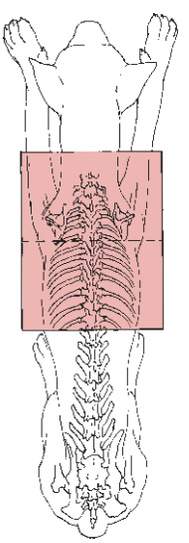

Figure 4-7. Positioning for dorsoventral or ventrodorsal thoracic radiograph.

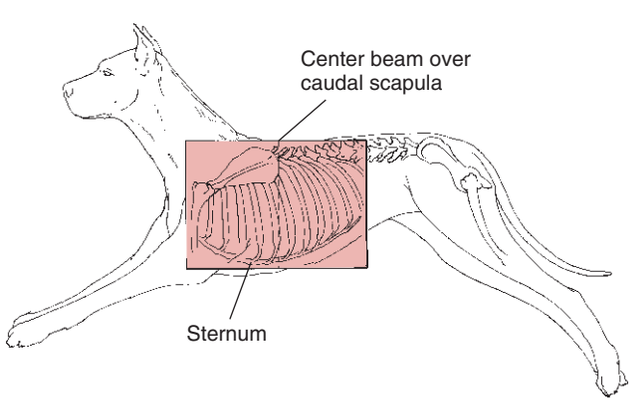

Figure 4-6. Positioning for lateral thoracic radiograph.

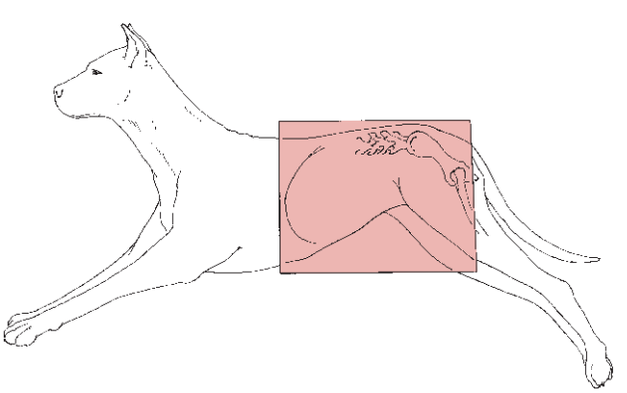

Figure 4-8. Positioning for lateral abdominal radiograph.

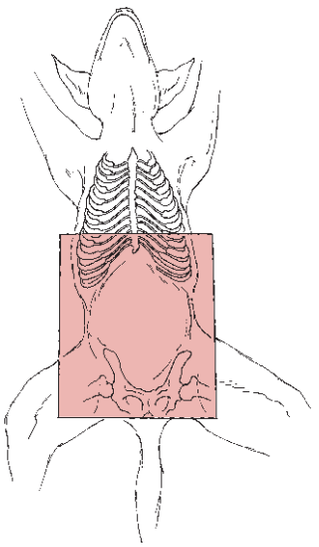

Figure 4-9. Positioning for ventrodorsal abdominal radiograph.

structures. The spoon can separate the colon from the urinary bladder to demonstrate the uterus, for example. Remember to reduce the kVp, because you are decreasing the thickness of the tissue being radiographed.

Extremities

For radiography of the extremities, the animal needs a clean, dry haircoat. Remove splints and bandages if possible. Place the limb to be radiographed closest to the film. Employ a high-mAs, low-kVp (50–70) technique to produce high-contrast radiographs. Collimate closely. Use tabletop (nongrid) techniques on parts less than 10 cm thick. Administer anesthesia or tranquilizers whenever needed. Use positioning devices. Measure the part to be radiographed over the thickest area. If the part thickness varies greatly, two exposures (e.g., lateral pelvis and femur) may be necessary. In the case of moderate variation, choose the greater measurement to set the exposure and "hot light" the slightly overexposed areas when reading the film. When long bones are being radiographed, include the joints proximal and distal.

▼ ***Key Point*** Radiograph the opposite limb for comparison to determine normal from abnormal.

Scapula and Shoulder Joint

Caudocranial

The animal is in dorsal recumbency, with the sternum rotated away from the side being radiographed. The leg is fully extended. Center the x-ray beam at the mid-scapula. For the shoulder joint, center the beam at the point of flexion for the joint.

Mediolateral (ML)

The animal is in lateral recumbency, with the down side to be radiographed. Extend the leg about 45 degrees from the vertebral column. Flex the opposite leg and place it over the thorax. Pull the head and neck back so that the cervical spine and trachea are not overlapping the joint space.

Humerus

Caudocranial

The animal is in dorsal recumbency, with the legs extended. Rotate the sternum away from the side being radiographed. Center the x-ray beam at the mid-humerus. The radiograph includes both the shoulder and the elbow joints.

Mediolateral

Place the animal in a position similar to that for the ML view of the scapula and the shoulder joint. Center the x-ray beam at the mid-humerus. The radiograph includes both the shoulder and the elbow joints.

Elbow Joint

Craniocaudal

The animal is in sternal recumbency, with the elbow joint in full extension. If the elbow cannot be completely extended, angle the x-ray beam 10 degrees to 20 degrees, craniodistal to caudoproximal.

Mediolateral

The animal is in lateral recumbency, with the elbow slightly flexed. Pull the opposite leg caudally. Center the beam on the palpable medial epicondyle. The elbow is in extreme flexion if identification of the anconeal process is of importance.

Craniolateral-Caudomedial Oblique

This aids in imaging of the lateral aspect of the medial coronoid.

Antebrachium

Craniocaudal

Place the animal in sternal recumbency. Extend the leg and position the elbow for a true craniocaudal projection. The film includes both elbow and carpus.

Mediolateral

The animal is in lateral recumbency, with the leg in the neutral position. Move the opposite limb caudally; center the beam on the midshaft radius. It may be easier to obtain the radiograph if the elbow is slightly flexed. Include the elbow and carpal joint on the film.

Carpus or Metacarpus

Dorsopalmar

By convention, positional terms change from cranial and caudal to dorsal and palmar distal to the radius. Place the animal in sternal recumbency, with the extremity extended. Allow the elbow to abduct slightly so that the carpus is in true dorsopalmar (DP) view. Center the x-ray beam on the carpus or metacarpus.

Mediolateral

Place the animal in lateral recumbency, with the affected leg down. Slightly flex the carpus; center the x-ray beam on the carpus. A lateral view of the metacarpus is often unrewarding.

Oblique Views

Place the animal in sternal recumbency, with the carpus/metacarpus in DP. Rotate the extremity 45 degrees in both directions for the two oblique views (dorsolateral to palmar medial oblique and dorsomedial to palmar lateral oblique).

Digits

Dorsopalmar

Place the paw flat against the cassette.

Mediolateral

Place the animal in lateral recumbency. Pull the specific digit to be examined dorsally with tape.

Oblique Views

Place the animal in sternal recumbency, with the carpus/metacarpus in DP. Rotate the extremity 45 degrees in both directions for the two oblique views (dorsolateral to palmar medial oblique and dorsomedial to palmar lateral oblique). Cotton can be placed between the digits to help with separation.

Pelvis

Tranquilization may be necessary for routine VD and lateral radiographs. General anesthesia is recommended for Orthopedic Foundation for Animals (OFA) or Penn-Hip radiographs.

Ventrodorsal Extended Hip

The animal is in dorsal recumbency, with the legs extended. The pelvis is straight; the femurs are parallel and as close to the cassette as possible. Patellae are superimposed over the distal femurs. Center the x-ray beam on the hip joints. Include the stifles on the radiographs. Legs are the same distance apart as the acetabula.

Lateral

The animal is in lateral recumbency, with the dependent leg pulled cranially. Elevate the nondependent leg with a foam block parallel to the tabletop.

Lateral Oblique

Place the animal in lateral recumbency. Place a foam wedge to elevate the pelvis approximately 20 degrees. Push the upper leg proximally to rotate.

Ventrodorsal Flexed Hip (Frog-Leg Position)

Place the animal in dorsal recumbency, and flex and abduct the femurs so that the stifles are lateral to the abdomen. Place the femurs at an angle of 45 degrees to the spine.

Femur

Craniocaudal

Place the animal in dorsal recumbency or in the erect sitting position, with the leg extended. Center the x-ray beam at mid-femur. Include the hip and stifle on the radiograph. Measure at the proximal femur.

Mediolateral

Place the animal in lateral recumbency with the leg to be examined on the cassette. Abduct the opposite leg and rotate out of the x-ray beam's path. Center the x-ray beam at mid-femur. Include the hip and stifle on the film.

Stifle

Caudocranial

Place the animal in ventral recumbency with the leg to be examined pulled caudally into maximum extension. In large dogs, angle the x-ray beam 15 degrees caudodistal to cranioproximal. Center the x-ray beam at the joint space.

Mediolateral

Position the animal as for the mediolateral femur view, with the x-ray beam centered on the joint space. Usually, the tarsus is away from the cassette, so you need to place a foam wedge under the hip and femur.

Tibia and Fibula

Caudocranial

Position the animal as for the caudocranial stifle view. The x-ray beam remains vertical and centered at the mid-tibia. Include stifle and tarsus on the film.

Mediolateral

Place the animal in lateral recumbency with the tibia and fibula included on the film.

Tarsus

Dorsoplantar

Place the animal in dorsal recumbency. Extend the leg, and center the x-ray beam at the proximal intertarsal joint.

Mediolateral

Place the patient in lateral recumbency. Slightly flex the tarsocrural joint. Center the x-ray beam at the proximal intertarsal joint.

Oblique Views

Dorsolateral to palmar medial oblique and dorsomedial to palmar lateral oblique. Position the animal in dorsal recumbency, then rotate 45 degrees in each direction (lateral and medial) for the two oblique views.

Metatarsus and Digits

Position the animal as for the metacarpus and digits of the forelimbs.

Spinal Positioning and Technique: General Principles

- Materials needed include sandbags, foam wedges, markers (right and left), and a Plexiglas trough to aid in positioning the animal without anyone in the room.
- Use general anesthesia or heavy sedation in all but the most subdued animals. Exceptions are suspected fracture, congenital malformation with instability, and other diseases in which the animal's condition or protective mechanisms that have maintained stability will be compromised.
- Short-scale, high-contrast (high-mAs, low-kVp) technique provides good detail. Use a grid and collimate to include only the spine.
- At least two radiographic views of the area of interest are needed: lateral and VD.
- In the average-size dog, five vertebral segments can be adequately evaluated per film. Because of the divergence of the x-ray beam, all areas of interest have to be centered to evaluate intervertebral disc spaces.

▼ ***Key Point*** Poor patient positioning and poor radiographic quality commonly occur when animals are not anesthetized or heavily sedated for spinal films. Many radiographic lesions can be obscured by poor technique. Conversely, a normal structure can be falsely identified as a lesion.

- Ideal spinal survey studies are listed in Table 4-5.

Cervical Spine

Measure at the caudal cervical spine for all views.

Lateral View

For radiography, the spine must be parallel to the cassette. In many cases, support the center of the neck with radiolucent positioning blocks (sponges). Place the head in a normal position (neither flexed nor extended) relative to the neck. The head must be lateral because it controls the position of the proximal neck. Pull the front legs back over the thorax to allow thinning of the tissues over the caudal neck. The thorax must be in the accurate lateral position because it controls the position of the caudal neck. Extending the entire neck may help open up the caudal cervical disc spaces. Include both occipital and cervicothoracic areas on the radiograph.

Ventrodorsal View

The spine is not parallel to the cassette because of the anatomic variation between the head and the thorax. The spine inclines away from the cassette at the thorax. Place the head in normal position (hard palate and dorsal nose at a 60 degree angle to the cassette). If the head is in a true VD position, an undesirable arch is pro-

Table 4-5. SPINAL SURVEY STUDIES

Study	Centering—Lateral	Centering—Ventrodorsal
Cervical spine (C1-5)	C3-4	C3-4
Cervical spine (C6-T2)	C6-7	C6–T1 (x-ray beam angled 15 degrees ventrocaudal to dorsocranial)
Occipitoatlantoaxial	C1 C1 flexion, C1 oblique	C1 (rostrocaudal open mouth to visualize the dens)
Thoracic spine (cranial)	T6-7	T6-7
Thoracolumbar spine (T12-13)	T12-13	T12-13
Lumbar spine	L3-4	L3-4
Lumbosacral spine	LS LS flexion LS extension	 LS
Post-trauma	Center on area of suspected lesion	Cross-table (horizontal beam); center on area of suspected lesion

duced in the cervical spine. The midplane of the head and thorax must be perpendicular to the cassette. Tilting the x-ray tube ventrocaudal to dorsocranial approximately 10 to 20 degrees permits imaging of the intervertebral disc spaces.

Thoracolumbar Spine

Lateral View

The midplane of the entire body must be parallel to the cassette. Most animals must have the sternum elevated for good lateral views of the spine. Pull the front legs cranially and the rear legs caudally to straighten the spine. Extending the entire neck may help open up the cranial thoracic disc spaces.

Ventrodorsal View

The midplane of the entire spine must be perpendicular to the cassette. When the dorsal spines are prominent, as in thin animals, radiolucent positioning blocks may be beneficial. The body may be held by placing tension on the legs.

Skull Radiography

- General anesthesia or deep tranquilization of the patient is essential, if not specifically contraindicated by the patient's physical condition, to obtain radiographs of good diagnostic quality.

▼ ***Key Point*** The lack of proper patient restraint is the most common cause of skull radiographs of nondiagnostic quality.

- The highest-resolution (detail) radiographic image of the skull is produced with a nonscreen film or an ultradetail film-screen combination. Nonscreen film necessitates a 10- to 20-fold increase in the mAs compared with film in par speed screen cassettes.
- The positioning of the patient and the number of projections needed for a complete study depend upon the area of the skull being evaluated. A minimum of two views is necessary.

Routine Skull

Lateral and DV views are used.

Nasal Cavity and Paranasal Sinuses

Lateral and DV occlusal (Fig. 4-10), VD open mouth (extraoral film) (Fig. 4-11), frontal (primary beam parallel to the hard palate) (Fig. 4-12), and lateral oblique (right and left) (Fig. 4-13) are used to evaluate small frontal sinuses.

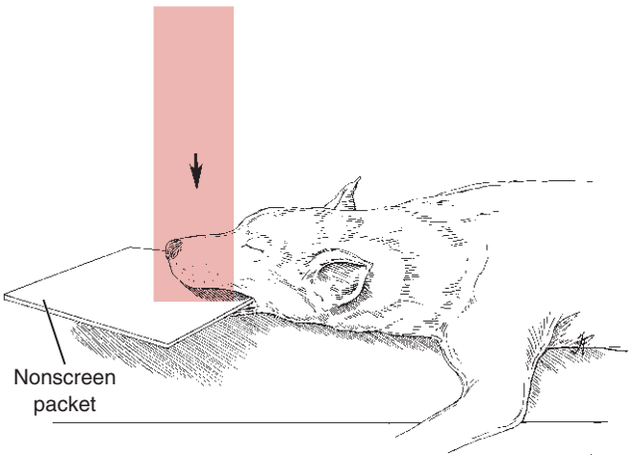

Figure 4-10. Positioning for dorsoventral occlusal (intraoral) radiograph of the skull.

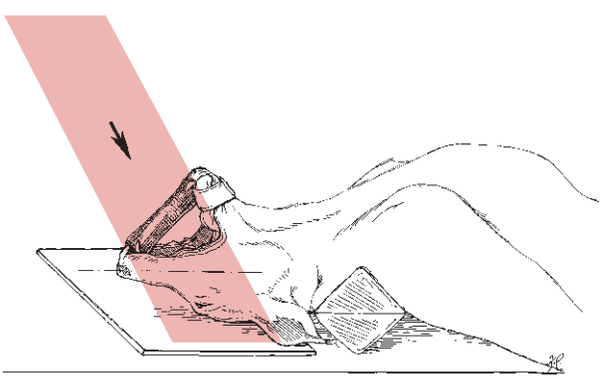

Figure 4-11. Positioning for the ventrodorsal (20° to 30° tube angle), open-mouth view of the skull.

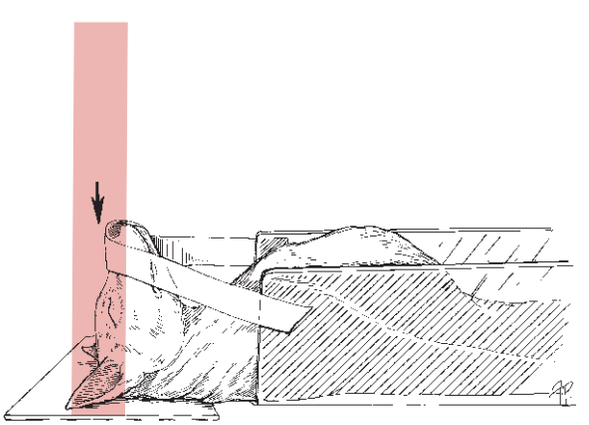

Figure 4-12. Positioning for the rostrocaudal (frontal) view of the skull.

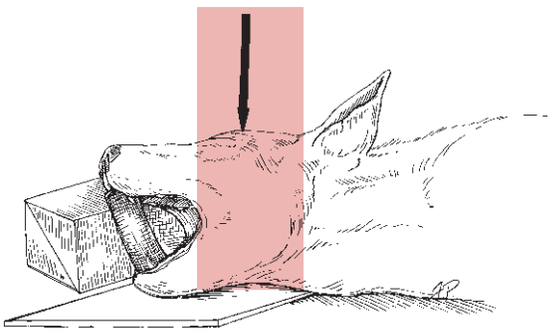

Figure 4-13. Positioning for the open-mouth lateral oblique (20° to 30°) view of the frontal sinuses.

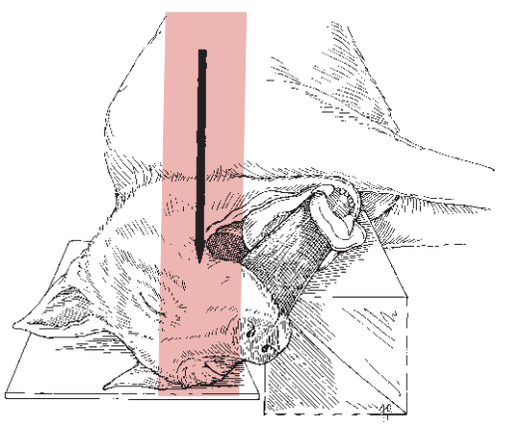

Figure 4-14. Positioning for the open-mouth lateral oblique (20° to 30°) view of the maxilla.

Dental Arches

- Maxillary: Right and left lateral obliques (20–30 degrees) (Fig. 4-14), VD open mouth (extraoral film), and DV occlusal.
- Mandibular: Right and left lateral obliques (20–30 degrees), open mouth (Fig. 4-15), and VD occlusal (Fig. 4-16).

Bisecting Angle Technique

Project the central beam perpendicular to an imaginary plane that bisects the angle formed by the long axis of the tooth (or teeth) and the plane of the film (Fig. 4-17).

Tympanic Bullae (Middle Ears)

DV, open mouth frontal. The primary beam bisects the angle of the opened temporomandibular joint (TMJ) (Fig. 4-18); right and left lateral obliques (30 × 30 degrees) (Fig. 4-19). Palpate the jugular processes; when these processes are oblique, the bullae will also be properly oblique.

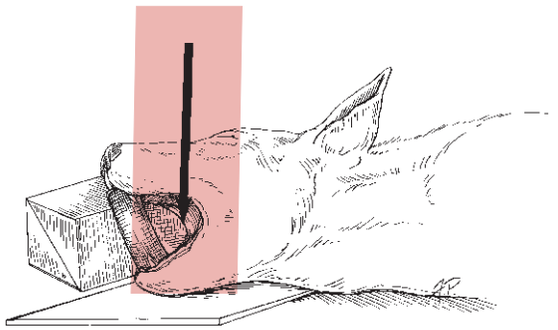

Figure 4-15. Positioning for the open-mouth lateral oblique (20° to 30°) view of the mandible.

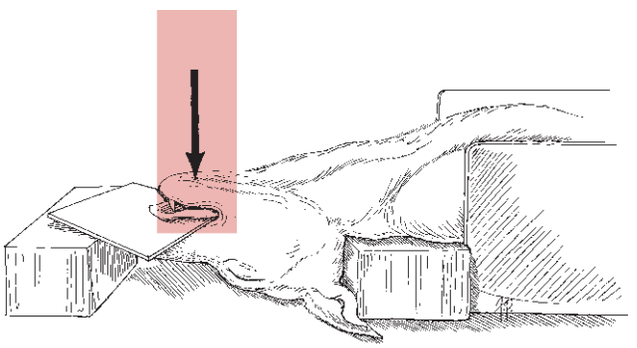

Figure 4-16. Positioning for the ventrodorsal occlusal (intraoral) view of the mandible.

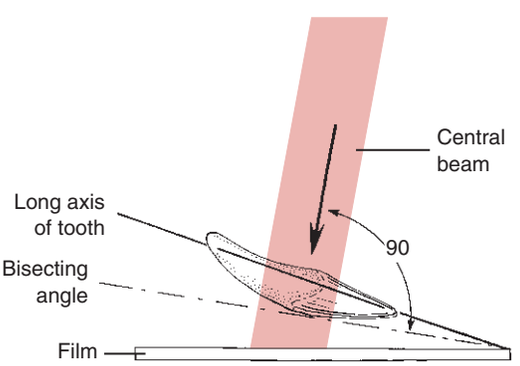

Figure 4-17. Bisecting angle technique for radiographing the teeth.

Foramen Magnum

Rostrodorsal-caudoventral oblique (fronto-occipital). The central beam passes between the eyes and exits through the foramen magnum (Fig. 4-20).

Temporomandibular Joint

DV, open mouth frontal (see Fig. 4-18). The primary beam bisects the angle of the opened temporomandibular joint; right and left lateral obliques (20–30 degrees) (see Fig. 4-13).

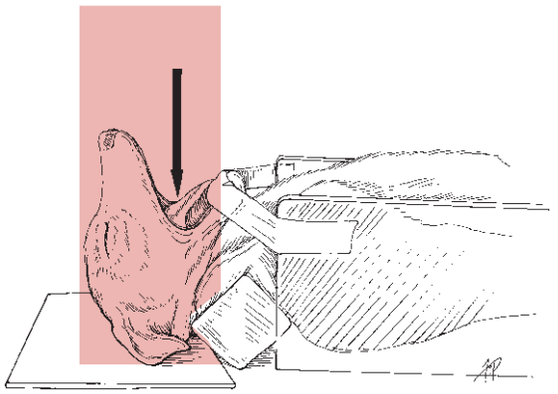

Figure 4-18. Positioning for the open-mouth rostrocaudal (basilar) view of tympanic bullae.

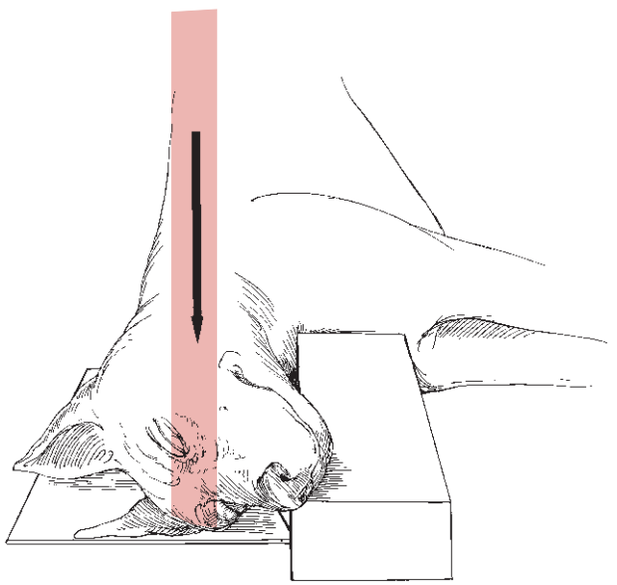

Figure 4-19. Positioning for the lateral oblique (30° nose elevated, then 30° oblique) view of tympanic bullae.

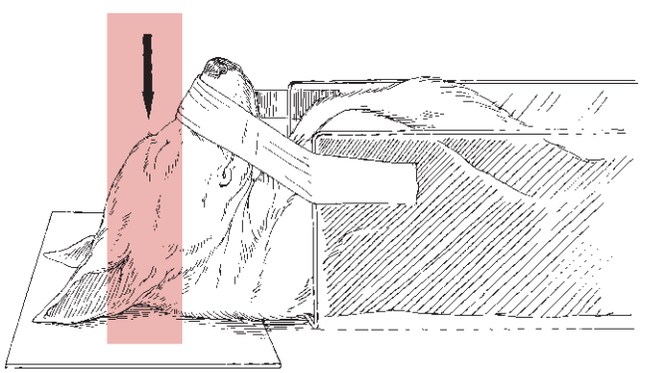

Figure 4-20. Positioning for the rostrodorsal-caudoventral (fronto-occipital) view of the skull.

Mandible

DV, lateral, and lateral oblique (right and left).

Maxilla

DV occlusal, VD open mouth, lateral, and lateral oblique (right and left).

Zygomatic Bone and Orbit

DV, lateral, and lateral oblique (right and left); frontal; and VD open mouth.

CONTRAST STUDIES

Contrast Medium

- Positive-contrast medium: iodine (ionic, nonionic), barium (liquid, paste) (Table 4-6)
- Negative-contrast medium: room air, carbon dioxide, nitrous oxide

Excretory Urogram (Intravenous Pyelogram, Intravenous Urogram)

- A well-prepared animal is important for this contrast study (excretory urogram[EU], intravenous pyelogram, and intravenous urogram are synonymous terms). Withhold food for 12 to 24 hours. Give enemas the night before and at least 2 hours before the study. Determine renal function (blood urea nitrogen and serum creatinine) before initiating the study.

▼ ***Key Point*** Always take scout films before performing contrast studies of the urinary tract.

- The primary contraindication in animals is dehydration. Contrast medium is hypertonic and will compromise an already unstable patient. Make sure the patient is properly hydrated before EU. Other contraindications in people include diabetes mellitus, multiple myeloma, heart failure, and known hypersensitivity to the contrast medium.
- Use a water-soluble, iodinated ionic contrast media (Renografin, Conray, Hypaque, Renovist, etc.). Dose is 2 ml/kg intravenously (approximately 300–400 mg/ml of iodine), not to exceed 90 ml or 35 g of iodine. For animals with impaired renal function, the dose may need to be doubled (4 ml/kg). Place an indwelling catheter to help avoid perivascular injections and to allow intravenous access if complications occur. Give the bolus as fast as possible.
- Increase radiographic technique (mAs) 5% to 10% over scout films. Keep the kVp approximately 70 to produce better differentiation between the kidney and the contrast medium.

Table 4-6. RADIOGRAPHIC CONTRAST AGENTS

Type of Contrast Agent	Brand Names	Manufacturers
Barium products	Intropaste (barium paste)	Lafayette Pharmacal (Lafayette, IN)
	Barosperse (barium suspension)	Mallinckrodt (St. Louis, MO)
	Novopaque (barium suspension)	Lafayette Pharmacal (Lafayette, IN)
	E-Z-ML- 196 (barium suspension)	E-Z-EM (Westbury, NY)
Iodinated gastrointestinal contrast agent	Gastrografin	Bracco Diagnostics (New Brunswick, NJ)
	Omnipaque (iohexol)	Amersham Health (Piscataway, NJ)
Iodinated contrast agent	Renografin 60 or 76	Bracco Diagnostics (New Brunswick, NJ)
	Hypaque-76	Amersham Health (Piscataway, NJ)
	Conray 30 or 400	Mallinckrodt (St. Louis, MO)
Myelographic contrast agent	Omnipaque (iohexol)	Amersham Health (Piscataway, NJ)
	Isovue (iopamidol)	Bracco Diagnostics (New Brunswick, NJ)

Technique

1. Immediate postinjection VD film demonstrates nephrographic phase.
2. VD and lateral films at 5 minutes.
3. In some cases, if there is poor filling of the renal pelvis, between 10 and 20 minutes following contrast administration place an abdominal wrap between the bladder and the kidney to compress the ureters, causing the pelvis and diverticula of the kidney to completely distend for better evaluation. This is contraindicated in cases of severely diseased bladder walls or mass lesions, in which it may cause rupture.
4. VD and lateral films at 15 minutes for evaluation of the pyelographic stage.
5. VD and lateral films at 30 minutes.
6. Remove the compression wrap and take lateral and VD radiographs.
7. Modify this technique as needed for the suspected disease entity. For example, to evaluate for ectopic ureters, take oblique films off lateral at the bladder trigone between 15 and 20 minutes. A pneumocystogram may also be helpful for identifying the distal ureters and vesicoureteral junctions.
   - Complications include perivascular injection, which can be treated by instilling saline into tissues to dilute; nausea or vomiting; adverse systemic (anaphylactoid) reaction; and contrast-induced renal failure. The study may be nondiagnostic when the kidneys become bright (contrast enhanced) and remain that way, but there is no opacification of the collecting system, ureters, or bladder. Be careful in VD positioning to avoid aspiration.

Cystography

- Contrast medium: For negative contrast, use nitrous oxide, room air, or carbon dioxide; for positive contrast, use a water-soluble iodinated ionic contrast medium (not barium).
- Catheters: Foley, tom cat, male dog, or metal female catheters
- Sterile lubricant gel
- Three-way stopcock
- Contrast studies
  - Negative-contrast cystogram (pneumocystogram)
  - Positive-contrast cystogram (technique of choice for identifying urinary bladder location and tears)
  - Double-contrast cystogram (superior for demonstrating lesions involving the urinary bladder wall and intraluminal filling defects)

Technique (Double Contrast)

1. Withhold food for 12 to 24 hours.
2. Administer warm-water cleansing enemas the night before and 3 to 4 hours before the procedure if needed.
3. Sedation or tranquilization may be necessary for catheterization, especially in cats and female dogs.
4. A small amount of 2% lidocaine (2–5 ml) infused into the urinary bladder before the contrast agent may reduce urinary bladder spasm.
5. Place the catheter tip within the bladder neck.
6. Empty the urinary bladder.
7. Infuse the positive-contrast medium (1–3 ml in cats and dogs <25 pounds; 4 to 6 ml in dogs >25 pounds), rotate the patient, and massage the bladder to distribute the contrast medium and coat the entire mucosal surface.
8. Slowly infuse negative-contrast material (approximately 10 ml/kg, but range is extremely variable). Complete distention is desirable and can be judged by palpation, back pressure felt on syringe plunger, or reflux of gas around catheter.
9. Take a lateral, two lateral obliques, and a VD radiograph to examine the bladder full on double-contrast cystograms.
10. Evacuate contrast material from the bladder after the study.

Technique (Positive Contrast)

- Increase exposure technique by 10% for a positive-contrast study.
- Only lateral and VD views are necessary for positive-contrast cystograms.

- Use the technique described previously for catheter placement.
- Administer 3 to 5 ml/kg of positive-contrast medium.

Complications

- Fatal air embolism (rare cases). An increased risk exists with ulcerative or erosive cystitis. Carbon dioxide is more soluble than room air in blood and thus less likely to cause this problem. Air embolism occurs immediately after the administration of negative-contrast medium. Place the animal in left lateral recumbency, and lower the head to maintain normal blood circulation through the heart. The air is trapped in the right ventricle.
- Iatrogenic trauma (hematuria or rupture) and infection (bacterial contamination or cystitis).

Urethrography

- Retrograde positive-contrast study of the urethra using iodine.
- Equipment includes catheter (Foley, metal, male dog), sterile gel, lidocaine, and water-soluble iodinated contrast medium.

Technique

1. Evacuate the colon with an enema, if needed, before the study; take scout films before the study to evaluate technique and preparation.
2. Pass a urinary catheter into the distal urethra. Inflate the balloon if a Foley catheter is used (in distal urethra for female dogs or cats and proximal to the os penis in male dogs when possible).
3. Administer 2 to 5 ml of 2% lidocaine before injecting contrast material to reduce urethral spasm.
4. Position male dogs with their legs drawn cranially.
5. Administer 10 to 20 ml of contrast medium for male dogs and 5 to 10 ml for female dogs and cats. Inject as a bolus and take radiographs during the last few milliliters of injection.
6. A lateral radiograph may be sufficient, but subsequent lateral and VD oblique views may be helpful.

Complications

- Iatrogenic trauma and bacterial contamination

Esophagography

Technique

1. Take survey cervical and thoracic radiographs.
2. Position the animal in lateral recumbency.
3. Administer contrast medium (see Table 4-6) (barium sulfate suspension, Esophotrast, barium burger) slowly into the buccal pouch.
4. Dose is variable (5–20 ml); use enough to induce swallowing and coat esophagus.
5. Obtain radiographs following swallows. The lateral view is most informative; additional views can be taken if needed. Follow-up radiographs may be helpful if a bolus of contrast material is retained within the esophagus.

Complications

- Aspiration.
- Leakage of barium into mediastinum. Low osmolality, nonionic iodinated contrast medium (iohexol) may be indicated if perforation is suspected.

Gastrography

▼ ***Key Point*** Before contrast studies of the gastrointestinal tract, discontinue all drugs that may influence motility.

Technique

1. Fast patient 12 to 24 hours before the study.
2. Give cleansing enema the night before and 3 to 4 hours before the study, especially if complete upper gastrointestinal study is to be done.
3. Take plain films before the study. Then pass a stomach tube for administration of contrast medium.
4. Obtain negative-contrast gastrogram (pneumogastrogram) by administering 6 to 16 ml of room air per kilogram of body weight using a stomach tube. Immediately take four views (right and left lateral, VD, and DV). This is often valuable in the diagnosis of radiolucent foreign bodies.
5. Obtain positive-contrast gastrogram using barium (suspension, 30% weight-to-volume) at a dose of 6 to 12 ml/kg (see Table 4-6). Administer through a stomach tube, and take films immediately (right and left lateral, VD, and DV). Use this procedure to document gastric displacement, certain gastric foreign bodies, and gastric perforation. Barium begins leaving the stomach within 5 to 15 minutes. The stomach is emptied by 30 to 60 minutes in cats and 1 to 2 hours in dogs.
6. A double-contrast gastrogram can be done as a separate study or during an upper gastrointestinal study. Give barium, 60% weight-to-volume at a dose of 1.5 to 3 ml/kg, and insufflate with room air at 10 ml/kg. Immediately take DV, VD, and right and left lateral films. This study is indicated in cases of suspected gastric wall and mucosal lesions.

Upper Gastrointestinal Study

- Preparation requires a 12- to 24-hour fast and an enema the night before and 3 to 4 hours before the study.
- Use barium suspension, 30% to 60% weight-to-volume, for routine studies (see Table 4-6). Dose is 8 to 16 ml/kg.
- Use iodinated contrast (ionic and nonionic) agents (see Table 4-6) with suspected perforation for quick determination of small intestine patency and location

and when endoscopy is planned immediately following the contrast study.
- For restraint in canines use acepromazine, and in felines use ketamine/acepromazine preparations. See Chapter 2 for doses. These sedatives have less effect on motility than do many others.

Technique

1. Take survey radiographs (right lateral and VD).
2. Immediately after administration of barium, take right and left lateral and DV and VD views. Obtain right lateral and VD radiographs at 15, 30, and 60 minutes. Be consistent unless a lesion is identified that is better evaluated by repositioning the animal. Then, proceed at hourly intervals until the contrast material reaches the colon.
3. Modify this protocol for each individual depending on the suspected disease entity or the lesions visualized during the procedure.
4. Expected transit time to the colon is 3 to 4 hours for dogs and 1 hour for cats.

Complications

- Aspiration of barium with or without gastric contents.
- Leakage of barium indicates a gastrointestinal (GI) perforation, which is a surgical emergency. Barium itself induces a chemical peritonitis that may make treatment of GI perforation more difficult.

▼ ***Key Point*** Whenever GI perforation is suspected, use nonionic iodinated contrast medium (e.g., iohexol) instead of barium.

Myelography

- Myelography is the radiographic evaluation of the spinal cord by injection of a positive-contrast agent into the subarachnoid space.
- Indications
  - To evaluate transverse myelopathy
  - To determine nature, location, and extent of a lesion prior to surgery
  - To identify multiple lesions when one lesion might be masked by another and therefore not detected clinically
- Contraindications
  - Diffuse myelopathy that is not amenable to surgery
  - Meningitis, which may be aggravated by contrast medium
  - Not indicated when survey radiographs and clinical signs are adequate for diagnosis
- Contrast medium (see Table 4-6)
  - Dose for cisternal tap: Cervical study (0.2–0.3 ml/kg); thoracolumbar study (0.45 ml/kg)
  - Dose for lumbar tap: Cervical study (0.45 ml/kg); thoracolumbar study (0.3 ml/kg)

▼ ***Key Point*** Always obtain survey spinal radiographs before myelography.

Basic Technique

1. Animals must be under general anesthesia.
2. Perform sterile preparation of the puncture site.
3. Collect and analyze cerebrospinal fluid (CSF) if deemed necessary.

Cisternal Tap Procedure

1. Position the animal in lateral recumbency.
2. Place the nose parallel to the tabletop and perpendicular to the spine.
3. Use a 20- or 22-gauge, 1.5- to 2.5-inch spinal needle with the bevel directed caudally.
4. Insert the needle on the dorsal midline between the occipital protuberance and the wings of the atlas.
5. Direct the needle toward the mandible.
6. If the needle hits bone, move the needle cranially or caudally until it falls into the atlanto-occipital (AO) space.
7. Remove the stylet and check for CSF flow often while advancing the needle.
8. Inject contrast material slowly after seeing CSF in the needle. Prior to injection, collect a specimen if CSF for later analysis is indicated.
9. Elevate the head for 5 minutes before taking radiographs.
10. Take lateral and VD radiographs (also VD oblique if necessary). Remove the endotracheal tube, if necessary, for the VD radiograph.

Lumbar Tap Procedure

1. Position the animal in lateral or sternal recumbency, and flex the rear legs to help open the interarcuate spaces.
2. Use a 20- or 22-gauge, 1.5- to 3.5-inch spinal needle.
3. Insert the needle through the L5-6 interarcuate space for small dogs and cats and L4-5 for large dogs. Place the needle on the dorsal midline just lateral to the dorsal spinous processes of L6 at a 50 to 60 degree angle in a cranioventral direction toward the interarcuate space at L5-6. In cats, insert the needle off the cranial edge of the L6 dorsal spinous process perpendicular to the long axis of the spine. Direct the needle ventrally through the interarcuate space.
4. Inject in either the dorsal or the ventral subarachnoid space. Always check for CSF flow before injection; however, it is not always obtained. Increase the likelihood of obtaining CSF by elevating the head and shoulders before placing the needle.
5. Perform a small test injection (0.25–0.50 ml) followed by a radiograph to check needle placement.
6. Slowly inject total dose. Take radiograph views based on localization determined by neurologic examination.

Complications

- Seizures (incidence is reduced with new contrast agents, e.g., iohexol)
- Exacerbation of clinical signs
- Hyperesthesia
- Apnea during injection
- Epidural injection will not negatively affect the health of the animal but negatively affects the quality of the myelogram.
- Central canal filling occurs when the needle is placed through the center of the cord. It usually appears thin on radiograph and sharply defined in the normal animal.

Interpretation

Lesions are divided into three categories (Fig. 4-21):

1. Extradural, characterized by
   a. Displacement of the spinal cord
   b. Narrowing or compression of the subarachnoid space
   c. Deviation of the subarachnoid space
   d. Spinal cord may appear wide on opposite view
2. Intradural extramedullary, characterized by
   a. Filling defect within the subarachnoid space ("golf tee" sign)
   b. Possibly associated extradural or intramedullary component
3. Intramedullary, characterized by
   a. Spinal cord widening in all views

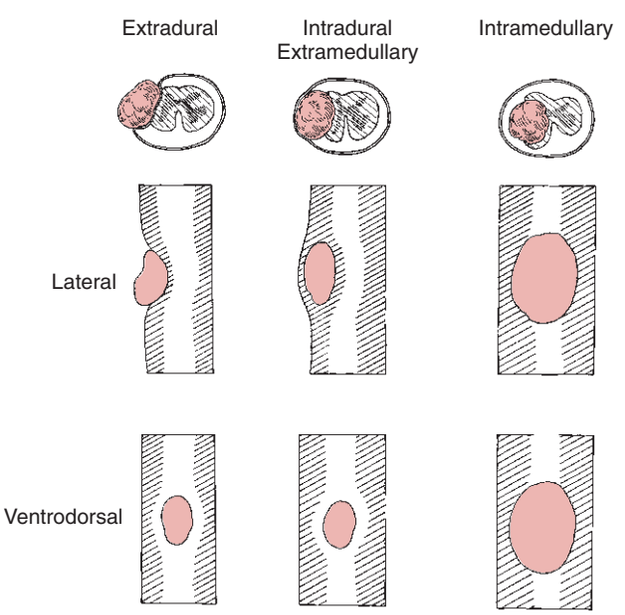

Figure 4-21. Radiographic patterns of myelographic lesions.

RADIATION SAFETY

Basic Radiation Safety

The objectives of radiation safety are to obtain the maximum amount of diagnostic information while keeping the radiation exposure to personnel and animals to a minimum.

▼ ***Key Point*** The responsibility for radiation safety lies solely with the owners of the practice.

Radiation protection in veterinary medicine is the subject of the National Council on Radiation Protection and Measurements (NCRP) Report No. 36, titled *Radiation Protection in Veterinary Medicine*. This report specifically outlines when radiation protection surveys are made. The report makes recommendations concerning tube housing, aluminum filtration, collimation types, and centering devices. A special section discusses radiography with portable and mobile diagnostic equipment. All practices need a copy of this report. Other NCRP reports that may be pertinent are No. 116, which discusses protection devices and provides recommendations for the maximum permissible dose (MPD); No. 107, which explains the concept of ALARA (as low as reasonably achievable) for medical and dental personnel; and No. 35, which discusses dental applications of diagnostic radiology.

The MPD was established to keep the radiation exposure of workers below a level at which adverse effects might be observed during a lifetime and to minimize the incidence of genetic effects in the entire population. The MPD does not apply to animal patients, to radiation emitted from natural background sources, or to radiation therapy. The actual risk to an individual exposed to MPD is small, but the risk is directly proportional to the received dose. Therefore, radiation exposure must be kept as low as possible. Radiation can cause both tissue and genetic damage. The effects of radiation can be demonstrated in a short time, or they can be cumulative and not observed for a long time.

Federal regulations regarding use of x-ray equipment and radiation protection are published in the Code of Federal Regulations, available at university and public libraries. Individual states publish radiation control regulations that are reprinted from the state codes. These regulations include information concerning the licensing of x-ray machines, the licensing fee, and the procedure to be followed in obtaining licensing. The goal in diagnostic radiology is to obtain radiographs with minimum exposure to both patient and personnel.

Maximum Permissible Dose

The MPD is currently 5 rem per year.

▼ ***Key Point*** Be familiar with federal, state, and local regulations regarding use of x-ray equipment and radiation safety.

Reducing Exposure

Three methods reduce radiation exposure: (1) increased distance between the individual and the radiation source, (2) decreased duration of exposure, and (3) protective barriers between the individual and the radiation source.

- Limiting radiation exposure
  - Limit the number of individuals within the room where the procedure is taking place. Use positioning devices, such as sandbags, sponges, tape, and Plexiglas or foam trough. Use chemical restraint whenever possible.

▼ ***Key Point*** When you must be present within the radiographic room during film taking, always wear protective clothing.

  - Protective lead apparel includes apron, gloves, thyroid shield, and protective goggles. Lead apparel is usually 0.5-mm lead equivalent. Hang aprons up to prevent the lead from cracking. Store gloves so that liners can dry. Check all protective clothing at least twice a year for cracks and tears. Place the items on a film cassette and radiograph them at an exposure of approximately 85 kVp.

▼ ***Key Point*** Never permit any portion of the body to be within the primary beam, even if covered with protective clothing.

  - Never hand-hold any x-ray tube. All x-ray tubes leak radiation from the housing.
  - Use a shielding device whenever possible to protect all or part of your body. Lead glass may be part of this shield so that you may continue to see the patient.
- When using a horizontal x-ray beam, never position any part of your body behind the cassette.
- Use collimation. An unexposed border on the radiograph demonstrates that the primary beam did not exceed the size of the cassette (film). This practice helps reduce scatter radiation by decreasing the interaction between the primary beam and the tissue, therefore increasing radiographic quality. Check the collimator light for accuracy; replace the bulb as needed.
- Use fast film, fast rare-earth screens, and high-kVp techniques to lower the exposure factors and the amount of radiation produced.
- Use a 2.0-mm aluminum filter installed at the tube housing port to remove the softer (less energetic) radiation portion of the x-ray beam. This aids in the reduction of scatter radiation and exposure to the patient.
- Individuals within the room should always stand as far from the radiation source as possible. If you double the distance from the source of radiation, you decrease your exposure level by a factor of 4 (inverse square law).
- All personnel working with radiation are required to wear a film badge or some other method of monitoring the amount of exposure if they have the potential to receive greater than $^1/_4$ MPD. Remember that wearing the device does not protect the individual, but it serves as a reminder of working in a potentially hazardous environment. For a monitoring device to be most helpful in determining exposure to radiation, wear it consistently in the same location on the body outside the apron at the neck. Film badges register when exposed to heat, light, water, or pressure. They can be purchased through companies listed in Table 4-7.

▼ ***Key Point*** Never permit anyone under the age of 18 or a pregnant woman in the room during a diagnostic procedure.

- Rotate personnel, thus reducing the amount of exposure to each person.
- Do not direct the x-ray beam into adjacent rooms that may be occupied.
- Use a gonadal shield for the patient.
- Always plan radiographic procedures (e.g., proper position and technique), thus reducing the number of films needed, which ultimately reduces the exposure to patient and personnel.

Table 4-7. SOURCES OF FILM BADGES

Company	Address	Phone Number	Website
Landauer	2 Science Rd. Glenwood, IL 60425	800-323-8830	www.landauerinc.com
Teledyne Brown Engineering	50 Van Buren Ave. Westwood, NJ 07675	201-664-7070	www.tbe.com

Clinic Construction

- Check with your state's health department (radiation protection division) for the latest laws on radiation safety and clinic construction.
- Register your x-ray machine with the state.
- Many states are now conducting "surprise spot checks" of x-ray machines and radiographic records. Maintain film and technique logs for complete records (Figs. 4-22 and 4-23).
- If constructing a new clinic, a drawing of the layout must be sent to the state radiation protection department. This drawing indicates the location of the x-ray machine and demonstrates how the space in the room where the x-ray machine is located will be used. The use of the adjoining rooms and an estimate of the degree of traffic in these areas are determined. The radiation safety department then sends a computerized layout of wall, ceiling, and floor materials to be used in certain areas of your clinic.

RADIOGRAPHIC INTERPRETATION

Radiology is a valuable adjunctive diagnostic tool. Do not interpret radiographs without considering the history, clinical signs, physical examination findings, and laboratory data. Radiographic signs are rarely pathognomonic; therefore, a specific diagnosis is seldom possible.

History + Physical exam + Lab findings + Radiographs = Differential list

From the differential list, additional tests can be done to help formulate a definitive diagnosis.

- Successful interpretation of radiographs depends on many factors.

▼ ***Key Point*** The most important factor in the successful interpretation of radiographs is the quality of the radiographs being examined.

- At least two views at right angles to each other are needed. The use of right or left lateral radiographs is based on the preference of the individual reading the radiographs. The same holds true for VD and DV views, but be consistent.
- Maximize viewing conditions.
- Dark, quiet room.
- At least two view boxes to evaluate two views simultaneously.
- Always place the film on the view boxes such that the anatomic structures are in the same position and direction: DV/VD radiograph with the animal's right to your left; lateral radiograph with the head to your left.
- Have a shielded, high-intensity (hot) lamp available.
- Read films slowly and thoroughly.
- Always have radiology and anatomy texts nearby.
- Evaluate the radiographs using a systematic approach. Evaluate the entire film before concentrating on obvious lesions.
- Use an area method, evaluating the radiograph either peripheral to center or center to peripheral.
- Use an organ system method. Evaluate all parts of a system before examining the next system.

Radiology Log and Film Inventory

Date	Client Name	Type of Study Performed	Film Size and Number of Films			
			8×10	10×12 24×30	11×14 30×35	14×17 35×43

Figure 4-22. Film usage and inventory log.

Name _____

Clinic number _____

Species _____ Breed _____

Sex _____ Date of Birth _____

Radiology Technique Log

Date	Exam	Patient Thickness	Views Taken	mAs	kVp	Tabletop/ Grid	Film size	Screen	Notes

Figure 4-23. Radiology technique log.

- However you choose to evaluate films, be consistent from case to case.
- Knowledge of normal radiographic anatomy is essential.

Radiographic Signs

- *Radiopacity:* Various radiographic opacities are caused by the differential absorption of x-rays. The opacity of surrounding material also influences the observed opacity of a structure. The five radiopacities in decreasing order (white to black) are those of metal, bone, soft tissue (fluid), fat, and gas. Metal is the only one that is not a biologic opacity.
- *Geometry:* Size, shape, position, margination, and number.
- *Function:* Excretion (intravenous urography), motility (upper gastrointestinal), patency, and integrity. Evaluation of function often requires contrast medium and multiple films.

COMPUTED TOMOGRAPHY

Computed tomography (CT) is a cross-sectional imaging technique that allows identification of structures without the superimposition present with radiographs. Like radiographs, CT uses x-rays to produce an image. There are many different types of CT machines, but all produce a thin fan of x-rays that are directed through the patient and strike a row of radiation detectors. The amount of radiation going through a specific part of the patient, and therefore reaching the detector, is related to the density of the body part. Based on numerous views of each part and the image density of different areas, a computer is used with various algorithms to form a cross-sectional, gray-scale image.

Similar to radiographs, when looking at a CT: bone = white, air = black, fat = dark gray, and soft tissues/fluid = various shades of gray. Once the image has been acquired, post-processing parameters can be adjusted to optimize viewing of certain areas (i.e., bone, soft tissue, lung, and brain). Thus, the term *soft-tissue* or *bone window* is commonly used when evaluating CT images. Often, the same study is viewed in multiple windows for a complete evaluation. For example, a CT of the thorax would need to be viewed in a soft-tissue window (for the mediastinum), a lung window (for the pulmonary parenchyma), and a bone window (for the ribs and spine). The adjustment in a bone versus a soft-tissue window is made by changing the window width and window level. The window width defines how many shades of gray are seen over a given density of tissue (providing a long or short scale of contrast). The window level is the midpoint of the window width.

CT studies are normally performed with slices in the transverse (axial) plane through the area of interest. This information can then be used to reformat the area

of interest into a different plane (sagittal, coronal, or oblique), therefore maximizing interpretation. Common areas to use CT in veterinary medicine are the nasal cavity, middle ears, skull (bone changes or trauma), skeletal (elbows and spine), thorax, abdomen, and areas of neoplasia (for surgical or radiation planning). Magnetic resonance imaging (MRI) is considered best for soft-tissue structures, particularly the brain and spinal cord.

Advantages

- The cross-sectional image is provided without superimposition of structures, allowing more accurate detection and assessment of the extent of disease.
- CT is considered better than MRI for evaluation of bone abnormalities (MRI is best for soft tissue).

Disadvantages

- Higher cost compared with radiographs (less expensive than MRI).
- The animal must not move during the CT study, so the patient must undergo general anesthesia in most cases.

MAGNETIC RESONANCE IMAGING

MRI is a cross-sectional imaging technique that is considered excellent for imaging soft tissues. CT is still considered the best cross-sectional imaging modality when assessment of bone is required. MRI utilizes a magnetic field, radiofrequency (RF) waves, and the hydrogen protons in the patient for creation of the images. The equipment consists of a magnet, receiving coils, and hardware and software of the control station.

MRI technology utilizes a magnet to polarize hydrogen atoms in the tissues and monitor the summation of the spinning energies within living cells. When a patient is put in a strong magnet, some of the atoms become aligned with the magnetic field. If an RF pulse is sent into the patient, the vector direction of the hydrogen protons can be changed. As the atoms realign themselves with the magnetic field, they give off an RF pulse that can be detected by the receiver coil. The amount of RF signal given off and the time at which it is released are characteristic for certain tissues. This information is again processed by a computer to provide a cross-sectional image with various shades of gray. The shade of gray of a certain tissue depends on the acquisition parameters. In other words, fluid may be dark gray in one acquisition and bright white in a different acquisition. *Cortical bone and air will always be black with MRI.* The images can be acquired in any plane without reformatting.

There are different types of magnets, ranging from low- to mid- to high-field units. The unit strength is termed the *Tesla.* Low-field magnets are less than 0.5 Tesla, mid-field magnets are 0.5 to 1 Tesla, and high-field magnets are more than 1 Tesla. Although all types of magnets are utilized, the cost of the machine and the time needed to acquire the image depend on field strength. In general, high-field magnets are more expensive, but images are acquired more quickly than from low-field units.

Images are acquired using different pulse sequences (imaging acquisition parameters). These different sequences are used because the signal intensity (appearance of the image) will vary depending on primarily the water, fat, and mineral content of the area being imaged. Typical sequences are termed T1-weighted, T2-weighted, and proton density. There are a variety of fat saturation techniques and variations in the sequences that are also utilized. Contrast material is generally given to patients and the T1-weighted sequences are repeated. The contrast material is a ferromagnetic substance that enhances signal intensity on T1-weighted sequences.

Advantage

- MRI is useful for areas that cannot be evaluated by more conventional methods (radiographs or ultrasound) such as the central nervous system, particularly the brain.

Disadvantage

- Limited access
- High cost

ULTRASOUND

Ultrasound is rapidly becoming an accepted imaging modality in small animal practice. New and used equipment is available at reasonable prices, and usefulness has increased to include ophthalmic, cardiac, abdominal, and reproductive disease diagnosis. It is a safe, noninvasive diagnostic technique that provides information about the internal architecture of organs within the abdomen and thorax. Functional information can also be obtained with echocardiography. Ultrasound is not meant to replace diagnostic radiography but to complement it. Ultrasound is operator dependent. The quality of the image and the information gained are directly related to the ability of the person doing the study.

Equipment

The major components of the diagnostic ultrasound imaging system are pulser, transducer, receiver, memory, and display. Electrical pulses are produced by the pulser, and these drive the transducer. The transducer produces ultrasound pulses for each electrical

pulse it receives. The transducer also produces electrical pulses for each ultrasound pulse (reflection) it receives from tissues. The electrical pulses go to the receiver, where they are converted to information that the memory can utilize. Information from the memory drives the display, which produces an image.

Suppliers of ultrasound equipment are listed in Table 4-8.

Machines

- Questions to consider before purchasing or leasing ultrasound equipment:
- What kind of scanning will I be doing (e.g., heart, abdomen, real-time, B-mode, or M-mode)?
  - How large or small are my patients?
  - Is someone in the practice willing to accept primary responsibility for learning and doing the procedures?
  - How much money can I invest?
- There are multiple types of transducers
  - A linear array scanner produces a rectangular image and can be used to evaluate broad areas, where no bony or gas-filled structures interfere. These scanners are usually less expensive. The major drawback is the transducer contact zone, which makes intercostal and subcostal (heart, liver, biliary tract, and right kidney) imaging difficult.
  - A sector scanner produces a pie-shaped image. A smaller contact zone is used, which makes intercostal and subcostal imaging less difficult.
  - Mechanical: In a mechanical (sector) scanner, the sound wave is focused a certain distance from the transducer (focal point). The sound wave is within focus for some distance on both sides of the focal point (focal zone). Resolution is best within this fixed focal zone. The scanner contains moving parts.
  - Electronic: These are linear or sector scanners with no moving parts; therefore, they are more durable than mechanical scanners. The beam is formed by adding together many small beams from an array of small crystals. The scanner has variable (dynamic) focusing. The focal zone therefore can be placed anywhere in the image depth.
- Image display
  - M-mode (motion-mode): Documents motion, especially that of the heart (echocardiography). A thin ultrasound beam is directed into the heart, is reflected back, and then is shown on the screen as numerous moving lines. Motion is indicated along the side, and time is shown along the bottom of the screen.
  - B-mode (brightness-mode): Echoes are displayed as dots. The brightness of the dot changes with the amplitude of reflection. The larger the reflection, the brighter the dot—no reflection, black dot. The location of the dot corresponds to the location of the reflector in the body.
  - Real time: The image is continually updated during the entire examination. This permits direct observation of moving structures (e.g., heart or bowel peristalsis).

Table 4-8. ULTRASOUND COMPANIES

Company	Address	Phone Number	Website
Aloka	10 Fairfield Blvd. Wallingford, CT 06492-7502	800-442-5652	www.aloka.com
Alliance Medical U.S.A.	112 N. Bridge St. Smithville, MO 64089	888-689-3070	
Classic Medical Supply	19900 Mona Road, Ste. 105 Tequesta, FL 33469	800-722-6838	www.classicmedical.com
Hitachi Medical Corp.	1959 Summit Commerce Park Twinsburg, OH 44087	800-800-3106	www.hitachimed.com
Jorgensen Laboratories	1450 N. Van Buren Ave. Loveland, CO 80538	800-525-5614	www.jorvet.com
Medelex	732 N. Pastoria Ave. Sunnydale, CA 94086	800-644-0692	www.medelex.com
Products Group International	447 Main St. P.O. Box 1807 Lyons, CO 80504	800-336-5299	www.productsgroup.com/vet_index.html
Sound Technologies	5939 Darwin Ct, Ste. 101 Carlsbad, CA 92008	800-268-5354	www.soundvet.com
SoundVision	417 Tory Dale Ct. Roseville, CA 95747	800-957-5565	www.soundvisionweb.com
Ultrasource	5241 Plainfield Ave. NE, Ste. Q Grand Rapids, MI 49525	888-680-6989	www.ultrasource.net
Universal Medical Systems	299 Adams St. Bedford Hills, NY 10507	800-842-0607	www.u-m-s.com

- New versus used equipment
  - New equipment purchase is ideal because some companies offer training (in-house or continuing education course) and a year-long warranty with service and parts (in-house service or another unit is made available while your unit is serviced by the company). Manufacturer-reconditioned units may provide a year-long or shorter warranty. The major disadvantage of new equipment obviously is the higher cost.
  - A great deal of used equipment is available with the advent of newer technology. Older, used, outdated equipment is being replaced with new equipment based on new technology. The price of old equipment is very attractive, sometimes as low as $1000. Although initial cost is low, some significant expense may be required, including service, maintenance, transducers, and accessories. If the appropriate frequency transducers do not come with the unit (often only 2- and 3-MHz transducers come with units that were used on human patients), the cost can increase 3 to 4 times to purchase 5- and 7.5-MHz transducers.

Transducers

- Transducers are available in a variety of frequencies (2–15 MHz). Low-frequency transducers provide greater depth of penetration, but because of large wavelength, resolution is poorer. High-frequency transducers provide excellent resolution, but the beam is rapidly attenuated in tissue. They are therefore used to evaluate superficial tissues.
- Use as high a frequency transducer as possible to maximize resolution but still allow penetration to the depth needed.
- For transducer uses, see Table 4-9.

Ancillary Equipment

This may include a guided biopsy attachment for the transducer, calipers, a screen-labeling device, and an M-mode/B-mode split screen. Portability of the machine must also be considered.

Ultrasonographic Accessories

- Positioners
  - V-trough is easily constructed from wood or Plexiglas.
  - Surgical table can be formed into a V-trough.
  - Cardiac table (wood or Plexiglas) with holes so that the transducers may be brought up under the recumbent patient. Lateral recumbency causes the heart to lie against the chest wall, providing an ultrasonographic window to the heart.
- Standoff pad to place between the transducer and the skin for imaging superficial tissues.
- Coupling gel is necessary to transmit sound from the transducer through the skin.
- Numerous brands are commercially available.
- Water-soluble, hypoallergenic gel is available.

Table 4-9. TRANSDUCER SELECTION

Transducer Type	Use
7.5 MHz	Eye, feline heart and abdomen, small canine abdomen (<25 lb), testicles
5.0 MHz	Medium-size canine (<55 lb) heart and abdomen
3.5 MHz	Very large-breed canine heart and abdomen

Image Storing

There are various methods of preserving the image for inclusion in the animal's medical record:

- Polaroid camera—Heat-sensitive, thermal-paper recorder
- Multiformat camera—Can record multiple images on x-ray film
- Videotape—Images are recorded, allowing evaluation by others at a later time
- Digital images or digital video

Ultrasound Technique

- Patient preparation
  - Tranquilization is usually not required, but the patient must always be adequately restrained.
  - The most common problem in obtaining good-quality images is poor transducer skin contact. Clip the hair over the area to be imaged with a #40 blade. Hair tends to trap air, acting as a barrier to the ultrasound. Clean the exposed skin to remove dirt, oil, and debris before applying the coupling gel to help achieve the best image.
- Patient positioning
  - Most abdominal imaging is done from the ventral surface. Alternate scanning planes from lateral and lateral intercostal can be chosen to avoid gas. When gas is a problem, gentle abdominal pressure from the transducer usually displaces it.
  - The heart is imaged through the intercostal spaces, usually while the animal is in lateral recumbency.
- Ultrasound image
  - It is a two-dimensional representation of a three-dimensional object.
  - Ultrasound reflects the anatomy tomographically (cross-sectionally).
  - Ultrasound permits identification of internal organ architecture.
- Image viewing
  - Abdomen (Figs. 4-24 and 4-25)
  - Cardiac
  - Longitudinal scan: Cardiac base to the right
  - Transverse scan: Pulmonary valve (outflow tract) on the right of the screen

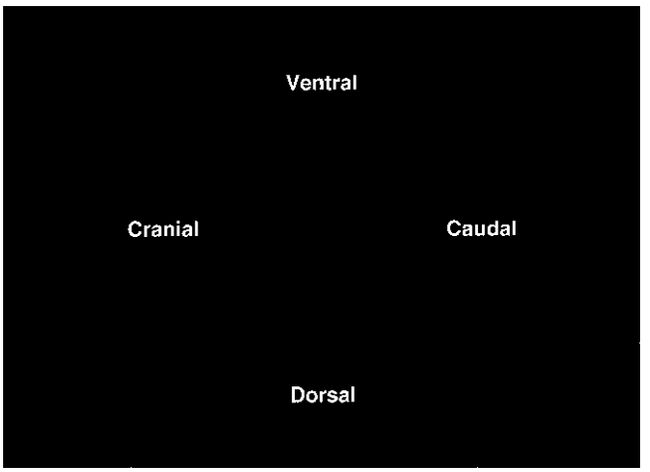

Figure 4-24. Viewing a longitudinal (sagittal) ultrasound image.

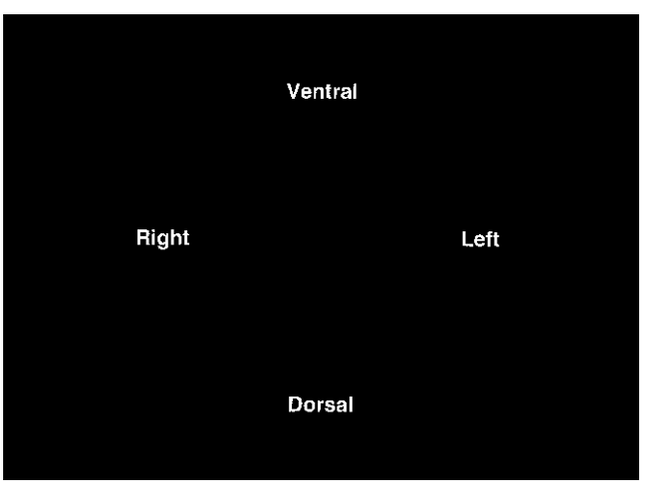

Figure 4-25. Viewing a transverse (axial) ultrasound image.

Principles of Interpretation

Ultrasound Terminology

- *Anechoic:* Area void of echoes (seen as black).
- *Hypoechoic:* Lower level of echogenicity (darker) than adjacent structures.
- *Hyperechoic:* Higher level of echogenicity (brighter) than adjacent structures.
- *Isoechoic:* Level of echogenicity similar to adjacent structures.
- *Complexly echogenic:* Area of multiple echogenicities.
- *Ultrasonographic barriers:* Highly reflective or absorptive interfaces within the body that cause an almost complete attenuation of the sound beam. Examples include bone, mineral, and air. This barrier results in an absence of echoes deep to the interface (acoustic shadow).
- *Ultrasonographic windows:* Soft-tissue organs adjacent to the body wall used to help avoid gas or bone and to facilitate deeper imaging. Examples include imaging through the spleen on the left lateral abdominal wall to identify the left kidney and imaging through the urinary bladder to identify the area where sublumbar lymph nodes are found.
- *Acoustic enhancement (through transmission):* Sound passes through an anechoic structure with little attenuation and emerges with more intensity than expected in surrounding echogenic areas. This occurrence is expected deep to fluid-filled structures (e.g., gallbladder and hepatic cyst).

Organ Echogenicity

- Rank of abdominal parenchymal organs from least to most echogenic:
  - Renal medulla
  - Renal cortex
  - Liver
  - Spleen
  - Prostate
  - Renal sinus

Ultrasound Use

See respective chapters for ultrasound use in specific diseases. See Table 4-10 for an overview of ultrasound in various organs.

Interventional Ultrasound

- Uses
  - Ultrasound-guided needle biopsy for histopathology and culture
  - Ultrasound-guided fine needle aspiration (FNA) for cytology and culture
  - Cystocentesis to obtain urine (small bladder, difficult animals)
  - Gallbladder aspiration for culture and cholangiography
  - Abscess diagnosis and drainage
  - Cyst diagnosis and drainage
  - Renal pyelocentesis
- Equipment
  - Real-time B-mode scanner
  - Transducer biopsy guide (or can be done freehand)
  - Needles, syringe, slides, culture medium, formalin containers
  - Sterile glove or transducer cover
  - Sterile ultrasound gel or alcohol
  - Sedatives, lidocaine
- Patient preparation
  - Complete an abdominal ultrasound examination.
  - Choose the site for FNA biopsy.
  - FNA: Rarely need sedation; sterile preparation of skin and transducer sterile glove cover.

Table 4-10. ULTRASOUND USES

Location	Pathology	Usefulness
Heart	Wall thickness	+++
	Wall motion	+++
	Valve morphology	+++
	Valve motion	+++
	Mass lesion	+++
	Pericardial disease	+++
Pleural space	Pleural effusion	+++
	Pleural mass	+++
Thorax (extracardiac)	Pulmonary mass*	+++
	Diaphragmatic hernia	++
	Mediastinal disease	++
Peritoneal cavity	Carcinomatosis	+
	Lymphadenopathy	+++
	Diffuse disease	+/++
	Neoplasia	++/+++
Liver	Abscess	++/+++
	Biliary disease	++/+++
	Portacaval shunt	+/++
	Nodular hyperplasia	+/++
	Diffuse disease†	+/++
Kidney	Hydronephrosis	+++
	Pyelonephritis	+/++
	Parenchymal disease‡	+/++
	Calculi	++/+++
	Perirenal disease	+++
Urinary bladder	Neoplasia	+++
	Calculi	+++
	Cystitis	+/++
Adrenal gland	Neoplasia	+++
	Hyperplasia	+/++
Gastrointestinal	Neoplasia	+++
	Enteritis	+
	Obstruction	++/+++
	Intussusception	+++
	Foreign body	++/+++
Pancreas	Neoplasia	++/+++
	Pancreatitis	+/++
	Pseudocyst	++
Reproductive tract	Ovary	+
	Testicular neoplasia	+++
	Peritesticular lesion	+++
	Pregnancy	+++
	Pyometra	+++
Prostate	Prostatitis	++
	Paraprostatic cyst	+++
	Neoplasia	++
Eye	Detached retina	+++

*If mass contacts thoracic wall.
†Lipidosis, steroid hepatopathy, suppurative hepatitis (dependent on severity of disease).
‡Glomerulonephritis, amyloidosis, ethylene glycol toxicity, renal dysplasia (dependent on severity of disease).
+++, good; ++, fair; +, poor.

- Tissue biopsy: Sedation and/or local anesthesia; general anesthesia is sometimes necessary. Surgical preparation of skin and transducer.
  - Sterile glove cover.
  - Determine packed cell volume (PCV); total plasma protein, activated clotting time, and platelet count.
  - Check prothrombin time and partial thromboplastin time.
  - Monitor patient closely for signs of internal hemorrhage for 3 to 4 hours following biopsy.
- Methods
  - Guided: Transducer has an attachable biopsy guide. Ultrasound machine has biopsy capabilities (software). Biopsy guide maintains needle in the scanning plane so that the entire procedure can be seen.
  - Directed: Image the organ or lesion of interest. Determine the location, entrance angle, and depth. Obtain biopsy or aspirate blindly without ultrasound observation. More dependent on sonographer's experience. Biopsy guide and biopsy-capable machine are not necessary.
  - Freehand: Localize biopsy site with transducer perpendicular to the skin. Place the needle with the other hand into the scanning plane to the desired depth. Biopsy procedure can be observed in real time and depends more on sonographer's experience. Biopsy guide and biopsy-capable machine are not necessary.
- Complications: Very low incidence with all procedures
  - Peritonitis
  - Hemorrhage
  - Tumor spread to local tissues

SUPPLEMENTAL READING

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Chapter 5

Fluid Therapy for Dogs and Cats

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Fluid therapy can be the single most important therapeutic measure used in seriously ill animals. Effective administration of fluids requires an understanding of fluid and electrolyte dynamics in both healthy and sick animals. An overview of a general approach to fluid therapy decision making can be found in Figure 5-1.

DECISION-MAKING CHECKLIST

Answer these questions to decide when fluid therapy is needed:

- Does the patient have a form of shock that requires fluid resuscitation?
- Does a serious deficit (or excess) of fluid or water exist?
- Is there an anticipated loss of substantial fluid volume?
- Are there serious electrolyte disturbances (excesses or deficits)?
- Is there a serious disturbance in the acid-base balance?
- Is there a serious disturbance in oncotic pressure or excessive protein loss?
- Is there an immediate need for full nutritional support with calories and protein?
- Does the patient have an anemia that may be affecting oxygen delivery?
- Does the patient have a coagulopathy?

Answer these questions in order to provide appropriate fluid therapy:

- What type(s) of fluids will be given?
- What volume of fluids will be given?
- How fast will fluids be given?
- Through what route will fluids be given?
- What, if any, supplements will be added to commercially available fluids?
- If more than one fluid type is being given, can they be administered together?
- If medications are to be administered with fluids, are they compatible?

▼ ***Key Point*** If no laboratory testing is immediately available, start correction of dehydration with isotonic-balanced electrolyte solutions.

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Figure 5-1. General decision tree for fluid therapy. (From Finco DR: A scheme for fluid therapy in the dog and cat. J Am Anim Hosp Assoc 8:178–180, 1972.)

INDICATIONS FOR FLUID THERAPY

- Most commonly for resuscitation from shock syndromes and the correction of dehydration, hypokalemia, and metabolic acidosis
- Less commonly for specific correction of other electrolyte disturbances (sodium, potassium, chloride, calcium, or magnesium), acid-base disturbances (metabolic alkalosis or mixed acid-base disorders), and disorders of oncotic pressure

- For parenteral nutrition (see Chapter 3)
- For treatment of anemia and coagulopathies (see Chapters 22 and 23)

DISTRIBUTION OF BODY WATER AND ELECTROLYTES

Water

- Total body water (TBW) represents 50% to 70% of body weight in adults. Usually 60% is arbitrarily chosen as an average figure, although cats possess slightly less water. Young animals and especially neonates possess more water (70%).
- Two-thirds of TBW is within cells, so intracellular water (ICF) represents on average about 40% of body weight.
- One-third of TBW is outside of cells, so extracellular water (ECF) represents on average about 20% of body weight. The ECF comprises both the interstitial fluid and the fluid in the intravascular space.
- The distribution of ECF between the interstitial and the intravascular spaces is about 75% to 25%, respectively. Thus the interstitial fluid comprises about 12% to 14% of the body weight, and the intravascular fluid comprises about 6% to 8% of body weight.

Electrolytes

- Sodium and chloride exist in high concentration in ECF and low concentration in ICF.
- Potassium, magnesium, and phosphorus exist in high concentration in ICF and low concentration in ECF.

MAINTENANCE REQUIREMENTS

Maintenance is defined as the volume of fluid (ml) and the amount of electrolyte (mEq or mg) that must be taken in on a daily basis to keep the volume of TBW and the electrolyte content normal. Obligatory losses of water and electrolytes occur daily as a consequence of normal metabolism. Water taken into the body in all of its forms is equal to the loss of water in the normal animal. See Figure 5-2 for specific maintenance requirements of electrolytes and water in caged dogs and cats that have normal food intake.

- Water can be taken in by drinking, combined mechanically with food, or derived from metabolism of food or tissue breakdown.
- Water is lost from the body through evaporation during breathing, from feces, and from urine.
- Obligatory loss of electrolytes occurs in fecal water and in urine, but the overall loss of electrolytes is proportionally less than the loss of water.

Figure 5-2. Maintenance fluid and electrolyte requirements for caged normal dogs and cats. (Finco after Harrison JB: J Am Anim Hosp Assoc 8:179, 1972.)

Table 5-1. DAILY FLUID REQUIREMENTS FOR HOSPITALIZED NON-ANORECTIC DOGS*

Body Weight (kg)	Total Daily Fluids (ml/day)	Total Daily Fluid per Body Weight (ml/kg/day)	Hourly Rate of Total Daily Fluid (ml/hr)
1	132	132	6
2	214	107	9
3	285	95	12
4	348	87	15
5	407	81	17
6	463	77	19
7	515	74	21
8	566	71	24
9	615	68	26
10	662	66	28
11	707	64	29
12	752	63	31
13	795	61	33
14	837	60	35
15	879	59	37
16	919	57	38
17	959	56	40
18	998	55	42
19	1037	55	43
20	1075	54	45
25	1256	50	52
30	1427	48	59
35	1590	45	66
40	1746	44	73
45	1896	42	79
50	2041	41	85
55	2182	40	91
60	2319	39	97
65	2453	38	102
70	2583	37	108
75	2710	36	113
80	2836	35	118
85	2960	35	123
90	3080	34	128
95	3200	34	133
100	3316	33	138

*Based on 104–132 × BW $(kg)^{0.75}$.

Table 5-2. DAILY FLUID REQUIREMENTS FOR HOSPITALIZED NON-ANORECTIC CATS*

Body Weight (kg)	Total Daily Fluids (ml/day)	Total Daily Fluid per Body Weight (ml/kg/day)	Hourly Rate of Total Daily Fluid (ml/hr)
1.0	80	80	3
1.5	108	72	5
2.0	135	67	6
2.5	159	64	7
3.0	182	61	8
3.5	205	58	9
4.0	226	57	9
4.5	247	55	10
5.0	268	53	11
5.5	287	52	12
6.0	307	51	13
6.5	326	50	14
7.0	344	49	14
7.5	363	48	15
8.0	380	48	16
8.5	398	47	17
9.0	416	46	17
9.5	433	46	18
10.0	450	45	19

*Based on 80 × BW $(kg)^{0.75}$.

- In most situations, the kidneys conserve sodium and excrete excess amounts of potassium, resulting in urine that typically has a much lower concentration of sodium and a higher concentration of potassium compared to plasma.
- The volume of fluid required daily varies with the size of the animal. Large patients (with low mass-to-body surface area ratios) require less fluid per kilogram on an individual basis than small animals (with high mass-to-body surface area ratios), as shown in Table 5-1 for dogs and Table 5-2 for cats.
- Maintenance volume is comprised of two subcomponents:
  - *Insensible losses* (not readily measured losses from respiratory evaporation and the passage of normal feces) are estimated at 20 ml/kg/day in normal animals but can increase during febrile states, panting, and high environmental temperatures.
  - *Sensible losses* (readily measured as urine production) are estimated to be 20 to 40 ml/kg/day in normal animals that are consuming food.
- Urine output can dramatically decrease during:
  - Acute intrinsic renal failure—Oliguria or anuria
  - Urinary obstruction—Anuria
  - Severe dehydration—Oliguria
- Urine output can dramatically increase during:
  - Polyuric renal failure
  - Post-obstructive diuresis
- Consider maintenance fluid therapy for hospitalized patients who are not eating and drinking on their own but are not dehydrated. Maintenance fluids should be low in sodium, chloride, and osmolality and high in potassium compared to normal plasma.

▼ ***Key Point*** Lactated Ringer's and 0.9% sodium chloride solutions are *not* ideal maintenance solutions because they contain too much sodium and chloride, are too high in osmolality, and do not contain enough potassium.

▼ ***Key Point*** A 0.45% sodium chloride solution (in water or in 2.5% dextrose) is more suitable as a maintenance solution due to its sodium and chloride content and its osmolality. It does not contain adequate potassium; therefore, potassium must be added.

DEHYDRATION (REPLACEMENT NEEDS)

Dehydration exists when TBW decreases to less than normal.

- Technically, dehydration refers to loss of pure water, but clinical fluid loss is usually accompanied by some loss of electrolytes.
- Acute fluid and electrolyte loss in any disease process is initially lost from intravascular fluid.
- Compensatory shifts of water and electrolytes from intracellular and interstitial compartments subsequently occur.
- The magnitude of these shifts depends on the tonicity and hydrostatic pressure of the remaining extracellular fluid. Consequently, dehydration can occur to different degrees in the various compartments.

Causes of Dehydration

Decreased Water Intake (Hypodipsia, Adipsia)

- Lack of food intake also decreases available water (water from oxidation and that physically present within the food).
- Appetite and thirst centers may be depressed in systemically ill animals.
- Accidental or deliberate deprivation of adequate water and food decrease available water.

Increased Water Loss

- Urinary (polyuria): Common
- Gastrointestinal (vomiting, diarrhea): Common
- Respiratory (fever, panting)
- Skin (burns, large wounds)
- Excessive salivation

▼ ***Key Point*** Fluid losses from the urinary and gastrointestinal tracts are the most frequent causes of dehydration.

Characterization of Dehydration (Type)

Disease processes can display a spectrum of fluid and electrolyte loss combinations, from mostly water loss (hypotonic loss) to water loss with significant quantities of accompanying electrolytes (isotonic or hypertonic). Evaluation of the tonicity and sodium concentration of the extracellular fluid in a dehydrated patient will give clues to the nature of the fluid that was lost and helps determine the type of fluid that will be given as replacement during treatment.

The type of dehydration is defined based on the serum sodium concentration at the time of dehydration.

- *Isotonic dehydration* is the type that occurs most commonly. It is defined by finding a normal serum sodium concentration (145–157 mEq/L) in the presence of dehydration. It occurs because of loss of water and electrolytes in proportion to that found in normal serum (isotonic loss).
- *Hypertonic dehydration* is the next most common type. It is defined by finding an elevated serum sodium concentration (158 mEq/L or greater) in the presence of dehydration. It occurs as a consequence of predominantly water loss or water lost in excess of solute found in normal serum (hypotonic loss).
- *Hypotonic dehydration* is the least common type. It is defined by finding a low serum sodium concentration (143 mEq/L or less) in the presence of dehydration. It theoretically occurs as solute is lost in excess of the concentration found in normal serum (hypertonic loss), but this is probably not the most significant mechanism. More likely, it is the loss of isotonic fluid and concurrent intake and absorption of hypotonic fluids (such as drinking of water) with the net dilutional effect on the remaining extracellular sodium concentration below normal.

Detection of Dehydration

Clinical tools to detect dehydration are limited in both sensitivity and specificity. There is no single test or procedure to accurately assess the magnitude of dehydration. Integration of historical findings, abnormalities on physical examination, and laboratory measurements will be necessary to quantify dehydration. Dehydration is not detectable by clinical means until approximately 5% of body weight in water has been lost. An acute loss of greater than 12% body weight in water is considered life threatening (Table 5-3).

History

History often leads the clinician to suspect dehydration and to assess its magnitude more accurately. Question

Table 5-3. PERCENTAGES OF DETECTABLE DEHYDRATION

Dehydration	Signs
<5%	Not detectable on physical exam; history is suggestive of losses; acute body weight changes
5%	Subtle loss of skin elasticity
6–8%	Mild delay of skin tent, slight prolongation of CRT, dry mucous membranes
8–10%	Obvious delay of skin tent, slight prolongation of CRT, dry mucous membranes, eyes slightly sunken in orbits
10–12%	Severe prolongation of skin tent, eyes sunken in orbits, dry mucous membranes, signs of shock likely present (prolonged CRT, tachycardia, weak pulses etc.)
>12%	Moribund

*CRT, capillary refill time.

the owner about volume of intake (adipsia, hypodipsia, polydipsia, or normal intake of water). Because volume of water intake may, in part, be a function stimulated by food intake, note also the presence or absence of anorexia. Abnormal losses of body fluid may be determined from owner responses to questions about vomiting, diarrhea, polyuria, panting, excessive salivation, or other bodily discharge. The duration of these historical signs and the magnitude of losses affect the magnitude of clinically detectable dehydration.

Physical Examination

Physical examination provides general guidelines for detecting dehydration but is subjective (see Table 5-3). Signs of listlessness and depression may occur from dehydration but may be partially attributable to the underlying disease or to concomitant electrolyte and acid-base abnormalities. As dehydration becomes more severe, decreased skin turgor, sunken eyes, dryness of mucous membranes, tachycardia, diminished capillary refill, and signs of shock may occur. An accurate and recent body weight, when available, can be used for comparison to evaluate change in body weight as an indicator of body water change.

▼ ***Key Point*** An acute increase or decrease in an animal's body weight often reflects acute gain or loss of body water. This is the most sensitive clinical tool for assessment of dehydration and rehydration. An acute loss or gain of 1 kg is the equivalent of losing or gaining 1 L of fluid.

Skin Turgor

Skin turgor assessment during physical examination is important for estimating the percentage of body weight loss due to dehydration. Skin turgor is evaluated by determining the time required for skin gently lifted from the body to return to its original position (referred to as the skin pinch or skin tent). Normal skin pliability (skin turgor) depends on hydration of the tissues in the area tested. Skin turgor is largely determined by hydration status of the interstitial tissues, although both vascular and intracellular hydration also contribute. Elastin and adipose within skin and subcutaneous tissues will also influence the apparent skin turgor. Choose skin from the trunk as a test area. Avoid dependent areas and skin from the neck. Normal skin returns immediately to its initial position when lifted a short distance and released. Dehydrated skin shows varying degrees of slow return to the original position. As dehydration progresses, the time required for the return of the skin pinch to its initial position becomes greater. The clinician assigns increasing percentages of dehydration to abnormal skin turgor of increasing severity (see Table 5-3).

Skin Turgor Artifacts

Many artifacts confuse interpretation of skin turgor.

- Skin turgor of obese animals may appear normal despite dehydration, owing to the large amounts of subcutaneous fat.
- The skin of an emaciated animal with normal hydration may fail to return to its normal position owing to a lack of subcutaneous fat and elastic tissue. Consequently, underestimating dehydration in obese animals and overestimating dehydration in emaciated animals can occur.
- Avoid testing cervical skin because redundant skin in the neck area confuses the result.
- Skin turgor changes in longhaired animals are more difficult to detect than those in shorthaired animals.
- Differences in turgor assessment can occur in the same animal in the standing versus recumbent positions.

▼ ***Key Point*** Dehydration may be as much as 5% of body weight loss in lean dogs and 10% or more in obese dogs before loss of skin turgor is detected.

Other Physical Examination Artifacts

- Dry mucous membranes may occur in animals that pant continually and in those given anticholinergics.
- Sunken eyes may be seen with catabolic diseases that decrease the soft tissue behind the globe or with atrophy of the muscles of mastication.

▼ ***Key Point*** Assessment of fluid, electrolyte, and acid-base status will frequently be in error if only the history and physical examination are available for interpretation. The more seriously ill an animal is, the more important evaluation of laboratory data becomes.

Laboratory Assessment of Dehydration

Packed Cell Volume and Total Plasma Protein

Simple laboratory testing is helpful in evaluation of intravascular hydration. Packed cell volume (PCV) recorded in percentages (SI unit: L/L) and total plasma protein (TPP) recorded in gm/dl (SI unit: g/L) can be rapidly and inexpensively determined using microhematocrit tubes and a refractometer. These two tests require only a few drops of blood and can be taken by capillary action from a 25-gauge venipuncture. TPP concentration may be more helpful in the detection of dehydration than PCV. Increased TPP and PCV provide documentation for intravascular dehydration. Simultaneous evaluation of PCV and TPP is recommended in order to minimize interpretation errors due to preexisting anemia or hypoproteinemia. (Table 5-4) Additional value is obtained when PCV and TPP are followed

Table 5-4. INTERPRETATION OF CHANGES IN PACKED CELL VOLUME (PCV) AND TOTAL PLASMA PROTEIN (TP)

PCV	Total Protein	Possible Interpretation
↑	↑	Dehydration
↑	**N** or ↓	Splenic contraction
		Erythrocytosis
		Hypoproteinemia with dehydration
N	↑	Hyperproteinemia
		Anemia with dehydration
		Hypertonic dehydration (RBC shrinkage)
↓	↑	Anemia with dehydration
		Anemia with pre-existing hyperproteinemia
↓	**N**	Non-blood-loss anemia, normal hydration
N	**N**	Normal hydration
		Dehydration, after secondary compartment shift
		Dehydration with pre-existing anemia + hypoproteinemia
		Acute hemorrhage
↓	↓	Blood loss anemia
		Overhydration

serially as increasing values identify progressive dehydration.

Urinalysis

Urinalysis (UA) is important in all cases of suspected dehydration. An elevated specific gravity (SG) represents the healthy kidneys' response to decreased perfusion. The finding of dilute urine (<1.030 SG) from a dehydrated animal immediately incriminates the kidneys as a major cause of, or contributor to, the dehydration.

Serum Biochemistry

Evaluation of serum electrolytes may help characterize the nature of the fluid that was lost.

Blood Gases

Abnormalities in blood-gas values may appear in dehydrated animals owing to net loss or gain of acid or buffer. The most common acid-base disturbance in dehydrated patients is metabolic acidosis that typically develops because of a decrease in urine production and an impaired ability of the kidneys to excrete the daily acid burden. In addition, moderate to severe forms of dehydration are accompanied by decreased perfusion to major tissue beds, resulting in a switch to anaerobic metabolism and the production of lactic acid.

▼ ***Key Point*** Animals may be severely dehydrated yet exhibit little or no change in their serum biochemical test results. Likewise, their PCV or TPP can be normal in the face of dehydration.

Anticipation of Dehydration with Specific Diseases

Dehydration should be anticipated in sick animals with certain disease syndromes known to predispose a patient to dehydration regardless of physical exam or laboratory findings. For example, a collapsed diabetic is very likely to be dehydrated, as is an animal with advanced chronic renal failure or a patient with upper intestinal obstruction.

Correction (Replacement) of Dehydration

The *volume of fluid* to be replaced is calculated as follows based on the assessed percentage of dehydration and the patient's present body weight:

- % dehydration × weight (kg) = L of fluid to be replaced.
- % dehydration × weight (lbs) × 500 = ml of fluid to be replaced.
- Alternatively, if a known recent body weight is available for comparison, replace 1 L of fluid for every kilogram (500 ml/lb) of acute body weight loss.
- The *type of fluid* that is chosen to accomplish this rehydration is based primarily on the patient's ability to tolerate a sodium challenge, the serum electrolyte (sodium, chloride, and potassium) concentrations, and the presence of any acid-base disturbances.

▼ ***Key Point*** Initial replacement with adequate fluid volume is usually more important than correcting minor electrolyte or acid-base disorders.

- Administer to the patient both the volume and the type of fluid that has been lost or continues to be lost from the body. Base the volume calculation on volumetric measurement of the losses or, more practically, from estimates. Base the type of the fluid on actual measurements from the patient or, more commonly, on the predicted biologic composition of fluid losses associated with a specific disease.

▼ ***Key Point*** Choose a fluid type or add supplements to stock fluids so that electrolytes deficient in the plasma or body are administered and those that are excessive in the plasma are avoided.

Contemporary (Ongoing) Losses

Although initiation of fluid therapy is aimed at replacing fluid lost from the patient, persistence of uncontrolled signs or untreated diseases will permit the dehydrating process to continue. Consider replacement of contemporary or ongoing losses that begin after fluid therapy has begun. Estimate gastrointestinal fluid loss (e.g., from vomiting or diarrhea). When ongoing loss is from the urinary tract, temporary urethral catheter collection may increase the accuracy of estimating the magnitude of the loss. Less invasive but feasible methods of estimation include collecting urine in a container (free

catch from dogs or litter box from cats) and measuring the volume or weight change of the container.

Volume To Be Administered

The initial volume of fluids to be administered over the first 24 hours can be calculated (Figure 5-3). The multiples of maintenance volumes method is less accurate but is acceptable for routine use in uncomplicated cases of simple dehydration (Table 5-5).

FLUID THERAPY FOR SHOCK

See Chapter 156 for a discussion of shock treatment.

TYPES OF FLUIDS AND THEIR SELECTION

Crystalloid Solutions

Crystalloid fluids contain no large macromolecules, allowing them to redistribute quickly from the vascular space to the interstitial and intracellular fluid spaces. Thus they exert their greatest effect in rehydration or replacement of prior fluid loss. Expansion of the vascular fluid space initially occurs, but with time, redistribution minimizes this effect.

Table 5-5. ALTERNATIVE METHOD TO CALCULATE MAINTENANCE + DEHYDRATION NEEDS*†

Maintenance +% Dehydration	Multiplication Factor	ml/kg/day	ml/lb/day
M + 5%	1.80	110	55
M + 6%	2.00	120	60
M + 7%	2.17	130	65
M + 8%	2.33	140	70
M + 9%	2.50	150	75
M + 10%	2.70	160	80

*Maintenance (M) is defined in this table as 60 ml/kg/day or 30 ml/lb/day.
†Contemporary fluid losses are not considered in these calculations.

Method 1

_____ml = **Deficit** = estimated % dehydration × weight (kg), or
= estimated % dehydration × weight (lb) × 500

\+

_____ml = Maintenance = **use Table 5-1 (dogs), or Table 5-2 (cats)**
= 40–60 ml/kg/day depending on patient size

_____ml **Total 24-Hour Needs**

÷ **24**

_____ml/hr **Hourly Needs**

\+

_____ml/hr **Hourly Contemporary Losses**
= accrued volume of loss observed over time ÷ hours in observation interval

_____ml/hr **Hourly Fluid Rate** (administered for same number of hours as observation interval above and then recalculated)

Method 2

_____ml = **Deficit** = estimated % dehydration × weight (kg), or
= estimated % dehydration × weight (lb) × 500

\+

_____ml = **Insensible** = 20 ml/kg/day (10 ml/lb/day)

_____ml **Total 24-Hour Needs**

÷ **24**

_____ml/hr **Hourly Needs**

\+

_____ml/hr **Hourly Sensible Losses** (measured)

_____ml/hr **Hourly Fluid Rate** (administered until sensible losses are measured again)

Figure 5-3. Two methods of calculating fluid needs.

Table 5-6. COMPOSITION OF COMMON COMMERCIAL FLUID TYPES

Fluid	Sodium (Na)	Potassium (K)	Chloride (Cl)	Calcium (Ca)	Magnesium (Mg)	Osmoles (OSM)	Bicarbonate Precursors
D5W (5% Dextrose in Water)	0	0	0	0	0	278	0
0.45% NaCl	77	0	77	0	0	154	0
0.45% NaCl + 2.5% Dextrose	77	0	77	0	0	290	0
0.9% NaCl	154	0	154	0	0	308	0
LRS	130	4	109	3	0	278	23 lactate
P-148, Norm-R	140	5	98	0	3	308	23 acetate/ 23 gluconate
3% NaCl	513	0	513	0	0	1026	0
5% NaCl	856	0	856	0	0	1712	0

Osmolality

Crystalloid fluids can be classified according to osmolality by comparison to the animal's normal serum osmolality of approximately 300 mOsm/kg. Table 5-6 lists the composition of a variety of commercially available crystalloid fluids. Osmolality of commercial fluids is largely determined by sodium and glucose concentrations. Fluids with osmolality of less than 300 mOsm/kg are hypotonic (e.g., 0.45% saline in water), those with osmolality of greater than 300 mOsm/kg are hypertonic (e.g., 5.0% dextrose added to 0.9% sodium chloride), while those with osmolality near 300 mOsm/kg are isotonic (e.g., lactated Ringer's solution, Plasma-Lyte 148, and Normosol-R). Physiologic saline (0.9% sodium chloride) at 308 mOsm/kg is also within the isotonic range. Lactated Ringer's solution is often referred to as an isotonic solution in some species, but at 272 mOsm/kg it is mildly hypotonic for small animals.

Replacement Fluids

Crystalloid fluids can also be classified by their intended function for maintenance or replacement. *Replacement fluids* must be formulated for specific electrolyte or alkali deficits. Additives such as potassium chloride, magnesium, calcium, or sodium bicarbonate will often be added to commercially available solutions, but this will vary greatly with the disease process and the patient's laboratory measurements. Replacement fluids are usually ideally suited to replenish fluid losses and resulting dehydration.

Maintenance Fluids

Maintenance fluids are polyelectrolyte solutions that differ greatly from serum as they are lower in sodium, contain additional potassium, and contain glucose. Although at administration they are isotonic, after the glucose is metabolized their effect is hypotonic. This class of fluids is intended for use in patients who have been rehydrated and are simply being maintained on IV fluids during hospitalization.

The amount of energy derived from dextrose in these fluids is insufficient to meet patient needs. Use parenteral nutrition solutions if nutritional support is necessary. The importance of introducing enteral nutrition in ill patients early in the course of hospitalization (when appropriate) also minimizes the need to switch to maintenance-type solutions after rehydration of the patient has been accomplished. Maintenance fluid and electrolyte needs can often be met with nutritional support rather than through maintenance crystalloid administration.

Patients with an intact renin-angiotensin-aldosterone axis should be able to excrete the higher sodium load present in replacement crystalloids if these fluids are utilized for a short-term basis after rehydration is accomplished. Maintenance crystalloid solutions with their lower sodium content are ideally suited for the treatment of patients with congestive heart failure or advanced liver or kidney disease, who cannot tolerate the sodium load present in replacement solutions, or of patients with true water losses and hypernatremia.

Colloid Solutions

Colloid solutions differ from crystalloids because they contain large macromolecules (natural or synthetic). These molecules, because of their size, do not readily pass through the normal endothelium, thus giving them oncotic pressure effects. This allows them to affect water movement from the interstitial fluid space. In addition, the large net negative charge carried by these molecules attracts sodium and thus water from the interstitial spaces, which contributes to their volume expanding effect. Depending on the clinical situation, colloid molecules exert most of their effect in the intravascular space, making them ideal for volume expansion of the intravascular space but less suitable for replacement of extravascular fluid losses.

Natural Colloids

Natural colloids are produced by the body, harvested from volunteer donors, and stored for later use. In small

Table 5-7. CHARACTERISTICS OF COLLOID SOLUTIONS

Fluid	Molecular Weight (MW) (KDa)	Range (KDa)	Solvent	Colloid Osmotic Pressure (COP)	Molar Subst'n
5% Albumin	69	—	—	20	—
25% Albumin	69	—	—	100	—
6% Dextran-70	70	10–80	0.9% NaCl or D5W	40	0.5
6% Hetastarch	480	10–3400	0.9% NaCl	30	0.7
10% Pentastarch	260–280	10–1000	0.9% NaCl	40	0.4–0.5
Oxypolygelatin	30–35	5.6–100	Electrolyte Solution	45–47	
Oxyglobin	200	65–500	Modified LRS	42	—

animal medicine, this group of fluids includes the blood transfusion components that possess albumin and other plasma proteins (whole blood and plasma). Indications for use of blood component therapy are covered elsewhere (see Chapter 22).

Concentrated Human Albumin

In human medicine, 5% and 25% concentrated albumin products are also manufactured. Unconcentrated natural colloids do not expand the vascular space except by the volume administered. Concentrated natural colloids will expand the vascular space by up to 5 times (25% albumin) their volume owing to their impressive oncotic pressure. Concentrated human albumin products have been used with success in small animals, but their use carries risk of adverse reaction. Most commonly, concentrated human albumin solutions are used when severe decreases (<12 mmHg) in colloid osmotic pressure (COP) are measured or the patient's albumin concentration is severely decreased (<1.5 g/L or <15 g/dl).

Synthetic Colloids

The commercially available *synthetic colloids,* which are currently finding more frequent use in small animal medicine, are all complex polysaccharide molecules. The reported average molecular weight, COP, and molar substitution ratio of these molecules are listed in Table 5-7. The complex behavior and pharmacokinetics of these molecules do not allow accurate prediction of actual biological behavior. As a result, the dose and duration of administration of these solutions vary with individual preference and the patient characteristics and requirements. In addition, availability of these products in some countries depends on national health and safety licensing.

In general, the smaller the average molecular weight, the more potent the effect on intravascular expansion. This is due generally to the higher COP of these solutions. Breakdown of synthetic molecules depends on their size (molecular size range) and the complexity of branching (molar substitution ratio). Molecules with higher size ranges and molar substitution ratios are more difficult to metabolize; thus these solutions tend to have a longer biological effect.

- Synthetic colloids should rarely be utilized by themselves but are useful adjuncts to standard crystalloid fluid therapy in several well-defined situations. Patients with hypoproteinemia and lowered oncotic pressure are likely to benefit from continuous infusions of hydroxyethyl starch (hetastarch or pentastarch) at doses of 20 ml/kg every 24 hours (cats—10–15 ml/kg every 24 hours) or more if needed. The measurement of COP is a useful monitoring tool to determine infusion rate and end point. In addition, synthetic colloid solutions may play a valuable role in shock resuscitation (see the previous section).
- Patients with diffuse vascular injury to the pulmonary vasculature and who are at risk for non-cardiogenic pulmonary edema formation may be very sensitive to sudden elevations in intravascular volume. Thus if increased oncotic pressure is desirable, continuous infusion rather than bolus administration of colloids is recommended.

▼ ***Key Point*** Use synthetic colloids with caution, and at very reduced doses, in patients with congestive heart failure and those with renal origin oliguria or anuria as rapid volume expansion could be detrimental.

- Of the three synthetic colloids mentioned in Table 5-7, dextran 70 has the most potential to interfere with hemostasis. While clotting times become elevated with use of the hydroxyethyl starches, clinically apparent hemostatic abnormalities are typically not encountered if the recommended dosages are utilized.
- Dextran 70 also carries a small risk of anaphylactic reaction, whereas reactions to administration of hydroxyethyl starches have not been reported. Consequently, and also as a result of the decreasing cost differential between dextrans and hydroxyethyl starch, dextrans are being used infrequently.

Fluids To Be Kept on Hand

▼ ***Key Point*** Clinical correction of most fluid problems can be accomplished by maintaining only a few stock solutions, usually lactated Ringer's solution, Plasma-Lyte 148, or Normosol-R; 0.9% sodium chloride; and 5% dextrose in water.

- It is convenient, although not essential, to have 2.5% dextrose with or without 0.45% sodium chloride available for use in patients who cannot tolerate high sodium loads. Mixing equal portions of 0.9% sodium chloride with 5% dextrose in water provides the same solution.
- An alkalinizing basic electrolyte solution (lactated Ringer's solution, Plasma-Lyte 148, Normosol-R) is most often chosen as a "physiologic" solution that is similar in composition to normal animal plasma with the exception of protein. It is usually the fluid of choice in the absence of laboratory data until more information about electrolyte, osmolality, and acid-base status is available from the laboratory.
- A 0.9% sodium chloride solution is chosen when "extra" sodium or chloride is needed to maintain volume expansion or for the correction of metabolic alkalosis.
- Low-sodium fluids (0.45% saline in 2.5% dextrose, Plasma-Lyte 56, Normosol-M, or 5% dextrose in water) are chosen when treating sodium-intolerant patients or patients with a water deficit (hypernatremia).
- It is useful to have one synthetic colloid solution available. Synthetic colloids should be administered in conjunction with crystalloids when there is lowered oncotic pressure or when rapid (and low volume) intravascular expansion is desired.

SUPPLEMENTATION OF PARENTERAL FLUIDS

After sodium, potassium considerations are most important. Hypokalemia is commonly encountered in hospitalized animals, particularly with prolonged anorexia and while receiving potassium-deficient fluids. Other supplements can include alkali, magnesium, dextrose, phosphate, calcium, and vitamins.

Potassium Supplementation

Potassium supplementation is usually provided as potassium chloride, although potassium phosphate is used in special situations. It is most common to use commercially available sterile vials with 2 mEq/ml of potassium for addition to fluids. Potassium supplementation to fluids is indicated if the serum potassium concentration is less than 3.5 mEq/L.

- The modified Sliding Scale of Scott (Table 5-8) recommends adding potassium chloride to maintenance fluid volumes proportional to the degree of hypokalemia; the lower the potassium concentration, the greater the amount of potassium added to the fluids. An exact number of milliequivalents for supplementation is not calculated using this method. Potassium supplementation using this scale can be started during correction of dehydration if fluids will be distributed evenly throughout the day.
- Alternatively, a fixed concentration of potassium from 20 to 30 mEq/L can be given in maintenance fluids and is particularly helpful when frequent monitoring of serum potassium is not possible. This concentration corresponds to the lower end of the Scott scale. Potassium up to 35 mEq/L can be given in subcutaneous fluids without irritation to local tissues.
- Potassium supplementation may still be indicated when its concentration is from 3.5 to 4.5 mEq/L and especially if ventricular arrhythmias are present. This can prevent the development of hypokalemia during fluid treatment and also can help replenish total body potassium deficits that are not yet reflected by the serum potassium concentration. High normal levels of potassium (>4.5 mEq/L) are helpful when managing arrhythmias because they reduce membrane hyperpolarization caused by low serum potassium levels.
- Maintenance needs for potassium in healthy dogs and cats is shown in Table 5-8 in mEq/day, but enhanced losses through the urine during fluid administration can be expected.

Table 5-8. MODIFIED SLIDING SCALE OF SCOTT

Serum K^+ (mEq/L)	mEq KCl Added to 250 ml	mEq KCl Added to 1000 ml	Maximal Infusion Rate (0.5 mEq/kg/hr)
<2.0	20	80	6 ml/kg/hr
2.1–2.5	15	60	8 ml/kg/hr
2.6–3.0	10	40	12 ml/kg/hr
3.1–3.5	7	28	18 ml/kg/hr
>3.5 < 5.0	5	20	25 ml/kg/hr

K^+, potassium; KCl, potassium chloride; mEq/L, milliequivalents per liter.

▼ ***Key Point*** Add approximately 20 to 30 mEq/L of potassium for maintenance fluids when serum potassium concentration is from 3.5 to 4.5 mEq/L.

- Caution should be used whenever potassium-enriched fluids are infused. The rate of potassium infusion is usually more important than the total number of milliequivalents. Do not exceed a rate of 0.5 mEq/kg/hr to lessen the risk for development of hyperkalemia or cardiotoxicity. Infusion of greater than 0.5 mEq/kg/hr should only occur in crisis situ-

ations and continue for no longer than 3 to 4 hours before the serum potassium is rechecked.
- Animals with alkalosis and translocation of potassium may not require vigorous potassium supplementation if the alkalosis can be corrected rapidly. Potassium can rapidly return from the cells to the ECF.
- Animals with severe emaciation have reduced lean body mass available for potassium uptake and should be less vigorously supplemented with potassium in their fluids.
- Reduced renal function and azotemia can lead to potassium retention and hyperkalemia during infusion of potassium-supplemented fluids, particularly if oliguria is present. Less vigorous potassium supplementation and careful monitoring is indicated in this situation.
- Potassium chloride supplementation increases the osmolality of fluids, particularly when high concentrations are provided. For example, potassium supplementation at 40 mEq/L increases the osmolality of the fluid by 80 mOsm/kg, 40 Osm each from potassium and chloride. If the infused potassium enters cells or is excreted, this lessens the effects of the osmolality.

▼ ***Key Point*** Although potassium supplementation is often beneficial, excessive supplementation can result in death of the patient due to hyperkalemia. Do not use potassium supplementation at higher concentrations unless serum potassium concentration can be measured on an urgent basis. Electrocardiographic monitoring may be needed during supplementation of fluids with potassium in animals that are at risk for development of hyperkalemia.

Alkali Supplementation

Addition of alkali to fluids is sometimes needed for partial correction of metabolic acidosis. It is not usually necessary or desirable to entirely correct metabolic acidosis to normal by supplementation alone.

- Add sodium bicarbonate to fluids when alkali replacement is needed quickly.
- Do not rely on bicarbonate precursors (lactate, gluconate, or acetate) in commercially available solutions to correct severe metabolic acidosis.
- Bicarbonate precursors require metabolic conversion to bicarbonate before they can contribute to correction of acidosis.
- Supplementation of bicarbonate is most safely accomplished when blood gas analysis is present to determine the contribution of the respiratory system to the acid-base disturbance.
- Bicarbonate buffers acid by combining with a proton to form carbonic acid, which is subsequently broken down by carbonic anhydrase into water and carbon dioxide ($HCO_3^- + H^+ \rightarrow H_2CO_3 \rightleftharpoons H_2O + CO_2$).
- Patients that do not have adequate ability to exhale CO_2 formed in this reaction are at risk for worsened acidosis by administration of bicarbonate.

▼ ***Key Point*** Patients with inadequate respiratory compensation for a metabolic acidosis or a mixed acidosis are at risk for worsened acidosis by administration of bicarbonate. Focus on fluid resuscitation, if they are in shock, or investigate the cause of respiratory dysfunction. Re-evaluate acid-base status using blood gas analysis prior to administration of bicarbonate.

▼ ***Key Point*** Do not add sodium bicarbonate to fluids that contain calcium (lactated Ringer's solution), as calcium precipitates may occur.

- Calculate alkali replacement from either the bicarbonate value reported on a blood gas analysis or the total CO_2 value on a serum biochemical profile. Total CO_2 (mEq/L) can be substituted for bicarbonate in these calculations since the difference is usually only 1 to 2 mEq/L.

Methods for Calculating Bicarbonate Dose

- Assume that normal HCO_3 is 24 mEq/L.
- Subtract measured patient HCO_3 from 24, which is equal to the HCO_3 deficit in mEq/L.

Method A

- HCO_3 deficit × 0.6 × body weight (kg) = "missing" mEq bicarbonate from TBW at the time of sampling
- Administer total calculated replacement mEq over 8 to 12 hours or longer; it may take as long as 18 hours for administered bicarbonate to equilibrate inside cells.

Method B

- HCO_3 deficit × 0.3 × body weight (kg) = "missing" mEq bicarbonate from ECF at the time of sampling
- Use this formula when multiple injections of bicarbonate are anticipated, ongoing production of acid or loss of alkali is anticipated, and access to multiple HCO_3 measurements is possible. Without access to blood gas analysis or total CO_2, it is difficult to know with any certainty the magnitude of need.

Empirical Method

If the clinical diagnosis and suspicion for metabolic acidosis is high, bicarbonate may be administered empirically.

- Estimate of mild acidosis: Give 3 mEq/kg bicarbonate over 24 hours

- Estimate of moderate acidosis: Give 6 mEq/kg bicarbonate over 24 hours
- Estimate of severe acidosis: Give 9 mEq/kg bicarbonate over 24 hours
- In crisis situations requiring bicarbonate, administer 0.5 to 1.0 mEq/kg of sodium bicarbonate over 5 to 10 minutes and reevaluate. Electrocardiographic monitoring is recommended during the injection if it is available.

Precautions for Bicarbonate

- Remember that along with bicarbonate, sodium is administered, which can result in hypernatremia, hyperosmolality, hypertension, overhydration, and volume overload if the administered sodium is not excreted.
- Overtreatment with alkali can result in alkalosis, paradoxical cerebrospinal fluid acidosis, shifts of ionized calcium, a shift of the oxyhemoglobin dissociation curve (decreasing oxygen unloading), and seizures.

Magnesium Supplementation

Magnesium has recently emerged as an important but seldom considered ion. It is a metabolic cofactor in hundreds of metabolic functions, most importantly as a cofactor in the sodium-potassium pump (NaK-ATPase). Deficiencies in magnesium can thus lead to potassium loss from the body. Hypokalemia and hypomagnesemia are often found concurrently in many ill or dehydrated patients. Magnesium is lost alongside other cations when urinary and gastrointestinal losses result in dehydration. Inadequate intake in anorexic patients will exacerbate hypomagnesemia.

- As magnesium is primarily an intracellular ion, serum measurements are often not reflective of total body stores. It is generally thought that low total serum magnesium is reflective of low total body magnesium status, but this is often a late finding. Ion-specific electrodes are more sensitive for detecting hypomagnesemia but are not in common use.

▼ ***Key Point*** In patients with documented hypokalemia, and especially hypokalemia that seems to be resistant to supplementation efforts, magnesium supplementation is indicated. In addition, patients with diabetic ketoacidosis, congestive heart failure, and ventricular arrhythmias (and concurrent hypokalemia) are likely to benefit from magnesium supplementation.

- Magnesium sulfate and magnesium chloride are the commonly available sources of magnesium. Magnesium sulfate is preferred to prevent excessive chloride administration. The dosage of magnesium sulfate supplementation is 2.5 to 5 mg/kg/hour and can be added to most commercially available fluid types. A loading dose of 30 mg/kg of magnesium sulfate can also be administered over 20 minutes to 1 hour prior to beginning the lower rate of hourly supplementation.
- Magnesium supplementation can be extremely helpful in achieving and maintaining high normal levels of potassium when treating cardiac arrhythmias.
- Do not use magnesium supplementation in oliguric patients as this is the primary route of excretion of excessive amounts.

Dextrose Supplementation

If supplementation with dextrose is necessary, use varying amounts of 50% dextrose to achieve the desired concentration or the percentage of dextrose in the final solution.

- To increase the dextrose concentration by 2.5%, add 25 g of dextrose or 50 ml of 50% dextrose to 1000 ml of stock solution (e.g., lactated Ringers solution). Long-term supplementation of dextrose through a peripheral vein should not exceed concentrations over 5%, as the hypertonicity can induce significant phlebitis.
- Indications include hypoglycemia due to sepsis, insulin overdosing, insulinoma, and liver disease. Dextrose supplementation at greater than 10% to 15% is necessary to provide sufficient calories for anorectic animals.

Vitamin Supplementation

The benefits of supplemental vitamins during parenteral fluid therapy in cats or dogs are plausible but not proven. Water-soluble vitamins can be conservatively added to parenteral fluids without known harm and may replenish rapidly depleted stores.

- Dogs or cats in polyuric renal failure may benefit from additional water-soluble vitamins in parenteral fluids because of urinary losses of these vitamins.
- Thiamine deficiency can be of clinical concern in cats and can develop during anorexia while on fluids, as the storage period of thiamine is short.
  - Initial signs of thiamine deficiency include anorexia, vomiting, and ataxia that can progress to dilated pupils and tonic ventriflexion of the neck, which may be confused with seizures. True seizures can also occur. Death usually occurs within 24 hours of onset of convulsions if the deficiency is not treated.
  - It is common practice to add 0.5 to 1.0 ml of water-soluble multi-vitamins to each liter of fluids to provide needed vitamins and to prevent thiamin deficiency.
  - B-complex vitamins are light sensitive, so the IV fluid bag should be covered to prevent degeneration. Fluids with B-complex vitamins added should

also be replaced every 24 to 48 hours to maximize the potential benefits of vitamin supplementation.

Calcium Supplementation

- Calcium gluconate and calcium chloride can be supplemented in replacement and maintenance fluids for the correction of symptomatic hypocalcemia. Many small animals with low serum albumin will have low total serum calcium concentrations. Most of these will not require calcium supplementation as the ionized calcium is not usually as depressed as the total calcium. When ionized calcium is substantially decreased, supplementation with calcium salts may be required.
- The percentage of calcium contained varies widely by the specific calcium salt. There is no difference in effectiveness of IV calcium salts to correct hypocalcemia when the dose is based on elemental calcium content. Calcium gluconate is often chosen as the calcium salt of choice because it is non-irritating if the solution is injected outside of a vessel. In contrast, calcium chloride is extremely irritating to tissues but provides more elemental calcium in each milliliter of solution.

Acute Infusion for Hypocalcemic Tetany

- Tetany or seizures due to hypocalcemia require treatment with IV calcium salts. Calcium is administered to effect at 5 to 15 mg/kg of elemental calcium (0.5–1.5 ml/kg of 10% calcium gluconate) over a 10- to 20-minute period.
- Monitor heart rate and electrocardiogram during acute infusion of calcium salts. Bradycardia may signal the onset of cardiotoxicity from an excessively rapid infusion rate of calcium.

▼ ***Key Point*** Treat severe symptoms of ionized hypocalcemia (tetany and seizures) by administering 0.5 to 1.5 ml/kg of 10% calcium gluconate intravenously over 10 to 20 minutes while observing a continuous electrocardiogram.

Continuous Intravenous Infusion

- Continuous IV infusion of calcium is recommended from 60 to 90 mg/kg/day of elemental calcium (2.5–3.75 mg/kg/hour) until oral medications provide control of serum calcium. Give initial doses in the higher range to patients with more severe hypocalcemia and decrease the dose according to calcium level achieved. Reduce the dose of IV calcium as oral calcium salts and vitamin D metabolites become more effective.
- Ten milliliters of 10% calcium gluconate provides 93 mg of elemental calcium. A convenient method to infuse calcium is available when IV fluids are given at a maintenance volume of 60 ml/kg/day (2.5 ml/kg/hour). Approximately 1, 2, or 3 mg/kg/hour of elemental calcium are provided by adding 10, 20, or 30 ml of 10% calcium gluconate, respectively, to each 250-ml bag of fluids.
- Do not add calcium salts to fluid therapy preparations that contain lactate, acetate, bicarbonate, or phosphates, since calcium salt precipitates can occur.
- Alkalinizing fluid therapy containing sodium bicarbonate decreases ionized calcium and may expose clinical signs of hypocalcemia in patients with borderline hypocalcemia; consequently, it should not be used.

Subcutaneous Injection

Never give calcium salts subcutaneously as severe skin necrosis and calcification have been observed in some patients, even when the calcium salts have been diluted prior to subcutaneous administration.

Phosphorus Supplementation

Hypophosphatemia is present when the serum concentration is less than 0.8 mmol/L (2.5 mg/dl). Mild hypophosphatemia (0.65–0.80 mmol/L or 2.0–2.5 mg/dl) is common and often transient. Hypophosphatemia often resolves quickly during therapy directed at the underlying cause. Severe hypophosphatemia (<0.48 mmol/L or <1.5 mg/dl) is uncommon but can be life threatening, particularly when less than 0.32 mmol/L (1.0 mg/dl). Use supplementation with phosphate salts when the serum phosphorus concentration is very low (<0.48 mmol/L or <1.5 mg/dl).

▼ ***Key Point*** Clinically significant hypophosphatemia that requires phosphate replacement therapy is most likely to be encountered in patients with diabetic ketoacidosis 12 to 48 hours after initiation of insulin therapy or in patients in whom enteral nutrition is initiated after prolonged periods of anorexia.

When necessary, sodium phosphate or potassium phosphate can be supplemented to replacement and maintenance fluids for the correction of symptomatic or severe hypophosphatemia.

- Do not add phosphate salts to fluids that contain calcium.
- Treat only if hypophosphatemia is severe and a concurrent likely cause is present.
- The dosage for phosphate supplementation is 0.01 to 0.03 mmol/kg/hour, intravenously, for 3 to 6 hours.
- Severe cases may require prolonged supplementation or higher dosages of phosphate (0.06–0.12 mmol/kg/hour intravenously).
- Continue supplementation only until the serum phosphorus concentration is greater than 0.65 mmol/L (2.0 mg/dl).

- Avoid oversupplementation that can cause hyperphosphatemia, hypocalcemia, tetany or seizures, soft-tissue mineralization, hyperkalemia (if using potassium phosphate), and hypernatremia (if using sodium phosphate).

GENERAL GUIDELINES FOR FLUID SELECTION

Serum Sodium Level as a Guide

Normal Sodium

If the serum sodium concentration is normal, the animal has isotonic dehydration and needs replacement fluids that are nearly normal in serum sodium concentration and osmolality. Lactated Ringer's solution, Plasma-Lyte 148, Normosol-R, or 0.9% sodium chloride would be appropriate selections.

Hypernatremia

If the serum sodium concentration is elevated, the animal has hypertonic dehydration and needs more water than salt for replacement (hypotonic fluid). Choose fluids that are effectively hypotonic (5% dextrose in water, 0.45% NaCl in 2.5% dextrose). Dextrose solutions in 2.5% to 5% concentration are considered effectively hypotonic because of rapid dextrose metabolism removing its contribution to osmolality. The magnitude of the elevation in serum sodium and the patient's clinical status will determine whether dextrose in water or dextrose in some concentration of saline should be administered. Lowering of severe hyperosmolality and hypernatremia excessively rapidly can be detrimental, particularly to the brain. A general guideline is to allow sodium concentration to fall no faster than 0.5 mEq/L/hour or no more than 12 mEq/L in 24 hours. Pure water without some electrolyte or glucose to add osmolality is not given as this can cause severe problems with hemolysis and rapidly decreased serum osmolality.

Hyponatremia

If the serum sodium concentration is low, the animal has hypotonic dehydration and needs additional sodium relative to water. Hypertonic fluid infusion is theoretically indicated, but clinically is not chosen unless the hyponatremia and hyposmolality are very severe and the patient is symptomatic. Isotonic fluids are usually chosen for replacement since the kidneys should excrete unnecessary water and reclaim needed sodium.

Other Laboratory Abnormalities

Further selection of fluid type requires laboratory measurement of albumin, total protein, potassium, chloride, magnesium, calcium, phosphorus, and blood gases. When serum concentration of an electrolyte is elevated, choose a fluid for infusion that is devoid or low in that electrolyte concentration. When serum concentration of an electrolyte is low, choose a fluid for infusion that contains high concentration of that electrolyte or provide supplementation of that electrolyte to the fluid. In some instances, supplemental electrolyte can be given to prevent deficits (as previously mentioned for potassium). Evaluate final osmolality of fluids for infusion following supplementation of base solutions to ensure that they are appropriate, as supplementation of base solutions often results in unappreciated hyperosmolality.

Selection of fluid type can be confusing when clinical problems dictate that disparate fluid types should be chosen; for example, use an acidifying solution (0.9% sodium chloride) in a patient that is severely acidemic, because high sodium content of this fluid is desirable. Thus in these situations, identify the most severe problem and choose the initial fluid to address this issue. Subsequently, as resolution of the most urgent problem is accomplished, correct secondary abnormalities. Fluid therapy is often dynamic, and changes of fluid type and additives are frequently needed over the course of therapy.

Preservatives

▼ ***Key Point*** Never use fluids containing preservatives of any kind for administration to cats, puppies, or small dogs because of the likelihood of severe toxic reactions.

- Benzoic acid derivatives are commonly used in fluids for their antibacterial and antifungal effects. Cats are extremely susceptible to toxic effects from these compounds even at low doses. Benzyl alcohol at 0.9% is commonly added to multiple dose vials of sodium chloride for injection.
- Clinical signs of toxicity are mostly neurological, and early signs include changes in behavior, apprehension, aggression, hyperexcitability (light and sound), salivation, marked ataxia, fasciculations of the muscles of the head and ears, widely dilated nonresponsive pupils, convulsions, coma, and death.

ROUTES OF ADMINISTRATION FOR PARENTERAL FLUIDS

The route of fluid therapy depends on the nature of the clinical disorder, its severity, its onset (acute versus chronic), the nature and magnitude of ongoing losses, and the composition of fluids to be given. The availability of personnel and equipment required for monitoring during IV therapy also influences decisions about the appropriate route of administration.

Subcutaneous Route

- Subcutaneous administration of fluids is common in dogs and cats; choose isotonic or mildly hypotonic fluids to enhance absorption.
- Subcutaneous infusions may be given under gravitational forces through IV administration tubing or by direct injection from a large-volume hypodermic syringe.

▼ ***Key Point*** Do not give 5% dextrose in water as an isotonic solution subcutaneously in cases of severe dehydration. Delayed absorption, with consequent equilibration of ECF electrolytes into the pocket of pooled, unabsorbed subcutaneous fluid, may occur.

- Absorption of subcutaneous fluid is unreliable in conditions characterized by peripheral vasoconstriction (e.g., shock, severe dehydration, or hypothermia). Never rely on this route for the emergency replacement of fluid in critically ill or severely dehydrated patients. This route may correct minimal dehydration or prevent dehydration in the anorexic animal.
- The volume of fluid that can be administered subcutaneously is limited by the patient's skin elasticity. Animals differ in their abilities to tolerate the infused volume comfortably.
- Choose the site of the subcutaneous infusions somewhere on the trunk so that the fluid does not gravitate into the limbs. Avoid areas with surgical wounds because fluid may drain from the incision or dissect through the healing tissues.

Intravenous Route

Give hypotonic, isotonic, and hypertonic fluids by the IV route as the need arises. Large volumes of fluid are more readily administered to a patient using the IV route. Rapid administration of fluid should always be administered intravenously.

▼ ***Key Point*** Use IV fluid administration whenever accurate delivery of fluid volume and potent pharmacotherapeutic agents are required.

Vein Selection

- The jugular vein and cephalic vein are most commonly chosen for indwelling IV catheterization. The lateral saphenous and femoral veins also may be used.
- Use the jugular vein in cats and small dogs to prevent occlusion of fluid flow when the animal's limb is bent.
- Use the jugular vein in serious diseases regardless of patient size. It is also easier to maintain aseptically if the patient has diarrhea.
  - Advantages of using the jugular vein include the ability to measure central venous pressure (CVP), the ability to administer hypertonic solutions and other irritating drugs because of greater dilutional effects from greater blood flow, and the ease of obtaining serial blood samples from the IV line (use care to avoid clotting within the line).
  - The prime disadvantage of peripheral veins is that limb position often changes the rate of fluid infusion owing to partial or complete occlusion of the indwelling catheter when gravity flow is used. When fluid pumps are used, this effect is minimized.

Catheter Selection

- In cats and small dogs use 20- to 22-gauge catheters; in medium and large dogs use 14- to 20-gauge catheters. Use short, larger-bore catheters, or catheterize two veins in emergency situations requiring rapid fluid administration. Clinician preference determines the type of catheter used.

Intravenous Catheter Care

- Always perform aseptic catheter placement using wide clipping of hair over the vein and a standard surgical scrub. After securing the catheter in the vein, place a gauze sponge with an antimicrobial cream over the puncture site.
- Catheter complications include thrombophlebitis, thromboembolism, bacteremia, bacterial endocarditis, and catheter-fragment foreign body.
- To minimize problems:
  - Place the catheter aseptically and keep the catheter site clean.
  - Check the catheter site once to twice daily. If no redness, swelling, pain, or patient discomfort when injecting are present, the catheter may be left in place. Routine catheter changes at 72 hours are no longer recommended.
  - Monitor the patient for fever, leukocytosis, and heart murmurs.
  - Ensure that all injections made into the IV catheter or lines are done aseptically.
  - Ensure that the IV line remains a closed and aseptic system. Do not disconnect the IV line unless absolutely necessary, and ensure aseptic technique is followed when changing IV fluid bags.
  - When the catheter is not in use, flush regularly to prevent clotting.

Intraperitoneal Route

- Severely anemic puppies and kittens may be transfused by this route (see Chapter 22 for details of blood transfusion).
- This route may be considered for rewarming very hypothermic animals.
- Use isotonic to mildly hypotonic fluids for rehydration (an IV route is preferred when possible).

Intraosseous Route

- Provides rapid access to circulation when venous catheterization is not successful or possible.
- Consider using in puppies and kittens and in emergency situations where immediate IV access is difficult.
- Blood and crystalloid solutions can be infused safely.
- Catheterize the bone marrow of the femur, tibia, or humerus with a bone marrow or spinal needle and secure it in place (see Chapter 3 for technique).

RATE OF FLUID INFUSION

The rate of fluid administration depends on the extent and rapidity of the fluid loss, as well as on the composition of the fluid to be infused. Rapid or extensive fluid losses demand rapid replacement. In chronic disorders, it is not always necessary to replace the dehydration deficit rapidly. Patients displaying symptoms of shock require a fluid resuscitation phase prior to correction of any dehydration that is present. For simple dehydration with no signs of shock, there are many acceptable methods to rehydrate the patient. Some clinicians prefer to calculate the dehydration deficit, add it to the daily maintenance requirements, and distribute this fluid load over 24 hours. Others prefer to replace part of the dehydration deficit over the first few hours (referred to as "front-end loading"). Deficit replacement of 75% to 80% on the first day and the remaining 25% deficit on the second day is recommended by some clinicians.

- Measure urine output during rapid fluid infusion as a guide to organ perfusion. With persistent oliguria, be careful about maximal fluid infusion and monitor CVP response to fluid challenge to avoid overhydration.

24-Hour Infusion Rate

- In less critical conditions, distribute fluids evenly throughout the day. Physiologically, this may be advantageous because it allows more time for adequate equilibration of water and electrolytes between the body compartments. Ideally, a constant or continuous infusion of IV fluids over a 24-hour period would accomplish this. This ideal situation may not be possible if very small volumes of fluid are being infused or if 24-hour monitoring of the IV lines is unavailable.
- Front-end loading of fluids to correct dehydration can be given over a 4- to 8-hour period when an animal's clinical condition dictates more rapid correction of dehydration. Maintenance and contemporary losses can then be infused evenly over the remaining hours of the day. If the intrinsic ability of the patient's tissues to absorb fluid is less than the volume of the fluid being administered, the difference will most likely be lost in the urine. In this situation, increased urine production is a misleading indicator of hydration status of the patient, so other physical examination and laboratory parameters as well as serial monitoring of the patient's weight must be considered.
- If fluid infusion can be observed for only part of the day, give the 24-hour needs over the number of hours that personnel can watch the drip, then flush the catheter with heparinized saline to maintain patency until infusion resumes. If severe dehydration has been corrected, give additional fluids subcutaneously until the IV drip can be restarted the next day.

Drip Rate

- The rate of infusion for the total 24-hour volume of fluid should be specified as to the required number of milliliters per hour and the number of drops per minute to ensure accurate delivery of prescribed fluids.
- IV administration sets are available in standard "macrodrip" volumes of 10, 15, or 20 drops/ml. Pediatric administration sets also are available in the "microdrip" volume of 60 drops/ml. Patient size and volume of fluid to be infused determine the choice between the microdrip and the macrodrip systems.
- The microdrip administration set is most suitable for cats and small dogs because it allows easier quantitation of small volumes of fluid for infusion.
- For small dogs and cats, consider the use of a Buretrol (Baxter Healthcare) or a similar device to accurately premeasure the volume of fluid to be administered. Fluids from the reservoir bag are then periodically used to reload the Buretrol device. The use of such a device minimizes the chances of overhydration because it allows controlled and accurate delivery of small volumes.
- Commercially available devices (Control-A-Flow; Baxter Healthcare) can also be used to limit gravitational flow to relatively accurate flow rates.
- Once the drip set has been adjusted to the desired rate, mark the IV bottle or bag with adhesive tape to monitor the hourly volume of fluids received. Disruptions of flow can be detected in this way to ensure that the desired volume of fluid is being administered over the desired timeframe.
- The rate of IV fluid infusion is important when considering fluids that have been supplemented with any additive or medication. Accuracy is enhanced by using infusion pumps or syringe pumps (see below).

"Ins and Outs"

- In hydrated animals with either severe oliguria or polyuria, measurement of urine output may be helpful for accurately matching the needs of the animal to the fluid therapy ("ins and outs"). Without

this technique, there is a tendency to overestimate the actual fluid needs in an oliguric animal (resulting in overhydration) and to underestimate the fluid needs in an animal undergoing extensive diuresis (resulting in failure to correct dehydration).

- Choose an observation interval (every 1–8 hours) and begin quantifying urine production. At the end of the first interval, a new fluid rate is calculated that will include the insensible losses for the upcoming interval (22 ml/kg divided by the observation interval) and the measured sensible (urine) losses from the previous observation interval. For example, a 10-kg dog will be placed on ins and outs every 6 hours. In the previous 6-hour period, 120 ml of urine was produced. The fluid amount to be given over the next 6 hours will be 120 cc plus insensible loss ($\{10 \times 22 = 37/6\}$ ml) to equal 157 ml of fluid.
- This type of close attention to fluid volume administration is of benefit in the initial management of critically ill animals, particularly when CVP and renal status are uncertain.
- Remember that with this technique the volume of fluid administered (ins) will exceed the volume of fluid (urine) that is measured (outs) by the daily insensible needs. If the patient is rehydrated, your calculations are accurate, and no other source of fluid loss exists, then the patient's weight should remain static.

Infusion Pumps

Infusion pumps provide an extremely accurate means of administering IV fluids.

- Enter ml/hr or drops/min depending on the type of machine.
- Most are equipped with an alarm system that indicates if fluid flow is interrupted.
- New pumps are expensive (refurbished, used machines may be surprisingly affordable).
- These pumps are especially useful for small dogs, cats, and animals receiving fluids supplemented with potassium or other agents.

Syringe Pumps

Syringe pumps provide an extremely accurate method of administering small volumes of medication or fluid into a patient's IV drip or directly into the IV catheter.

- Sophisticated machines exist that allow complex dosages (such as µg/kg/min) to be easily programmed.
- Drug administration errors because of mathematical error can thus be eliminated, and rapid changes to new dosing rates are easily and accurately accomplished.
- Most machines allow extremely accurate dosing of very small volumes (0.1–0.01 ml).
- Refurbished machines are becoming more widely available, making them cost effective for many practices.

MONITORING EFFICACY OF FLUID THERAPY

Perform a physical examination several times daily during the initial fluid management to document rehydration, prevent overhydration, and detect contemporary fluid loss. The indicators of successful fluid therapy are normalization of skin turgor, moistening of mucous membranes, strengthening of pulses, increased perfusion (decreased refill time), and increased alertness. Table 5-9 provides guidelines to assess the success of fluid therapy, and Table 5-10 lists possible reasons dehydration has not been adequately corrected.

Body Weight

- Increased body weight should occur during successful rehydration. An acute gain or loss of 1 kg suggests an increase or decrease of 1000 ml of body water (1 lb = 500 ml).

Table 5-9. DATA BASES TO EVALUATE EFFICACY OF FLUID THERAPY

	Minimum (Mildly Ill/Dehydrated)	Extended (Severe Dehydration/Collapse)	Advanced (Shock/Oliguria/ Heart Failure)
Body Weight	✓	✓	✓
PCV/TPP	✓	✓	✓
Urine Specific Gravity	✓	✓	✓
Electrolytes (Na, K, Cl)		✓	✓
Bicarbonate (Total CO_2)		✓	✓
Electrocardiogram		✓	✓
Blood Gas (ven ± art)			✓
Lactate			✓
Central Venous Pressure (CVP)			✓
Ionized Calcium (Ca)/Magnesium (Mg)			✓

Na, Sodium; K, potassium; Cl, Chloride.

Table 5-10. REASONS FOR FAILURE TO CORRECT DEHYDRATION ADEQUATELY

1. Calculation and mathematical error
2. Error in assessment of initial degree of dehydration
3. Larger contemporary losses than expected
4. Too-rapid infusion resulting in diuresis and loss of fluid from body
5. Mechanical catheter problems, calculated volume not infused
6. Increased sensible loss not appreciated (fever, panting)
7. Increased sensible loss not appreciated (polyuria)

- An anorexic animal, however, loses 0.1 to 0.3 kg of its body weight per day per 1000 calories of daily caloric requirement owing to tissue catabolism. Measure and record body weight accurately at least once daily.

Packed Cell Volume and Plasma Protein

- Follow PCV and TPP serially during fluid therapy. Decreases in both PCV and TPP suggest successful intravascular rehydration (see Table 5-4).

Central Venous Pressure

- In difficult cases (particularly those with renal or heart failure), monitor CVP to minimize chances of overloading the heart and causing pulmonary edema when administering fluids rapidly.
- Monitor CVP with a jugular catheter, the tip of which is in the cranial vena cava or near the right atrium. Normal CVP is 0 to 5 cm H_2O.
- A sudden increase in CVP during fluid therapy indicates the inability of the cardiovascular system to accommodate the rate of fluid administration. Reduce the rate of administration accordingly.
- A persistent increase in CVP following administration of a fluid challenge indicates adequate volume expansion of the patient. Patients with mild or moderate degrees of hypovolemia will have a rapid return to baseline CVP following fluid challenge.
- Signs of overhydration, unfortunately, can still occur even without a change in CVP.

Electrolyte and Acid-Base Status

- Closely monitor all animals receiving fluid therapy. Determine serial serum electrolyte values and acid-base status in severely dehydrated animals receiving fluid therapy at least every 12 to 24 hours. Ideally, animals that had serum electrolyte deficiency or excess or severe acid-base disturbances will show improvement toward normal values after appropriate therapy.
- Follow electrolyte determinations and acid-base status in those cases that had initially normal values to detect the possible consequences of volume expansion and changes in the underlying disease process.

▼ ***Key Point*** Successful fluid therapy ultimately depends on the clinician's ability to detect and correct the underlying cause for the loss of fluid and loss or retention of electrolytes. Identifying and stopping ongoing fluid losses is particularly important.

OVERHYDRATION

Overhydration rarely occurs as a spontaneous disorder; it usually is iatrogenic following fluid therapy. Inability to excrete free water, which can occur in a variety of renal and liver diseases and in congestive heart failure, predisposes a patient to overhydration.

Clinical Signs

- Body weight increases above and beyond that expected to accomplish rehydration.
- CVP is persistently elevated or increases suddenly.
- Increased volume and/or frequency of urinations may be noticed as the patient attempts to rid the body of excess water, but the volume excreted may not be sufficient to prevent overhydration.
- A gelatinous feel to the subcutaneous tissues may precede the development of obvious peripheral edema.
- Pulmonary edema, manifested as lung crackles and tachypnea, may be detected.
- Vomiting, diarrhea, serous discharge from the nose and eyes, and chemosis can develop.
- Venous overdistension may also be noted.

Laboratory and Radiographic Findings

- Progressive decreases in PCV and total protein may be measured (see Table 5-4).
- Radiographs may reveal increased lung density compatible with pulmonary edema; cardiac enlargement or pulmonary venous distension may be noted if congestive heart failure is imminent.

Treatment

- Immediate correction may be difficult when renal or cardiac function is impaired.
- Discontinue all IV infusions, and give furosemide from 2 to 4 mg/kg IV. Give another dose of furosemide (4–8 mg/kg IV) if no diuresis is seen within 15 minutes.
- Morphine may be considered as a treatment to increase compliance of pulmonary vessels.

Chapter 6

Pain Management in the Surgical Patient

Richard M. Bednarski

Like anesthesia, the perioperative assessment of pain and the provision of analgesia have become an integral part of companion animal medicine. Regardless of the type of medical or surgical procedure performed, pain management must be considered a part of the perianesthetic drug plan.

▼ ***Key Point*** The keys to developing a successful perianesthetic analgesia plan include (1) understanding basic concepts of pain transmission and modulation; (2) recognizing and differentiating the signs of pain; (3) gaining a working knowledge of the pharmacology of analgesic drugs and techniques associated with their use; and (4) knowing how to integrate these drugs and techniques into a perianesthetic plan.

A multimodal approach to analgesia is generally more effective than reliance on a single drug or technique. One or multiple sites in the anatomic pain pathway are targeted. A multimodal approach involves choosing more than one drug or technique from the available categories of analgesic drugs. These are opioid analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs), local anesthetics, alpha-2 agonists, and dissociative N-methyl-D-aspartate (NMDA) receptor antagonists. Several texts describe in detail the pharmacology and techniques associated with these drugs (see "Supplemental Reading"). This chapter suggests some perioperative analgesic protocols and techniques that can be used commonly in small animal practice.

DEFINITIONS

- *Pain:* Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage. The inability to communicate in no way negates the possibility that an individual is experiencing pain and is in need of appropriate pain relieving treatment.
- *Nociceptor:* Specialized sensory nerve endings that respond to the mediators of tissue damage. These mediators are mechanical, thermal, and chemical.
- *Nociception:* The sensing and ascending neural transmission of a noxious stimulus. Nociception that is centrally processed can be interpreted as pain.
- *Somatic pain:* Pain caused by activation of nociceptors within the skin and musculoskeletal tissue. This is usually described in people as sharp and localized when associated with superficial tissue and dull or aching when associated with deeper tissues.
- *Visceral pain:* Pain that is poorly localized and described by people as a pressure-like or squeezing sensation. It is associated with activation of nociceptors within a body cavity.
- *Neuropathic pain:* Pain related to nervous system damage. This is usually described in people as a burning sensation.
- *Acute versus chronic pain:* Acute pain is the normal response to an inciting stimulus, such as the pain resulting from surgical stimulation, trauma, or thermal injury. Perioperative analgesic plans are formulated to minimize this type of pain. Chronic pain persists longer than that associated with healing of an acute condition or that associated with a malingering condition. Perianesthetic analgesia can temporarily alleviate this type of pain.
- *Preemptive analgesia:* The concept of administering analgesic drugs to prevent central sensitization of pain pathways (see below). Often erroneously referred to as simply administering analgesics preoperatively.

PAIN PATHWAYS

- *Transduction:* Tissue injury releases chemical mediators (prostaglandins, histamine, and cytokines) that can activate nociceptors. Continued nociceptive stimulation sensitizes the nociceptors (peripheral nociceptive sensitivity), resulting in hyperalgesia (increased response to a painful stimulus) and allodynia (pain from a normally non-painful stimulus) localized to the area of insult.

▼ ***Key Point*** NSAIDs and local anesthetics can block or modify transduction. Preventing or reducing

nociception prior to applying the inciting stimulus can reduce pain perception. This is the concept behind preemptive analgesia.

- *Transmission:* Nociceptive signals are transmitted to the spinal cord by primary afferent A-delta or C fibers. The thinly myelinated A-delta fibers conduct rapidly and are responsible for rapid reflex responses such as limb withdrawal from the inciting stimulus. The non-myelinated C fibers conduct more slowly. Cell bodies of these fibers are located in the spinal cord dorsal horn. Axons from these neurons synapse in the superficial layers of the spinal cord dorsal horn. Activated dorsal horn neurons send their impulses toward the brain via ascending spinal tracts. Interneurons located within the dorsal horn can modify the nociceptive signals via the release of endogenous opioids. Continued C-fiber dorsal horn stimulation increases sensitivity of these neurons to nociceptive stimulation (central sensitization), resulting in allodynia in anatomic areas adjoining the area of initial insult. This central sensitization is referred to as "wind-up."
- *Perception:* Ascending nociceptive transmission results in perception or awareness of pain in some part of the body. Cortical and limbic systems of the brain are involved. This evokes the autonomic and affective behavioral aspect of pain.
- *Modulation:* Descending inhibitory signals from the brain act in the dorsal horn to modify nociceptive signals via opioids, norepinephrine, serotonin, and γ-aminobutyric acid (GABA).

▼ ***Key Point*** Opioid analgesics, alpha-2 agonists, GABA-mimetic drugs, and NMDA-receptor antagonists can modify nociception within the spinal cord dorsal horn.

PAIN ASSESSMENT

- Pain is an individual experience and can be difficult to quantitate given the diversity of species, breeds, and individual temperament.
- Pain-related behaviors such as vocalizing, guarding, lameness, and trembling are easily recognized. However some animals, particularly cats, will not develop these "obvious" signs (Table 6-1). Furthermore, vocalization can be a manifestation of emergence from anesthesia, breed or individual temperament, or opioid induced dysphoria.
- As yet, no one blood chemical value specifically relates to pain. Plasma glucose, cortisol, catecholamine, and endorphin concentrations are not specific for pain.
- Changes in physiologic variables such as heart rate, blood pressure, and respiratory rate are nonspecific for pain and can change in response to anesthetic recovery.
- In addition to recognizing the commonly perceived signs of pain, anticipating pain related to a type of procedure facilitates preemptive treatment (Table 6-2). In general, the greater the degree of tissue trauma related to a surgical procedure, the greater the pain. The degree of tissue trauma also relates to the surgeon's experience and skill as well as the duration of the procedure.

Table 6-1. SIGNS OF PAIN

Behavioral Signs
Vocalization
Withdrawal, avoidance, fear, and fear biting
Unwillingness to move
Refusal to lie down, sleep, or groom
Refusal to bear weight
Guarding
Trembling
Licking or mutilation of site
Withdrawal to the back of the cage or enclosure
Refusal to eat
Physiologic Signs
Tachycardia
Tachypnea
Bradypnea
Mydriasis
Ptyalism

PAIN SCORING SYSTEM

- Use a pain scoring system when assessing pain. A standardized scoring system minimizes person-to-person inconsistency in evaluation. A pain scoring system minimizes observer bias based on breed characteristics.
- Scoring systems range from extensive to simple and take into account combinations of physiologic, behavioral, and neurochemical responses. A simplified scoring system that relies on observation of behavior can be performed quickly (Table 6-3).

Table 6-2. PROCEDURES ASSOCIATED WITH SIGNIFICANT PAIN

Amputation, particularly of proximal limb
Fracture repair, particularly of proximal limb
Extensive soft tissue resections*
Total ear canal ablation
Thoracotomy, particularly median sternotomy
Onychectomy
Sectioning and extraction of large teeth
Extensive open abdomen procedures

*Generally significant tissue mass resection and severing of major nerve trunks result in relatively greater pain response.

Table 6-3. SIMPLIFIED PAIN SCORING SYSTEM

Reaction to Gently Probing of Wound While Animal Is Awake	
No response	0
Looks at wounded area, may slightly withdraw affected area	1
Turns toward wounded area, withdrawal of affected area, some vocalization	2
Dramatic response such as violent withdrawal, loud vocalization	3
Comfort	
Asleep, calm and resting quietly	0
Refusal to lie down or assume normal posture but willing to approach when coaxed	1
Severe vocalizing, thrashing, extreme guarding of affected area, withdrawn and motionless, unresponsive to coaxing	2
Physiologic Responses	
Normally expected postoperative changes in heart rate and respiratory rate	0
Tachycardia, tachypnea not explainable by other physiologic causes (dehydration, stress, hypoxemia, etc.), dilated pupils	2
Respiratory Pattern	
Normal	0
Guarded, mild abdominal	1
Marked abdominal	2
Observation and scoring must be influenced by observation of behavior prior to induction of painful stimulus	
Minimum score (no pain)	= 0
Maximum score (maximum pain)	= 9
Any score other than zero warrants consideration of analgesic therapy, with higher scores suggesting more potent and multimodal therapy	

- Regardless of the pain score, use common sense. If a given procedure would cause you pain, then administer perioperative analgesic therapy. If you think the animal is experiencing pain, administer analgesia.

ANALGESIC DRUGS AND TECHNIQUES

(Tables 6-4 to 6-8)

General Principles

- Consider preemptive analgesia as a part of every anesthetic plan.
- Consider multimodal analgesic therapy with some combination of opioid, NSAID, local anesthetic, NMDA-receptor antagonist, and alpha-2 agonist for more painful procedures (see Table 6-2) or for animals with higher pain scores.
- Analgesic drugs and techniques are compatible with general anesthesia. As with anesthetic drugs, their selection should be influenced by preoperative patient status (see Chapter 2).
- Assess postoperative pain using a pain scoring system (see Table 6-3) and treat for pain whenever indicated.
- Do not rely on drugs used to induce and maintain anesthesia (propofol, thiopental, isoflurane, or sevoflurane) to provide preemptive analgesia or postoperative control of pain.

Opioid Agonists

Opioid agonists (e.g., morphine, hydromorphone, fentanyl, oxymorphone, and meperidine) are generally considered the most potent analgesics for treating acute pain. Opioids are controlled substances and are subject to state and federal regulations.

Duration of Action

- Morphine, hydromorphone, and oxymorphone provide 4 to 6 hours of analgesia.
- Meperidine is relatively short acting (less than 1 hour), so it must be re-dosed more frequently than the other opioid agonists.
- Fentanyl is very potent but short acting (15–20 minutes). It is most suitably administered by continuous intravenous (IV) administration or a transdermal patch.

Administration

- Opioids combine well with acepromazine, alpha-2 agonists, and benzodiazepines for preoperative sedation and preemptive analgesia.
- They are most often administered parenterally as discrete boluses or they can be administered by infusion. Preservative free morphine is useful for epidural analgesia.
- Cats are more sensitive to opioid-induced dysphoria; give relatively low doses.

Side Effects

- Bradycardia is the most common cardiovascular side effect. Respiratory depression can occur during general anesthesia but is not generally an issue in awake animals.
- Prolonged opioid administration (days) can result in urinary retention and the need to periodically express the bladder or insert a urinary catheter.
- Opioids can induce dysphoric behavior (vocalizing and pacing) that can be confused with pain behavior. Opioid-induced dysphoria can be treated using small incremental boluses of naloxone (1–2 μg/kg), an opioid antagonist.

Opioid Agonist-Antagonist (Butorphanol) and Partial Agonist (Buprenorphine)

These two drugs are generally considered less potent analgesics than the opioid agonists. They are controlled substances and are subject to state and federal regulations.

Duration of Action

- Butorphanol lasts up to 2 hours in a cat but less than 1 hour in a dog.
- Buprenorphine is effective up to 8 hours. Onset of action is relatively slow (30 minutes), so it is not useful for immediate pain relief.

Table 6-4. OPIOID DRUGS FOR TREATING PAIN IN DOGS AND CATS

Drug	Dog Dose (mg/kg) (IV, IM, SC)	Cat Dose (mg/kg) (IV IM, SC)	Duration of Action (hr)	Comments	DEA Schedule
Morphine	0.2–1.0	0.1–0.2	2–4 in dogs 4–5 in cats	Histamine release possible with large IV bolus dose; CRI*: 0.1–0.3 mg/kg/hr; Epidurally†: 0.1 mg/kg preservative free product	II
Hydromorphone	0.1–0.2	0.1–0.2	2–4 in dogs 4–5 in cats		II
Oxymorphone	0.05–0.1	0.05–0.1	2–4		II
Fentanyl	0.004–0.008	0.002–0.004	<20 min	CRI*: 2–6 µg/kg/hr	II
Fentanyl Transdermal patch	25 µg/kg/hr in small dogs; 50 µg/kg/hr in medium dogs; 75 µg/kg/hr in large dogs; 100 µg/kg/hr in giant breeds	25 µg/kg/hr size	3–4 days	At least 6–12 hr (cat) and 18 hr (dog) to reach therapeutic concentrations	
Meperidine	2–5	2–5	0.5–1.0	Do not administer IV due to histamine release	II
Butorphanol	0.1–0.4	0.1–0.4	<1 in dogs; ≤2 in cats		IV
Buprenorphine	0.005–0.02	0.005–0.02	6–8	Useful orally in cats bid–tid; Epidurally†: 5 µg/kg	V
Pentazocine	2–3	1–2	≤2	Higher doses provide ≤2 hr	IV

*CRI, constant rate infusion; usually preceded by a bolus dose to rapidly achieve therapeutic plasma concentration. Use lower end of infusion rate in cats.
†Duration of action after epidural use is up to 24 hours for morphine and buprenorphine.

Table 6-5. OTHER SEDATIVE AND ANESTHETIC DRUGS FOR TREATING PAIN IN DOGS AND CATS

Drug	Dog Dose	Cat Dose	Duration of Action	Comments	DEA Schedule
Ketamine	CRI*: 2–10 µg/kg/min	CRI*: 2–10 µg/kg/min	Duration of infusion	Subanesthetic dose, useful as analgesic adjunct when given with other analgesics Epidurally: 2 mg/kg diluted in sterile 0.9% NaCl; 1 ml/4.5 kg body weight	III
Xylazine	0.1–0.2 mg/kg IV, IM	0.1–0.2 mg/kg IV, IM	<1 hr	Sedation accompanies analgesia, not recommended if cardiovascular compromise present	—
Medetomidine	2–10 µg/kg IV, IM	10–20 µg/kg IV, IM	1–2 hr	Sedation accompanies analgesia, not recommended if cardiovascular compromise present	—
Morphine/lidocaine/ketamine†	CRI*: 0.2/3.0/0.6 mg/kg/hr	0.2/3.0/0.6 mg/kg/hr	Duration of infusion and several hours beyond	Useful as an adjunct to inhalation anesthesia in dogs, compatible with other perioperative analgesics and anesthetics	Morphine: II Ketamine: III

*CRI, constant rate infusion.
†To 500 ml of crystalloid, add 10 mg of morphine SO_4, 150 mg of 2% lidocaine HCl, and 30 mg of ketamine HCl. Administer at 10 ml/kg/hr intra-operatively. Concentration can be adjusted (increased) to be compatible with postoperative maintenance fluid rates.

Table 6-6. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS FOR TREATING PAIN IN DOGS AND CATS

Drug	Dog Dose (mg/kg)	Cat Dose (mg/kg)
Aspirin	10–22 PO bid	10 PO q 48 hr
Carprofen	2 PO, SC, bid or 4 PO, SC, sid	4 one time only
Deracoxib	3–4 PO sid for ≤7 days	Not recommended
Etodolac	10–15 mg PO sid	Not recommended
Ketoprofen	2 PO, SC, initially followed by 1 PO daily	2 PO, SC, initially followed by 0.5–1.0 PO, SC
Meloxicam	0.2 PO, SC, initially followed by 0.1 daily for 2–3 days	0.3 SC, one time only
Naproxen	1.2–2.2 PO q 1–2 days	Not recommended
Tepoxalin	10–20 PO first day followed by 10 PO sid subsequent days'	Not recommended
Firocoxib	5 PO, sid	Not recommended

Administration

- Buprenorphine is effective and well accepted orally in cats. It is useful for "at home" administration.
- Buprenorphine can be used epidurally (see Table 6-4).

Side Effects

- Side effects are similar to those listed for opioid agonists.

Alpha-2 Agonists (Xylazine, Medetomidine)

Medetomidine and xylazine produce dose related analgesia for mild to severe pain. Analgesia is accompanied by a dose dependent sedation; it can be difficult to separate analgesia from sedation.

Table 6-7. LOCAL ANESTHETIC DRUGS

Drug	Duration of Action (hr)	Constant Rate Infusion (µg/kg/min)*	Nerve Block or Local Infiltration (mg/kg)†	Epidural (mg/kg)
Lidocaine	1	20–60	1–2	4
Bupivacaine	2–6	—	1–2	1–2
Ropivacaine	2–6	—	1–2	1–2

*Not recommended for use in cats because of cardiovascular depression.
†Includes maxillary and mandibular nerve blocks; nerve blocks for onychectomy; splash blocks; intercostal nerve blocks; and incisional line blocks.

Table 6-8. SAMPLE PAIN TREATMENT PROTOCOLS*

Example	Drug(s)	Comments
Ovariohysterectomy, castration, cystotomy, exploratory laparotomy or any elective surgical procedure with minimum to moderate tissue trauma	Parenteral opioid and or alpha-2 agonist as part of preanesthetic regimen; NSAID immediately pre- or post-surgery. For cats, oral buprenorphine continued for 1–3 days post-surgery	Any opioid listed in Table 6-4 is acceptable as long as attention is given to dosing interval. For onychectomy, also perform local nerve block of feet. Continue analgesic support for at least 24 hours post-surgery.
Fractures and severe soft tissue trauma†	Parenteral opioid agonist as part of the premedication plus one or more of the following: epidural opioid for rear limb fractures, abdominal procedures, and perineal surgery; local anesthetic nerve blocks for maxillectomy, mandibulectomy, or thoracotomy; Fentanyl patch applied 12–18 hours preoperatively; CRI‡ of morphine, fentanyl, lidocaine, or ketamine; CRI of a morphine, lidocaine, and ketamine combination.	Maximum analgesia is needed. Combinations involving several categories (multimodal) are most useful. For example, preoperative opioid pre-med with an epidural opioid, CRI opioid, or opioid combination. Continue postoperative analgesia for at least 48–72 hours.
Arthritis	NSAID	Use only if normal liver and kidney function are present. Follow manufacturer's recommendations for pre- and post-administration patient evaluation.

*Refer to drug tables for choice of specific drugs and dosing regimens. For procedures requiring general anesthesia, these recommended drugs are given perioperatively as part of the anesthetic plan (see Chapter 2). Pain treatment protocols depend on drug availability and the availability of qualified personnel to administer controlled drugs. Depending on the pain score, additional analgesic drugs may need to be administered.
†Tissue trauma of increasing magnitude requires relatively high doses and multimodal therapy using more than one category of drug.
‡CRI, constant rate infusion.

Duration of Action

- Xylazine: Less than 1 hour
- Medetomidine: 1 to 2 hours

Administration

- IV or intramuscular (IM) (also see Chapter 2)

Side Effects

- Cardiovascular effects include hypertension, bradycardia, bradyarrhythmia, and reduced cardiac output.

Local Anesthesia

The local anesthetic techniques described below are intended to augment, not replace, general anesthesia for the surgical procedures.

Local Anesthetic Drugs

- Lidocaine, ropivacaine, bupivacaine

Duration of Action

- Bupivacaine and ropivacaine have a 4- to 8-hour duration and lidocaine has a less than 1-hour duration of action after local infiltration or regional nerve blockade.
- Onset of action is shorter with lidocaine (a few minutes) than with ropivacaine or bupivacaine (30 minutes).

Administration

- Local anesthetic drugs are used for local tissue infiltration, regional nerve blockade, epidural administration, or intravenous infusion.
- Local infiltration or regional nerve blockade results in sensory and motor blockage.
- Lidocaine can be administered by intravenous infusion in dogs to treat mild to moderate pain.

Local Anesthesia for Onychectomy

See Chapter 114.

Nerve Blocked

- Br. of median, ulnar, radial.

Area Blocked

- Digits

Technique

Use ropivacaine or bupivacaine; note that both of these drugs are commercially available in varying concentrations. It is important to use the least concentrated formulation (0.2% for bupivacaine or 0.25% for ropivacaine) to provide sufficient volume for the block.

- Dose = 1 to 2 mg/kg. Approximately 1.5 ml per leg per 3-kg cat. This volume would be further divided if the procedure is performed on four limbs.
- Infiltration using a 25-gauge needle is just proximal to carpus and deep to the flexor tendons (palmar) and extensor tendons (dorsal).

Anesthesia of Mandible

For mandibular biopsy, mandibulectomy, and dental procedures, see Chapters 99 and 64.

Nerve Blocked

- Inferior alveolar branch of the mandibular nerve

Technique

- Insert a needle approximately 1 cm rostral to the angular process (caudal edge) of mandible against the medial surface to mandibular foramen.
- Inject 1 to 2 ml of 0.2% ropivacaine or 0.25% bupivacaine (less in cats).

Anesthesia of Upper Jaw

For maxillary biopsy, maxillectomy, and dental procedures, see Chapters 99 and 64.

Nerve Blocked

- Maxillary nerve deep at vertical portion of palatine bone

Area Blocked

- Maxilla and associated teeth

Technique

- Insert a 1- or 1.5-inch needle ventral to the zygomatic process and anterior to the ramus of the mandible.
- The needle is advanced until it contacts the palatine bone.
- Inject 1 to 2 ml of 0.2 % ropivacaine or 0.25% bupivacaine.

Intercostal Nerve Block

For thoracotomy, see Chapter 167.

Nerves Blocked

- Intercostal nerves proximally and at the caudal edge of the ribs

Area Blocked

- Chest wall

Technique

- Two intercostal spaces cranial to and two caudal to and including the space receiving the surgical incision

- Ropivacaine (0.2%) or bupivacaine (0.25%); 1 to 2 mg/kg divided among the five intercostal spaces

Epidural Anesthesia or Analgesia

For surgery of the caudal abdomen, tail, perineum, or anus.

- Opioids, local anesthetics, alpha-2 agonists, and ketamine have all been injected into the epidural space for analgesia (see Tables 6-4, 6-5, and 6-7).
- Local anesthetics produce a dose related sensory and motor blockade (epidural anesthesia).
- Opioids, alpha-2 agonists, or ketamine induce dose-related analgesia with minimal motor blockade (epidural analgesia).

Area Blocked

- Caudal abdomen, tail, perineum, and anus

Anatomy and Landmarks

- The lumbo-sacral space is located on the midline on a line drawn between the left and the right cranial-dorsal iliac spines.
- Palpate the spinous process of vertebrae L7 and the median sacral crest. The space is located midway between these structures.
- The spinal cord ends at L7 in the dog and between L7 and S1 in the cat.

Technique

- Position the animal in lateral or sternal recumbency.
- Clip hair and do an aseptic preparation. Surgical gloves should be worn when performing the procedure.
- A 22-gauge, 1- to 3-inch spinal needle is inserted on the midline. Advance the needle through the yellow ligament until a sudden loss of resistance is felt as the needle enters the epidural space. Depth of insertion will vary from 0.5 cm in a cat to 7 cm in a large-breed or obese dog.
- Slowly inject and withdraw the needle.
- The appropriate dose (mg/kg) is delivered in a 1 ml/4.5 kg volume.

Lidocaine Constant Rate (IV) Infusion

- Can be used as an adjunct to other analgesic therapy.
- Better for soft tissue pain rather than orthopedic.
- Dosage = 20 to 60 µg/kg/min, IV
- Begin with mid-range dosage for dogs. Cats may develop cardiovascular depression from lidocaine infusion.

Nonsteroidal Anti-inflammatory Drugs

These drugs traditionally have been used to treat chronic pain and to reduce inflammation as a result of their inhibition of the cyclooxygenase (Cox) 1 and 2 enzymes. Cox 1 is the normally present constitutive enzyme, and Cox 2 is induced during inflammation. Both enzymes may be involved in normal renal function.

- They potentiate the action of opioid analgesics.
- Injectable NSAIDs can be administered immediately before or after surgery. Oral NSAIDs can be prescribed postoperatively. NSAIDs do not produce sedation.
- They can cause gastrointestinal ulceration, liver, and kidney damage, and they should be used cautiously if at all in animals with hypotension, gastrointestinal, or renal disease.
- Do not use NSAIDs with corticosteroids.

SUPPLEMENTAL READING

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Mathews KA (ed): Veterinary Clinics of North America: Management of Pain. Philadelphia: WB Saunders, 2000.

Thurmon JC, Tranquilli WJ, Benson GJ: Lumb and Jones' Veterinary Anesthesia, 3rd ed. Philadelphia: Williams & Wilkins, 1996.

Section 2

Infectious Disease

Robert G. Sherding

Chapter 7

Vaccination Guidelines for the Dog and Cat

Richard B. Ford

Proposed changes in vaccination protocols for companion animals, the safety of licensed vaccines, and advances in vaccine technology are among the most important issues practicing veterinarians face as we enter the 21st Century. While many would argue that these are already issues, the future promises to be especially challenging as the vaccines we use and the protocols we recommend undergo unprecedented change.

HISTORICAL BACKGROUND

Prior to 1998, vaccination recommendations were limited to the Compendium of Animal Rabies Prevention and Control, published annually by the National Association of State Public Health Veterinarians (at www.nasphv.org). In 1998, the American Association of Feline Practitioners (AAFP) published the first report of an Advisory Panel on Feline Vaccines recommending that *adult* cats be vaccinated every 3 years, rather than annually, against *feline parvovirus* (panleukopenia). Reaction to this report was profound. Veterinarians throughout North America voiced concerns that anything other than annual vaccination of adult cats against panleukopenia was inappropriate, irrational, and quite possibly detrimental to the health of the cat population. In December of 2000, the same Advisory Panel published a second iteration of the Guidelines for Feline Vaccination. In that report, the Panel expanded the "every 3 year" booster recommendation to include feline herpesvirus-1, feline calicivirus, and panleukopenia.

Then, in March 2003, the American Animal Hospital Association (AAHA) Canine Vaccine Task Force released its Guidelines on canine vaccination. In that document, 3-year booster intervals in adult dogs are recommended for distemper, parvovirus, adenovirus-2, and parainfluenza virus.

In 2004, some vaccine manufacturers announced results of challenge studies verifying the ability of their canine distemper, parvovirus, and adenovirus-2 combination vaccines to protect dogs against virulent challenge, thereby validating the recommendations outlined in the canine vaccination guidelines.

FUTURE VACCINATION ISSUES

It is important to remember, however, that despite the controversy over 3-year booster intervals for some vaccines, there are several strategic issues justifying the need for veterinarians to reassess recommendations for the selection and use of vaccines. Included among these issues are vaccine safety profiles, profound variation in exposure risk of individual dogs and cats, and changes in vaccine technology (e.g., recombinant vaccines). These issues will take on even more importance in the future as new vaccines continue to be introduced and as more veterinarians question the need for and safety of these products.

The introduction of so many vaccines in the past 10 years, and the promise of more to come, justify the need for the veterinary profession to critically address which

vaccines are administered to which patients and at which stage of life.

▼ ***Key Point*** To merely accept any and all newly licensed vaccines as part of an annual protocol for all patients is, quite simply, *wrong*.

THE VACCINE GUIDELINES

First, and most importantly, the published Canine and Feline Vaccination Guidelines do *not* represent vaccination *standards*. The Guidelines were never intended to be used as a set of enforceable requirements against which all practices would be held accountable. They are merely *guidelines*. However, the published guidelines are becoming templates for the standard of care appropriate to vaccination practices in the United States. For that reason alone, they are worth reading.

▼ ***Key Point*** Current editions of both the Canine and Feline Vaccination Guidelines and updates on new vaccines can be reviewed at www.dvmvac.com.

Secondly, the Canine and Feline Vaccination Guidelines *do* ***not*** *represent a vaccination protocol*. Attempting to use the Guidelines as *a defined protocol* in practice would be frustrating. Instead, the Guidelines serve as a tool for clinicians to use in developing a rational vaccination protocol appropriate for the individual patient. Vaccine selection and use in veterinary medicine remain the responsibility of the individual practitioner.

CORE VERSUS NON-CORE VACCINES

Canine and Feline Vaccination Guidelines are developed around the concept of **Core** and **Non-Core** vaccines. It is important to understand that Vaccination Guidelines merely suggest, *they do not mandate,* which vaccines should be Core or Non-Core. However, it is in the interest of the individual practice to establish which vaccines meet the definition of Core, then ensure that information is communicated to *all* professional staff, technicians, and office staff, thereby assuring consistent, clear communication to clients.

Core Vaccines

Core vaccines are those vaccines recommended for administration to every dog or cat presented to the practice. Recommendations for designating a particular vaccine as **Core** are determined by: (1) severity of disease caused by the agent, (2) the risk of transmission of the agent to susceptible animals, and (3) the potential for a particular infection to be zoonotic.

Non-Core Vaccines

Non-Core vaccines, on the other hand, are those vaccines recommended for administration to a dog or cat that has a reasonable risk of exposure to a known infectious agent. Examples include the feline leukemia virus (FeLV) and canine Lyme borreliosis (*Borrelia burgdorferi*) vaccines.

DURATION OF IMMUNITY

Perhaps one of the greatest paradigms challenged by the publication of Canine and Feline Vaccination Guidelines is the time-honored "annual booster recommendation." Recommendations that some vaccines can be administered 3 years (or more) apart without reduction in protective immunity have not been universally accepted. However, the fact remains that over the last decade, the quality of companion animal vaccines has improved. Recent studies have clearly shown that the duration of immunity for many, although not all, canine and feline vaccines is well beyond 1 year. Clearly there is a growing body of data that validates triennial booster vaccination in adult dogs and cats for those vaccines listed in the guidelines as "Core." However, some vaccines (e.g., *Bordetella bronchiseptica,* leptospirosis*, and Chlamydophila felis* vaccines*)* may *not* consistently provide a 1-year duration of immunity, despite a product label (package insert) stipulating "annual booster recommended."

ANNUALIZED VACCINATION PROTOCOLS

The fact that the Canine and Feline Vaccination Guidelines recommend triennial vaccination for certain vaccines in no way stipulates that adult dogs and cats should *only* be vaccinated every 3 years. In fact, annual vaccination does represent a high standard of medical care *as long as the vaccination appointment incorporates a thorough health and wellness examination.*

Considering the large population of pet dogs and cats and the remarkable spectrum of risk factors for exposure to infectious pathogens, it is quite unreasonable to assume that a single vaccination protocol would be applicable in all patients seen in practice. Two of the most important variables to consider when assessing risk are: (1) the **age of the patient**, and (2) the patient's **"lifestyle."** In implementing a vaccination protocol in clinical practice, it is critical for the clinician to consider these factors for the individual patient when recommending for, or against, Non-Core vaccines.

Tables 7-1 through 7-12 show *annualized* vaccination protocols for dogs and cats at moderate risk (applies to most), high risk, and low risk of exposure to infectious agents, while also taking into consideration the recommendations set forth in the Canine and Feline Vaccination Guidelines.

Table 7-1. ANNUALIZED VACCINATION PROTOCOL FOR DOGS AT **MODERATE RISK** OF EXPOSURE

Age at Vaccination	Vaccine
6–8 weeks	Distemper (MLV or recombinant) Parvovirus Adenovirus-2 Optional + Parainfluenza virus
10–12 weeks	Distemper (MLV or recombinant) Parvovirus Adenovirus-2 Rabies (1 dose at 12, 14, or 16 weeks of age) Optional + Parainfluenza virus + *B. bronchiseptica* (killed-parenteral, 2 doses required, 3–4 wks apart) + Leptospirosis (serovars as indicated at 12 wks or older)
14–16 weeks	Distemper (MLV or recombinant) Parvovirus Adenovirus-2 Rabies (now or at 12 wks) Optional + Parainfluenza virus + *B. bronchiseptica* (live-intranasal, 1 dose or the 2nd killed-parenteral dose) + Leptospirosis (serovars as indicated)
+1 year	Distemper (MLV or recombinant) Parvovirus Adenovirus-2 Rabies (booster required) Optional + *B. bronchiseptica* (intranasal or parenteral) + Parainfluenza + Leptospirosis (serovars as indicated)
+2 years	Optional + *B. bronchiseptica* (intranasal or parenteral) + Leptospirosis (serovars as indicated)
+3 years	Optional + *B. bronchiseptica* (intranasal or parenteral) + Leptospirosis (serovars as indicated)
+4 years	Distemper (MLV or recombinant) Parvovirus Adenovirus-2 Rabies Optional + *B. bronchiseptica* (parenteral) + Parainfluenza + Leptospirosis (serovars as indicated)
+5 years	Optional + *B. bronchiseptica* (parenteral) + Leptospirosis (serovars as indicated)
+6 years	Optional + *B. bronchiseptica* (parenteral) + Leptospirosis (serovars as indicated)
+7 years	Distemper (MLV or recombinant) Parvovirus Adenovirus-2 Rabies Optional + *B. bronchiseptica* (parenteral) + Parainfluenza + Leptospirosis (serovars as indicated)
Beyond 7 years	Cycle repeats as indicated

For any vaccine preceded by "+," see defining criteria in Table 7-2.
NOTE: All intranasal *B. bronchiseptica* vaccines also contain parainfluenza virus; some also contain canine adenovirus-2.
NOTE: In some States or municipalities, annual **rabies** vaccination may be required.

Table 7-2. DEFINING CRITERIA FOR **MODERATE-RISK** CANINES (APPLIES TO MOST DOGS)

***B. Bronchiseptica* Vaccination Is Indicated If**
Dog is ever boarded in a commercial kennel
Dog requires occasional grooming
Dog regularly has supervised walks/runs outside with likelihood of contact with other dogs

Parainfluenza* Vaccination Is Indicated If
Dog is ever boarded in a commercial kennel
Dog requires occasional grooming
Dog regularly has supervised walks/runs outside with likelihood of contact with other dogs

***Leptospira* Vaccination Is Indicated If**
The dog is 12 wks of age or older
Dog has opportunities for unsupervised outdoor activities
Cases of leptospirosis are known to have been confirmed in the area†
Dog has access (supervised or otherwise) to areas inhabited by "reservoir" hosts (e.g., opossum, skunk, raccoon, vole) or other domestic animals such as cattle, pigs, or horses

Lyme Borreliosis Vaccination Is Not Indicated Unless
Dog will travel to known endemic areas (Northeast or upper Midwest) and will spend time outside
Lyme borreliosis cases have been diagnosed (via IDEXX Snap 3Dx or Western Blot analysis) in the community
Dog is not receiving any form of topical tick preventative (e.g., fipronil)

*Note: Parainfluenza vaccine is combined with all intranasal *B. bronchiseptica vaccines.*
†Note: Risk of exposure is *not* limited to rural areas.

Table 7-3. ANNUALIZED VACCINATION PROTOCOL FOR DOGS AT **LOW RISK** OF EXPOSURE

Age at Vaccination	Vaccine	Age at Vaccination	Vaccine
6–8 weeks	Distemper (MLV or Recombinant) Parvovirus Adenovirus-2 Optional + Parainfluenza virus	+3 years	Health Examination Non-Core vaccines considered if risk assessment changes
		+4 years	Distemper (MLV or Recombinant) Parvovirus Adenovirus-2 Rabies (required in most States) Optional + Parainfluenza
10–12 weeks	Distemper (MLV or Recombinant) Parvovirus Adenovirus-2 + Rabies (1 dose at 12, 14, or 16 wks of age) Optional + Parainfluenza virus	+5 years	Health Examination Non-Core vaccines considered if risk assessment changes
14–16 weeks	Distemper (MLV or Recombinant) Parvovirus Adenovirus-2 + Rabies (now or at 12 wks) Optional + Parainfluenza virus	+6 years	Health Examination Non-Core vaccines considered if risk assessment changes
		+7 years	Distemper Parvovirus Adenovirus-2 + Rabies (required in most states) Optional + Parainfluenza
+1 year	Distemper (MLV or Recombinant) Parvovirus Adenovirus-2 Rabies (required in most states) Optional + Parainfluenza	Beyond 7 years	Cycle repeats as indicated
+2 years	Health Examination Non-Core vaccines considered if risk assessment changes		

For any vaccine preceded by "+," see defining criteria in Table 7-4.
Note: All intranasal *B. bronchiseptica* vaccines also contain parainfluenza virus; some also contain canine adenovirus-2.
Note: In some states or municipalities, annual **rabies** vaccination may be required.

Table 7-4. DEFINING CRITERIA FOR **LOW-RISK** CANINES (ONLY CORE VACCINES NEED BE ADMINISTERED)

***B. Bronchiseptica* Is Not Indicated Because**
Dog is never boarded in a commercial kennel
Grooming is not an issue
Dog lives exclusively indoors
Dog has no exposure to other dogs (or it occurs rarely)

Parainfluenza* Vaccination Is Indicated If
Dog is ever boarded in a commercial kennel
Dog requires occasional grooming
Dog regularly has supervised walks/runs outside with likelihood of contact with other dogs

***Leptospira Canicola*, *L. Icterohemmorhagiae*, *L. Pomona*, and *L. Grippotyphosa* Vaccinations Are Not Indicated Because**
There is no exposure to other dogs
There is no opportunity for unsupervised outdoor activity
The dog lives exclusively indoors
Leptospirosis is not known to occur in the area

Lyme Borreliosis Vaccination Is Not Indicated Because
Dog does not reside in a known Lyme borreliosis endemic area
Dog does not travel to known endemic areas
Dog neither lives in or travels into a known tick-vector area
Dog is reliably treated with topical flea and tick preparation
Dog has never known a tick and never will

*Note: Parainfluenza vaccine is combined with all intranasal *B. bronchiseptica* vaccines.

Table 7-5. ANNUALIZED VACCINATION PROTOCOL FOR DOGS AT **HIGH RISK** OF EXPOSURE

Age at Vaccination	Vaccine
6–8 weeks	Recombinant Distemper Parvovirus Adenovirus-2 Parainfluenza *B. bronchiseptica* (*intranasal* recommended)
10–12 weeks	Recombinant Distemper Parvovirus Adenovirus-2 Parainfluenza Rabies (at 12, 14, or 16 weeks) *B. bronchiseptica* (*intranasal* recommended) Optional + Leptospirosis + Lyme borreliosis (recombinant)
14–16 weeks	Recombinant Distemper Parvovirus Adenovirus-2 Parainfluenza *B. bronchiseptica* (*intranasal* recommended) Rabies (now or at 12 wks) Optional + Leptospirosis + Lyme borreliosis (recombinant)
+1 year	Distemper (MLV or recombinant) Parvovirus Adenovirus-2 Parainfluenza *B. bronchiseptica* (intranasal or parenteral) Rabies (required) Optional + Leptospirosis + Lyme borreliosis (recombinant)
+2 years	*B. bronchiseptica* (intranasal or parenteral) Optional + Leptospirosis + Lyme borreliosis (recombinant)
+3 years	*B. bronchiseptica* (intranasal or parenteral) Optional + Leptospirosis + Lyme borreliosis (recombinant)
+4 years	Distemper (MLV or recombinant) Parvovirus Adenovirus-2 Parainfluenza *B. bronchiseptica* (intranasal or parenteral) Rabies (required) Optional + Leptospirosis + Lyme borreliosis (recombinant)
+5 years	*B. bronchiseptica* (intranasal or parenteral) Optional: + Leptospirosis + Lyme borreliosis (recombinant)
+6 years	*B. bronchiseptica* (intranasal or parenteral) Optional: + Leptospirosis + Lyme borreliosis (recombinant)
+7 years	Distemper (MLV or recombinant) Parvovirus Adenovirus-2 Parainfluenza *B. bronchiseptica* (intranasal or parenteral) Rabies (required) Optional + Leptospirosis + Lyme borreliosis (recombinant)
Beyond 7 years	Cycle repeats as indicated

For any vaccine preceded by "+," see defining criteria in Table 7-6.
Note: All intranasal *B. bronchiseptica* vaccines also contain parainfluenza virus; some also contain canine adenovirus-2.
Note: In some states or municipalities, annual **rabies** vaccination may be required.

Table 7-6. DEFINING CRITERIA FOR **HIGH-RISK** CANINES

***B. Bronchiseptica* Booster Is Indicated If**
Dog is regularly boarded in a commercial kennel
Dog is routinely groomed at a facility where other dogs are maintained
Dog is regularly allowed outdoors and is unsupervised
Dog has regular exposure to other, unknown dogs
Dog is on a first-name basis with animal control officers

Annual *Leptospira* spp Booster Is Indicated If
Dog lives outside and is not constrained to a gated kennel
Dog lives on a farm and has ample outdoor activity
Dog is regularly allowed to roam freely
Dog lives exclusively outdoors.
Dog is used for hunting or other extended outdoor activity
Cases of leptospirosis are known to have been confirmed in the area
Dog has access (supervised or otherwise) to areas inhabited by "reservoir" hosts (e.g., opossum, skunk, raccoon, vole) or other domestic animals such as cattle, pigs, or horses

Annual Lyme Borreliosis Booster Is Indicated If
Dog resides in a known Lyme borreliosis endemic area (e.g., Northeast or upper Midwest)
Dog lives outside most or all of the time and does have tick exposure
Dog regularly travels to known endemic areas
Cases of Lyme borreliosis have been identified by serologic testing (IDEXX Snap 3Dx or Western Blot analysis) among dogs in the patient population
Dog is inconsistently treated with topical flea and tick preparation
Dog is only treated with over-the-counter tick preparations
Ticks are known to be constant companions for this dog

Table 7-7. ANNUALIZED VACCINATION PROTOCOL FOR CATS AT **MODERATE RISK** OF EXPOSURE

Age at Vaccination	Vaccine	Age at Vaccination	Vaccine
9–10 weeks	Panleukopenia (MLV) Herpesvirus-1 and Calicivirus (MLV) Optional + FeLV (recombinant, transdermal)	+4 years	Panleukopenia (MLV) Herpesvirus-1 and Calicivirus (MLV) + Rabies (recombinant)
		+5 years	+ Rabies (recombinant)
12–14 weeks	Panleukopenia (MLV) Herpesvirus-1 and Calicivirus (MLV) + Rabies (recombinant) Optional: + FeLV (recombinant, transdermal)	+6 years	+ Rabies (recombinant)
		+7 years	Panleukopenia (MLV) Herpesvirus-1 and Calicivirus (MLV) + Rabies (recombinant)
+1 year	Panleukopenia (MLV) Herpesvirus-1 and Calicivirus (MLV) + Rabies (recombinant) Optional + FeLV (recombinant, transdermal)	+8 years	+ Rabies (recombinant)
		+9 years	+ Rabies (recombinant)
		+10 years	Panleukopenia (MLV) Herpesvirus-1 and Calicivirus (MLV) + Rabies (recombinant)
+2 years	+ Rabies (recombinant, transdermal)	Beyond 10 years	Cycle repeats as indicated
+3 years	+ Rabies (recombinant)		

For any vaccine preceded by "+," see defining criteria in Table 7-8.

Table 7-8. DEFINING CRITERIA FOR **MODERATE-RISK** FELINES (APPLIES TO MOST CATS)

FeLV Vaccine Is Indicated If

Cat lives indoors predominately, but *not* exclusively, *and*
Cat is less than 6 months of age, *and*
Cat is known to occasionally have contact with other cats of unknown health status, *or*
Other cats in the household are known to be FeLV infected, *or*
Other cats live in the household but are of unknown FeLV status, *or*
Other cats in the household are known to roam at will, *or*
Owner may bring stray cats into the household

***Bordetella Bronchiseptica* and *Chlamydophila Felis* Vaccines Are Not Indicated If**

Cat is an adult (current literature suggests that clinical *B. bronchiseptica* infections are most likely to occur in kittens), *and*
Cat does not have exposure to other cats, *and*
Any other cats in the household are known to be strictly indoor cats, *and*
Owner is unlikely to bring stray cats into the household

Rabies Vaccination in Cats

Is *not* required by many states and municipalities; however, in accordance with the Feline Vaccination Guidelines, rabies is a Core vaccine and is highly recommended for all cats.

Table 7-9. ANNUALIZED VACCINATION PROTOCOL FOR CATS AT **LOW RISK** OF EXPOSURE

Age at Vaccination	Vaccine	Age at Vaccination	Vaccine
9–10 weeks	Panleukopenia (MLV) Herpesvirus-1 and Calicivirus (MLV)	+5 years	+ Rabies (recombinant)
		+6 years	+ Rabies (recombinant)
12–14 weeks	Panleukopenia (MLV) Herpesvirus and Calicivirus (MLV) + Rabies (recombinant)	+7 years	Panleukopenia (MLV) Herpesvirus-1 and Calicivirus (MLV) + Rabies (recombinant)
+1 year	Panleukopenia (MLV) Herpesvirus-1 and Calicivirus (MLV) + Rabies (recombinant)	+8 years	+ Rabies (recombinant)
		+9 years	+ Rabies (recombinant)
		+10 years	Panleukopenia (MLV) Herpesvirus-1 and Calicivirus (MLV) + Rabies (recombinant)
+2 years	+ Rabies (recombinant)		
+3 years	+ Rabies (recombinant)		
+4 years	Panleukopenia (MLV) Herpesvirus-1 and Calicivirus (MLV) + Rabies (recombinant)	Beyond 10 years	Cycle repeats as indicated

For any vaccine preceded by "+," see defining criteria in Table 7-10.
Note: Although administration of rabies vaccine to cats may not be required by state or local statutes, it is recommended for all cats, regardless of risk.

Table 7-10. DEFINING CRITERIA FOR **LOW-RISK** FELINES (PROTOCOL CENTERS AROUND CORE VACCINES)

FeLV and FIV Vaccines Are Not Indicated If

Cat is known to be a strictly indoor cat, *and*
Any other cats in the household are known to be both FeLV and FIV-free and were tested within the last 12 months, *and*
Other cats in the household are known to be strictly indoor cats
Owner does not bring stray cats into the household

***Bordetella Bronchiseptica* and *Chlamydophila* Vaccines Are Not Indicated If**

The cat is an adult (current literature suggests that clinical *B. bronchiseptica* infections are most likely to occur in kittens), *and*
The cat does not have exposure to other cats, *and*
Any other cats in the household are known to be strictly indoor cats
Owner does not bring stray cats into the household

Rabies Vaccination in Cats

Is *not* required by many states and municipalities; however, in accordance with the Feline Vaccination Guidelines, rabies is a Core vaccine and is highly recommended for all cats.

Table 7-11. ANNUALIZED VACCINATION PROTOCOL FOR CATS AT **HIGH RISK** OF EXPOSURE

Age at Vaccination	Vaccine
9–10 weeks	Panleukopenia (MLV) Herpesvirus-1 and Calicivirus (MLV) Optional + FeLV (recombinant, transdermal) + *B. bronchiseptica* + *Chlamydophila* (non-adjuvanted) + FIV
12–14 weeks	Panleukopenia (MLV) Herpesvirus-1 and Calicivirus (MLV) + Rabies (recombinant) Optional + FeLV (non-adjuvanted) + *B. bronchiseptica* + *Chlamydophila* (non-adjuvanted) + FIV
+1 year	Panleukopenia (MLV) Herpesvirus-1 and Calicivirus (MLV) + Rabies (recombinant) Optional + FeLV (recombinant, transdermal) + *B. bronchiseptica* + *Chlamydophila* (non-adjuvanted) + FIV
+2 years	+ Rabies (recombinant) Optional + FeLV (recombinant, transdermal) + *B. bronchiseptica* + *Chlamydophila* (non-adjuvanted) + FIV
+3 years	+ Rabies (recombinant) Optional + FeLV (recombinant, transdermal) + *B. bronchiseptica* + *Chlamydophila* (non-adjuvanted) + FIV
+4 years	Panleukopenia (MLV) Herpesvirus-1 and Calicivirus (MLV) + Rabies (Recombinant) Optional + FeLV (recombinant, transdermal) + *B. bronchiseptica* + *Chlamydophila* (non-adjuvanted) + FIV
+5 years	+ Rabies (Recombinant) Optional + FeLV (recombinant, transdermal) + *B. bronchiseptica* + *Chlamydophila* (non-adjuvanted) + FIV
+6 years	+ Rabies (recombinant) Optional + FeLV (recombinant, transdermal) + *B. bronchiseptica* + *Chlamydophila* (non-adjuvanted) + FIV
+7 years	Panleukopenia (MLV) Herpesvirus-1 and Calicivirus (MLV) + Rabies (recombinant) Optional + FeLV (recombinant, transdermal) + *B. bronchiseptica* + *Chlamydophila* (non-adjuvanted) + FIV
+8 years	+ Rabies (recombinant) Optional + FeLV (recombinant, transdermal) + *B. bronchiseptica* + *Chlamydophila* (non-adjuvanted) + FIV
+9 years	+ Rabies (recombinant) Optional + FeLV (recombinant, transdermal) + *B. bronchiseptica* + *Chlamydophila* (non-adjuvanted) + FIV
+10 years	Panleukopenia (MLV) Herpesvirus-1 and Calicivirus (MLV) + Rabies (recombinant) Optional + FeLV (recombinant, transdermal) + *B. bronchiseptica* + *Chlamydophila* (non-adjuvanted) + FIV
Beyond 10 years	Cycle repeats as indicated

For any vaccine preceded by "+," see defining criteria in Table 7-12.
Note: *Chlamydia psittaci* has been renamed *Chlamydophila felis* (the name on vaccine label may not reflect the new classification).

Table 7-12. DEFINING CRITERIA FOR **HIGH-RISK** FELINES

Both FeLV and FIV Vaccines Are Indicated If

Cat is known to roam at will and engage in fighting (risk of FIV in male cats is 4 times greater than in female cats), *or*
There is likely exposure to other cats with unknown health status, *or*
There are other cats in the household that are known to roam at will and engage in fighting, *or*
Owner regularly adopts (or hoards) cats

***Bordetella Bronchiseptica* and *Chlamydophila Felis* Vaccines Are Indicated If**

Cat is a kitten and resides within a cluster household (current literature suggests that clinical *B. bronchiseptica* infections are most likely to occur in kittens), *or*
Cat has regular exposure to other cats of unknown health status, *or*
There are other cats in the household known to roam at will and have contact with other cats, *or*
Owner regularly adopts (or hoards) cats

Rabies Vaccination in Cats

Is *not* required by many states and municipalities; however, in accordance with the Feline Vaccination Guidelines, rabies is a Core vaccine and is highly recommended for all cats.

SUPPLEMENTAL READING

Ford RB (ed): Veterinary Clinics of North America: Small Animal Practice. Philadelphia: WB Saunders, 2001.

Report of the American Animal Hospital Association (AAHA) Canine Vaccine Task Force: 2003 Canine Vaccine Guidelines and Recommendations. J Am Anim Hosp Assoc 39:119–131, 2003. (the complete report, including supporting literature, is available to AAHA members at www.aahanet.org).

Richards J, Rodan I, Elston T, et al: 2000 Report of the American Association of Feline Practitioners and Academy of Feline Medicine Advisory Panel on Feline Vaccines, Nashville, TN.

Chapter 8

Feline Leukemia Virus

Robert G. Sherding

ETIOLOGY

Feline leukemia virus (FeLV) is an RNA retrovirus that is a transmitted both vertically (mother to fetus) and horizontally (cat to cat). FeLV infects cats worldwide and causes lymphoma, leukemia, bone marrow suppression, immunodeficiency, and a variety of other clinical syndromes. Fortunately, widespread testing and vaccination since the mid-1980s have resulted in a substantial decrease in the prevalence of FeLV infection.

Structure of the Virus

Certain structural components of the FeLV virion have clinical implications.

- *Core* contains the viral RNA and reverse transcriptase enzyme that allows DNA copies of the virus to be transcribed and inserted into the genome of infected host cells.
- *Core protein* (p27) is the group-specific FeLV antigen detected by conventional FeLV diagnostic tests.
- *Envelope glycoprotein* (gp70) defines the FeLV antigenic subgroup as A, B, C, or combinations of these; determines infectivity, host range, and pathogenicity; and elicits the protective host neutralizing-antibody response that occurs with natural exposure or vaccination. Only subgroup A is infectious.
- *Envelope protein* (p15e) is a mediator of FeLV-related immunodeficiency.

Prevalence

The prevalence of FeLV varies with age, health, environment, and lifestyle. Kittens less than 4 months of age are much more susceptible to infection than adults. Resistance develops with age, but even healthy adults can become infected. The prevalence of FeLV infection and related diseases, such as lymphoma, has been steadily declining over the last 2 decades because of client education, FeLV testing, and vaccination. Recent epidemiological surveys are few, and most of the older published surveys overstate the prevalence of FeLV compared with what is seen today. In the prevalence statistics below, the dates for earlier surveys are shown:

- Purebred catteries—Less 0.1% (if testing and vaccination are used)
- Healthy pet cats—Less than 1%
- Free-roaming stray and feral cats—1% to 4%
- Cats seen at U.S. teaching hospitals—2% (of 409,417 cats; 1972–1998)
- Cats tested at Tufts Laboratory—Decreased from 8% to 4% from 1989 to 1995 (of 13,000 cats)
- High-risk and clinically sick cats—13% (of 27,976 cats; 1990–1991)
- In highly endemic households with many viremic cats—30% to 70% of unvaccinated kittens compared with only 10% to 20% of unvaccinated adult cats

▼ ***Key Point*** Most purebred catteries have completely eliminated FeLV, and infection is rare in household pet cats. FeLV is most frequently found in multi-cat households that take in untested strays, especially kittens.

Transmission

▼ ***Key Point*** FeLV is contagious through prolonged close contact with infected cats. Transmission is primarily through saliva.

- Persistently viremic cats continuously shed large amounts of virus in saliva and, to a lesser extent, in naso-ocular secretions. Infected queens shed large amounts of virus in milk. Feces, urine, and fleas are less likely sources of infection.
- Transmission most often occurs through direct oronasal contact with infectious saliva during mutual grooming and sharing of food and water bowls or through bite wound inoculation of saliva.
- Transplacental transmission can occur, but milk-borne infection in nursing kittens is more common.
- Iatrogenic transmission of FeLV can occur through contaminated blood transfusions, needles, surgical and dental instruments, and endotracheal tubes.
- FeLV usually does not survive more than a few hours outside of the cat, up to a maximum of 48 hours

under optimal temperature and moisture conditions. Heat, drying, detergents, and disinfectants readily destroy FeLV.

▼ ***Key Point*** The risk of FeLV transmission is minimal in shelters and veterinary hospitals that house cats in separate cages and routinely use hand washing and disinfection procedures for cages, food and water dishes, and litter pans.

PATHOGENESIS

Sequence of FeLV Infection

The sequence of FeLV infection includes inoculation followed by replication in local lymphoid, systemic lymphoid, bone marrow, and polyglandular tissues.

- After oronasal or percutaneous inoculation, FeLV replicates in local lymphoid tissues and then in systemic lymphoid tissues throughout the body, such as lymph nodes, spleen, and thymus. Viral antigen may first become detectable in the blood (antigenemia) at this stage with enzyme-linked immunosorbent assay (ELISA) tests (see "Diagnosis"). A successful immune response may terminate the infection at this stage or even before antigenemia is detectable.
- If infection progresses, FeLV infects the bone marrow, leading to circulation of virus-infected leukocytes and platelets (cell-associated viremia) that are detectable in the blood by the immunofluorescent antibody (IFA) test (see "Diagnosis"). This usually indicates that FeLV has overwhelmed the host immune response and that the infection is likely to persist indefinitely.
- Concurrent with the development of viremia, FeLV infects glandular cells throughout the body (e.g., salivary glands, lacrimal glands, mammary glands, and mucosal epithelial glands). This leads to shedding of virus in most body secretions, with especially high concentrations of virus in saliva and the milk of lactating queens. At this stage, FeLV-infected cats are contagious to other cats in close contact, and queens can infect their nursing kittens.

Host Immune Response

Immunity to FeLV is the collective result of humoral antibody, cytotoxic T lymphocytes and other cell-mediated immune mechanisms, complement, and interferon. Humoral antibody responses have been characterized as follows:

- *Antiviral response* is mediated by neutralizing antibody directed against FeLV envelope antigens. Transient infection and recovery occur if the immune response is successful, whereas bone marrow infection and persistent viremia occur if the virus overwhelms the host immune response.
- *Antitumor response* is mediated by antibody directed against FeLV-associated antigens on the surface of FeLV-induced neoplastic cells.

Categories of Infection

The outcome of FeLV exposure depends on many factors, including viral dose and route of exposure, environmental conditions, and host factors such as the cat's age, innate immunity, vaccination status, and health status. Cats exposed to FeLV can be categorized as noninfected, persistently infected, transiently infected, or latently infected.

Cats That Resist Infection

Many cats exposed to FeLV do not get infected, either because of an inherent resistance to infection or because of insufficient exposure. The most important factor is age-related resistance in cats over 4 months of age.

Transient Infection

The majority of cats exposed to FeLV develop a transient replicating ("regressive") infection that is subsequently rejected by a vigorous immune response, resulting in a full clinical recovery.

- Transiently infected cats usually eliminate the virus swiftly within 4 to 6 weeks after exposure, with either no detectable antigenemia or a transient antigenemia lasting 1 to 5 weeks. However, FeLV-infected cats can potentially eliminate the virus at any stage, rarely even after many months or years as a persistent carrier.
- Many cats are vaccinated against FeLV, and upon exposure, most will resist persistent infection and instead go through a brief transient infection (see "Vaccination").
- Transiently infected cats frequently develop latent infection as they recover (see the next section).

Latent Infection

Non-viremic cats that "recover" from transient infection often become latent carriers of non-replicating FeLV for a variable period of time.

- In latent FeLV infection, non-replicating FeLV provirus remains dormant within the DNA genome of bone marrow and lymphoid cells of the cat. This can only be detected by specialized virus culture techniques or polymerase chain reaction (PCR) assays (see "Diagnosis"); thus, it is difficult to distinguish cats that have truly cleared the virus from cats with latent infection.

▼ ***Key Point*** Latent FeLV infection cannot be detected by conventional immunochromatographic (IC), ELISA, and IFA diagnostic tests.

- In most transiently infected cats, the latent stage of infection eventually is eliminated uneventfully within 6 to 9 months as part of the normal recovery process, but it sometimes can take a year or more. Latent infection persists indefinitely in an estimated 10% of "recovered" cats.
- The clinical significance of FeLV latency is the rare possibility of reactivation to a replicating infection, either spontaneously or in response to immunosuppression (e.g., corticosteroid-induced). In addition, reactivation of infection in latent-infected queens may rarely transmit FeLV to kittens in utero or during nursing.
- Latent infected cats have minimal risk of developing FeLV-related disease. They also have minimal risk of being contagious to other cats, except for the rare occurrences of reactivation mentioned above.

Persistent Infection

Cats with persistent or "progressive" FeLV infection have generalized lymphoid, bone marrow, and polyglandular infection with persistent cell-associated viremia and continuous shedding of virus. This widespread replicating FeLV infection persists for the remainder of the cat's life with only rare exceptions.

- Persistent infection eventually leads to fatal FeLV-related disease in most cats after a variable disease-free interval. The mortality rate in persistent FeLV-positive cats is 30% at 6 months, 60% at 2 years, and 90% at 4 years.
- Persistent infection will develop in approximately 10% to 30% of unvaccinated cats that receive continuous heavy exposure, such as living in an endemically infected household. In this situation, kittens less than 4 months of age are most susceptible, and the persistent infection rate can reach 70% in this group.
- Vaccination prevents persistent infection in many cats. Reducing the risk of exposure combined with vaccination has greatly decreased the prevalence of persistent FeLV infection.

CLINICAL DISEASE SYNDROMES

The clinical manifestations of FeLV are attributable to the oncogenic, cytopathic, and immunosuppressive effects of the virus. FeLV-induced neoplasia can be lymphoid or myeloid. Degenerative and cytopathic effects on various cells include bone marrow cells (anemia, neutropenia, thrombocytopenia), lymphocytes (T lymphocyte depletion, lymphoid atrophy, lymphoid hyperplasia), intestinal cells (enteritis), and the fetus and placenta (abortion, stillbirth). The immunosuppressive effects of FeLV cause profound immunodeficiency, resulting in susceptibility to a wide variety of opportunistic infections. In addition, FeLV-related immune dysfunction has been associated with immune-mediated and autoimmune diseases.

Nonspecific Clinical Signs

Presenting clinical signs that are common in FeLV-infected cats include weight loss, fever, dehydration, oculonasal discharge, anemia, diarrhea, stomatitis, and lymphadenopathy.

▼ ***Key Point*** The majority of FeLV-infected cats are asymptomatic at the time they are identified on routine screening tests during wellness exams.

Lymphoma and Leukemia

FeLV can be a primary cause of lymphoma, leukemia, and myelodysplasia. For additional information regarding diagnosis and treatment of these neoplastic conditions, see Chapters 26 and 27. In the mid-1970s, 70% of cats with lymphoma and leukemia were FeLV positive. Virus-negative alimentary lymphoma was uncommon. However, with the decline in prevalence of FeLV infection, FeLV-negative lymphomas now comprise 85% to 90% of the lymphomas seen in cats, and alimentary lymphoma is the predominant form. Some of these FeLV-negative lymphomas have molecular evidence of FeLV provirus, but most feline lymphomas are now caused by factors other than FeLV.

Alimentary Lymphoma

- Mesenteric lymph nodes—Palpable enlargement
- Stomach—Vomiting, anorexia, and weight loss
- Intestine—Diffuse infiltrative thickening of the intestinal wall or palpable obstructing mass (weight loss, vomiting, diarrhea, and inappetence)
- Liver—Diffuse hepatomegaly or nodular tumor masses within the liver (icterus, weight loss, vomiting, and abnormal liver tests)
- Spleen—Diffuse splenomegaly

▼ ***Key Point*** FeLV-negative alimentary lymphoma affecting middle-aged and older cats (mean age of 8 years) is now the predominant form of lymphoma in cats.

Mediastinal Lymphoma

Characterized by a cranial mediastinal mass due to lymphoma of the mediastinal lymph nodes or thymus.

- Pleural effusion (dyspnea)
- Tracheal compression (dyspnea, cough)
- Esophageal compression (dysphagia, regurgitation)
- Sympathetic trunk impingement (Horner's syndrome)
- Decreased cranial thoracic compressibility
- Mass palpable at thoracic inlet

Multicentric Lymphoma

- Generalized involvement of external and internal lymph nodes.
- Bone marrow, liver, spleen, and other extranodal sites are often affected.

Extranodal Forms of Lymphoma

Renal Lymphoma

- Signs—Nonspecific signs (early); renal failure and uremia (late)
- Kidneys palpably enlarged and nodular ("lumpy")

Ocular Lymphoma

- Retrobulbar mass—Mimics retrobulbar abscess
- Third eyelid mass—Mimics "cherry eye"
- Corneal infiltration—Mimics eosinophilic keratitis
- Uveal infiltration and hemorrhage—Mimics anterior uveitis or chorioretinitis

Neural Lymphoma

- Brain—Seizures, ataxia, blindness, behavior aberrations, motor deficits, and cranial nerve signs
- Spinal (usually extradural)—Paresis or paralysis
- Peripheral nerve—Variable neuropathies

Cutaneous Lymphoma

- Multiple firm, non-painful cutaneous nodules

Other Extranodal Sites for Lymphoma

- Nasal cavity, lung, heart, and urinary bladder.

Leukemia and Myelodysplasia

FeLV infection of bone marrow hemopoietic cells can result in acute lymphoid leukemia, non-lymphoid leukemia, or myelodysplasia (preleukemia). Clinical signs include pallor (anemia), petechial and ecchymotic hemorrhages (thrombocytopenia), fever, lethargy, weight loss, hepatosplenomegaly, and mild lymphadenopathy. Abnormal blast cells are usually identified in the blood and bone marrow. For additional information, see Chapters 22 and 27.

Acute Lymphoid Leukemia

- Acute lymphoblastic leukemia is characterized by extensive infiltration of the bone marrow with neoplastic lymphoblasts, often accompanied by neoplastic infiltration of the liver, spleen, and lymph nodes.
- The complete blood count (CBC) shows nonregenerative anemia, other cytopenias, and circulating lymphoblasts. Bone marrow cytology is diagnostic.

Acute Myeloid (Non-lymphoid) Leukemia

- This group of neoplastic diseases is characterized by the proliferation of one or more cell lines in the bone marrow at the expense and to the eventual exclusion of normal hemopoietic cells. These disorders are classified on the basis of the cellular origin of the abnormal cells as acute myeloblastic leukemia, acute myelomonocytic leukemia, acute monocytic leukemia, and erythroleukemia.
- Diffuse hepatomegaly, splenomegaly, and lymphadenopathy occur from extramedullary hematopoiesis and/or neoplastic infiltration. Neoplastic infiltration of the liver may cause jaundice.
- Anemia and thrombocytopenia are common, and the diagnosis is based on identification of neoplastic blast cells in the blood and bone marrow.
- Non-lymphoid leukemias are poorly responsive to chemotherapy.

Myelodysplasia

- Myelodysplasia (preleukemia) is characterized by anemia and other cytopenias caused by abnormal hemopoietic cell maturation in the bone marrow. The bone marrow is hypercellular and dysplastic, and it may have myelofibrosis.
- Myelodysplasia may progress to overt acute myeloid leukemia after a few weeks to months.
- The prognosis is poor, but blood transfusion and supportive care may be palliative.

Anemia and Other Cytopenias

FeLV-Related Anemia

Anemia is a common primary presenting clinical sign in FeLV-infected cats (see Chapter 22). Nonregenerative anemia is most common and is indicated by an absent or minimal reticulocyte response. Regenerative anemia with reticulocytosis also can occur.

Pathogenesis

- Nonregenerative anemia is associated with primary FeLV infection of bone marrow hemopoietic stem cells and supporting stromal cells, resulting in destruction, suppression, and abnormal maturation of erythrocyte precursors.
- Nonregenerative anemia can also be caused by disruption of the bone marrow from leukemia or myelodysplasia (see the previous section).
- Regenerative anemia associated with FeLV infection can result from immune-mediated hemolysis; from opportunistic hemotropic infections, such as *Mycoplasma haemofelis, Mycoplasma haemominutum* (formerly hemobartonellosis), *Ehrlichia,* and *Babesia;* or from blood loss related to thrombocytopenia.

Diagnosis

- Clinical signs of severe anemia are lethargy, weakness, tachypnea, mucous membrane pallor, anemic murmur, splenomegaly, retinal hemorrhages, and pica.

- CBC usually shows normochromic-normocytic or macrocytic nonregenerative anemia (packed cell volume [PCV] <10%).
- Reticulocytosis indicates regenerative anemia. Consider hemolytic causes. Evaluate blood smears for hemotropic organisms, and consider *Mycoplasma* PCR, which is more sensitive, or a therapeutic trial of doxycycline (see Chapter 22).
- Leukopenia or thrombocytopenia may accompany nonregenerative anemia, especially in myelodysplasia and leukemia.
- Bone marrow cytology in FeLV-related nonregenerative anemia is usually hypoplastic or aplastic, but it can be hypercellular, dysplastic, or neoplastic.

Treatment

- For regenerative anemia, treat the associated underlying cause of hemolysis.
- For nonregenerative anemia, use blood transfusion and palliative supportive care (median survival with treatment in 49 cats was 4 months).
- Recombinant human erythropoietin (Epogen, Amgen; 35 to 100 IU/kg SC q48h until PCV rises, then weekly) has been beneficial in some cats with FeLV-related nonregenerative anemia, but most do not respond. Endogenous erythropoietin is already elevated in many cases.

FeLV-Related Neutropenia

Neutrophils and myeloid precursors are often infected in FeLV (see Chapter 22).

- FeLV-induced neutropenia can be transient (in the first 3 to 5 weeks of bone marrow infection), persistent, or cyclic (8- to 14-day intervals). Neutropenia also can be associated with FeLV-induced leukemia or myelodysplasia.
- Signs include chronic or recurrent fever, bacterial infections, or life-threatening sepsis.
- Myeloblastopenia (panleukopenia-like syndrome) is characterized by profound panleukopenia (white blood cell count is 300–3000/µl) and acute enterocolitis with fever, vomiting, and bloody diarrhea. Intestinal epithelial cells are infected heavily with FeLV. Coinfection with panleukopenia virus is likely.
- Treat complicating bacterial infections with antibiotics. Some cats with persistent or cyclic neutropenia respond to prednisolone (2–3 mg/kg PO q24h).
- Recombinant human granulocyte colony-stimulating factor (rhG-CSF) (Neupogen, Amgen; 5 µg/kg SC daily) has been beneficial for stimulating myelopoiesis in some cases of FeLV-associated neutropenia; however, cats form antibodies against this human protein after a few weeks that limit the effectiveness of this treatment.

FeLV-Related Thrombocytopenia

Platelets and megakaryocytes are often infected in FeLV.

- Thrombocytopenia can be associated with FeLV-induced leukemia, myelodysplasia, or immune-mediated disease. This may lead to petechial and ecchymotic hemorrhages and gastrointestinal (GI) blood loss.
- Macroplatelets with bizarre shapes are a common incidental finding in viremic cats, especially those with severe anemia. These may be miscounted as red blood cells by electronic counters.
- Platelet dysfunction occurs but is clinically insignificant.
- Treat life-threatening thrombocytopenia with transfusion of whole blood or platelet-rich plasma. Treat suspected immune-mediated thrombocytopenia with prednisolone (2–3 mg/kg PO q24h).

Secondary Infections from Immune Suppression

FeLV causes profound lymphoid depletion and immune suppression (especially T lymphocytes). In addition, neutrophil, complement, and cytokine responses may be impaired. Thus, FeLV-infected cats have increased susceptibility to a wide variety of opportunistic infections. Some examples follow:

- Viral—Feline infectious peritonitis, herpesvirus
- Fungal—*Cryptococcus, Aspergillus,* dermatophytosis
- Protozoal—*Toxoplasma, Cryptosporidium*
- *Mycoplasma—M. haemofelis, M. haemominutum*
- Bacterial
  - Oral—Gingivitis, periodontitis, stomatitis
  - Respiratory infections—Rhinitis, sinusitis, pneumonia, pyothorax
  - Enteritis—*Salmonella, Campylobacter,* diarrhea of undetermined cause
  - Cutaneous—Pyoderma, non-healing sores, abscesses, draining fistulas
  - Septicemia

Peripheral Lymph Node Hyperplasia

- FeLV occasionally causes severe, generalized, nonpainful enlargement of peripheral and visceral lymph nodes (especially mandibular nodes) up to 3 times normal size. This lymphadenopathy is not neoplastic.
- This has been seen mostly in young adult cats (6 months to 2 years of age); 50% are asymptomatic and 50% have fever, anorexia, and depression.
- Most cases resolve in 2 to 4 weeks either spontaneously or in response to corticosteroids, cyclophosphamide, and vincristine. In some cats the lymphadenopathy recurs or develops into lymphoma months to years later.

Immune-Mediated Disorders

Several immune-mediated disorders have been associated with FeLV infection. The exact role of FeLV in these disorders is not fully understood, but it presumably involves viral antigen-antibody complexes or FeLV-induced disruption of immune regulation.

- Immune-mediated hemolytic anemia
- Immune-mediated thrombocytopenia
- Immune-complex glomerulonephritis
- Chronic progressive polyarthritis
- Pemphigus-like mucocutaneous disorders
- Systemic lupus erythematosus-like syndrome

Reproductive Failure

FeLV-infected breeding queens frequently have reproductive failure associated with transplacental or milk-borne transmission of FeLV. Presenting clinical signs can include infertility, fetal resorption, abortion, stillbirth, "fading kitten syndrome" (viremic kittens), or milk-borne transmission to nursing kittens.

Miscellaneous

A role for FeLV in the following disorders has been suggested but unproved: multicentric osteochondromatosis (multiple skeletal tumors in young cats), olfactory neuroblastoma (a rare nasal tumor), chronic enteritis, seborrheic dermatitis, eosinophilic granuloma complex, cutaneous horns, idiopathic anisocoria, neurologic dysfunction, and degenerative myelopathy.

DIAGNOSIS

Diagnostic testing for FeLV infection is one of the most frequently performed procedures in clinical practice. FeLV tests are used to diagnose FeLV-related illnesses, to routinely screen healthy cats for subclinical infection, and to identify and eliminate FeLV infections in multicat households and catteries.

Diagnostic kits are widely available for rapid in-office screening for FeLV infection. These are based on ELISA or other IC technologies. Commercial diagnostic laboratories offer these as well as the IFA test. PCR assay and virus isolation are confirmatory tests that require a specialized laboratory.

▼ ***Key Point*** ELISA and other IC screening tests detect soluble FeLV antigen in serum or plasma (antigenemia). The IFA test detects intracellular virus in circulating leukocytes and platelets (cell-associated viremia), indicating bone marrow infection.

Indications for FeLV Testing

The American Association of Feline Practitioners recommends that the FeLV status of all cats should be known. Identification of FeLV-infected cats provides the opportunity to treat these cats and to prevent the spread of infection to other cats. FeLV status should be known before vaccination because it is useless to vaccinate a cat that is already infected. This also prevents preexisting infections being mistaken as vaccination failures. Indications for FeLV testing are listed in Table 8-1.

▼ ***Key Point*** To maintain a FeLV-negative household, test all new cats before entry.

ELISA and Immunochromatographic Tests

▼ ***Key Point*** ELISA and other IC tests are the preferred screening tests for FeLV, because they are rapid, widely available, slightly more sensitive, and detect infection earlier than the IFA test.

The membrane-based ELISA and other IC test kits detect soluble FeLV p27 antigen, a major viral core protein. These are sensitive screening tests that provide accurate results in less than 10 minutes. They are designed for rapid, point-of-care diagnosis of FeLV infection (Table 8-2).

Table 8-1. INDICATIONS FOR FELINE LEUKEMIA VIRUS TESTING

Test cats that have never been tested.
Test kittens at any age. Kittens can be born infected, or nursing kittens can be infected via milk.
Test cats prior to vaccination for FeLV.
Test cats that are newly adopted.
Test new cats before entering them into a household of healthy cats.
Test cats with potential recent exposure.
Test all cats in a cattery or household with FeLV, then separate infected and uninfected cats.
Test outdoor cats at least annually since they have ongoing risk of exposure.
Test cats with signs of illness consistent with FeLV.

Modified from the guidelines of the American Association of Feline Practitioners (www.aafponline.org).

Table 8-2. IC AND ELISA TEST KITS FOR FELINE LEUKEMIA VIRUS

Test Kit	Manufacturer	Format
Witness FeLV	Synbiotics	Membrane rapid immunomigration
ViraCHEK/FeLV	Synbiotics	Microwell ELISA
ASSURE/FeLV	Synbiotics	Saliva wand and tube ELISA
SNAP FeLV	IDEXX	Membrane ELISA
SNAP FIV/FeLV Combo	IDEXX	Membrane ELISA (also tests for FIV)

ELISA, enzyme-linked immunosorbent assay; FeLV, feline leukemia virus; FIV, feline immunodeficiency virus; IC, immunochromatographic.

▼ ***Key Point*** For the most accurate ELISA or IC results, use non-hemolyzed serum or plasma rather than whole blood. Tests that use saliva and tears are unreliable and not recommended.

- For testing clinically ill cats, consider using a combination test kit that simultaneously tests for FeLV and feline immunodeficiency virus (FIV), since the clinical manifestations of these two diseases are often indistinguishable.
- ELISA and other IC tests detect viral antigen, not antibodies; thus, these tests are not affected by vaccination or maternal antibodies.

ELISA Test Interpretation

- Positive ELISA or IC test results indicate FeLV antigenemia. Both transient and persistent FeLV infections can be ELISA positive.
- Confirm positive ELISA or IC results, especially in healthy cats where the prevalence of infection is low, by retesting in 4 to 6 weeks and again at 3 months to distinguish transient from persistent infection and to rule out the occasional false positive caused by laboratory error. For retesting, consider using the IFA test as the confirmatory test, because the IFA correlates better with persistent infection and is slightly less susceptible to false-positive results (the see next section).
- Interpret weakly positive ELISA or IC reactions as suspicious or inconclusive, and repeat the test, preferably using a different testing method such as the IFA test or an outside laboratory.
- False-negative ELISA or IC results are highly unlikely because of the inherently high sensitivity of these tests. However, cats tested in the early stages of infection may not yet be antigenemic at the time of the first test. Most cats become antigenemic within 4 weeks of exposure, but it can take up to 3 months and in rare cases longer. Thus, retest all ELISA-negative cats that have a possibility of recent exposure 4 weeks later and again at 3 months.

Immunofluorescent Antibody Test

▼ ***Key Point*** The IFA test is the preferred confirmatory test for FeLV, because it is slightly more specific than ELISA and other IC tests, and it correlates highly with persistent infection.

The IFA test is a confirmatory test performed by commercial labs to detect FeLV p27 antigen within the cytoplasm of circulating neutrophils and platelets on blood smears. A positive IFA indicates established FeLV infection involving the bone marrow.

- The IFA test is very specific for FeLV and is highly correlated with persistent infection and the results of virus isolation; thus, use the IFA test to confirm positive ELISA or IC results.
- Provide the lab with at least two high-quality, air-dried, unfixed blood or bone marrow smears.

Immunofluorescent Antibody Test Interpretation

- Positive IFA results indicate an advanced stage of FeLV infection. Up to 96% of IFA-positive cats remain persistently infected. However, in healthy IFA-positive cats, retest monthly for up to 3 months to be certain whether infection is persistent or transient.
- False-positive IFA results are very rare but can occur from poor-quality blood smears that are too thick and cause nonspecific binding of the conjugate. Platelet clumping and eosinophilia also can cause rare false-positive results.
- False-negative IFA results may occur in cats with low neutrophil and platelet counts. Perform the IFA test on bone marrow smears in this situation.
- The IFA may be negative in early and transient ELISA-positive infections, because the IFA does not become positive until the virus is established and replicating in the bone marrow.

Discordant Test Results

Discordance is when conflicting results occur with different tests, most often when a cat is ELISA positive and IFA negative. This can result from laboratory error (most often a false-positive ELISA result) or from biologic factors.

- Discordant results can indicate early or transient infection when ELISA-positive antigenemia can precede the bone marrow replication stage required for a positive IFA. Early infections may be only ELISA positive for a few weeks until bone marrow replication starts and the IFA becomes positive. Transient infections are usually eliminated by a successful immune response within 3 months or less; thus, retesting monthly for up to 3 months usually resolves whether the infection is transient or persistent.
- The rare phenomenon of persistently discordant test results, i.e., when a cat is repeatedly IFA negative but persistently antigenemic (ELISA positive), can be explained by sequestration of replicating FeLV infection in sites other than the bone marrow or by defective replication that produces FeLV antigens but not the whole virus. PCR testing (see below) is helpful in such cases.

Polymerase Chain Reaction Testing

PCR is a highly sensitive confirmatory test that detects FeLV nucleic acid sequences in blood, bone marrow, or biopsy specimens. PCR requires special laboratory expertise and a validated assay; thus, PCR is not yet widely available. Improper sample handling or technique can readily cause inaccurate results with PCR assays.

- For routine blood testing, PCR has no significant advantage over conventional FeLV tests; however, PCR may be helpful for determining the true status of cats with discordant results on conventional tests.
- PCR may be useful for detecting latent (non-replicating but reactivatable) FeLV infection.

Virus Isolation

Isolation of FeLV by culturing the virus from blood or bone marrow is a confirmatory test used primarily in research and is not readily available for clinical use. It is the preferred "gold standard" for validating the accuracy of other testing methods. Bone marrow culture can be used to detect latent, non-replicating, but reactivatable FeLV infection.

Neutralizing Antibody Tests

Serum neutralizing antibody titers are of limited usefulness in the diagnosis or clinical evaluation of FeLV infection. A positive titer merely indicates prior exposure to FeLV through infection or vaccination, but a titer does not confirm current active infection. Vaccine-induced antibody titers do not correlate well with the level of protective immunity.

TREATMENT

There is no proven effective treatment for FeLV, although various immune modulator and antiviral drugs have been used. The quality of life and possibly longevity of FeLV-infected cats are enhanced by general health care, palliative therapy, and treatment of secondary infections that arise.

General Recommendations

When a cat is found to be FeLV positive, optimize general wellness care for the cat and take measures to prevent the spread of infection to other cats. FeLV-infected cats can live for months to several years, especially healthy carriers identified on routine screening tests. The decision to treat or euthanize a cat with FeLV infection is an individual decision based on factors other than just the results of FeLV tests.

Preventing the Spread of Infection

- Confine FeLV-infected cats indoors to prevent the spread of infection to other cats and to reduce the cat's exposure to infectious agents carried by other animals.
- If the cat lives in a multi-cat household, test all other cats and separate infected and uninfected cats. It is especially important that FeLV-infected cats be isolated from kittens, because they are most susceptible. Prevent sharing of food and water dishes, litter pans, and any other item that could be a source of cross-contamination. Vaccinate all uninfected cats, but it is important to recognize that vaccination alone will not prevent infection in all cats.
- Spay or neuter FeLV-infected cats. This prevents mother-to-kitten transmission in utero or via infected milk. It also reduces roaming, aggression, and other stressful behaviors of sexually intact cats.

General Health Care

- Feed cats a nutritionally balanced and complete feline diet. Do not cats feed raw meat, uncooked eggs, or unpasteurized milk, because the risk of food-borne bacterial and parasitic infections is higher in immunocompromised cats.
- Provide optimal wellness care, including parasite control, core vaccinations, dental care, and a thorough semi-annual physical examination with a CBC, blood chemistry profile, urinalysis, and fecal examination. This facilitates early detection and treatment of FeLV-related conditions.
- Diagnose and treat secondary infections that arise because of immunosuppression promptly and aggressively.
- Avoid using corticosteroids and other immunosuppressive drugs except when clearly indicated.

Antiviral Therapy

Antiviral drugs are intended to directly inhibit virus infection and replication. Many anti-retroviral drugs developed for humans are not suitable for treatment of cats because of excessive toxicity, prohibitive cost, or lack of availability. Protease inhibitors developed for humans are species specific and not effective in cats. Two antiviral agents that may have a role in treating FeLV are interferons and zidovudine (AZT). Cats treated with antiviral drugs remain FeLV positive.

Interferons

Recombinant forms of interferon given parenterally in high doses can have both antiviral and immunomodulatory effects.

Feline Interferon-Omega

Recombinant feline interferon-omega (rFeIFN-ω) (Virbagen Omega, Virbac) has become available in Europe, and preliminary results look promising for treatment of FeLV. A placebo-controlled study in 81 FeLV-infected cats showed significant benefit in survival rate, clinical signs, and hematologic parameters with rFeIFN-ω given at 1,000,000 U/kg SC daily for 5 consecutive days in three cycles beginning on day 0, 14, and 60. No serious adverse effects were seen. Expense could be prohibitive for some owners.

Human Interferon-Alpha

A parenteral high dose (100,000–1,000,000 U/kg) of recombinant human interferon-alpha (rHuIFN-α) (Roferon, Hoffman-LaRoche; Intron-A, Schering-Plough) was shown to initially decrease virus load (i.e., FeLV p27 antigenemia) in FeLV-infected cats; however, this is unlikely to be effective as a long-term treatment because cats develop antibodies against the human protein within 6 to 7 weeks that inhibit the drug's activity.

Zidovudine

Zidovudine, a nucleoside reverse transcriptase inhibitor also known as AZT (Retrovir, GlaxoSmithKline; 5 mg/kg PO or SC q12h), has improved stomatitis associated with FeLV and FIV infections in a placebo-controlled study. Another study failed to show a beneficial response in chronically infected cats. Further evaluation is needed before AZT can be routinely recommended for treating FeLV. AZT causes dose-dependent myelosuppression in cats, so the CBC is monitored for nonregenerative anemia. Mild anemia in the first weeks of treatment is common and usually resolves. If the PCV drops below 20%, treatment is discontinued until the PCV recovers (usually 2–3 weeks), then AZT is restarted at half the original dose. Before administration, dilute injectable AZT in 5 ml isotonic sodium chloride to reduce local irritation.

Immune Modulator Therapy

Immune modulators are intended to stimulate the compromised immune function of FeLV-infected cats. Anecdotal reports of clinical improvement with these agents have not been substantiated by controlled studies; thus, conclusive evidence of a significant clinical benefit is lacking. Treated cats usually remain FeLV positive.

Human Interferon-Alpha

Interferons have antiviral effects at high doses (see the previous section) and immunomodulating activity at low doses. There are numerous anecdotal reports of clinical improvement in FeLV-infected cats treated with low-dose oral rHuIFN-α (Roferon, Hoffman-LaRoche; Intron-A, Schering-Plough), diluted to 30 U/ml and given at 30 units PO q24h for 7 days on alternate weeks. The mechanism of action is unknown but is presumed to involve a local immune-modulating effect on oropharyngeal lymphoid tissue. One placebo-controlled study in chronic FeLV-positive cats failed to show improvement in hematologic and clinical parameters.

Acemannan

Acemannan is a carbohydrate polymer derived from the aloe vera plant. For treatment of FeLV, acemannan (Carrisyn; Carrington Laboratories) has been given at 2 mg/kg intraperitoneally weekly for 6 weeks. In uncontrolled studies, no significant improvement was found in clinical and hematologic parameters, FeLV status, and clinical outcome.

Propionibacterium acnes

A commercial bacterial product of *Propionibacterium acnes* (ImmunoRegulin, ImmunoVet; 0.25–0.5 ml, IV, twice weekly then every other week for 16 weeks) has reportedly been beneficial for FeLV infection, but this has not been documented in placebo-controlled studies.

Staphylococcal Protein A

Staphylococcal protein A (SPA) (Sigma) is a purified bacterial cell wall polypeptide that has been given at 10 μg/kg intraperitoneally twice weekly for 10 weeks. Despite anecdotal reports of efficacy in FeLV, controlled studies have failed to show significant beneficial effects on survival, clinical findings, hematology, immune function, or viremia.

PIND-ORF

PIND-ORF (Baypamun, Bayer) is derived from inactivated parapox ovis virus and has been used in Europe as a nonspecific immune stimulant to treat FeLV. Despite anecdotal reports of improvement, a double-blind placebo-controlled study in 150 FeLV-infected cats failed to show significant benefit in survival rate, viremia levels, immune parameters, clinical scores, or hematology scores.

Palliative Therapy

Palliative care, such as antibiotics for secondary bacterial infections, fluid therapy, and nutritional support, may prolong survival in selected patients. Untreated lymphoma and leukemia are usually fatal within a few weeks to months, but anticancer chemotherapy can induce remission in many cats (see Chapters 26 and 27). The prognosis for cats with FeLV-related nonregenerative anemia or myelodysplasia is poor, although blood transfusions may prolong survival (see Chapter 22).

PREVENTION AND CONTROL

Because of the devastating consequences of FeLV infection and its prevalence in the cat population, prevention is of vital importance. Preventive measures include vaccination of individual cats to reduce susceptibility, restriction of free roaming outdoors to reduce exposure, and control measures to reduce the spread of FeLV in catteries.

▼ ***Key Point*** Vaccination reduces the risk of FeLV infection, but not all vaccinated cats are protected; therefore, effective prevention also requires measures that reduce the risk of exposure.

Kittens less than 4 months of age are most susceptible; thus, keep kittens isolated from other cats to minimize the risk of FeLV infection.

Vaccination

Adjuvanted and non-adjuvanted inactivated parenteral vaccines and a canary pox-vectored transdermal vaccine are currently available for prevention of FeLV. The pros and cons of FeLV vaccination are controversial, but overall, FeLV vaccine is considered a "non-core" vaccine that is used according to an individual benefit-risk assessment of each patient (see Chapter 7).

Indications

- Vaccination is recommended for cats with potential risk of exposure to FeLV, especially kittens. This should include cats allowed outdoors, cats living in multi-cat households with infected cats, or cats exposed to other cats of unknown status.
- Vaccination is not recommended for mature cats with minimal to no risk of exposure, such as cats restricted to closed, indoor, FeLV-negative environments.

▼ ***Key Point*** Vaccination is most indicated for cats living in multi-cat households (and shelters) with frequent exposure to new cats and for outdoor cats at risk of contact with other cats of unknown health status.

Administration

- If vaccination is deemed appropriate, administer two doses of vaccine 3 to 4 weeks apart, beginning as early as 8 weeks of age, followed by an annual booster (see Chapter 7). Give FeLV vaccines subcutaneously in the lateral aspect of the distal left rear limb.
- FeLV testing at or before the first vaccination is highly recommended. There is no proven beneficial or detrimental effect from vaccinating a cat for FeLV that already is infected.

Adverse Vaccine Effects

- Acute side effects are infrequent and include local swelling or pain, transient listlessness or fever, and injection site granuloma. Acute hypersensitivity signs (face and paw edema, vomiting, diarrhea, collapse) occur rarely. These effects are attributable mostly to adjuvants.
- Inflammatory nodules occasionally develop at the vaccination site. These can develop into vaccine-associated sarcomas in some cats weeks to years later (incidence is 1 per 10,000 vaccines). Excise or biopsy vaccination site lesions if they persist more than 3 months, are larger than 2 cm, or increase in size 1 month post-injection.
- For cats at risk of exposure, the benefits of FeLV vaccination far outweigh the risk of injection site sarcoma. However, the risk of vaccine-associated sarcoma may be greater than the risk of FeLV infection in well-controlled catteries and for indoor pet cats where the prevalence of infection is virtually nonexistent today.

Efficacy

- In general, many vaccinated cats that are exposed to FeLV develop transient viremia and sometimes latent infection despite vaccination; however, most vaccinated cats apparently are protected against persistent viremia and therefore against FeLV-related disease.
- As a general guideline for discussing vaccination expectations with animal owners, expect 70% to 90% of vaccinated cats older than 4 months of age to be protected against persistent FeLV infection.

Control in Multi-cat Households and Catteries

Control in FeLV-Positive Catteries

The following "test and removal program" is highly effective for eliminating FeLV from a household or cattery:

- Test all cats on the premises for FeLV (up to 30% may be persistently infected), and remove or strictly isolate all confirmed FeLV-positive cats.
- Quarantine the cattery so that there is no movement of new cats into the cattery.
- Vaccinate all FeLV-negative cats.
- Clean and disinfect the premises.
- Clean and disinfect or replace food and water dishes, litter pans, bedding, and toys.
- If infected and uninfected cats are separated but remain in the same household or facility, caretakers must take special precautions to prevent cross-contamination.
- Retest all cats every 1 to 3 months and continue to remove any confirmed FeLV-positive cats.
- Once all cats on the premises have had negative results on two successive tests 3 months apart, the cattery is considered "FeLV free."
- Then isolate all new incoming cats and test as described in the following section.

Control in FeLV-Negative Catteries

The following precautions should be taken for incoming cats:

- Obtain incoming cats from a source with a negative FeLV history.
- Screen incoming cats with ELISA; if test results are negative, vaccinate and then hold them in isolation for 3 months (in case they were recently exposed and are incubating FeLV).
- After a second ELISA-negative result at the end of the 3-month quarantine, new cats can join the cattery.

- ELISA-positive results should be confirmed by IFA or repeat ELISA; however, in cattery situations, the safest course is to consider any cat that has been ELISA positive at any time as too risky to allow into the cattery.

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Chapter 9

Feline Immunodeficiency Virus

Robert G. Sherding

ETIOLOGY

- Feline immunodeficiency virus (FIV) is a member of the lentivirus subfamily of retroviruses. It is an RNA virus with outer envelope and nucleocapsid. FIV originally was isolated in 1986 from a cattery in northern California; however, retrospective assays of stored cat sera have shown that FIV has been widely distributed worldwide since at least the 1960s.
- FIV causes a lifelong infection and gradually progressive decline in immune function that leads to an acquired immunodeficiency syndrome. Manifestations include chronic weight loss, opportunistic infections, chronic inflammatory conditions, and increased risk for malignant neoplasia.
- At least 5 FIV subtypes (clades A through E) have been identified based on genetic differences. Subtypes vary in regional distribution and influence cell tropism and pathogenicity. Subtype A predominates in the Western United States, and subtype B is seen most often in the Eastern United States.
- Numerous wild feline species are susceptible to various subtypes of FIV, including lions, tigers, jaguars, snow leopards, panthers, and bobcats.

Epidemiology

Prevalence

The serologic prevalence of FIV infection has been surveyed in many countries, regions, and cat populations. FIV has been found worldwide.

- The prevalence in indoor pet cats in single-cat households is less than 1%.
- The prevalence in well-controlled purebred catteries is less than 2%.
- The prevalence in free-roaming stray and feral cats in the United States is 2% to 4%.
- The prevalence in a 1991 IDEXX survey of 27,976 sick and high-risk cats in the United States presenting to veterinarians was 7.4%. This included sick cats that had a prevalence of 11.6% and asymptomatic high-risk cats (defined as outdoor pet cats, cats exposed to outdoor cats, or cats in large multicat households) that had a prevalence of 4%.
- The prevalence in some countries in areas with a high density of free-roaming cats, such as Japan and Italy, may reach 25% to 30%.

Age and Gender Distribution

- FIV affects cats of all ages (reported range is 2 months to 18 years); however, the incidence increases with age, and FIV is most prevalent in cats 6 years of age and older.

▼ ***Key Point*** Because of a prolonged asymptomatic latent period, most FIV-infected cats with clinical signs are older than 6 years of age.

- Adult male cats outnumber females 3 or 4 to 1 (see "Transmission").

High-Risk Factors

- Adult, male cats living outdoors or exposed to free-roaming outdoor cats.
- Sexually intact males are at increased risk for fighting behavior that can lead to bite-wound transmission.
- Cats in high-density habitats are at increased risk for territorial fighting that can lead to bite-wound transmission.
- Cats living in large multicat households (>6 cats) that frequently introduce new cats.

Public Health Risks

- FIV is a feline host-specific virus, and there is no evidence that it causes human infection. People who have had intimate contact with infected cats or direct exposure to FIV through cat bites or lab accidents do not develop antibodies, illness, or any other evidence of infection.
- Because of their immunosuppressed state, FIV-infected cats may harbor a variety of other opportunistic pathogens that can infect humans who are immunocompromised.

Transmission

- FIV is shed in saliva and transmitted primarily through direct bite-wound inoculation during territorial fights (hence the higher prevalence in males). Experimentally, a single-tooth puncture wound from a FIV-infected cat is an efficient method of transmitting FIV.

▼ ***Key Point*** Direct inoculation of saliva through biting is the principal mode of FIV transmission. The highest risk for FIV is associated with territorial fighting and biting behavior in sexually intact, adult male cats living outdoors.

- Transmission through intimate contact during cohabitation is unlikely but not impossible. In a study that confined FIV-positive and FIV-negative cats together in the same cages for 2 years, only 1 of 20 negative sentinel cats became infected. Contact transmission has been suspected in rare cases in catteries, but the mode of transmission in most of these cases is undetermined. Fomite transmission is highly unlikely.
- Transmucosal transmission of FIV can occur experimentally through direct atraumatic contact of FIV with oral, vaginal, or rectal mucosa and through artificial insemination; however, these routes are unlikely to be important under natural conditions.
- Experimentally, acute and chronically infected queens may transmit FIV vertically to their kittens in utero or during passage through the birth canal (congenital infection) or postnatally through ingestion of infected milk (lactogenic infection). However, transmission from mother to offspring in these ways is infrequent under natural conditions. More commonly, infected queens pass colostral FIV antibodies to their nursing kittens, causing a false-positive FIV antibody test (e.g., ELISA or Western blot) for up to 6 months (see "Diagnosis").
- Transmission of FIV can readily occur through intravenous transfusion of contaminated blood.

Pathogenesis

- FIV has a primary tropism for lymphocytes but also infects macrophages, salivary glands, and the central nervous system.
- FIV primarily infects and gradually destroys subpopulations of T lymphocytes. This cytopathic effect causes a progressive loss of CD4+ lymphocytes, inversion of the CD4/CD8 ratio, and eventual loss of CD8+ lymphocytes in the late stages of infection. Cell-mediated immunity is impaired to a greater extent than antibody-mediated immunity.
- In addition, impaired production and dysregulation of various cytokines plays a role in the pathogenesis of disease.
- After a prolonged, clinically silent latent period that can extend for years, the progressive loss of T lymphocytes results in an immunodeficiency syndrome characterized by chronic and recurrent infections. FIV infection is lifelong and eventually fatal. The natural incubation period for FIV averages 5 years, corresponding to this lengthy latency.
- FIV has various mechanisms for evading the host immune response so that it can persist and replicate for life.

CLINICAL SIGNS

The clinical disease caused by FIV is influenced by the age and health of the cat, the strain of the virus, the dose and route of exposure, and the interaction with concurrent infectious agents.

▼ ***Key Point*** The most common clinical signs associated with FIV infection are stomatitis-gingivitis (50% of cases), recurrent rhinitis-conjunctivitis, progressive weight loss ("wasting"), diarrhea, and fever.

Acute Primary Infection

This initial phase begins within 4 to 6 weeks after exposure associated with initial viremia. The effects are mild and transient, and usually go unnoticed.

- Transient fever
- Neutropenia and lymphopenia
- Generalized lymphadenopathy characterized by follicular hyperplasia and plasmacytic infiltration
- Infrequent complications: sepsis, cellulitis, pustular facial dermatitis, anemia, diarrhea, and stomatitis

Asymptomatic Latent Infection

This is a prolonged latency period following seroconversion that usually persists several years before signs of immunodeficiency occur. Persistent lymphadenomegaly sometimes is seen during this stage.

▼ ***Key Point*** It is typical for FIV-infected cats to remain clinically healthy for several years before developing clinical signs of disease.

Chronic Disease Syndromes

Advanced FIV infection causes an acquired immunodeficiency syndrome and predisposes the cat to chronic or recurrent opportunistic infections and chronic inflammatory conditions that wax and wane and progressively worsen over months or years. This may involve any combination of the following manifestations.

General Manifestations

- Progressive weight loss and debilitation ("chronic wasting")
- Chronic recurrent bacterial infections that may resolve partially with antibiotics but recur
- Recurrent fevers of unknown origin
- Generalized lymphadenopathy
- Polyclonal hypergammaglobulinemia
- Persistent or recurrent anemia, leukopenia (neutropenia, lymphopenia), or thrombocytopenia

Chronic or Recurrent Bacterial Infections

- *Oral cavity* (most common)—Stomatitis, gingivitis, periodontitis (suppurative or plasmacytic)
- *Respiratory*—Purulent rhinitis and conjunctivitis; pneumonia; pyothorax
- *Intestinal*—Acute or chronic diarrhea due to enterocolitis that can be ulcerative, necrotizing, or pyogranulomatous
- *Cutaneous*—Pustular dermatitis, abscesses, purulent otitis
- *Urinary*—Recurrent urinary tract infections (cystitis, pyelonephritis)

Specific Opportunistic Infectious Diseases

- Viruses—Calicivirus, herpesvirus, poxvirus, papillomavirus
- *Chlamydophila felis*
- *Mycoplasma haemofelis*
- Bacteria—*Staphylococcus, Pseudomonas, Mycobacterium, Yersinia*
- Fungi—*Candida, Cryptococcus, Aspergillus,* dermatophytes
- Protozoa—*Toxoplasma, Giardia, Cryptosporidium*
- Parasites—*Demodex, Notoedres*

Stomatitis

- Chronic ulceroproliferative, lymphocytic-plasmacytic stomatitis is the most frequent clinical manifestation of FIV, affecting up to 50% of cats. Lesions often begin in the fauces (faucitis) and spread rostrally along the maxillary gingivae. Clinical signs include oral pain, inappetence, foul odor, and loss of teeth.
- Concurrent oral infection with calicivirus is found in most cases, suggesting it may be a cofactor.
- Teeth cleaning and medical treatments (e.g., antivirals, immunomodulators, antibiotics, or corticosteroids) usually provide only temporary improvement (see "Treatment" and Chapter 64). The most effective treatment for resolving this condition is full-mouth dental extractions with complete removal of all roots.

Neurologic Disease

- The likelihood of developing neurologic disease is age dependent (especially young kittens) and strain dependent.
- Pathogenesis—FIV is neurotropic, directly infecting microglia and astrocytes and leading to neuronal damage.
- Signs (variable)—Dementia, behavior abnormalities (agitation, rage, hiding, disrupted sleep pattern, loss of litter training), compulsive roaming, circling, facial twitching, licking motions, lip-sucking, gait abnormalities, and seizures.
- Neurologic exam (variable)—Abnormal mentation, anisocoria, delayed papillary reflexes, gait abnormalities, and abnormal postural reflexes.
- Electrodiagnostics (e.g., electroencephalogram, brain stem auditory evoked potential, visual evoked potential, and nerve conduction velocity; see Chapter 125) are often abnormal.
- Some cats improve neurologically with zidovudine (see "Treatment").

Neoplasia

- FIV-infected cats have increased risk of B cell lymphoma and myeloproliferative neoplasia.
- Various other neoplasms occur sporadically, for example, squamous cell carcinoma and adenocarcinoma.
- Tumors in FIV-infected cats are most likely secondary to impaired immune function rather than a direct oncogenic effect of FIV.

Other Feline Immunodeficiency Virus-Associated Diseases

- Ocular—Anterior uveitis, chorioretinitis, glaucoma, pars planitis, retinal hemorrhages, and retinal degeneration
- Lymphocytic polymyositis (immune mediated?)
- Nephropathy—Chronic renal failure, proteinuria, and renal lesions of glomerulosclerosis, microcystic tubular dilatation, and interstitial nephritis and fibrosis

DIAGNOSIS

- The routine diagnosis of FIV depends on the detection of anti-FIV serum antibodies using assays such as enzyme-linked immunosorbent assay (ELISA), immunofluorescent antibody (IFA), or Western blot. The American Association of Feline Practitioners recommends that the FIV antibody status for all cats over 6 months of age be known. Furthermore, periodic retesting is justifiable in cats with high risk of exposure, such as outdoor cats.
- Assays for virus are not routinely used because the concentration of FIV in the blood is low, making detection difficult. Virus isolation and polymerase chain reaction (PCR) are used in specialized research labs for detecting virus or viral antigen. Virus isolation is prohibitively expensive and time-consuming.

Assays using PCR are not yet sufficiently reliable or standardized to be recommended for routine clinical diagnosis.

Indications for Feline Immunodeficiency Virus Testing

- When cats are sick
- Healthy cats not previously tested
- Newly adopted cats
- Cats with potential exposure, such as bite wounds from any cat of unknown FIV status
- Before vaccinating cats with FIV vaccine
- Annual retesting of cats with high risk of exposure, such as cats living with an FIV-positive cat or going outdoors unsupervised

Assays for Antibody

▼ ***Key Point*** A confirmed positive FIV antibody test indicates persistent, lifelong FIV infection, except when interpretation is unclear because of antibodies induced by prior FIV vaccination or because of passively acquired maternal antibodies in young kittens (<6 months of age).

- Seroconversion usually occurs within 4 to 6 weeks after exposure; however, this is highly variable and it can take up to 6 months for FIV antibodies to appear in some cats.
- Maternal FIV antibodies acquired from colostrum in nursing kittens can cause positive test results in uninfected kittens up to 6 months of age; thus, reevaluate all positive kittens at 2-month intervals until 6 months of age to determine whether they are infected or not.

▼ ***Key Point*** Regardless of whether a positive or negative test result is obtained for FIV antibody, all kittens younger than 6 months of age must be retested after they reach 6 months of age to determine their actual status.

ELISA Antibody Test

- ELISAs are sensitive, accurate, and considered the preferred screening tests for FIV.
- ELISAs are simple and rapid enough for convenient in-office or point-of-care screening, such as SNAP FIV/FeLV Combo (IDEXX) that tests simultaneously for FIV antibodies and FeLV antigen.
- Occasional false positives occur; thus, confirm all positive ELISA results by Western blot or IFA at a commercial lab.
- False-negative results can occur in the early stages of acute infection before seroconversion has occurred or rarely in the terminal stages of immunodeficiency when antibody levels can fall below detectable levels.

Immunofluorescent Antibody Test

- Available in some commercial laboratories
- Accuracy comparable to ELISA tests but less convenient

Western Blot Test

- Detects antibodies against specific viral proteins, and is considered the "gold standard" for confirming ELISA-positive results
- Available in research and commercial laboratories

Assays to Detect Virus

- Virus isolation and PCR assays can be used to detect FIV in the blood, tissues, or body fluids of infected cats.

PCR Assay

- FIV is difficult to detect reliably by PCR because of wide genetic variability among field strains and because of low virus levels in blood during the prolonged asymptomatic latent phase of infection when most testing is performed.
- PCR assays would theoretically be useful in place of the antibody tests for early detection of infection prior to seroconversion and for diagnosis of terminal stages of infection when antigen levels may be high and antibody levels are depressed. Virus assays could also be used as an alternative to antibody testing in vaccinated cats.
- Based on the rate of false-positive and false-negative results, commercial PCR assays for FIV are generally too unreliable to be recommended. Although PCR assays are promising for the future, currently available commercial assays are not yet adequately standardized or validated. In addition, it is uncertain whether PCR assays detect all field strains of FIV found in cats.

Virus Isolation

- Virus isolation (culture) is a valuable research tool but is too impractical for use as a clinical diagnostic aid.

TREATMENT

▼ ***Key Point*** No currently available treatment is effective for eliminating FIV once infection is established; thus, assume that confirmed infections are lifelong and incurable.

- Even though FIV is incurable, healthy FIV-positive cats can live for years before developing clinical signs, and symptomatic cats often can be managed for months to years with supportive care, antiviral

therapy, immune modulators, and antibiotics as needed to control secondary infections.

- The goal of therapy in FIV is to decrease the virus load with antiviral therapy or to increase the host immune response through immune modulator drugs. Although some studies have shown clinical improvement in sick FIV-positive cats with these treatments, there is little or no evidence that immune modulation and antiviral therapy benefit health or increase longevity in otherwise healthy FIV-infected cats.

Specific Antiviral Therapy

- Current and future antiretroviral therapies developed for human immunodeficiency virus (HIV) may or may not be applicable to cats. Many of these drugs have not been suitable for treatment of FIV because of excessive toxicity, lack of efficacy, prohibitive cost, or lack of availability.

Zidovudine

- Zidovudine, a nucleoside reverse transcriptase inhibitor also known as AZT, is the most well-studied antiviral for treating FIV infection. In cats infected with FIV, zidovudine inhibits viral replication, decreases virus burden, improves immunologic parameters (such as the CD4/CD8 ratio), reduces clinical disease, and increases survival time. One placebo-controlled study showed regression of FIV stomatitis. Clinical improvement in various other FIV-related manifestations is reported.
- Give zidovudine (Retrovir, GlaxoSmithKline) at dosages of 5 mg/kg PO or SC q12h. Compound oral AZT in gelatin capsules or flavored syrup. Dilute injectable AZT in 5 ml of isotonic sodium chloride to reduce local irritation.
- Zidovudine has been well tolerated in cats treated for over 2 years. However, the drug is myelosuppressive, so monitor the complete blood count for nonregenerative anemia. Mild anemia in the first weeks of treatment is common and usually resolves. If the packed cell volume (PCV) drops below 20%, discontinue treatment until PCV recovers (usually 2–3 weeks), then restart at half the original dose.
- Unfortunately, mutation of the virus allows drug-resistant strains to emerge after several months of therapy.

Interferon

- Recombinant forms of interferon given parenterally in high doses can have both antiviral and immunomodulatory effects. Feline interferon-omega and human interferon-alpha have both been shown to significantly inhibit replication of FIV, but feline interferon-gamma has no antiviral effect and actually enhances FIV replication.
- Recombinant feline interferon-omega (rFeIFN-ω) has become available in Europe, and preliminary results look promising for treatment of feline leukemia virus and possibly FIV. Treatment with rFeIFN-ω (Virbagen Omega, Virbac) is given at 1,000,000 U/kg SC daily for 5 consecutive days in three cycles beginning on day 0, 14, and 60. Expense will be prohibitive for some owners.
- A parenteral high dose (100,000–1,000,000 U/kg) of recombinant human interferon-alpha (rHuIFN-α) (Roferon, Hoffman-LaRoche; Intron-A, Schering-Plough) may initially decrease virus load, but this is unlikely to be effective long term because cats develop antibodies against the human protein after 6 to 7 weeks that inhibit the drug's activity.

Other Antiviral Drugs

- Stampidine, an experimental nucleoside reverse transcriptase inhibitor, shows promise as a future treatment for FIV. In a preliminary study in chronically FIV-infected cats, stampidine given orally significantly decreased the virus load with minimal side effects.
- Protease inhibitors are a class of drugs that are frequently used to treat humans with HIV; however, protease inhibitors developed for HIV are species specific and not effective against FIV.

Immune Modulator Therapy

- Immune modulators are intended to stimulate the compromised immune function of FIV-infected cats. Anecdotal reports of clinical improvement with these agents have not been substantiated by controlled studies; thus, conclusive evidence of efficacy is lacking.
- Immune modulator agents that have been used to treat FIV include low-dose oral human interferon-alpha (Roferon, Hoffman-LaRoche; Intron-A, Schering-Plough; 30 units PO, daily on alternate weeks), bovine lactoferrin (40 mg/kg PO q24h), acemannan (Carrisyn, Carrington Labs), *Propionibacterium acnes* (ImmunoRegulin; ImmunoVet), and *Staphylococcus* protein A (SPA).

General Supportive Therapy

- Use antibiotics to treat cats with FIV-related bacterial infections, using culture and sensitivity guidance whenever possible. Response to antibiotics can be dramatic in some cases.
- For palliative treatment of stomatitis, use metronidazole (10 mg/kg PO q12h) and clindamycin (12.5 mg/kg PO q12h). Stomatitis may also improve with the immunotherapeutic agent, bovine lactoferrin (40 mg/kg PO or topically q24h), zidovudine (see "Specific Antiviral Therapy"), or anti-inflammatory doses of prednisolone (5 mg/cat PO q12h). Full-mouth dental extraction is required in refractory cases.
- Use fluid therapy and nutritional support as indicated by the patient's needs.

- Keep FIV-positive cats indoors to prevent exposure of the immunosuppressed cat to infectious diseases carried by other animals and to decrease the spread of FIV to other cats.
- Continue routine vaccinations in FIV-positive cats, although killed products are preferred. Studies have shown FIV does not interfere with the response to vaccination until the terminal stages.
- Avoid the use of griseofulvin to treat dermatophytes in FIV-positive cats because of an increased risk of griseofulvin-induced neutropenia.

PROGNOSIS

Healthy FIV-positive cats can live for several years before developing clinical signs. Even symptomatic cats can live for months to years with good quality of life. In one study of FIV-positive cats, 18% died in the first 2 years and another 18% had progression of clinical signs; however, more than 50% remained asymptomatic for the 2-year follow-up period.

PREVENTION

Prevent Exposure

▼ ***Key Point*** The best prevention for FIV is to prevent cats from roaming freely outdoors.

- Spay and neuter cats that go outdoors to reduce roaming and fighting behavior.
- Prevent exposure to high-risk cats, such as stray and feral cats or untested outdoor cats.
- Keep infected cats indoors and isolated from uninfected cats to reduce the risk to other cats. The risk of transmission among housemates that do not fight is considered low but possible.
- Spay and neuter FIV-positive cats. It is especially important to remove FIV-infected females from breeding programs.

Vaccination

- A killed, adjuvanted, dual-subtype, whole-virus FIV vaccine is currently available that contains FIV subtypes A and D (Fel-O-Vax FIV, Fort Dodge). The range of crossprotection against the other natural subtypes of FIV is uncertain. Until additional evidence of efficacy in the field becomes available, FIV vaccination is not recommended as a core vaccine for cats.
- Immediately prior to vaccinating any cat for FIV, first determine that the FIV antibody test is negative.

▼ ***Key Point*** FIV antibodies from vaccination and infection are indistinguishable; thus, cats vaccinated for FIV will be positive for FIV antibodies for at least 12 months, thereby eliminating the diagnostic usefulness of FIV antibody tests.

- Kittens born to vaccinated queens will be positive for passively acquired FIV antibodies for up to 12 weeks.
- An effective vaccine for HIV in humans has yet to be developed despite intensive efforts. New vaccine strategies are under development for both HIV and FIV. The natural host immune response to FIV infection is almost never effective, and what is needed to elicit protective immunity is not yet understood. This suggests that conventional approaches to vaccine development may not be successful for these lentiviruses.

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Chapter 10

Feline Infectious Peritonitis (Feline Coronavirus)

Robert G. Sherding

Feline infectious peritonitis (FIP) is a progressive and highly fatal systemic disease of cats caused by feline coronavirus. Feline coronavirus most frequently causes inapparent enteric infection with fecal shedding of virus. Mild enteritis and diarrhea are seen rarely (see Chapter 14). A mutation of feline coronavirus during intestinal replication enables it to infect macrophages and cause FIP. Despite its name, the lesions of FIP are widespread and not restricted to the peritoneum. Effusive and non-effusive forms of FIP occur. Since its recognition in the 1950s, FIP has been one of the most studied diseases of cats, yet a definitive diagnostic test, an effective treatment, and a reliable vaccine are lacking. With the decline in prevalence of feline leukemia virus from vaccination, FIP has become the deadliest infectious disease of cats.

ETIOLOGY

Feline Coronavirus

- Feline coronavirus (FCoV) is a single-stranded enveloped RNA virus with distinctive petal-shaped peplomers projecting from the surface. There are two serotypes of FCoV that differ in cell culture characteristics. Serotype I predominates in North America and Europe, whereas Serotype II is more closely related to canine coronavirus (CCV) and predominates in Japan.
- Coronaviruses are found in many animals and are generally adapted for infecting epithelial cells of the respiratory or gastrointestinal tract. FCoV is closely related to CCV, swine transmissible gastroenteritis virus (TGEV), porcine respiratory virus, and some human coronaviruses. The CCV that causes enteritis and diarrhea in dogs (see Chapter 14) can infect cats and cause antibodies that crossreact with FCoV. Experimentally, CCV can cause enteritis, diarrhea, and even FIP in cats.

Pathogenesis of Feline Infectious Peritonitis

▼ ***Key Point*** FIP-causing coronaviruses are genetic mutants of harmless enteric FCoV.

- It was previously thought that cats were infected by two similar but distinct coronaviruses, the innocuous feline enteric coronavirus and the deadly FIP virus, but these are now considered phenotypic variants (biotypes) of the same virus. The non-mutated enterotropic FCoV typically causes a clinically inapparent infection of intestinal epithelial cells with fecal shedding of virus. During replication in the cat's intestinal tract, FCoV mutates frequently, especially in kittens, and this sporadically results in critical genetic mutations that enable FCoV to infect and replicate in macrophages.

▼ ***Key Point*** Any cat with inapparent FCoV infection has the potential to develop FIP if the virus mutates during replication to allow the mutated FCoV variant to infect macrophages. Viral replication in macrophages is the defining event in FIP.

- Macrophages then replicate the mutated coronavirus and carry it to target tissues such as the peritoneum, pleura, kidney, uvea, and nervous system, resulting in widespread immune-mediated vasculitis, disseminated perivascular pyogranulomatous inflammation, and exudative fibrinous polyserositis. These are the characteristic lesions of FIP.
- The pathogenesis involves circulating immune complexes, complement fixation, cytokine release, apoptosis of activated T lymphocytes, and vascular damage with necrosis and increased permeability.

▼ ***Key Point*** It is not the virus that causes widespread damage in FIP. The disease is a consequence of the cat's immune reaction to the virus.

- Natural immunity to FCoV is poorly understood but is presumed to be cell mediated rather than antibody mediated. Circulating FCoV antibodies can actually enhance progression of the disease.

EPIDEMIOLOGY

Prevalence

- FCoV is ubiquitous in cats worldwide. In many regions, 50% of cats are positive for coronaviral antibodies (i.e., seroprevalence). The majority of these seropositive cats represent current or past inapparent infection with non-mutated FCoV. Only some of these develop into mutated FIP-causing infections; thus, the prevalence of FIP is much lower.
- The prevalence of FCoV infection is highest in cats confined in crowded groups, such as catteries, shelters, and multiple cat households, where the seroprevalence ranges from 50% to 90%.
- In endemic catteries where the seroprevalence approaches 90%, most FCoV-infected cats remain healthy and only 5% develop FIP.
- The seroprevalence of FCoV in free-roaming feral and stray cats is 12% to 15%. The lower prevalence is presumed to relate to less social interaction and less exposure to fecally excreted virus than cattery cats.
- The seroprevalence in single-cat households is 15% or less.
- In a large survey of North American veterinary teaching hospitals, FIP was diagnosed in 1 of every 200 new feline accessions. This population mostly represents sick cats seen by veterinarians.
- FCoV can infect most wild felids, including the lion, cougar, cheetah, jaguar, leopard, bobcat, sand cat, caracal, serval, and lynx. Cheetahs are especially susceptible to developing FIP.

Risk Factors

▼ ***Key Point*** Whenever FCoV exists in a cat, so does the potential for developing FIP.

- FCoV infection occurs most often in young kittens after maternal antibodies dissipate, between 6 and 16 weeks of age; thus, the infection rate is highest in catteries where kittens are raised in association with virus-excreting adult cats.
- Young cats have increased risk for developing FIP. The peak incidence for FIP is between 6 months and 3 years of age, although cats of any age can be affected.
- Crowded group confinement (multicat households, purebred catteries, shelters) increases risk.
- Factors intrinsic to the shelter experience increase fecal shedding of FCoV up to 1 million-fold after 1 week.

▼ ***Key Point*** Most cats with FIP come from catteries and shelters.

- Any factor that increases FCoV replication in the intestines of an infected cat will increase the probability of the virus mutating to a form that can cause FIP. Thus, viral load, stress, immune impairment, corticosteroids, surgery, and concurrent disease (e.g., feline leukemia virus or feline immunodeficiency virus) can be risk factors for FIP.
- Inherited genetic susceptibility to FIP is a factor in some purebred cats and in cheetahs.

Transmission

- FCoV is primarily excreted in feces from cats with inapparent enteric infection. Healthy carriers often shed FCoV in their feces for at least 10 months, and some cats shed persistently for many years, possibly for life. One-third of healthy FCoV-seropositive cats are actively shedding virus. In high-density endemic catteries, up to 60% of healthy cats may be shedding virus at any given time.
- FCoV is usually inactivated in 24 to 48 hours at room temperature, but the virus can survive up to 7 weeks in dried fecal debris; thus, environmental contamination with small particles of used litter is an important source of infection. Contaminated surfaces, food and water dishes, and human clothing, shoes, and hands can act as fomites. Most disinfectants and detergents easily destroy FCoV.
- Transmission to uninfected cats most frequently occurs through oronasal contact with virus-containing feces or contaminated material from the environment. Contaminated litter and dust particles deposited on the fur are ingested during normal grooming activity.

▼ ***Key Point*** Indoor confinement in crowded groups increases exposure to large doses of infectious virus in feces in shared litter boxes.

- In catteries, kittens are most frequently infected as they lose maternal-derived immunity after 6 weeks of age through contact with feces from virus-shedding adult cats. Removing kittens from contact with adult cats at 5 to 6 weeks of age prevents infection (see "Prevention").
- FCoV can also be excreted in saliva, respiratory secretions, and urine, but these are unlikely to be important sources of infection.
- Transplacental transmission is possible but uncommon.
- Cats with FIP shed mostly the avirulent non-mutated FCoV, not the virulent mutated virus that causes FIP; thus, FIP itself is not directly contagious. Cats with FIP also excrete less FCoV than healthy carriers.

CLINICAL SIGNS

Cats with non-mutated FCoV infection of the intestinal tract infrequently develop clinical signs (see Chapter 14). This section describes the clinical manifestations of mutated, FIP-producing FCoV infection. Cats with FIP often present initially with nonspecific and non-localizing signs, such as fever, anorexia, inactivity, weight loss, vomiting, diarrhea, dehydration, and pallor (anemia). As the disease progresses, these signs worsen and additional clinical signs develop that indicate either body cavity effusions in the "wet" form of the disease or organ-specific abnormalities in the non-effusive or "dry" form (Table 10-1). Approximately 75% are effusive and 25% are non-effusive. Some cats manifest features of both effusive and non-effusive disease or change over time from one form to the other.

Incubation and Clinical Course

Incubation and Onset of Feline Infectious Peritonitis

- The natural incubation period is extremely variable, ranging from a few weeks to several years. Cats are at greatest risk for developing FIP within the first 6 to 18 months after initial infection with FCoV.
- This encompasses the unpredictable but often prolonged period of time it takes a carrier of the harmless, non-mutated FCoV to develop the critical viral mutation and then the time it takes the mutated virus to produce clinical disease.
- The onset of clinical signs is often insidious, but occasionally it is sudden, especially in young kittens.

Table 10-1. CLINICAL SIGNS AND LABORATORY ABNORMALITIES IN FELINE INFECTIOUS PERITONITIS

Nonspecific Signs
Chronic unresponsive fever of unknown origin
Unexplained anorexia, lethargy, and weight loss
Effusion Signs
Fluid distension of the abdomen
Dyspnea due to pleural effusion
Muffled heart sounds due to pericardial effusion
Scrotal swelling
Organ-Specific Signs
Abdominal disease
Enlarged, firm, irregular kidneys
Icterus and hepatomegaly
Intestinal pyogranulomatous mass
Splenomegaly
Pancreatitis
Mesenteric lymphadenopathy
Omental adhesions and mass
Neurologic signs (multifocal and progressive)
Uveitis (iridocyclitis; chorioretinitis)
Pyogranulomatous interstitial pneumonia
Testicular enlargement (orchitis)
Laboratory Abnormalities
Anemia (nonregenerative)
Neutrophilic leukocytosis or leukopenia; lymphopenia
Elevated serum protein (hyperglobulinemia)
Elevated serum liver enzymes and bilirubin (also bilirubinuria)
Azotemia of primary renal origin
Proteinuria of renal origin
Pyogranulomatous or fibrinous body cavity effusion
Elevated CSF protein and leukocytes (neutrophils)

CSF, cerebrospinal fluid; FIP, feline infectious peritonitis.

▼ ***Key Point*** Chronic fluctuating fever that is unresponsive to antibiotics is a frequent early sign of FIP.

Clinical Course

- Once viral dissemination occurs and clinical illness develops, FIP is virtually always progressive and fatal. However, there is considerable variation in the duration of clinical illness before death; 3 to 6 weeks is typical, but prolonged illness exceeding 6 months can occur, as can intermittent illness punctuated by periods of remission.
- For effusive FIP, the clinical course is usually acute (days to weeks).
- For non-effusive FIP, the course is often chronic and insidious (weeks to months).
- Cats with only ocular involvement sometimes survive for a year or more.

Effusive (Wet) Form of Feline Infectious Peritonitis

▼ ***Key Point*** In cats with the effusive (wet) form of FIP, the predominant location of the inflammatory fluid is the abdominal cavity in 62%, the thoracic cavity in 17%, or both cavities in 21%.

Abdominal Effusion (Peritonitis)

- Effusive FIP involving the peritoneal cavity causes progressive, non-painful, fluid distension of the abdomen.
- Effusion is detected by palpation and percussion of a fluid wave. In the early stages, a small amount of abdominal fluid may be detected by palpation of intestinal loops that feel excessively slippery, as though the serosal surfaces are highly lubricated. Pain on palpation is infrequent.
- Extension of the peritoneal inflammation may involve the gastrointestinal tract (vomiting, diarrhea), hepatobiliary system (jaundice), or pancreas (vomiting due to pancreatitis).
- Scrotal swelling may occur in intact males as a direct extension of the peritoneal inflammation and effusion into the testicular tunics.
- Adhesions may organize the mesentery, omentum, and viscera into an irregular, firm mass that is palpable in the cranioventral abdomen.

- Abdominal effusion is confirmed by radiography, ultrasonography, or abdominocentesis, and the results of fluid analysis are highly indicative of FIP (see "Diagnosis").

Thoracic Effusion (Pleuritis)

- Dyspnea, tachypnea, and exercise intolerance are the major presenting signs because lung expansion is restricted by compression from fluid in the pleural space.
- Cats with pleural effusion may prefer a sitting or sternal recumbent posture to facilitate breathing. Increased respiratory distress may occur with exercise, with physical restraint in the hospital, or with repositioning in lateral recumbency (i.e., orthopnea).
- Thoracic effusion may cause muffled heart and lung sounds on auscultation and hyporesonance and a horizontal fluid line on thoracic percussion.
- Thoracic effusion is confirmed by radiography or thoracocentesis (see Chapter 164). The results of fluid analysis are highly indicative of FIP (see "Diagnosis").

Pericardial Effusion

- Pericardial effusion due to fibrinous pericarditis may occur in FIP, with or without other effusions. In one survey, FIP was the second most frequent cause of feline pericardial effusion, accounting for 14% of cases.
- Pericardial effusion in FIP does not usually cause overt clinical signs. It may be suspected from auscultation (muffled heart sounds), thoracic radiography, or electrocardiography, and it is confirmed by echocardiography (see Chapter 151).

Non-effusive (Dry) Form of Feline Infectious Peritonitis

▼ ***Key Point*** The non-effusive (dry) form of FIP is characterized by multifocal pyogranulomatous inflammation and necrotizing vasculitis in various organs, such as the abdominal viscera (e.g., liver, spleen, kidneys, pancreas, and intestines), eyes, central nervous system (CNS), and lungs.

Pyogranulomas appear as multiple discreet or coalescing gray-white nodular masses of variable size on the surface and within the parenchyma of affected organs. These are often mistaken for tumors. Effusion is often minimal or absent. The specific organs affected and the degree of resulting organ failure determine the presenting clinical signs.

Kidney Disease

- Pyogranulomatous nephritis causes the kidneys to become palpably enlarged, firm, and irregular ("lumpy"), associated with pyogranulomas scattered over the surface and infiltrating throughout the renal cortex.
- Extensive renal involvement occasionally causes renal failure with polyuria-polydipsia and azotemia (increased blood urea nitrogen [BUN] and serum creatinine).
- Proteinuria is a frequent laboratory finding in renal FIP. In addition, large quantities of circulating immune complexes may lead to subclinical glomerulonephritis with any of the other forms of effusive and non-effusive FIP.

Liver Disease

- Pyogranulomatous hepatitis (hepatomegaly, jaundice, and signs of hepatic failure) may occur in FIP.
- The most consistent laboratory abnormalities are bilirubinuria and hyperbilirubinemia. Mild to moderate elevations of serum liver enzymes (alanine aminotransferase, alkaline phosphatase) and serum bile acids also may occur.

Disease in Other Abdominal Organs

- Pyogranulomatous lesions may cause palpable enlargement of the visceral lymph nodes, spleen, or omentum.
- Pyogranulomatous enterocolitis may cause diarrhea and diffuse or masslike intestinal thickening, especially in the ileocecocolonic region.
- Pancreatic involvement can occasionally cause pancreatitis and, rarely, diabetes mellitus.

Ocular Disease

- Ocular lesions of FIP are usually bilateral and affect the vascular tunic or uvea (uveitis). Lesions may sometimes cause blindness.
- Manifestations of exudative anterior uveitis (iridocyclitis) may include miosis, aqueous flare, keratic fibrinocellular precipitates, hypopyon ("mutton-fat" deposits of cells and fibrin), hyphema, anterior chamber adhesions (synechia), corneal edema, and deep neovascularization of the cornea (see Chapter 136).
- Chorioretinitis from posterior uveal involvement is detected by ophthalmoscopic examination and may include perivascular cuffing, exudative retinal detachment, and retinal hemorrhages (see Chapter 138).

Neurologic Disease

- Multifocal pyogranulomatous meningoencephalitis and myelitis are frequent in FIP. Inflammatory lesions are perivascular and often involve the meningeal and ependymal layers. In one report, 29% of cats with FIP developed neurologic signs. In a retrospective survey of 286 cats with neurologic disease, lesions indicating FIP of the CNS were found in 16%. In another large

survey, FIP was the most common spinal disease in cats.
- The neuroanatomic distribution of the lesions determines clinical signs; some of the most common are ataxia, tremors, vestibular dysfunction, seizures, posterior paresis, hyperesthesia, and behavioral changes. The relentless progression and multifocal nature of the signs are characteristic features of neural FIP.
- Neuropathies occasionally involve the cranial nerves (e.g., trigeminal or facial) or peripheral nerves (e.g., brachial or sciatic).
- Cats with neural FIP often develop secondary hydrocephalus when the inflammatory process obstructs the flow of cerebrospinal fluid (CSF). In one study of 24 cats with neural FIP, 75% had hydrocephalus. Dilatation of the ventricular and central canal system is identified on computed tomography (CT) and magnetic resonance imaging (MRI) scans. Meningeal enhancement also is seen on MRI.
- The diagnosis of neural FIP depends on CSF analysis (see the section on diagnosis).

Pulmonary Disease

- Pyogranulomatous pneumonia can be found in cats with FIP on thoracic radiographs or at necropsy, but in most cases this is clinically silent or only causes a mild cough.
- This appears radiographically as a diffuse, poorly defined, patchy or nodular interstitial pulmonary infiltrate.

Reproductive Disease

- Testicular enlargement caused by pyogranulomatous orchitis has been reported in FIP.
- Contrary to what has been speculated in the past, FCoV is not directly associated with cattery reproductive problems, neonatal deaths, or birth of weak or "fading" kittens.

DIAGNOSIS OF ENTERIC FELINE CORONAVIRUS

Fecal Virus Detection

- Non-mutated FCoV infection is characterized by persistent viral replication in enterocytes and fecal shedding of virus. Active fecal shedding of FCoV can be confirmed by reverse transcription polymerase chain reaction (RT-PCR) assay of feces (see the later section on RT-PCR assay) or by electron microscopy of feces. False negatives occur with both of these diagnostic techniques.
- The quantity of fecal virus can fluctuate, so ideally feces should be checked daily for 4 to 5 consecutive days before determining a cat is a non-shedder.

Intestinal Biopsy

- Intestinal biopsy shows nonspecific lesions of villous tip injury, with stunting and fusion of villi.
- Immunofluorescence or immunohistochemical staining for viral antigen in intestinal biopsies is confirmatory.

DIAGNOSIS OF FELINE INFECTIOUS PERITONITIS

The diagnosis of FIP is usually suspected from clinical signs and the results of routine laboratory evaluations (see Table 10-1). There is no single reliable confirmatory test for FIP; thus, base the clinical diagnosis of FIP on the combined results of well-chosen laboratory evaluations (e.g., hematology, serum chemistry, cytology, serology, and virology), diagnostic imaging, and histopathology (Table 10-2).

▼ ***Key Point*** Clinical signs and laboratory abnormalities in cats with FIP are not specific for the disease; however, collectively these may provide strong circumstantial evidence for a presumptive diagnosis of FIP.

Routine Laboratory Evaluations

- Hematology often reveals nonspecific abnormalities reflecting the chronic inflammatory response, such as nonregenerative anemia, neutrophilic leukocytosis or leukopenia, and stress lymphopenia.
- Total serum protein and serum globulins (especially gamma and alpha$_2$) are increased by the chronic immune stimulation in 70% of non-effusive cases and 50% of effusive cases, whereas serum albumin is often decreased. One study showed that a decreased serum albumin-to-globulin ratio (A/G < 0.8) indicates a high probability of FIP (92% positive predictive value); while an A/G > 0.8 suggests that FIP is unlikely (61% negative predictive value). Serum protein electrophoresis is usually not necessary.
- Serum chemistries may detect involvement of abdominal organs such as the liver (increased serum liver enzymes, bilirubin, and bile acids), kidneys (increased creatinine and BUN), or pancreas (increased pancreatic lipase immunoreactivity).
- Urinalysis findings may include proteinuria or bilirubinuria.
- Disseminated intravascular coagulation sometimes develops in FIP, resulting in prolonged coagulation times, decreased platelets, and increased fibrin degradation products (see Chapter 23).

Diagnostic Imaging

Diagnostic imaging is useful for identifying organ sites of involvement in FIP. Imaging also facilitates procurement of diagnostic fluid or biopsy specimens.

Table 10-2. DIAGNOSTIC FEATURES OF FELINE INFECTIOUS PERITONITIS

Parameter or Procedure	Findings Suggestive of FIP
Age	6 mo to 3 yr (but all ages affected)
Habitat	Cattery or multicat household
Signs (see Table 10-1)	Fever (unresponsive)
	Effusion (abdominal, thoracic)
	Liver disease (jaundice, etc.)
	Renal disease (renomegaly)
	Intestinal disease (GI signs)
	Ocular disease (uveitis)
	CNS disease (multifocal)
	Pulmonary disease (cough)
Clinical course	Progressive
Complete blood count	Anemia (nonregenerative)
	Neutrophilia or neutropenia; left shift
	Lymphopenia
	Neutrophil inclusions (immune complexes?)
Plasma proteins	Increased total serum protein
	Hyperglobulinemia (gamma, alpha$_2$)
	A/G ratio < 0.8
	Hyperfibrinogenemia (400–700 mg/dl)
Serum chemistries	Abnormal liver tests (increased ALT, ALP, bile acids, bilirubin)
	Azotemia (increased BUN, creatinine)
	Increased PLI assay (pancreatitis)
Urinalysis	Proteinuria, bilirubinuria
Radiography and ultrasonography	Effusions (abdominal, thoracic)
	Organomegaly (liver, kidney, intestine, etc.)
	Organ infiltration (lung)
CT and MRI brain imaging	Hydrocephalus, meningeal enhancement
Fluid analysis of effusion:	Yellow, clear, sticky, foamy, fibrinous
Protein	4–10 g/dl (A/G ratio < 0.8, globulin > 50%, gamma globulin > 32%)
Leukocytes	1,000–20,000 cells/µl
Cytology	Pyogranulomatous exudate
Cerebrospinal fluid analysis:	
Protein	50–350 mg/dl
Leukocytes	100–10,000 cells/µl
Cytology	Neutrophils > mononuclear
Serology	High FCoV antibody titer (see text)
RT-PCR assay	FCoV nucleic acid (in blood, fluid, or tissue)
Histopathology	Vasculitis and pyogranulomatous inflammation
	Positive immunofluorescence and immunohistochemistry

A/G, albumin-to-globulin ratio; ALP, alkaline phosphatase; ALT, alanine transaminase; BUN, blood urea nitrogen; CNS, central nervous system; CT, computed tomography; FCoV, feline coronavirus; FIP, feline infectious peritonitis; GI, gastrointestinal; MRI, magnetic resonance imaging; PLI, pancreatic lipase immunoreactivity; RT-PCR, reverse transcription polymerase chain reaction.

Radiography and Ultrasonography

Radiography is useful for confirming abdominal or thoracic effusion, abdominal organ enlargement (e.g., kidney and liver), or pulmonary infiltration. Affected abdominal organs (liver, kidney, spleen, pancreas, intestines, omentum, and lymph nodes) also can be imaged, aspirated, and biopsied using ultrasonography.

CT and MRI of the CNS

In cats with neurologic FIP, secondary obstructive hydrocephalus is a common finding on CT and MRI scans. Contrast enhancement of the meninges and ependyma also may be seen on MRI.

Fluid Analysis of Effusions

▼ ***Key Point*** Fluid analysis is usually sufficient for the clinical diagnosis of effusive FIP. The typical fluid in effusive FIP is a highly proteinaceous pyogranulomatous exudate.

- FIP fluid appears clear, viscous, and straw yellow or golden. It may be tenacious or sticky and contain

flecks or strands of fibrin. The fluid gets frothy when shaken because of its high protein concentration, and it may clot when refrigerated.

- FIP fluid has a high protein concentration, approaching that of plasma, ranging from 4 to 10 g/dl. Effusive FIP is highly likely if the total fluid protein is more than 3.5 g/dl and the globulin portion is greater than 50%. The A/G is usually less than 0.8. A gamma globulin percentage of greater than 32% by fluid protein electrophoresis is also highly indicative of FIP. An A/G ratio of greater than 0.8, or an albumin percentage greater than 50%, indicates that a disease other than FIP is highly likely.
- FIP fluid usually has a nucleated cell count ranging from 1,000 to 20,000 cells/µl, which is low compared with other exudates.
- The cytologic pattern of FIP fluid is pyogranulomatous exudate. The predominant cells are well-preserved (non-degenerate) neutrophils and macrophages with variable numbers of plasma cells and lymphocytes.
- Additional evaluations on effusions can include assay for anti-FCoV antibodies (see "Coronaviral Antibody Tests") and RT-PCR assay to detect coronaviral nucleic acid (see the later section on PCR assay). Antibody and RT-PCR assays on effusions may have higher diagnostic value than serum testing.
- Staining macrophages in effusions for intracellular FCoV antigen using either immunofluorescence or immunohistochemistry is the most definitive confirmatory test for effusive FIP, with 100% positive predictive value (see "Immunofluorescence and Immunohistochemistry").

Cerebrospinal Fluid and Aqueous of the Eye

- Analyses of CSF for neural FIP and aqueous fluid from the anterior chamber of the eye for ocular FIP have high diagnostic value. Both the protein concentration and the nucleated cell count (neutrophils, macrophages, lymphocytes) are increased in the CSF of most cats with neural FIP (see Table 10-2) and in the aqueous humor of cats with intraocular FIP.
- CSF and anterior chamber fluid can also be evaluated for the presence of anti-FCoV antibodies (see the following section). In FIP, the ratio of CSF or ocular antibodies to serum antibodies is generally much higher than the ratio of CSF or ocular total protein to serum total protein.
- A PCR assay of CSF and anterior chamber fluid for coronaviral nucleic acid is not as useful (see the section on PCR assay).

▼ ***Key Point*** Neurologic FIP is highly likely in cats that have the combination of progressive neurologic signs (especially if multifocal), increased CSF protein and leukocytes (especially neutrophils), and hydrocephalus on imaging.

Coronaviral Antibody Tests

Testing for coronaviral serum antibodies is informative as an epidemiological screening tool and as a diagnostic aid for FCoV and FIP if a reliable laboratory is used and the results are interpreted properly.

Principles of Feline Coronavirus-Antibody Testing

▼ ***Key Point*** A positive coronaviral antibody test means only that a cat has been exposed to some coronavirus at some time.

- Serology does not provide a definitive diagnosis of FIP because the antibodies in cats infected with harmless non-mutated FCoV are not distinguishable from the antibodies in cats with FIP. A large percentage of the healthy cat population is seropositive for FCoV antibodies, and most of these cats never develop FIP. In addition, seropositivity does not distinguish active from past infection.
- Antibodies to the related non-FCoVs (e.g., CCV and TGEV) crossreact with FCoV antibodies, lowering specificity further.
- Seroconversion after initial exposure to FCoV takes 1 to 3 weeks.

▼ ***Key Point*** A positive coronaviral antibody test does not confirm a diagnosis of FIP, and the absence of FCoV antibodies does not rule out a diagnosis of FIP.

- Many commercial diagnostic labs measure FCoV-antibody titers; however, methodologies are variable; thus, results cannot be compared between labs. For example, whether a feline or non-feline viral antigen is used in the test procedure will influence the titer values that indicate the lowest and highest titer levels.
- Use a reliable commercial diagnostic laboratory that measures quantitative FCoV-antibody titer levels. Avoid using rapid in-office enzyme-linked immunosorbent assay (ELISA) tests that merely report positive or negative results without titer quantification—this is less useful than titer information, and these tests give less consistent results than conventional serologic tests.
- Commercially available ELISA tests for detection of antibody to the 7b gene have been marketed as "FIP-specific tests." However, mutation of this gene is not specific for FIP, and this test has no advantage over conventional serologic assays.
- Serum or plasma samples for FCoV antibody testing can be refrigerated or stored at −20°C without affecting the test.
- FCoV antibodies also can be measured in effusions, CSF, or anterior chamber fluid (aqueous). Some studies suggest that these are more diagnostically

useful than serum testing but have similar interpretation pitfalls.

Indications

▼ ***Key Point*** Use the FCoV-antibody titer as a diagnostic aid for FIP rather than as a definitive diagnostic test. Interpret a positive titer to indicate that FIP is *possible* (low titer) or *probable* (high titer), when accompanied by supportive clinical findings. Interpret a negative titer to indicate that FIP is *unlikely.*

- Diagnostic aid in sick cats suspected of FIP
- Diagnostic aid in cats suspected of FCoV enteritis
- Healthy cats that have been exposed to cats with FIP or FCoV
- Screening catteries for the presence of FCoV
- Aid the process of creating an FCoV-free cattery
- Screening new cats before entering FCoV-free catteries

Positive Antibody Test Results

A positive FCoV-antibody titer in a cat can indicate any of the following:

- Clinical FIP caused by a mutant variant of FCoV
- Healthy carrier of non-mutant FCoV
- Recovered from previous FCoV infection
- Seroconversion to other non-FCoVs
- False-positive as a result of recent vaccination

Guidelines for Interpretation

▼ ***Key Point*** Coronaviral-antibody titers are not sufficiently specific to be used as a definitive diagnostic test. A positive titer, no matter how high, does not confirm a diagnosis of FIP.

- In healthy cats, the height of the antibody titer correlates with the virus replication rate in the intestine, the likelihood of fecal shedding, and the amount of virus shed in the feces.
- In general, low titers have the least diagnostic value.
- The highest measurable titer level for the assay used by the lab is highly suggestive of FIP but is still not confirmatory by itself. One study found 94% probability of FIP at the highest titer level.
- Rising antibody titers are not helpful because they are seen in healthy cats with non-mutated FCoV, and titers fluctuate unpredictably in both FIP and avirulent infections.
- Healthy carriers of non-mutated FCoV living in endemic cattery and multicat environments tend to have higher titers than individual pet cats; thus, high titers might be less meaningful in cattery cats. Less than 10% of cattery cats with titers ever develop FIP.

▼ ***Key Point*** A healthy cat that is negative for antibodies is likely to be free of FCoV and thus is not shedding virus, is not infectious to other cats, and is not at risk for FIP.

- False-negative test results are infrequent but occur in up to 10% of confirmed FIP cases; thus, a negative titer does not entirely rule out FIP. False-negative titers can result from low antibody levels seen with peracute infection (less than 10 days after exposure), the terminal stages of infection, or with consumption of antibody in immune complexes. A laboratory error or an insensitive assay system also explains some false negatives.
- The evaluation of FCoV antibodies in effusions was found to have good predictive value for FIP (90% positive, 79% negative), suggesting that fluid testing may be more diagnostically useful than serum testing.

Polymerase Chain Reaction

▼ ***Key Point*** Interpret the RT-PCR test with other clinical findings, and do not use this as the sole basis for diagnosis of FIP.

- The RT-PCR viral assay is used to detect coronaviral nucleic acid in blood, fluids, tissue, or feces.
- A positive result indicates the presence of FCoV, but it does not distinguish between the mutated, FIP-producing variants and non-mutated FCoV. Viremia occurs not only in FIP but also in healthy FCoV carriers. One study found that up to 80% of cats in endemic catteries can be viremic and RT-PCR–positive, and this was not predictive of FIP. Thus, RT-PCR by itself is not a reliable confirmatory diagnostic test.

▼ ***Key Point*** PCR assays do not distinguish between mutated and non-mutated FCoV.

- In general, effusions and tissue specimens are more likely than blood to be positive in cats with FIP. Plasma is more sensitive than serum. The lowest yield is in CSF and urine, so these are not recommended for routine PCR testing.
- Fecal RT-PCR can be used to document fecal shedding of FCoV, especially in healthy cats as a component of a cattery control program. Evaluate feces daily for 4 to 5 consecutive days. Retesting over several months is required to identify chronic persistent shedders.
- A false-negative RT-PCR results from degradation of sample RNA and poor laboratory technique. The primers used also may not detect all strains of FCoV.
- Samples for PCR require careful handling to avoid invalid results. Keep samples frozen and assay them as soon as possible for optimal results.

Histopathology

- Histopathology is considered the "gold standard" for confirming FIP. Thus, biopsy of affected tissues is a valuable diagnostic procedure for identifying the distinctive FIP lesions of vasculitis and pyogranulomatous inflammation.
- Coronavirus can be identified in tissue specimens by PCR, immunofluorescent antibody, and immunohistochemistry techniques (see the next section).

Immunofluorescence and Immunohistochemistry

- Staining of macrophages in tissue specimens and effusions for intracellular FCoV antigen using either immunofluorescence or immunohistochemistry is the most definitive confirmatory test for effusive FIP, with 100% positive predictive value (i.e., virtually no false positives).
- Do not rule FIP out when these tests are negative. False negatives occur frequently when there are insufficient infected macrophages in the specimen or when the viral antigen is masked by competitive binding with FCoV antibodies.

TREATMENT

▼ ***Key Point*** No treatment has been proved to reduce the risk of developing FIP in healthy antibody-positive FCoV carriers.

Treatment has not been proved to lower the high mortality rate of FIP (>95%) or to slow progression of the disease. Various antiviral, immunomodulating, and immunosuppressive drugs have been used to treat FIP, but efficacy is highly questionable. Some cats show temporary improvement of clinical signs with supportive care and anti-inflammatory therapy using corticosteroids. The best candidates for palliative medical therapy are cats that are eating, active, and in good body condition. Spontaneous remissions occur but are extremely rare. Euthanasia is appropriate in severely affected cats with poor quality of life.

▼ ***Key Point*** Nearly all cats with confirmed clinical FIP eventually die, regardless of treatment.

Antiviral Therapy

- Some antiviral drugs (e.g., acyclovir and zidovudine [AZT]) have no activity against FCoV. Other antiviral drugs (e.g., ribavirin) show in vitro activity against FCoV but are either too toxic for cats or ineffective when used clinically to treat FIP.
- Ribavirin-treated kittens, for example, had more severe clinical signs and a shortened survival time compared with untreated kittens. Ribavirin also causes serious side effects of hemolysis, bone marrow toxicity, and liver toxicity in cats.
- Interferons in high doses have both immunomodulating and antiviral activity (see below).
- New anticoronaviral drugs under development for treatment of human severe acute respiratory syndrome coronavirus might have future application in cats.

Immunomodulator Therapy

- Immunomodulators are intended to stimulate compromised immune function. Anecdotal reports of clinical improvement with these agents have not been substantiated by controlled studies; thus, conclusive evidence of efficacy in FIP is lacking.
- Nonspecific immune stimulation can theoretically potentiate the immune-mediated consequences of FIP.
- Immunomodulator agents that have been used unsuccessfully to treat FIP include *Propionibacterium acnes* (ImmunoRegulin), thioproline (Promodulin), acemannan (Carrisyn), levamisole, and cyclosporine.
- Human and feline interferons have been used to treat FIP (see below).

Interferon Therapy

Recombinant forms of interferon given parenterally in high doses can have both antiviral and immunomodulatory effects. Feline interferon-omega and human interferon-alpha have both been used to treat FIP.

Feline Interferon-Omega

- Recombinant feline interferon-omega (rFeIFN-ω) is available in Europe and Japan. To treat FIP, rFeIFN-ω (Virbagen Omega, Virbac) has been given at 1,000,000 U/kg SC every other day until clinical remission then once or twice weekly. Expense will be prohibitive for many owners.
- In a preliminary uncontrolled study of 12 FIP cats using rFeIFN-ω with prednisone (2 mg/kg PO q24h, tapered to 0.5 mg/kg q48h), 33.3% of the cats achieved complete remission for more than 2 years, 33.3% achieved partial remission but died after 2 to 5 months, and 33.3% failed to respond and died.

Human Interferon-Alpha

- Parenteral high-dose human interferon-alpha (rHuIFN-α) (100,000–1,000,000 U/kg IM) does not appear to be effective in FIP, and it is unsuitable for long-term treatment because cats develop antibodies against the human protein after 3 to 7 weeks that inhibit the drug's activity.
- Oral low-dose human interferon-alpha (Roferon, Hoffman-LaRoche; Intron-A, Schering-Plough) diluted to 30 U/ml and given at 30 units PO, daily for 7 days on alternate weeks, has reportedly improved appetite and well-being with minimal side effects. The rHuIFN-α given orally is destroyed by gastric acid

and does not achieve systemic levels, but it may exert immunomodulating activity on oropharyngeal lymphoid tissue leading to cytokine release.

Palliative Medical Therapy

Some cats transiently improve with supportive care combined with palliative medical therapy using a high dose of corticosteroid, with or without a cytotoxic alkylating agent such as chlorambucil or cyclophosphamide (Table 10-3).

- Corticosteroids and alkylating drugs have no effect on the virus, but by virtue of their anti-inflammatory and immunosuppressive effects, they are aimed at controlling the widespread immune-mediated inflammatory reaction that occurs in FIP.
- These drugs may adversely affect cellular immunity mediated by T lymphocytes and macrophages and thus have the potential to promote the viral infection.

▼ ***Key Point*** Only use immunosuppressive drugs to treat overt FIP. In healthy FCoV carriers and seropositive cats, these drugs could have the unwanted effect of promoting the onset of FIP.

- The principal side effects of alkylating drugs are anorexia and bone marrow suppression; thus, monitor a complete blood count periodically (see Chapter 26 for more details on the use of these drugs).
- Persistent drug-induced anorexia is a frequent problem when these drugs are given daily. An alternative is pulse administration, using a large dose of the drug once every 2 to 3 weeks. In this way, a few days after each dose the appetite usually rebounds and is maintained between treatment cycles.
- Regardless of the regimen chosen, if no response is noted within the first 2 to 4 weeks, consider the therapy ineffective and either modify or discontinue it. If a positive response occurs, continue the treatment indefinitely.

Supportive Treatment

These measures may improve quality of life and possibly survival time.

- Minimize stress as an exacerbating factor.
- Perform intermittent body cavity drainage of effusion as needed to relieve dyspnea.
- Give parenteral fluid therapy.
- Give nutritional support (via tube-feeding techniques; see Chapter 3).
- Give aspirin (10 mg/kg q72h) to inhibit platelet aggregation caused by vasculitis.
- Give antibiotics as needed to control complicating bacterial infections.
- Treat anterior uveitis with topical corticosteroids and atropine (see Chapter 136).
- Give blood transfusions (for severe nonregenerative anemia).

Table 10-3. TREATMENT FOR FELINE INFECTIOUS PERITONITIS

Mechanism of Action	Drug or Treatment*	Dosage
Immunomodulator and antiviral	Feline interferon-omega (Virbagen Omega)	1 million U/kg SC q48h until remission, then weekly
Immunomodulator	Human interferon-alpha (Roferon, Intron-A)	30 units PO q24h for 7 days on alternating weeks
Anti-inflammatory and immunosuppressive	Prednisone	2–4 mg/kg, q24h, PO
Immunosuppressive†	Chlorambucil (Leukeran) *or*‡	20 mg/m^2, every 2–3 wks, PO
	Cyclophosphamide (Cytoxan)	2–4 mg/kg, 4 days each week, PO, *or* 200–300 mg/m^2, every 2–3 wks, PO
Platelet aggregation inhibitor	Aspirin	10 mg/kg, q72h, PO
	Ozagrel HCl	5 mg/kg, q12h, SC
Topical ophthalmic for uveitis	Prednisone acetate (1%)	2–3 drops/eye q6h
	Atropine (1%)	1–3 drops/eye up to q6h for mydriasis
Supportive treatment	Minimize "stress"	—
	Parenteral fluid therapy	As needed to maintain hydration
	Nutritional therapy via tube feeding	See Chapter 3
	Body cavity drainage (thoracentesis)	As needed to relieve dyspnea
	Blood transfusion	As needed for severe anemia
	Antibiotics for complicating infections	Dosage based on the drug

*Cats most likely to respond are in good physical condition, are eating, and are free of neurologic signs, severe anemia, and feline leukemia virus or feline immunodeficiency virus infections.

†For conversion of body weight to body surface area (m^2), refer to conversion tables in Chapter 26.

‡Choose only *one* of these two alkylating agents, and combine with a corticosteroid.

PREVENTION

Vaccination

▼ ***Key Point*** The currently available FIP vaccine does not appear to be effective and is not recommended.

- A modified-live, temperature-sensitive strain of FIP coronavirus became available in 1991 as an intranasal vaccine for use in cats 16 weeks of age and older (Primucell FIP, Pfizer).
- The vaccine virus replicates locally in the nasopharynx and intestines but not systemically because of temperature sensitivity. It is supposed to stimulate local nasal and gut mucosal immunity, salivary immunoglobulin A antibody, and cell-mediated immunity. It does not protect against enteric FCoV infection.
- The lack of proven efficacy in kittens younger than 16 weeks of age is a fundamental pitfall, because under most circumstances kittens first become infected with FCoV between 6 and 16 weeks of age.
- The 2000 Report of the American Association of Feline Practioners Panel on Feline Vaccines states: "At this time there is no evidence that the vaccine induces clinically relevant protection and its use is not recommended."
- Various genetically engineered recombinant vaccines are under development and may become available in the future.

Control of Feline Infectious Peritonitis in Catteries

Control of FCoV infection in catteries, shelters, and multicat households is aimed at limiting virus spread, minimizing exposure, and reducing stress. Infection with FCoV is ubiquitous, so complete eradication is rarely feasible, and even if eradication is successful, reinfection frequently occurs. Test and removal based on FCoV antibody testing is not practical since it is typical for 80% to 90% of cats in endemic catteries to be seropositive. Depopulation and starting over would be required.

General Principles

▼ ***Key Point*** Do not consider healthy FCoV antibody-positive cats to be harmless. Seropositive cats frequently shed FCoV in their feces that contaminates the environment and infects other cats, and FCoV always has the potential to mutate and cause FIP.

- Be familiar with risk factors and transmission of FCoV (see "Epidemiology").
- Use good husbandry practices (e.g., good sanitation, ventilation, and feeding practices) and limit feco-oral contamination.
- Minimize overcrowding and stress. High-density housing allows a high level of fecal contamination of the environment, facilitating feco-oral spread of infection.
- Control feline leukemia virus in the cattery with vaccination, testing, and removal (see Chapter 8).
- Do not breed male and female cats that have a history of producing kittens that later developed FIP, because they potentially may pass on a genetic susceptibility to FIP.
- The risk of infection from cat shows and breeding exchanges is considered low; however, in these situations do not allow sharing of food, water, or litter.
- Only allow healthy seronegative cats to enter a coronavirus-free cattery. Ideally, before a cat can be safely mixed with other cats, confirm the absence of fecal shedding based on at least 4 consecutive negative fecal RT-PCR tests (although this may not be practical in many situations).

Control of Viral Exposure

The greatest source of viral contamination of the environment is from small particles of fecal debris and litter that are carried throughout the facility by movement of air, animals, and people. Any contaminated material can end up on the fur and thus be ingested by the cats. Consider the following control measures to reduce the environmental virus load and to minimize exposure:

- Use at least one litter box for every two cats. Locate litter boxes away from food and water bowls to avoid cross-contamination. Ensure that the area is easy to clean and disinfect.
- Scoop feces from litter boxes daily, and replace litter and disinfect litter boxes as often as possible (at least weekly).
- Dispose of used litter in sealed plastic bags.
- Use dedicated food and water bowls for each animal, and clean and disinfect bowls regularly.
- Brush the fur of cats regularly to remove contaminated fecal particles and litter that could be ingested during grooming.
- Reduce cross-contamination between cats by housing cats individually or in stable small groups of four or less.
- Avoid having too many kittens because they shed the greatest amount of virus.
- Ideally, identify and eliminate persistent carriers that continuously shed large amounts of virus by using fecal RT-PCR tests repeated over several months.

Control of Viral Spread in Kittens

Isolation and early weaning can be effective for controlling the spread of FCoV in kittens, as well as herpesvirus and calicivirus.

- Isolate queens 1 to 2 weeks pre-partum so that queens can give birth and nurse kittens in isolation from other cats in the cattery.
- Wean the kittens early and remove them from the mother at 5 to 6 weeks of age, coinciding with the time when maternal-derived immunity dissipates, then keep the litter of kittens isolated from all other cats until at least 16 weeks of age.
- Maintain strict quarantine procedures to prevent environmental or fomite transfer of FCoV.
- Confirm seronegativity at 12 to 16 weeks of age or prior to moving kittens to a new home to document effectiveness.
- The disadvantages of this approach are that it requires facilities for isolation and quarantine and that early weaning may adversely affect social development of the kittens.

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Chapter

11 Feline Infectious Respiratory Disease

Robert G. Sherding

ETIOLOGY

Feline infectious respiratory disease is caused by a variety of viruses and bacteria, especially feline herpesvirus and calicivirus. The clinical signs that result from these infectious agents overlap and are often indistinguishable; thus, these infections are collectively referred to as feline infectious respiratory disease or upper respiratory infection (URI).

Viruses

Most infectious upper respiratory disease in cats is caused by these two highly contagious viruses:

- *Feline herpesvirus-1 (FHV-1):* Also known as feline viral rhinotracheitis (FVR)
- *Feline calicivirus (FCV):* A member of the vesivirus (vesicle-forming) genus

Bacteria

- *Chlamydophila felis* (formerly *Chlamydia psittaci*)
- *Bordetella bronchiseptica*
- *Mycoplasma felis*

TRANSMISSION

Routes of Infection

Transmission can occur by contact, fomites, and aerosol. Direct contact with infected cats and fomites are the most important sources of infection. The greatest risk of infection is in young kittens, unvaccinated cats, and cats confined in high-density groups (e.g., shelters, catteries, or multicat households).

▼ ***Key Point*** Overcrowded group confinement contributes to the spread of feline respiratory infections.

- *Direct contact:* Oral, nasal, and ocular discharges are infective.
- *Fomites:* These etiologic agents can survive and remain infectious on fomites such as contaminated cages, examination tables, food and water dishes, and human hands and clothing.
- *Aerosol:* Sneezing and coughing can propel aerosolized microdroplets with virus up to 4 feet.

Subclinical Carriers as Sources of Infection

Most cats that recover from FHV and FCV infection become subclinical carriers and shed the virus for prolonged periods. Subclinical carriers that are persistently infected (FCV) or latently infected (FHV) perpetuate these viruses within the cat population and serve as the principal source for outbreaks in catteries, multicat households, research colonies, veterinary hospitals, and shelters.

▼ ***Key Point*** Despite vaccination, subclinical viral carriers are common and account for the widespread prevalence of infections caused by FHV and FCV.

Feline Herpes Virus

- In recovered carriers, FHV persists lifelong in a latent form in the trigeminal ganglia and other tissues. Carriers may shed the virus intermittently coinciding with reactivation of latent virus infection. Recrudescence of shedding and clinical signs in latent FHV carriers can be triggered by stress, parturition, lactation, or glucocorticoids.
- Episodes of shedding generally persist for 2 weeks and can be accompanied by mild clinical signs.
- FHV survives up to 24 hours outside the host, causing a moderate risk of fomite transmission.
- FHV is susceptible to drying and most disinfectants.

▼ ***Key Point*** Shedding of FHV often is triggered by parturition and lactation in latent carrier queens at the time when their newborn kittens are most susceptible. This is an important source of URI in young kittens.

Feline Calicivirus

- Recovered FCV carriers shed the infectious virus from the oropharynx continuously for many months and sometimes years. Subclinical carriers are prevalent. Isolation rates of FCV from healthy cat

populations are 5% to 10% for pet cats, 20% for show cats, and 40% for colony cats.
- FCV is highly resistant with survival outside the host of 8 to 10 days, causing a high risk of fomite transmission.
- The preferred disinfectant is a 1:32 dilution of 5% sodium hypochlorite (bleach).

Chlamydophila felis

- Primarily shed from conjunctival secretions; prolonged shedding up to 18 months has been documented after experimental infections
- Survives for several days in conjunctival discharges
- Inactivated by lipid solvents, detergents, and 1:1000 quaternary ammonium

Bordetella bronchiseptica

- *B. bronchiseptica* can be isolated from many healthy cats, indicating a widespread subclinical carrier state. Prolonged oronasal shedding for at least 19 weeks after experimental infection has been documented.

CLINICAL SIGNS

Typical clinical signs of feline URI are sudden onset of anorexia, depression, fever, and naso-ocular discharge. Other signs specific to each etiologic agent are detailed in the following sections. Illness is more severe in young kittens and milder in previously vaccinated cats. Clinical disease caused by FHV and FCV is usually self-limiting within 5 to 10 days; however, some cats take 3 weeks to recover. See Table 11-1 for a comparison of the clinical manifestations of FHV and FCV.

Feline Herpesvirus

- FHV has an affinity for conjunctival, nasal, and upper airway (laryngotracheal) epithelium. Multifocal epithelial necrosis at these sites causes rhinitis, tracheitis, laryngitis, and conjunctivitis. FHV can also cause nasal turbinate necrosis and osteolysis.
- Signs include sneezing, lacrimation, serous to mucopurulent naso-ocular discharge, cough, hypersalivation, and loss of voice.
- Corneal involvement causes keratitis and herpetic ulcers. Ulcers can have a punctate, oval, or branching (dendritic) pattern (see Chapter 134).
- Infection during pregnancy may result in abortion or in a severe generalized form of infection in newborn kittens, characterized by fatal encephalitis or focal necrotizing hepatitis. Neonates also may develop panophthalmitis (ophthalmia neonatorum) that can permanently damage the eyes.
- Secondary bacterial complication of the lesions may worsen and prolong FHV disease. Bacterial pneumonia is a serious complication in young kittens.
- Extensive turbinate damage may lead to fibrosis and stenosis of the nasal passages and predispose the patient to chronic rhinitis.
- Ulcerative skin lesions are seen infrequently.

Table 11-1. CLINICAL MANIFESTATIONS OF FELINE VIRAL RESPIRATORY DISEASE

Manifestation	Feline Herpesvirus (FHV-1)	Feline Calicivirus (FCV)
Incubation	2–6 days	1–5 days
Duration	5–10 days (rarely to 3 weeks)	5–7 days (rarely to 2 weeks)
Anorexia, depression	Severe and frequent	Mild and inconsistent
Fever	Frequent	Inconsistent (diphasic)
Nasal signs	Sneezing—severe Discharge—marked Ulcerated nares Turbinate necrosis Sequelae—chronic rhinosinusitis, nasopharyngeal stenosis	Sneezing—mild Discharge—mild or absent Ulcerated tip of nose
Ocular signs	Conjunctivitis—severe (serous to mucopurulent discharge, chemosis, photophobia) Ulcerative keratitis Panophthalmitis (neonates) Sequelae—sicca, corneal sequestrum	Conjunctivitis—mild
Oral signs	Hypersalivation, rare ulcers	Frequent oral ulcers (tongue, palate) Sequelae—chronic stomatitis, gingivitis, faucitis
Pulmonary signs	Rare bacterial pneumonia	Occasional viral pneumonia
Other signs	Abortion Peracute neonatal death (hepatic necrosis) Ulcerative dermatitis	Limping syndrome (arthritis, arthralgia, myalgia) Interdigital paw ulcers Enteritis (diarrhea and vomiting) Acute hemorrhagic fever syndrome
Postrecovery carrier	Lifelong	Months to years
Shedding pattern	Intermittent (after stress; lasts 1–2 wks)	Persistent

Feline Calicivirus

▼ ***Key Point*** The pathogenicity of different FCV strains is highly variable, producing a diversity of clinical syndromes. The most consistent feature of FCV is oral ulceration.

FCV Respiratory Disease

- FCV has an affinity for oropharyngeal epithelium and alveolar pneumocytes of the lung.
- Infection is manifested most often as oral ulceration (tongue, palate, and fauces), mild rhinitis (sneezing), and conjunctivitis. Oral ulcers begin as vesicles that subsequently rupture and ulcerate. In some cats, the tip of the nose may be ulcerated and crusted.
- Viral interstitial pneumonitis may occur, but it is usually subclinical.

Other FCV Syndromes

- One FCV isolate reportedly causes consistent footpad and interdigital ulcers along with oral ulcers ("paw and mouth disease").
- FCV has been isolated from cats with chronic ulcerative or proliferative lymphocytic gingivitis, stomatitis, and faucitis. This may be a hypersensitivity response to persistent FCV infection, but the role of FCV in chronic oral disease is uncertain.
- Some FCV strains cause acute synovitis, fever, and joint pain (arthralgia and myalgia), with or without concurrent respiratory signs.
- FCV has been isolated from the intestines and feces of cats with acute and chronic enteritis.
- FCV has been isolated from the urine of cats with lower urinary tract disease, but a causative role has not been established.

Acute Hemorrhagic Fever Syndrome

- Highly virulent, variant strains of FCV have recently emerged in North America associated with several outbreaks of a systemic, acute febrile hemorrhagic syndrome. Most outbreaks have originated in hospitalized shelter cats.
- Clinical signs usually include high fever, upper respiratory signs, oral ulcers, and ulcerative dermatitis and subcutaneous edema of the face, pinnae, and distal limbs. Signs of systemic involvement are variable and include dyspnea, jaundice, vomiting, diarrhea, hematochezia, and epistaxis. Some cats develop pulmonary edema, pleural and abdominal effusion, hepatic necrosis, pancreatitis, disseminated intravascular coagulation (DIC), or gastrointestinal ulceration. The mortality rate is up to 50%.
- Widespread susceptibility is seen regardless of age, health, or vaccination status. Healthy, well-vaccinated adult cats can succumb rapidly to the disease. FCV vaccines do not appear to crossprotect against these variant strains of FCV.

Feline Chlamydophilosis

- *C. felis* is a primary conjunctival pathogen. Ocular signs predominate as acute or chronic follicular conjunctivitis with chemosis and mucopurulent discharge that can begin unilaterally and later become bilateral (see Chapter 133).
- Mild nasal discharge and sneezing are infrequent.
- Subclinical pneumonia (pneumonitis) is uncommon and only detectable histologically.

Feline Bordetellosis

- *B. bronchiseptica,* a cause of infectious tracheobronchitis (kennel cough) in dogs, may be a primary or secondary respiratory pathogen in cats, especially in kittens.
- Outbreaks of fatal bronchopneumonia have been attributed to *B. bronchiseptica;* however, infections are usually subclinical or characterized by mild self-limiting signs of fever, sneezing, and nasal discharge of less than 10 days in duration. Coughing is an inconsistent sign.

Complications and Chronic Sequelae

Subclinical Carrier States

- Cats recovered from FHV and FCV are subclinical carriers and infectious for other cats (see "Transmission").
- Recrudescence of latent FHV may be associated with recurrence of clinical signs as well as viral shedding.

Chronic Nasal Disease

Chronic rhinitis or sinusitis and nasal obstruction can occur after FHV infection. Potential causes are:

- Complicating bacterial sinusitis
- Permanent turbinate damage resulting from necrosis and osteolysis
- Obstructed nasal passages because of nasopharyngeal fibrosis and stenosis

Chronic Ocular Disease

FHV has been associated with the following chronic ocular conditions in cats. The role of FHV in the pathogenesis of some of these is unclear:

- Chronic bacterial or follicular conjunctivitis (see Chapter 133)
- Tear duct blockage or infection (dacryocystitis) (see Chapter 139)
- Keratoconjunctivitis sicca (see Chapter 139)
- Chronic ulcerative keratitis and stromal keratitis (see Chapter 134)
- Corneal sequestrum (see Chapter 134)
- Eosinophilic keratitis (see Chapter 134)
- Anterior uveitis (see Chapter 136)

Chronic Oral Disease

- Chronic lymphoplasmacytic stomatitis, gingivitis, and faucitis may be linked to chronic FCV infection (see Chapter 64).

DIAGNOSIS

For individual mildly infected cats, a diagnosis of "viral respiratory disease" or URI based on clinical signs and likelihood of exposure is adequate for patient management. Cultures, virus isolation, and polymerase chain reaction (PCR) assays allow definitive diagnosis and are indicated for evaluation of disease outbreaks in groups of cats.

▼ ***Key Point*** Severe naso-ocular signs are most consistent with FHV infection. Corneal ulceration is indicative of FHV, whereas oral ulceration is most suggestive of FCV. Persistent conjunctivitis is the predominant sign in chlamydophilosis.

Confirmatory Tests for Viruses

Direct Immunofluorescence

- Collect smears of nasal mucosa or conjunctiva.
- This is most useful for FHV. This also can be used for FCV, but it is less reliable than virus isolation.

Virus Isolation

- Submit cell culture swabs from the oropharynx, nasal cavity, or conjunctiva. Use viral transport media on ice.
- This is the gold standard for confirming FCV. It also is useful for FHV.

Polymerase Chain Reaction

- PCR assays can be used to identify FHV, FCV, *Chlamydophila,* and *Mycoplasma* in nasal, conjunctival, corneal, and oropharyngeal mucosal specimens. Submit mucosal swabs or scrapings in 1 ml of phosphate-buffered saline (PBS) and freeze at –20°C.
- *FHV:* PCR assay is the most sensitive diagnostic method for FHV.
- *FCV:* Reverse transcriptase-PCR assay is useful, but it is less sensitive than virus isolation.

Bacterial Culture

- *Bordetella:* Submit nasal, pharyngeal, or bronchial specimens for culture on selective media. For transport, use charcoal Amies transport medium (Beckton Dickenson).
- *Chlamydophila:* Submit conjunctival swabs in chlamydia transport media for cell culture.
- *Mycoplasma:* Submit conjunctival, nasal, or tracheobronchial specimens for specialized culture.

Detection of Inclusion Bodies

- *FHV:* Intranuclear inclusions can occasionally be identified in conjunctival biopsies (hematoxylin-eosin stain).
- *Chlamydophila:* Intracytoplasmic inclusions can be identified in some cases in scrapings of conjunctival epithelium (Diff-Quik stain), mostly during the first 2 weeks of infection.

Serology

- Serology is generally not very helpful because most cats have vaccine-induced antibody titers.
- A rising neutralizing antibody titer in serum from a convalescent animal indicates a presumptive diagnosis of FCV.

Ancillary Diagnostics

Complete Blood Count and Serum Chemistries

- Results of complete blood count (CBC) and other routine laboratory evaluations (e.g., serum chemistry profiles) are usually normal except in severe infections complicated by bacteria, in which a neutrophilic leukocytosis may be seen.
- Findings in caliciviral acute hemorrhagic fever can include hyperbilirubinemia, elevated serum liver enzymes, hypoalbuminemia, and coagulopathies (DIC).

Tests for Retroviruses

Persistent or recurrent signs of URI often develop in immunodeficient cats. Evaluate cats for underlying infections of feline immunodeficiency virus (FIV antibody test; see Chapter 9) and feline leukemia virus (FeLV antigen test; see Chapter 8) in the following situations:

- Cats with recurrent episodes of infectious respiratory disease
- Vaccinated adult cats with unusually severe signs
- Cats with signs that persist longer than 2 weeks

Diagnostic Imaging

- Consider thoracic radiography in severe cases suspected to have complicating bronchopneumonia.
- Use nasal radiography and computed tomography to evaluate cats suspected of having chronic nasal sequelae, such as frontal sinusitis, severe turbinate damage, or nasopharyngeal stenosis.

TREATMENT

▼ ***Key Point*** Treat infectious respiratory disease in cats on an outpatient basis whenever possible to prevent cross-infection of other hospitalized cats.

Feline infectious respiratory disease is self-limiting in most cats within 5 to 10 days. Treatment is mainly supportive in nature, often combined with antibiotics and antiviral therapy, depending on the severity. Rarely, severe or complicated infections may require parenteral fluid therapy, oxygen therapy, or intensive nutritional support therapy.

Supportive Treatment

- Provide rest and warm ambient temperature (inhibits FHV replication).
- Clean discharge from eyes and nares as needed.
- Provide fluid and nutritional support as needed. Advise owners to offer a variety of flavorful, aromatic foods and broths to encourage continued intake. Soft or liquefied foods are better tolerated in cats with inflammation of the oral cavity and pharynx. Cyproheptadine or oxazepam may stimulate eating in some inappetant cats. In cats with prolonged anorexia, parenteral fluid therapy and esophagostomy or gastrostomy tube feeding may be needed (see Chapter 3).
- To minimize inspissation of respiratory secretions, prevent dehydration (using parenteral fluid therapy if necessary) and promote airway humidification (humidifier or steamed room).
- Irrigate necrotic oral lesions with 0.2% chlorhexidine solution (Nolvadent).
- Oxygen therapy may be required in cats with bronchopneumonia and hypoxemia (see Chapter 3).

Antiviral Therapy

- The oral antiviral drugs used in human herpes (e.g., acyclovir and valacyclovir) are not active against FHV, are too toxic for cats, or both. Ribavirin is active against FCV in cell culture but is too toxic for cats.
- Topical antiviral drugs have a role in treating ophthalmic manifestations of FVR (see "Ophthalmic Therapy").
- Human interferon (human IFN-α_2; Roferon-A) and recombinant feline interferon have been empirically used orally and topically as nose drops or eye drops, but there is little or no evidence of efficacy.

L-Lysine Therapy

- Preliminary evidence suggests that daily supplementation of L-lysine may reduce replication and shedding of FHV in cats with acute and chronic latent infections. Arginine is an essential amino acid for FHV replication that acts as a growth promoter for FHV. Presumably through competitive inhibition, large doses of L-lysine antagonize the growth promoting effects of arginine and inhibit FHV replication.
- Administer L-lysine at 250 mg PO bid for kittens and 500 mg bid for adult cats. Give in an oral paste form (Enisyl-F; Vetoquinol/EVSCO) or as a powder added to the food. Vomiting occurs if not given with food.

Antibiotic Therapy

- In viral infections, consider broad-spectrum antibiotics to control secondary bacterial infection, such as oral amoxicillin/clavulanate, doxycycline, cephalosporin, or fluoroquinolone. Liquid forms are best for cats with painful swallowing.
- For *Bordetella, Chlamydophila,* and *Mycoplasma,* give doxycycline (5 mg/kg PO q12h; use liquid form, or give with food or water to prevent esophagitis). An alternative is a fluoroquinolone such as orbifloxacin (2.5–7.5 mg/kg, PO, q24h). Choose antibiotics for *Bordetella* based on a culture and sensitivity whenever possible.

Ophthalmic Therapy

- For herpetic corneal ulcer and other severe or refractory corneal manifestations of FHV, consider using a topical antiviral agent. These are expensive and often irritating. To be effective, apply every 4 to 6 hours for 2 to 3 weeks.
  - Idoxuridine (only available from compounding pharmacies)
  - Vidarabine (Vira-A; Parke Davis)
  - Trifluridine (Viroptic; Burroughs Wellcome): Most expensive and most irritating
- For *Chlamydophila* and *Mycoplasma,* use tetracycline ophthalmic ointment for 3 to 4 weeks.
- For complicating bacterial conjunctivitis, use triple-antibiotic ophthalmic ointment.
- Do not use topical corticosteroids in FHV. If an anti-inflammatory ophthalmic therapy is needed, use 0.2% cyclosporine (Optimmune) or another nonsteroidal agent.

PREVENTION

Incorporate FHV and FCV into all feline vaccination programs. Use good husbandry and other control measures to prevent the spread of disease in groups of cats confined together in catteries and shelters.

Vaccination

▼ ***Key Point*** Vaccination for FHV and FCV helps prevent clinical illness, but it does not prevent infection. It also does not prevent or eliminate the chronic carrier state or virus shedding.

- Modified live virus (MLV) injectable, inactivated virus (killed) injectable, and MLV intranasal vaccines are available. Intranasal vaccines induce faster and better protection while avoiding adjuvant-related side effects. However, injectable vaccines are also reasonably effective.
- Protection with FCV vaccination is variable because of the heterogeneity of FCV strains in cats. Vaccina-

tion probably does not induce crossprotection against all FCV strains.

- *FHV and FCV vaccines:* Initially give kittens at least two doses 3 weeks apart (usually 9 and 12 weeks of age or every 3–4 weeks until 12 weeks of age), then revaccinate 1 year later and revaccinate every 3 years thereafter (see Chapter 7). Do not use MLV vaccines in pregnant cats.
- *Chlamydophila and Bordetella vaccines:* These are not recommended for routine use but may be considered for cats in high-risk multicat environments (see Chapter 7). Vaccine efficacy and duration of immunity are not well established.

Vaccine Side Effects

- Local reactions and injection site sarcomas have been associated with adjuvanted killed vaccines.
- Transient fever, arthralgia, and myalgia can be seen after MLV vaccines.
- Mild postvaccinal sneezing and oculonasal discharge are common after intranasal vaccination. Oronasal exposure to the viral strains in injectable MLV vaccines by inadvertent aerosolization or licking from the haircoat also can cause clinical disease with sneezing, oculonasal discharge, and oral ulcers.
- MLV vaccines that are produced in feline kidney cell culture systems contain renal antigens that may stimulate anti-kidney antibodies in vaccinated cats; however, the significance of this is not yet known.

Control in Catteries and Shelters

- Vaccinate all cats against FHV and FCV. When faster immunity is needed (such as in outbreaks), use intranasal vaccine. In catteries apparently free of respiratory disease, consider using a killed injectable vaccine to avoid introducing an MLV strain into the group.
- Avoid incoming cats from infected sources. Isolate cats with signs of illness.
- FHV and FCV are perpetuated in catteries by virus shed from subclinical carriers and spread by contact, fomite, and aerosol transmission.

▼ ***Key Point*** Subclinical shedders of respiratory viruses are prevalent. Cats free of signs of disease are not necessarily free of infection, even if they have been well vaccinated.

- When introducing a new cat, there is always a risk that the incoming cat is a subclinical carrier that can be the source for an outbreak. Vaccinate and then isolate all incoming cats for 3 weeks. This protects the incoming cat from viruses in the cattery and protects the cattery from a new cat that might be incubating a viral infection or undergoing stress-induced shedding.
- In housing facilities for cats, avoid overcrowding, provide adequate ventilation (10 or more air changes per hour), maintain a warm nonfluctuating temperature, control humidity at approximately 50%, and provide separate cages or pens with solid partitions and separate food and water dishes.
- To prevent fomite transmission, clean and disinfect cages (1:32 sodium hypochlorite bleach solution) and minimize cross-contamination by personnel.
- Identify cats infected with *Bordetella* or *Chlamydophila,* and treat them with oral doxycycline and topical tetracycline ophthalmic ointment.

Control in Endemic Breeding Catteries

- In endemic catteries, kittens lose their maternal immunity at 5 to 7 weeks of age and often become infected by virus shed from carrier adults, especially their own lactating mother.
- To boost maternal antibody levels in kittens, vaccinate queens before breeding or during pregnancy. Only use inactivated vaccine in pregnant cats.
- Move queens into isolation 3 weeks before giving birth to prevent exposure of newborn kittens to carriers in the colony.
- Wean kittens early at 4 to 5 weeks of age and raise them in isolation to reduce risk of acquiring infection from a carrier mother.
- Use intranasal vaccine in kittens starting at 6 weeks of age, because it can induce local protection rapidly despite the presence of interfering maternal antibody. Maintain isolation until 1 week after the last dose of vaccine at 12 weeks.
- When possible, avoid using confirmed or suspected carriers in breeding programs, especially queens with a history of producing infected litters.

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Chapter

12 Canine Infectious Tracheobronchitis (Kennel Cough)

Robert G. Sherding

Canine infectious tracheobronchitis (ITB), also known as kennel cough, is a collection of highly contagious infectious diseases of the canine respiratory tract that cause acute tracheobronchitis and sudden onset of a paroxysmal cough lasting several days.

ETIOLOGY

- The two most important causes of canine ITB are canine parainfluenza virus (CPIV) and *Bordetella bronchiseptica,* a gram-negative, aerobic coccobacillus.
- Other infectious agents occasionally isolated from coughing dogs include canine adenoviruses (especially CAV-2), canine herpesvirus, reoviruses (types 1, 2, and 3), and mycoplasmas; however, these are considered to be of minor importance.
- Clinical outbreaks of disease often involve concurrent infection with more than one of these agents. Clinical disease is more severe in animals co-infected with more than one agent.
- Cats can also occasionally develop clinical respiratory disease associated with *B. bronchiseptica* (see Chapter 11).

Transmission

▼ ***Key Point*** Canine ITB is highly contagious through direct contact with aerosolized respiratory secretions (via cough and sneezing) from infected dogs.

- These agents also can be transmitted by fomites (e.g., personnel, cages, and food and water bowls).
- Dogs infected with CPIV or CAV-2 shed the virus for only 1 week following recovery; however, dogs infected with *B. bronchiseptica* or mycoplasmas can become chronic carriers with persistent shedding.

▼ ***Key Point*** Canine ITB is commonly spread in dogs that are confined in high-density facilities with poor ventilation (e.g., boarding kennels, animal shelters, pet shops, veterinary hospitals, and lab animal facilities).

Pathogenesis

- Incubation period is usually 5 to 7 days (range of 3–10 days).
- Individually, these infectious agents cause mild self-limiting disease or are harbored in the airways of asymptomatic carriers. Mixed infections are common and have a synergistic effect in producing more severe clinical disease.
- The primary target of these agents is the upper airway epithelium. The result is epithelial injury, acute inflammation, and dysfunction of the airway cilia.

▼ ***Key Point*** In young puppies and immunocompromised animals, mixed infections or secondary bacterial invasion of the lower respiratory tract may cause life-threatening bronchopneumonia.

CLINICAL SIGNS

- Infection can occur at any time of year, but the highest incidence is in summer and fall.
- Acute onset of a loud, paroxysmal, hacking cough is due to tracheobronchitis. Even though the cough is sometimes described as dry-sounding, ITB is characterized by increased production of mucus.
- Cough may be high-pitched because of laryngitis and swollen vocal folds.
- Cough may be more frequent during exercise, excitement, or changes in temperature and humidity of inspired air.
- Cough may be elicited by tracheal palpation or pressure from the collar.

▼ ***Key Point*** Episodes of paroxysmal cough may be followed by gagging or retching that can be mistaken for vomiting or choking.

- Mild, serous, or mucopurulent naso-ocular discharge can be seen.
- Typically, affected dogs continue to eat, remain active and alert, and are nonfebrile. In severe cases, anorexia, depression, and fever may be present.

- Complicating bacterial pneumonia and even rare fatalities can occur with severe disease, especially in mixed infections in young or unvaccinated puppies from crowded environments such as pet shops and animal shelters.
- *Clinical course:* Clinical signs usually last 7 to 14 days in uncomplicated cases.

DIAGNOSIS

Consider ITB based on exposure history and clinical signs, especially the sudden onset of a severe cough in a previously healthy dog. A recent history of exposure to other dogs, especially under kennel conditions, is typical but not found in all cases. Hematology, radiography, airway cytology, and culture are not indicated unless ITB is severe with fever and bronchopneumonia. In typical uncomplicated ITB, these diagnostics are unremarkable or reveal nonspecific findings.

Hemogram

- *Mild ITB:* The complete blood count (CBC) is usually normal or shows a stress response (mature neutrophilia, lymphopenia).
- *Severe ITB:* Neutrophilic leukocytosis with a left shift is seen with complicating pneumonia.

Thoracic Radiography

- *Mild ITB:* Usually normal; a mild increase in interstitial lung density is seen occasionally.
- *Severe ITB:* Interstitial and alveolar pattern with lobar consolidation is seen with complicating bronchopneumonia.

Airway Cytology

- Evaluation of airway cytology is only indicated in severe, febrile, or complicated ITB. Obtain specimens by transtracheal aspiration, endotracheal tube lavage, or bronchoscopic lavage or swab (see Chapter 158).
- Findings include increased mucus, mucopurulent exudate, and sometimes bacteria.

Cultures

- Nasal swabs or tracheobronchial specimens can be cultured for *Bordetella* and mycoplasma.
- Isolation of *Bordetella* or mycoplasma allows only presumptive diagnosis, because these organisms can be harbored in the respiratory tract of subclinical carriers.

Virology and Serology

- Virus isolation can identify CPIV and CAV-2 from nasopharyngeal or tracheal swabs but is impractical for clinical use.
- Serology (paired acute and convalescent titers) can demonstrate viral exposure but has limited usefulness.

TREATMENT

Because many of the principles of treatment for bronchitis and bacterial pneumonia can be applied to dogs with ITB, refer also to Chapters 162 and 163.

General Guidelines

- Treat ITB on an outpatient basis whenever possible to prevent transmission to other hospitalized animals.
- For typical ITB, the disease is mild and self-limiting in 7 to 14 days; thus specific therapy may not be required. However, in most cases the empirical use of an antibiotic is justified along with an antitussive drug to control cough. If needed, an anti-inflammatory dose of a glucocorticoid can be used for the first few days in uncomplicated ITB.
- For severe, complicated ITB, treat aggressively for life-threatening bacterial bronchopneumonia (see Chapter 163). Avoid antitussives or glucocorticoids if bronchopneumonia is suspected.
- For cough that persists more than 14 days, consider causes other than ITB and evaluate further with thoracic radiographs, CBC, airway cytology and culture, and other diagnostics as appropriate.

Antibiotics

- For mild self-limiting ITB, antibiotics are optional, but most cases are treated empirically for possible *Bordetella* infection and to limit opportunistic secondary infections using one of the following:
  - Doxycycline (5–10 mg/kg PO q12h) for 2 to 4 weeks; effective for both *Bordetella* and mycoplasma
  - Amoxicillin/clavulanate (12.5–25 mg/kg POq12h) for 2 to 4 weeks
  - Azithromycin (5 mg/kg PO, once daily) for 5 to 7 days.
  - Others: enrofloxacin, trimethoprim/sulfa
- For severe ITB complicated by bronchopneumonia or for refractory *Bordetella* infection, choose antibiotics based on culture and susceptibility testing whenever possible.
- For refractory *Bordetella* infection, aerosolize gentamicin, 50 mg diluted in 2 to 3 ml saline, with a handheld nebulizer for 10 minutes every 12 hours for 3 to 5 days. Aerosolized antibiotic may be more effective against *Bordetella* because the bacteria attach to the cilia on the mucosal surface and are hard to reach with systemic antibiotics.

Antitussives

- In diseases with a productive cough, it usually is recommended to avoid antitussives, but in uncompli-

cated ITB (no fever or evidence of bronchopneumonia), the cough can be such a nuisance and source of discomfort for owner and patient that antitussives are often needed for relief.
- *Examples:* Hydrocodone (0.22 mg/kg PO q6–12h) and butorphanol (0.55–1.1 mg/kg PO q6–12h).
- Over-the-counter human cough medicines (dextromethorphan, guaifenesin) are not effective for treating ITB.

Corticosteroids

- Use anti-inflammatory dosages of corticosteroids (prednisolone 0.25–0.5 mg/kg PO q12h) as needed to control refractory cough in uncomplicated ITB. Limit use to 5 days or less, and do not use in dogs with bronchopneumonia.

Bronchodilators

- Efficacy of bronchodilators in ITB is not established, but these may reverse reflex bronchoconstriction triggered by airway irritation, thereby reducing discomfort and cough.
- *Examples:* Theophylline, aminophylline, albuterol, and terbutaline (see Chapter 162 for dosages).

Supportive Care

- Provide adequate fluid intake, airway humidification, nutritional support, and rest.

PREVENTION

Prevention strategies include vaccination and kennel management practices.

Vaccination

Guidelines for routine canine vaccination usually incorporate CAV-2 and CPIV. In dogs with high risk of exposure, *Bordetella* vaccination is an optional consideration, although it has only moderate efficacy. For specific vaccination recommendations, see Chapter 7.

- Both injectable and intranasal (IN) vaccines are available for CAV-2, CPV, and *Bordetella*. Vaccines for CAV-2 and CPIV contain modified live virus. *Bordetella* vaccines are derived from killed bacterins (injectable) or avirulent live culture (IN).
- The IN vaccines have advantages of stimulating local immunity, protection after one dose, more rapid onset of protection, and minimal interference from maternal antibody, allowing use in puppies as young as 2 to 4 weeks of age. Side effects of IN vaccines may include nasal discharge, sneezing, and cough beginning 2 to 5 days after vaccination.
- The maximum duration of immunity for these vaccines following initial puppy vaccination and a 1-year booster is not well established; however, immunity for CAV-2 and CPIV is expected to last for at least 3 years, whereas immunity for *Bordetella* may be only 6 months or less.
- For *Bordetella,* a booster is recommended 1 to 2 weeks prior to known exposure (e.g., boarding or showing) if the dog has not been vaccinated within the previous 6 months.

Kennel Prevention

- Avoid overcrowded, high-density confinement.
- Isolate infected (coughing) animals. In recovered animals, ITB viruses may be shed for 1 to 2 weeks, and *Bordetella* and mycoplasmas may be shed for 3 months or longer.
- Use caretaker hygiene to prevent fomite spread.
- Ensure proper kennel ventilation (at least 12 air changes per hour; 15–20 is optimal).
- Use disinfectants such as sodium hypochlorite (Clorox), chlorhexidine (Nolvasan), and benzalkonium Cl (Roccal-D).

PUBLIC HEALTH CONSIDERATIONS

Humans are potentially susceptible to *B. bronchiseptica,* especially if immunocompromised; however, the risk of acquiring infection from an infected pet is considered minimal.

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Chapter

13 Canine Distemper

Robert G. Sherding

Canine distemper is a severe, highly contagious viral disease of dogs and other carnivores with profound effects on the respiratory tract, gastrointestinal tract, nervous system, and lymphoid tissue. It is seen worldwide.

ETIOLOGY AND EPIDEMIOLOGY

Canine distemper virus (CDV) is an RNA *Morbillivirus* in the *Paramyxoviridae* family. It is closely related to human measles virus.

Epidemiology

- *Distribution:* Enzootic worldwide.
- *Incidence:* All ages can be affected; however, the incidence is highest in young dogs (2–6 months of age), especially unvaccinated puppies that are exposed following the loss of passive immunity from maternal colostral antibodies.
- *Host susceptibility:* Domestic dogs and many wild carnivores, including the following:
  - *Canidae* family—Fox, dingo, coyote, wolf, jackal
  - *Mustelidae* family—Ferret, mink, weasel, marten, skunk, badger, otter
  - *Procyonidae* family—Raccoon, kinkajou, coati
  - Large *Felidae*—Cheetah, lion, jaguar, margay, ocelot
  - Others—Bear, panda, hyena, mongoose

Transmission

- Infected animals shed virus in all body secretions and excretions.
- The primary route of infection is by inhalation of the virus from aerosolized secretions or from fomites.
- The greatest opportunity for spread occurs where dogs are kept in groups (e.g., pet shops, kennels, animal shelters, and research colonies).
- Transplacental transmission is a rare source of distemper in neonates.
- Viral shedding usually ceases 1 to 2 weeks after recovery; therefore, "carrier state" transmission is not a big problem. Shedding for 60 to 90 days has been reported but is rare.
- The virus is labile in the environment, usually surviving only a few hours and no more than a few days outside of the host. It is readily destroyed by drying and by most disinfectants, such as phenols and quaternary ammonium.

PATHOGENESIS

The pathogenesis and severity of disease is affected by the viral strain and dose, the animal's age, and the effectiveness of the host's immune response.

Stages of Infection

- *Day 1:* Airborne exposure leads to infection of tissue macrophages of the upper respiratory tract.
- *Days 2 to 4:* Infection spreads to local lymphoid tissues of the tonsils, retropharyngeal lymph nodes, and bronchial lymph nodes.
- *Days 4 to 6:* Widespread infection of systemic lymphoid tissues involves the liver, spleen, abdominal lymph nodes, and lamina propria of the gastrointestinal tract. This corresponds to a transient fever spike and the onset of lymphopenia caused by viral damage to T and B lymphoid cells.
- *Days 6 to 8:* Viremia occurs.
- *Days 8 and 9:* The virus is disseminated to epithelial tissues (epitheliotropism) and the central nervous system (CNS) (neurotropism).
- *Days 9 to 14:* The subsequent outcome varies depending on the host's immune response and can include recovery, severe multisystemic clinical disease, or CNS localization.

Host Immune Response

- If the immune response fails to develop by days 9 to 14, the outcome is rapid, widespread dissemination of the virus to skin; glandular and epithelial organs, such as the respiratory and gastrointestinal tracts; and the CNS, causing acute encephalomyelitis. The results are multisystemic signs, a second fever spike, and a high mortality rate, especially in young puppies.
- If the immune response is sluggish or partial, multisystemic signs are mild or absent and recovery occurs; however, CNS localization can result in chronic

demyelinating encephalomyelitis with delayed onset of neurologic signs.
- If the immune response is rapid and effective, the infection is subclinical with complete recovery and elimination of the virus without clinical illness (by day 14 postinfection). It is estimated that more than 50% of CDV infections are subclinical. Delayed-onset CNS disease is occasionally seen in this group.

Role of Immunosuppression

- CDV causes severe immunosuppression associated with widespread lymphoid damage (apoptosis), impaired B and T cell–mediated immunity, circulating lymphopenia, thymic atrophy, and impaired cytokine responses.

CLINICAL SIGNS

The clinical signs of distemper are multisystemic and extremely variable. The mortality rate is variable depending on the virulence of the CDV strain and the age and immune status of the host.

General Systemic Signs

- Severe depression, anorexia, and dehydration
- Fever of 103°F to 105°F (39.5–41°C); diphasic (signs usually coincide with the second fever spike)

Respiratory System

- Rhinitis and conjunctivitis result in serous to mucopurulent naso-ocular discharge.
- Productive cough, tachypnea, dyspnea, and auscultation abnormalities are caused by pneumonia. This begins as an interstitial pneumonitis (primary viral effect) that rapidly develops into generalized bronchopneumonia complicated by secondary bacterial infection.

Gastrointestinal System

- Vomiting and diarrhea are the result of acute gastroenteritis.

Eyes

- Keratoconjunctivitis results in serous to mucopurulent ocular discharge.
- Chorioretinitis results in hyperreflective fundic lesions of retinal atrophy.
- Optic neuritis or serous retinal detachments results in blindness.

Nervous System

Acute encephalomyelitis predominantly destroys gray matter (neurons), whereas subacute or chronic nonsuppurative encephalomyelitis predominantly affects white matter (demyelination). CNS signs can occur simultaneously with other multisystemic signs or can be delayed in onset for 1 to 3 weeks or even months after apparent recovery from systemic illness. In some dogs, CNS involvement can occur as the only apparent clinical manifestation of infection. (For additional details concerning the neurologic manifestations of CDV, see Chapter 126.)

▼ ***Key Point*** Any region of the CNS can be affected by CDV. Diffuse or multifocal CNS involvement is typical. CNS signs tend to be progressive and can occur during, after, or in the absence of multisystemic illness.

- *Acute encephalitis:* Generalized seizures, so-called chewing-gum seizures, pacing, circling, and behavior changes
- *Midbrain, cerebellar, and vestibular:* Ataxia and other disturbances of gait
- *Spinal cord:* Disturbances of gait, abnormal spinal reflexes, paresis, and abnormal proprioception
- *Peripheral and cranial neuropathies:* Cranial nerve deficits including optic neuritis
- *Myoclonus:* Rhythmic, repetitive motor movements or muscle twitches

Other Clinical Manifestations

- Dental enamel hypoplasia (pitted teeth) can result from infection before eruption of the permanent teeth.
- Naso-digital hyperkeratosis of the foot pads and nasal planum ("hard pad disease"), which may be more frequent in dogs with CNS involvement.
- Abdominal pustular dermatitis.
- Viral cardiomyopathy has been observed in neonatal (<7 days old) infections.
- Young, growing large-breed dogs can develop metaphyseal osteosclerosis of the long bones.

DIAGNOSIS

▼ ***Key Point*** A presumptive diagnosis of canine distemper is based on typical clinical signs in a young dog (2–6 months of age) with a history of inadequate vaccinations and possibility of exposure to the virus.

In suspected cases of distemper, perform a complete blood count to assess leukocyte responses and thoracic radiographs to assess pneumonia. In dogs presenting with neurologic disease suspected to be due to CDV, use routine cerebrospinal fluid (CSF) analysis to distinguish CDV infection from other diseases. The presence of a CDV-specific antibody in CSF can confirm the diagno-

sis but requires a special laboratory. Special virology techniques can help substantiate a diagnosis of distemper; however, this is not practical or necessary in most clinical situations, and false-negative results are common.

Hematology

- Lymphopenia (beginning with the initial fever spike).
- Neutrophilic leukocytosis occurs later (associated with secondary bacterial complications such as pneumonia).
- Distemper inclusions are seen rarely in circulating lymphocytes, monocytes, neutrophils, and erythrocytes.

Thoracic Radiography

- Diffuse interstitial pneumonitis is seen early.
- A diffuse alveolar and bronchial pattern, air bronchograms, and lobar consolidation are seen later with secondary bacterial bronchopneumonia.

Cerebrospinal Fluid Analysis

- CSF may have increased cells (mostly lymphocytes) and/or protein, but normal findings do not rule out CDV (see Chapters 125 and 126).
- The presence of a CDV-specific antibody in CSF in greater concentration than serum is diagnostic of CDV, but not all cases have CSF antibodies.

Serology

- A single positive immunoglobulin G (IgG) titer is of no benefit, because it does not distinguish current infection from previous vaccination or exposure.
- The demonstration of a rising serum neutralizing an antibody titer or a CDV-specific IgM titer is suggestive but not diagnostic of recent CDV infection.

Virology

Various methods are available for demonstrating the virus or viral antigen in cells or tissues; however, with any of these procedures negative results do not rule out CDV.

- Intracytoplasmic viral inclusion bodies can sometimes be detected in peripheral blood cells, epithelial cells (cytology specimens), or biopsies, but inclusions are absent in many cases.
- Viral antigen can be identified by immunohistochemistry or fluorescent antibody techniques in cells from blood, CSF, cytology specimens (e.g., conjunctival scraping or tracheobronchial aspirate), or frozen tissue specimens.
- Virus isolation is difficult and expensive, and it mostly uses postmortem tissues.
- Polymerase chain reaction (PCR) assays have been used to test peripheral blood monocytes and tissues for CDV. These tests appear to be highly sensitive and specific under experimental conditions, but they are not yet readily available for clinical use.

TREATMENT

There is no effective antiviral treatment for CDV; therefore, treatment is supportive and symptomatic. Whenever possible, treat distemper in an isolation facility to prevent aerosol exposure of other hospitalized animals.

Symptomatic Treatment

- Give broad-spectrum antibiotics (extended-spectrum cephalosporin, fluoroquinolone, etc.) for secondary bacterial infection, especially pneumonia (see Chapter 163).
- For pneumonia, give antibiotics for secondary bacterial infection, maintain hydration with parenteral fluid therapy, and perform chest coupage (see Chapters 162 and 163).
- For vomiting and diarrhea, restrict food intake and administer antiemetics (see Chapter 67) and antidiarrheals (see Chapter 69) as necessary.
- For seizures, give a single dose of dexamethasone (1–2 mg/kg IV) for CNS edema, and consider anticonvulsant therapy using phenobarbital, diazepam, or potassium bromide (see Chapter 127).
- Provide general supportive care, such as eyes and nose kept clear of discharges; nutritional support; and adequate fluid intake or parenteral fluid therapy.

Prognosis

- Mortality rate varies but is highest in young puppies, especially those with high fever, severe multisystemic disease, severe pneumonia, or progressive neurologic disease.
- The neurologic deficits caused by CDV are often progressive and irreversible. It is justified to recommend euthanasia for patients with progressive neurologic signs that are severe and incapacitating.

▼ ***Key Point*** Do not be too optimistic with the owner, even with mild cases of distemper. The disease is often progressive despite therapy; and even animals that seem to be recovering can have a delayed onset of progressive, incapacitating neurologic disease.

Client Education

- Discuss the multiplicity of signs, likelihood of progression, and guarded to poor prognosis.
- Advise owners to isolate their animal from others to prevent spread of infection.

- Educate the client about proper immunization procedures for future reference.
- Recommend routine disinfection procedures and a 1-week waiting period before bringing another dog onto the premises.

PREVENTION

Passive Maternal Antibody

- The neonatal pup acquires passive immunity against CDV from its dam. Most of this maternal-derived antibody (Ab) comes from colostrum absorbed during nursing in the first few hours after birth.
- Maternal Ab protects most pups until after weaning and then gradually disappears between 8 and 14 weeks of age.
- When present, maternal Ab interferes with the response to vaccination; however, in most dogs it decreases to a level that allows successful immunization by 12 weeks of age.

Vaccination

▼ ***Key Point*** CDV vaccination is highly recommended for all dogs, and the efficacy of recombinant and modified live virus (MLV) vaccines is considered high. Vaccinate puppies at 6 to 8 weeks, 9 to 11 weeks, and 12 to 14 weeks of age. Give the first booster 1 year later and additional boosters every 3 years thereafter (see Chapter 7).

- Measles virus vaccine is not as protective as CDV vaccine, but a single IM dose can be used to provide temporary, partial protection in the presence of interfering maternal antibodies in young puppies 4 to 12 weeks of age who are in high-risk environments. This must be followed by CDV vaccine after 12 weeks of age.
- Rarely, postvaccinal encephalitis has occurred from 7 to 15 days after MLV distemper vaccination, primarily in neonatal puppies (<4 weeks of age); in severely ill, stressed, or immunocompromised dogs; or in very young puppies infected with parvovirus.

SUPPLEMENTAL READING

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Chapter

14 Intestinal Viruses

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Parvoviruses, coronaviruses, and rotaviruses are established causes of viral enteritis and diarrhea in dogs and cats and are discussed in this chapter. In addition, numerous other viruses of uncertain significance and enteropathogenicity have been found in the feces or intestines of dogs and cats.

- In dogs these include herpesvirus, enteroviruses, calicivirus, parainfluenza virus, adenovirus, and picornavirus.
- In cats these include astrovirus, calicivirus, reoviruses (types 1, 2, and 3), torovirus, and togavirus.
- In addition, the intestine may be involved as part of generalized viral infections in disorders such as canine distemper in dogs (see Chapter 13), and feline leukemia virus (see Chapter 8), feline immunodeficiency virus (see Chapter 9), and feline infectious peritonitis (see Chapter 10) in cats.

CANINE PARVOVIRUS

Etiology and Epidemiology

Canine parvovirus type 2 (CPV-2), a non-enveloped, single-stranded DNA virus, causes an acute, highly contagious enteritis of dogs that has been prevalent worldwide since the late 1970s. CPV is believed to have evolved from the feline panleukopenia virus or a closely related virus. Since 1980, variants designated CPV-2a and CPV-2b have evolved, the latter now being the predominant strain in North America. Both of these variants and a newer CPV-2c variant can also infect and replicate in cats.

Transmission

CPV infection occurs by the fecal-oral route. During acute illness, and for about 1 to 2 weeks after recovery, massive amounts of parvovirus (over 1 billion virions per gram of feces) are shed in the feces of infected dogs. Because the virus can survive and remain infectious for 5 to 7 months in the environment, fomites and environmental contamination play a major role in transmission. A peak seasonal incidence in the months of July, August, and September was found in a Canadian study, but this may vary by climatologic region.

Incubation

Signs of enteric disease usually begin 4 to 7 days after exposure, coincident with localization of virus in the mitotically active zones of intestinal crypt epithelia.

Age Incidence

Dogs of any age can be infected, but the incidence of clinical disease is highest in puppies between weaning and 6 months of age. Puppies younger than 6 weeks of age generally are protected by passive maternal antibody, whereas most mature animals have been immunized or have seroconverted from natural exposure.

Breed Incidence

All dogs are susceptible to infection; however, certain breeds have a higher risk for parvovirus infection and appear to be more susceptible to a severe form of the disease. These include rottweilers, Doberman pinschers, American pit bull terriers, German shepherds, and possibly Labrador retrievers. The biologic basis for these breed susceptibilities is unclear.

Pathogenesis

▼ ***Key Point*** CPV has an affinity for the rapidly dividing cells of the intestines, bone marrow, and lymphoid tissues and thus causes intestinal crypt necrosis, severe diarrhea, leukopenia, and lymphoid depletion.

- Intestinal epithelial damage from CPV causes breakdown of the intestinal mucosal barrier. This allows translocation of bacteria (especially *Escherichia coli*) and absorption of endotoxin, predisposing to bacteremia, endotoxemia, and the development of fatal systemic inflammatory response syndrome (SIRS).

Clinical Signs

- CPV causes sudden onset of anorexia, depression, fever, vomiting, diarrhea, and severe dehydration. The diarrhea can be profuse, foul smelling, and hemorrhagic. Abdominal palpation may reveal intestinal

loops that are painful and distended with fluid and gas.
- Hypothermia, hypovolemic shock, icterus, hemorrhagic diathesis (disseminated intravascular coagulation), and pulmonary edema because of acute respiratory distress syndrome may develop terminally in cases complicated by bacterial septicemia, endotoxemia, and SIRS.
- Death may occur in severe cases, particularly in very young puppies and in the highly susceptible breeds, and is usually attributable to dehydration, electrolyte depletion, endotoxic shock, or overwhelming bacterial sepsis associated with severe leukopenia. Septic puppies often develop hypoglycemia.
- The severity of clinical illness may be increased by factors such as stress, overcrowded or unsanitary kennel conditions, secondary bacterial infection, and concurrent diseases such as canine distemper, coronavirus, salmonellosis, campylobacteriosis, and intestinal parasitism (e.g., nematodes or giardia).
- In susceptible mature dogs, mild or inapparent infection that results in seroconversion without obvious clinical signs is common.
- In utero or postnatal infection can cause acute neonatal myocarditis in neonatal puppies that did not receive maternal antibodies. However, this form of perinatal parvoviral infection is rare because most nursing puppies receive abundant maternal antibodies from colostrum. Signs of parvoviral myocarditis include dyspnea caused by acute heart failure, sudden death caused by arrhythmias, and sometimes delayed-onset chronic congestive heart failure caused by chronic myocardial fibrosis.

Diagnosis

Suspect parvovirus infection in young dogs that have an abrupt onset of vomiting and foul-smelling bloody diarrhea, especially if associated with severe depression, fever, or leukopenia or if these signs follow potential exposure to infected dogs or fomites.

▼ ***Key Point*** Because of the difficulty in breaking through maternal antibody interference with vaccination in young puppies, prior vaccination does not necessarily exclude parvoviral infection, especially in puppies 6 to 20 weeks of age.

Hematology

- A complete blood count is particularly useful because approximately 50% of dogs with parvoviral enteritis develop severe leukopenia caused by lymphopenia and granulocytopenia, often with a total of only 500 to 2000 leukocytes/μl and sometimes less. Depletion of circulating mature neutrophils is caused by extensive loss of neutrophils through the damaged intestinal mucosa coupled with impaired myelopoiesis caused by bone marrow disruption from the virus. The severity of the leukopenia is generally proportional to the severity of the clinical illness. A rebound neutrophilia is a positive indicator of impending recovery.
- The hematocrit is variable. The PCV is often normal but can be moderately decreased (especially after rehydration with fluids) in some dogs because of intestinal hemorrhage. In some dogs, the PCV can be elevated initially because of hemoconcentration from dehydration.

Serum Chemistries

Serum chemistry abnormalities are variable and nonspecific. Findings may include electrolyte abnormalities (most frequently hypokalemia), prerenal azotemia, hypoglycemia, hypoalbuminemia, increased bilirubin, and increased liver enzymes (alanine transaminase and alkaline phosphatase).

Abdominal Radiography

Gas and fluid distention of the gastrointestinal (GI) tract due to generalized ileus is frequent in parvoviral enteritis and must be differentiated from small intestinal obstruction (e.g., foreign body or intussusception). Carefully palpate the abdomen to help rule out mechanical obstruction, including complicating intussusception. Barium contrast radiography often reveals mucosal irregularity (corrugation or scalloping) and prolonged transit time.

Serology

- Determination of an anti-CPV antibody titer in serum is not sufficient for diagnosis because up to 95% of dogs in the population have seroconverted from prior vaccination or natural exposure.
- Detection of early-appearing immunoglobulin (Ig) M antibodies by an indirect fluorescent antibody (IFA) test or 2-mercaptoethanol procedure provides presumptive evidence of recent infection because IgM antibodies are only found during or a few weeks after infection.

Virology

▼ ***Key Point*** Definitive diagnosis of parvoviral enteritis requires demonstration of active excretion of virus or viral antigen in the feces.

- Massive quantities of virus are shed in the feces during the acute illness, and shedding is over within 1 to 2 weeks after recovery. The most practical methods for detecting parvovirus in the feces are the commercially available, rapid in-office tests; including the enzyme-linked immunosorbent assays (ELISAs), such as the SNAP-Parvo Test (IDEXX Lab-

oratories) and ASSURE-Parvo Test (Synbiotics), or the rapid immunomigration assay, such as Witness CPV (Synbiotics). These tests are sensitive and accurate.
- Consider that false-positive results are occasionally seen on these CPV immunoassays 5 to 12 days following vaccination with modified live virus (MLV) vaccines. False-negative results occur rarely when fecal antigen is bound to neutralizing antibodies or viral shedding stops early.
- Other methods for detecting fecal excretion of parvovirus, such as hemagglutination, latex agglutination, electron microscopy (EM), virus isolation, and polymerase chain reaction (PCR) assay, are less convenient for routine clinical use because they require a commercial or research laboratory.

Necropsy

Necropsy diagnosis of parvovirus is based on identification of the characteristic intestinal lesions of necrosis of the intestinal crypt cells with secondary villous collapse and dilatation of the crypts with necrotic debris. Myeloid degeneration and widespread lymphoid depletion also are seen. Parvovirus can be demonstrated in frozen tissue samples by immunofluorescence and in fixed specimens by PCR.

Treatment

The treatment of parvovirus is mainly supportive and similar in most ways to the treatments used for other types of severe gastroenteritis. The intensity of the treatment depends on the severity of the signs. In dogs with fully developed clinical signs, withhold food and water for 12 to 24 hours to rest the GI tract, administer IV crystalloids to replace fluid and electrolytes, and give parenteral antibiotics to control bacterial complications. Initiate therapy whether or not definitive tests are done or while awaiting the return of results.

Fluid Therapy

▼ ***Key Point*** The cornerstone of treatment for CPV infection is IV fluid and electrolyte therapy.

See Chapter 5 for specific guidelines and procedures for fluid and electrolyte therapy.

- Use the intravenous route for fluid and electrolyte replacement using a balanced crystalloid solution (e.g., lactated Ringer's solution, Plasma-Lyte 148, or Normosol-R). For animals presented in hypovolemic shock, administer up to 90 ml/kg IV in the first 1 to 2 hours to restore hemodynamic stability (see Chapter 156), then switch to a maintenance rate. For most other animals, correct dehydration over the first 24 hours, then use a maintenance rate for fluids plus replacement of ongoing losses. Two to three times normal maintenance levels are often required. Continue fluid therapy until vomiting ceases and oral intake resumes.
- Add potassium (20–30 mEq/L) to IV fluids to control hypokalemia.
- Add dextrose to IV fluids at a 2.5% solution to control complicating hypoglycemia of sepsis. Monitor serum glucose and increase to 5% if needed to maintain serum glucose from 120 to 160 mg/dl.
- Consider supplementing magnesium according to guidelines in Chapter 5, as magnesium is often deficient in severe cases of parvoviral enteritis.
- Infuse colloid solution (e.g., hetastarch) at 20 ml/kg, IV, if infusion of balanced crystalloid solution does not restore hemodynamic stability or if serum albumin drops below 2 g/dl.
- Avoid administration of fluids by the subcutaneous route, especially in dogs with severe leukopenia, because this has been associated with secondary infection, cellulitis, and skin necrosis at administration sites.
- Monitor fluid therapy by tracking body weight, physical parameters, urine output, estimates of ongoing fluid losses (vomitus, diarrhea), and hematocrit and total plasma protein. Also evaluate serum potassium concentration daily and adjust potassium level added to IV fluids accordingly.

Antibiotics

- Administer bactericidal, broad-spectrum antibiotics to control bacterial complications. Initially, administer antibiotics parenterally.
- Use cefazolin or ampicillin in mild cases.
- Use cefazolin, ampicillin, or penicillin combined with an aminoglycoside (e.g., gentamicin or amikacin) or a fluoroquinolone (e.g., enrofloxacin) in severe and leukopenic cases. Fluoroquinolones may damage joint cartilage in young, growing pups. If an aminoglycoside is used, maintain hydration to prevent nephrotoxicity and monitor the urine daily for casts and proteinuria as early indicators of nephrotoxicosis.
- Consider a third-generation cephalosporin (e.g., ceftiofur; Naxel) combined with clindamycin in dogs with severe life-threatening bacterial sepsis.

Dietary Restriction

- Give nothing per os (fluid needs are met by IV infusion) for the first 12 to 24 hours. Prolonged food restriction may be detrimental to intestinal recovery. One study showed improved outcome in dogs treated with early enteral nutrition (using a nasoesophageal tube feeding starting at 12 hours) compared with dogs treated by prolonged dietary restriction.
- Persistent vomiting can sometimes take 3 to 5 days to abate in severe cases, sometimes requiring partial parenteral nutrition.

- When feeding is resumed, give small, frequent feedings of a bland and digestible diet, such as a commercial GI diet or cooked skinless chicken and rice, until GI function appears to have recovered. The transition back to regular feeding should be gradual.

Antiemetics

- For frequent or persistent vomiting associated with delayed gastric emptying that sometimes occurs in parvoviral infection, administer metoclopramide, a dopaminergic antagonist, at 0.5 mg/kg every 8 hours SC or most effectively as a constant rate infusion of 1 to 2 mg/kg every 24 hours diluted in IV fluids.
- For gastritis, control gastric acid secretion with an H_2 receptor blocker, for example, ranitidine (Zantac; 2 mg/kg IV, q8–12h), or famotidine (Pepcid; 0.5 mg/kg IV, q12–24h).
- If these are unsuccessful for controlling vomiting, consider the broad-spectrum phenothiazine antiemetic, chlorpromazine (0.5 mg/kg SC or IM, q6–12h), but not until dehydration has been corrected because phenothiazines have a hypotensive effect. Avoid the use of metoclopramide and chlorpromazine together because they can produce central nervous system excitation and, rarely, seizures.
- For persistent vomiting that is refractory to other treatments, give ondansetron (Zofran; 0.1–0.2 mg/kg slow IV, q6–12h), a serotonin-antagonist antiemetic.
- Avoid the use of anticholinergics in parvoviral enteritis because they can worsen GI hypomotility.

Antidiarrheals

- Parvoviral diarrhea is usually self-limiting, and treatment to control diarrhea is rarely needed as long as fluid needs are met; however, when diarrhea is profuse and persistent, administer loperamide (Imodium; 0.2 mg/kg PO, q8h).

Infusion of Whole Blood or Plasma

- Consider whole blood transfusion (5–10 ml/kg IV) for treatment of severe blood loss anemia and hypoproteinemia.
- Consider plasma infusion (5–10 ml/kg IV) for cases that develop disseminated intravascular coagulopathy. Plasma may also help correct hypoproteinemia, but hetastarch is a preferred source of colloid for raising colloid osmotic pressure. Plasma may also provide anti-CPV antibodies, but the benefit of this is questionable.

Treatment for Septic Shock

- Use the recommendations in Chapter 156 for fluid therapy in shock.
- Dexamethasone (2–4 mg/kg IV) can be used as a single dose to treat septic shock.
- Flunixin meglumine (Banamine), a nonsteroidal anti-inflammatory drug, is an alternative to corticosteroids as a single injection to treat septic shock. Beware of gastric ulceration; do not give repeated doses or combine with corticosteroids.
- Equine-origin, antiendotoxin hyperimmune serum (Septi-Serum, Immvac) is intended to bind and neutralize endotoxin, but efficacy is uncertain.

Immunotherapy

The following experimental treatments have been used for CPV infection:

- Recombinant human granulocyte colony-stimulating factor (rhG-CSF) has been used to treat other causes of neutropenia, but studies have failed to show improved survival or any beneficial effects in parvoviral neutropenia.
- Recombinant human bactericidal/permeability-increasing protein is used to treat human SIRS, but in a preliminary study in dogs with CPV enteritis it did not decrease circulating endotoxin or improve survival.
- Recombinant feline interferon-omega (rFeIFN-ω) (Virbagen Omega, Virbac), 2.5 million U/kg IV, daily for 3 consecutive days, decreased the severity of enteritis and improved survival in dogs with CPV enteritis in preliminary studies. This product is currently available in France but needs further study as a treatment for CPV.

Prognosis and Complications

▼ ***Key Point*** Most dogs with CPV enteritis recover if treated appropriately to control dehydration and bacterial complications.

- Most animals that survive the first 3 to 4 days of illness recover uneventfully. The survival rate with intensive therapy is 80% to 95%.
- Some animals succumb to bacterial sepsis and endotoxemia resulting from leukopenia, immunosuppression, and breakdown of the intestinal mucosal barrier caused by CPV. In general, the mortality rate is highest in young puppies.
- Complications may include hypoproteinemia, anemia, hypoglycemia (secondary to sepsis), disseminated intravascular coagulation (sepsis), SIRS, intussusception, liver disease, central nervous system signs (likely due to concomitant canine distemper), and various secondary bacterial infections, such as endocarditis, thrombophlebitis, pneumonia (caused by aspiration in some dogs), urinary tract infection, injection site abscesses, and intestinal salmonellosis and campylobacteriosis.

Prevention by Minimizing Exposure

- Dogs with CPV infection shed massive amounts of virus in the feces during their illness. The excreted virus as well as the fomites and premises that become contaminated are highly infectious for other dogs. Thus, instruct the owner of a CPV-infected dog to keep the dog isolated from other dogs until at least 1 week after full recovery.
- CPV is ubiquitous, and because it is so stable outside of the animal and easily transmitted by fomites, prevention of exposure is almost impossible. Nevertheless, until vaccinations are complete, keep young puppies isolated as much as possible from other animals and from potentially infected premises.

▼ ***Key Point*** Elimination of CPV from infected premises is difficult because the virus is so resistant; however, cleanup followed by disinfection with a 1:32 dilution of sodium hypochlorite bleach is effective.

Prevention by Vaccination

Vaccination is highly effective for prevention and control of parvovirus infection.

Maternal Antibody Interference

Although widespread vaccination against parvovirus has markedly reduced the incidence of the disease in North America, parvoviral enteritis continues to be a problem in puppies as they are nearing the end of their maternal antibody protection between 6 and 18 weeks of age. This is because of a period of susceptibility when maternal antibodies are too low to protect but at the same time high enough to interfere with the response to vaccination, especially when killed or low-titer MLV vaccines are used.

▼ ***Key Point*** In puppies from dams with high CPV titers, maternally derived antibody can persist at interfering levels for 18 weeks or more; thus, killed and low-potency MLV vaccines may not be able to break through this maternal antibody interference until as late as 18 weeks of age.

- In the first weeks of life, maternal antibody protects the puppy from infection, but at the same time it also interferes with active immunization.
- As the level of this maternal antibody gradually declines, there is a period of 2 to 4 weeks when puppies may be refractory to vaccination but susceptible to infection if exposed.
- Most suspected "vaccination failures" in puppies probably result from exposure to infection during this critical period of susceptibility.
- Because the age at which pups can respond to vaccination for CPV is unpredictable, vaccination protocols for puppies use a series of vaccinations in 3- to 4-week intervals.
- Attenuated (MLV) CPV-2 vaccines that are high titer and low passage (i.e., contain a high titer of a highly immunogenic strain of virus) are most effective at breaking through maternal antibody interference at a young age.

Recommendations for Routine Vaccination

▼ ***Key Point*** Vaccination against CPV is highly recommended for all dogs, and the efficacy of MLV vaccines is considered high.

- Vaccinate puppies using high-titer MLV CPV-2 vaccines at 6 to 8 weeks, 9 to 11 weeks, and 12 to 14 weeks of age. Give the first booster 1 year later and additional MLV boosters every 3 years thereafter (see Chapter 7).
- Advantages of MLV CPV-2 vaccines over killed vaccines are as follows:
  - Better magnitude of protection
  - More rapid onset of protection (as early as 1–3 days)
  - Longer duration of protection (≥3 years)
  - Better able to break through maternal antibody interference
  - Prevention of shedding of virulent CPV if exposed (killed vaccines protect only against clinical disease but do not prevent subclinical infection or shedding)

▼ ***Key Point*** Commercially available CPV-2 vaccines effectively crossprotect against all known field strains and variants of CPV.

- In unvaccinated dogs 16 weeks of age or older, give two initial doses of vaccine 2 to 4 weeks apart, although when high-titer MLV vaccine is used, a single primary dose is probably adequate.
- Avoid vaccinating pregnant dogs, but if necessary, use killed CPV vaccine instead of MLV. Also use killed instead of MLV in puppies less than 5 weeks of age, such as when early vaccination is needed in colostrum-deprived pups.

CANINE CORONAVIRUS

Etiology

Canine coronaviral enteritis is an acute contagious disease of dogs caused by an epitheliotropic virus that preferentially invades the mature enterocytes of the villous tips. The resulting villous damage, atrophy, and fusion cause diarrhea of variable severity. Canine coronavirus (CCV) is an enveloped, single-stranded RNA virus.

- CCV is considered of minor importance as a cause of enteritis in dogs.
- CCV is shed subclinically for months postinfection in chronic carriers and spreads rapidly by fecal-oral transmission. The incubation period is 1 to 4 days.
- CCV is closely related to feline coronavirus (see Chapter 10). Cats experimentally infected with CCV develop enteritis and sometimes feline infectious peritonitis.

Clinical Signs

- CCV rarely causes clinical disease, and when signs do occur they are typically mild and self-limiting. Acute diarrhea is the most frequent clinical sign. This may be accompanied by mild anorexia, depression, and vomiting. The character of the diarrhea varies from soft to watery and sometimes contains mucus. Bloody diarrhea and fever are infrequent.
- The signs are mild and easily confused with various other nonspecific causes of mild diarrhea of brief duration.

▼ ***Key Point*** Most CCV infections are subclinical; however, occasional epizootics of severe enteritis have occurred, primarily in puppies associated with kennels and dog shows.

Diagnosis

Consider coronaviral enteritis in dogs with an acute onset of signs of gastroenteritis, especially if other dogs on the premises are affected. Because coronaviral enteritis is usually non-fatal and the only treatment is supportive, definitive laboratory confirmation is not needed for effective case management except to document an epizootic outbreak. Coronaviral enteritis should, however, be distinguished from parvoviral infection, a more serious systemic infection.

▼ ***Key Point*** In contrast to CPV infection, fever, leukopenia, hematochezia, and fatalities are not typical of coronaviral enteritis.

- Routine hematology, serum chemistries, and abdominal radiography are usually normal.
- Definitive diagnosis requires laboratory detection of CCV in feces by EM, virus isolation, or PCR during the acute illness. Fecal examination by EM requires fresh feces (specimens can be kept refrigerated but not frozen). Both false-positive and false-negative results are a problem with EM because of misidentification of fecal particles. Virus isolation and PCR are performed in research labs and are not readily available to the clinician.

▼ ***Key Point*** The mere identification of CCV in a dog's feces is not proof that it is the cause of diarrhea or illness because CCV is shed in the feces of many healthy dogs.

- Serology can provide only a retrospective diagnosis via demonstration of a fourfold or greater rise in serum antibody titer in paired sera (at the time of illness and 2–6 weeks later).

Treatment

Treat coronaviral enteritis with nonspecific supportive measures such as fluid therapy and dietary restriction for 12 to 24 hours. Antibiotics are not necessary. Most dogs recover rapidly, although occasionally diarrhea persists 3 to 4 weeks. Rare fatalities have been reported, especially in neonates and mixed infections involving CPV or enteropathogenic bacteria.

Prevention

- Killed (inactivated) and modified-live CCV vaccines are commercially available; however, the efficacy, duration of immunity, and benefit from these products is questionable. Thus, CCV vaccination is not routinely recommended for most dogs (see Chapter 7). The CCV vaccine may be considered in selected situations in which exposure risk is high, such as in show and field trial dogs and kenneled (boarded) dogs.
- In general, immunity to coronaviruses is brief and is mediated by local (immunoglobulin A) immunity rather than the serum antibodies that would result from a parenteral vaccine. Parenteral vaccination does not prevent CCV infection, but it may reduce intestinal replication of virus and minimize clinical signs.

CANINE ROTAVIRUS

Etiology

Rotaviruses are non-enveloped, double-stranded RNA viruses that frequently cause neonatal diarrhea in humans and many other species of mammals and birds; however, canine rotavirus rarely causes diarrhea or clinical illness in dogs.

▼ ***Key Point*** Canine rotavirus is not an enteropathogen of major clinical importance in the dog.

- Antirotavirus antibodies are prevalent in surveys of normal dogs, indicating widespread subclinical infection.
- Rotaviruses are highly infectious and can persist in the environment for prolonged periods. Transmission is by the fecal-oral route.
- Rotaviruses replicate exclusively in the mature enterocytes of the villus tip, causing damage and blunting of the tips of the small intestinal villi.

Clinical Signs

- In adult dogs, rotaviral infection is usually subclinical. In young puppies, clinical signs of acute enteritis occasionally are seen.
- The diarrhea, which may be watery to mucoid, is usually self-limiting and of brief duration (5–7 days), although rare fatalities attributable to dehydration have been reported.
- Experimental inoculation of newborn gnotobiotic puppies with canine rotavirus results in diarrhea and mild to moderate villous atrophy. Deprivation of colostrum predisposes the patient to much more severe diarrhea.
- It is not possible to produce clinical disease or signs from experimental rotavirus infection in dogs older than 6 months of age.

Diagnosis

Definitive diagnosis is based on detection of rotavirus in feces by EM, virus isolation, or PCR. ELISA-based kits marketed for humans may not be reliable for detecting canine rotavirus.

Treatment

Rotaviral enteritis is treated like other types of acute diarrhea, with emphasis on supportive measures such as fluid therapy and dietary restriction or modification. Antibiotics are not needed. Most animals recover uneventfully with minimal treatment.

Prevention

Vaccines are not available for canine rotavirus. In neonates, the only group significantly threatened by rotavirus infection, the best protection is to ensure nursing of colostral antibodies in the first hours after birth.

FELINE PANLEUKOPENIA VIRUS

Etiology

Feline panleukopenia virus (FPV) is a severe, highly contagious parvoviral infection of cats. Panleukopenia is now a relatively rare disease in pet cats because of highly effective vaccines. Occasional infections are seen in unvaccinated kittens, especially those from shelters, farms, and urban stray populations. Cats also are susceptible to the closely related CPV variants CPV-2a, CPV-2b, and CPV-2c, but these only seem to infect cats sporadically.

- FPV can infect all species of *Felidae* as well as raccoon, ferrets, and mink.
- FPV is shed in all body excretions for up to 6 weeks, especially feces.
- FPV is very resistant to inactivation but can be inactivated with a 1:32 dilution of sodium hypochlorite bleach.
- FPV is ubiquitous in the environment, where it can survive readily for more than 1 year and can be transmitted by oropharyngeal contact with contaminated fomites.
- FPV has a predilection for rapidly dividing cells, particularly the following:
  - Intestinal crypt epithelium, resulting in acute enteritis
  - Hemopoietic tissue, resulting in panleukopenia
  - Lymphoid tissues, resulting in lymphoid depletion
  - In utero fetus, resulting in fetal death or cerebellar hypoplasia

Clinical Signs

Subclinical Infection of Adult Cats

Infection in susceptible adult cats is often subclinical. Acute enteritis and panleukopenia occur rarely in healthy adults. One study has identified FPV in heart tissue from cats with myocarditis and idiopathic cardiomyopathy using a PCR assay. The clinical significance of this finding is uncertain.

Generalized Infection of Kittens

The incidence and mortality rate are highest in young kittens. Clinical features are similar to those of canine parvoviral enteritis, with acute onset of anorexia, depression, a high fever from 104°F to 106°F (40–41°C), persistent vomiting, diarrhea, and progressive dehydration. Vomitus is usually a bile-stained fluid, and feces may be watery, mucoid, or bloody. Intestinal loops may be palpably thickened and firm (rope-like), fluid filled, and painful. There is increased susceptibility to bacterial sepsis and endotoxemia.

Perinatal Infection of Neonates

In utero infection of the fetus at the end of gestation or of the neonate in the first 2 weeks after birth may permanently damage the central nervous system and cause cerebellar hypoplasia. Affected kittens show nonprogressive signs of ataxia, hypermetria, falling to the side, broad-based stance, and intention tremors.

FPV also may invade the thymus of neonates, causing thymic atrophy and early neonatal mortality (fading kitten syndrome), and it may invade the retina, causing retinal dysplasia.

In Utero Infection of the Fetus

The only manifestation of infection in the pregnant cat may be transplacental infection of the developing embryo or fetus, leading to early embryonic resorption

(infertility), fetal death, fetal mummification, abortion, or stillbirth.

Diagnosis

Feline panleukopenia usually is diagnosed presumptively on the basis of typical clinical signs and leukopenia in a susceptible (unvaccinated) kitten.

▼ ***Key Point*** Profound leukopenia (total leukocyte count often <500/µl) is frequent and usually lasts 2 to 4 days before rebounding during recovery. The degree of leukopenia is proportional to the severity of clinical illness.

- Serum chemistry abnormalities are nonspecific and occur inconsistently but can include electrolyte depletion (especially hypokalemia), prerenal azotemia, and increased bilirubin and liver enzymes.
- If leukopenia persists more than 5 days or is accompanied by severe nonregenerative anemia, consider the panleukopenia-like syndrome that is associated with feline leukemia virus infection (see Chapter 8). Other panleukopenia "look-alike" diseases include acute salmonellosis, acute bacterial sepsis with endotoxemia, and GI foreign body with perforation and peritonitis (e.g., linear foreign body).
- Presumptive serologic diagnosis is based on paired neutralizing antibody titers. Definitive diagnosis requires fecal PCR or virus isolation, but these are not routinely available in clinical practice.
- Necropsy diagnosis is based on lesions of severe necrosis of intestinal crypts.

Treatment

- The treatment for feline panleukopenia is similar to that for canine parvoviral enteritis, mainly nonspecific supportive treatment such as intensive fluid therapy, parenteral antibiotics, antiemetics, nursing care, and restriction of dietary intake followed by enteral or parenteral feeding.
- In young kittens with panleukopenia, the mortality rate is high (50–90%). A guarded prognosis is justified until impending recovery is indicated by cessation of vomiting and diarrhea, return of appetite to normal, return of body temperature to normal, and rebound leukocytosis. However, serious complications that frequently indicate an impending fatal outcome include hypothermia, septic shock, overwhelming bacterial infection, jaundice, and disseminated intravascular coagulation.

Prevention

▼ ***Key Point*** Vaccination is highly effective for prevention of feline panleukopenia.

- Both attenuated (MLV) and inactivated (killed) FPV vaccines are available, but MLV vaccines are more effective and produce a more rapid onset of immunity. This can be an important consideration in high-risk environments such as shelters, where cats are housed in groups. Side effects associated with adjuvants in killed vaccines are avoided when MLV vaccines are used. Parenteral and intranasal MLV vaccines are available.
- Vaccinate kittens for FPV at least twice 3 weeks apart (usually 9 and 12 weeks of age) or every 3 to 4 weeks until 12 weeks of age. Give the first booster 1 year later and additional boosters every 3 years thereafter (see Chapter 7). Annual revaccination as recommended by manufacturers is not needed because antibody titers and resistance to FPV challenge persist 3 years or more after vaccination.
- Give two doses of vaccine, 3 to 4 weeks apart, for primary vaccination of adult cats.

▼ ***Key Point*** Use only killed FPV vaccine in pregnant cats and in kittens younger than 4 weeks of age. MLV vaccine given perinatally can infect the unborn fetus or the neonatal cerebellum.

FELINE CORONAVIRUS

Etiology

Feline coronavirus is a ubiquitous enteric virus in the cat population that invades the epithelium of the villous tip, resulting in villous atrophy and mild enteritis. A mutant variant of feline coronavirus causes feline infectious peritonitis (see Chapter 10).

▼ ***Key Point*** Feline coronavirus is shed in the feces of many normal cats, and a high percentage of cats are seropositive, indicating that inapparent infection is extremely prevalent.

Clinical Signs

- In young kittens, especially those 4 to 12 weeks of age, feline coronavirus causes an acute onset of mild enteritis with diarrhea. Feces are soft to fluid and rarely contain mucus and blood.
- Diarrhea is infrequently accompanied by vomiting, low-grade fever, anorexia, and lethargy.
- Clinical signs are usually mild and self-limiting within 2 to 4 days. Rare fatalities have been seen in kittens.
- In a small percentage of infected carrier cats, mutation of this coronavirus enables the virus to infect macrophages, leading to systemic dissemination and fatal feline infectious peritonitis (see Chapter 10 for a detailed discussion of FIP).

Diagnosis

Serology can identify a convalescent rise in coronaviral antibody titer. Subclinical coronavirus infection is widespread in cats; thus, seropositivity does not distinguish active and past infection. EM and PCR can be used to identify active shedding of coronavirus in fresh feces, but sensitivity is low with both of these diagnostic techniques.

Treatment

Uncomplicated coronaviral enteritis is usually self-limiting. Routine supportive measures such as fluid therapy and dietary restriction may be beneficial.

Prevention

This virus appears to be practically ubiquitous and spreads very efficiently through catteries; thus, prevention may not be practical. An intranasal feline coronavirus vaccine is available, but it does not appear to be effective and is not recommended.

FELINE ROTAVIRUS

Etiology

As in the canine, rotavirus has been isolated from the feces of both normal and diarrheic cats, especially kittens, but its enteropathogenic significance is unclear. Infection is restricted to the GI mucosa. Subclinical infection in mature animals is probably frequent, as indicated by surveys that found antibodies to rotavirus in 26 of 94 clinically healthy British cats and 23 of 50 cats in Louisiana.

Clinical Signs

Subclinical infection is typical, except in neonatal kittens that may develop mild diarrhea of 1 to 2 days duration.

Diagnosis

As in dogs, feline rotavirus can be detected in feces by EM, PCR, or ELISA.

Treatment

Rotaviral enteritis is self-limiting but, as for other types of acute diarrhea, supportive measures such as fluid therapy and dietary restriction may be beneficial. Most cats recover uneventfully with minimal or no treatment.

Prevention

Vaccines are unavailable for rotavirus. Because natural immunity is short lived, vaccination is unlikely to be warranted.

FELINE ASTROVIRUS

Etiology

Very little is known concerning this viral agent, but a few reports have identified astroviruses in the feces of cats with diarrhea, and mild diarrhea was reproduced experimentally in kittens. A survey of British cats determined a seroprevalence of less than 10%. Astrovirus infections in other species are limited to infection of the mature villous epithelial cells of the intestinal mucosa. Transmission is by the fecal-oral route.

Clinical Signs

Feline astrovirus appears to cause mild, nonspecific diarrhea 4 to 14 days in duration. Transient low-grade fever, depression, and inappetance also may occur, but affected cats otherwise remain well. Rarely, astrovirus has been implicated in diarrhea outbreaks in catteries. As with other enteropathogenic viruses, kittens are most likely to be affected.

Diagnosis

Feline astrovirus is detected in feces by EM or PCR. Some cats shed the virus subclinically. Serum antibody to astrovirus has been identified in cats, but its significance is uncertain.

Treatment

Diarrhea caused by astrovirus is treated like any other acute diarrhea with supportive measures such as fluid therapy and dietary restriction. Most animals recover uneventfully with minimal or no treatment.

Prevention

No preventive measures are available.

TOROVIRUS AND REOVIRUS TYPE 2

A syndrome of mild diarrhea in conjunction with idiopathic protrusion of the nictitating membrane (third eyelid) has been observed in cats, in some cases affecting clusters of cats in the same household. In a small number of these cats, type 2 reoviruses and a novel torovirus have been identified in the feces. Each of these viruses produced mild diarrhea in experimentally inoculated kittens, but protrusion of the nictitating membrane did not occur. The clinical significance of these viral agents is uncertain.

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Chapter 15

Rabies and Pseudorabies

Robert G. Sherding

RABIES

Etiology

- Rabies virus is a rhabdovirus (genus *Lyssavirus*) that can cause fatal infection in all warm-blooded mammals. The virus primarily attacks the nervous system and salivary glands, and it is shed in saliva.
- Rabies has public health importance as a zoonotic infection that causes highly fatal encephalitis in humans. The incidence of human rabies in the United States is very low. Several countries are considered rabies free, including Great Britain, Australia (except for a bat variant), New Zealand, and the Scandinavian countries. Hawaii is also free of rabies.
- Rabies is transmitted in saliva from the bite of an infected animal. For both humans and domestic animals, the usual source is the bite of a rabid domestic animal or wild animal, especially reservoir species such as skunks, raccoons, bats, foxes, or coyotes. Some of these wild animals can shed rabies virus for prolonged periods in their saliva without evidence of clinical signs.
- Rabies virus is very labile outside the host, and it is readily inactivated by many disinfectants.

▼ ***Key Point*** Rabies is rare in dogs and cats in the United States; however, cats are more susceptible, and the incidence in cats is higher than in dogs. Wild animals are the principal reservoirs of infection.

Pathogenesis

Rabies virus is transmitted in saliva into a deep bite wound, where it enters the peripheral nervous tissue and spreads retrograde (centripetally) along peripheral nerves to the spinal cord and brain. Centrifugal spread then occurs along peripheral nerves from the central nervous system (CNS) to other tissues, such as the salivary glands. The incubation period before CNS signs occur is extremely variable, but it is usually 2 to 8 weeks. Incubation periods of up to 24 weeks have been reported in dogs and cats. Virus shedding in saliva begins a short time (less than 10 days) before neurologic signs appear and continues until the animal dies. The clinical course is 3 to 10 days.

Clinical Signs

The clinical progression of rabies, although variable, is divided classically into three phases: prodromal, furious, and paralytic. Death usually occurs within 3 to 10 days from the onset of signs; however, some animals develop atypical rabies and do not progress through these stages.

Prodromal Phase (2–3 Days)

This phase often passes unnoticed, but there may be subtle signs of erratic behavior, fever, slow corneal and palpebral reflexes, and chewing at the bite site due to pruritus.

Furious Phase (2–4 Days)

Initially, the forebrain region of the CNS is invaded, resulting in signs of erratic and unusual behavior (i.e., "mad dog syndrome") such as irritability, restlessness, barking, episodic aggression, vicious attacks on inanimate objects, pica, unexplained roaming, and abnormal sexual behavior. Ataxia, disorientation, seizures, and paralysis may develop.

Paralytic Phase (2–4 Days)

This form is most common. Progressive lower motor neuron paralysis develops, causing signs of ascending paresis or paralysis of the limbs (often affecting a bitten extremity first) or signs of cranial nerve paralysis, such as laryngeal paralysis (change in bark, dyspnea), pharyngeal paralysis (drooling, dysphagia), and masticatory paralysis (dropped jaw). These are followed by generalized paralysis, depression, coma, and death from respiratory paralysis.

Atypical Rabies

Some animals develop subclinical, chronic, or recovered infections rather than the typical furious and paralytic forms. This has been observed in dogs, cats, bats,

and skunks. These animals may survive and shed virus for extended periods.

Diagnosis

▼ ***Key Point*** Rapid laboratory confirmation of animal rabies is essential so that exposed humans can receive proper prophylaxis as early as possible. Definitive diagnosis requires laboratory testing of postmortem tissues.

Antemortem tests for rabies are too unreliable to be recommended; thus, always evaluate postmortem tissue specimens for diagnosis, especially the brain. For laboratory analysis of brain and salivary tissue for the presence of rabies virus or antigen, submit the animal's head chilled on wet ice in a leak-proof container, along with appropriate information and biohazard labeling. Specimens can be stored by refrigeration but not freezing, because thawing will ruin the specimen for subsequent virus detection.

Direct Fluorescent Antibody Test

This is the test of choice used by most laboratories for rapid, reliable confirmation of rabies antigen in tissues. Brain tissue is most often used for routine testing, but salivary glands can also be evaluated. The direct fluorescent antibody (DFA) procedure has also been used for antemortem detection of rabies antigen in skin biopsies; however, a high percentage of false-negative results limits the usefulness of the skin test.

Histopathology

This older, less sensitive test identifies intracytoplasmic neuronal inclusions called Negri bodies, which are found in 75% of rabid dogs but rarely in cats.

Mouse Inoculation Test

This is a backup confirmatory test in which DFA-positive brain suspensions are inoculated intracerebrally into mice; the mice then are sacrificed and their brains are examined by DFA testing 5 to 6 days postinoculation. The correlation between DFA and mouse inoculation tests is reportedly 99.9%.

Tissue Culture Inoculation Test

This test is similar to the mouse inoculation test except that cell cultures are inoculated and then examined by DFA testing 24 to 72 hours later.

Monoclonal Antibody Techniques

These techniques are used to identify specific antigenic variants of rabies virus and to differentiate vaccine virus strains from wild-type strains in DFA-positive brains.

Molecular Techniques

Rabies virus genomic RNA can be detected in brain tissue using molecular techniques such as polymerase chain reaction (PCR) and hybridization techniques. These are generally reserved for specimens with questionable DFA results.

Treatment

Rabies is almost always fatal in domestic animals. Because of the extreme public health danger, treatment is not warranted; therefore, quarantine or euthanize all animals suspected of rabies, and notify local health department authorities.

Prevention in Dogs and Cats

Rabies prevention requires vaccination and preventing pets from having contact with wild animals.

Vaccination

▼ ***Key Point*** Vaccinate all dogs, cats, and ferrets against rabies in accordance with local public health regulations and the Compendium of Animal Rabies Prevention and Control, published annually by the National Association of State Public Health Veterinarians (available at www.nasphv.org).

- Vaccinate as early as 3 months of age and 1 year later, then booster every 3 years in accordance with the product recommendations. Maternal antibodies from vaccinated females will protect neonates until 3 months of age. Immunity is not fully developed until 28 days after the initial rabies vaccination.
- *Side effects:* Adjuvants may cause local soreness, lameness, fever, lethargy, palpable inflammatory nodules, and rarely, injection-site sarcomas in cats. The rare neurologic complications of earlier attenuated (modified live virus [MLV]) vaccines are no longer a problem because only inactivated and recombinant rabies vaccines are currently available in the United States. In other countries where MLV vaccines are available, only use MLV vaccines that are derived from high egg passage or cell culture.
- Rabies serum titers may not correlate with protection and should not be used to determine the need for booster vaccination.
- Do not vaccinate wild animals or hybrids against rabies, even if they are kept as pets. The safety and efficacy of parenteral rabies vaccination in wildlife and hybrids (wild animal–domestic animal crossbreds) have not been established, and no vaccines are licensed for these animals.

Postexposure Management

Report all human and animal exposures to the local public health authorities. Recommendations for dogs

and cats exposed to rabies (bitten by a known rabid animal or a wild animal that is unavailable for testing) are as follows:

- In a previously vaccinated dog or cat that has been exposed, revaccinate immediately and keep under the owner's control for 45 days to observe for illness suggestive of rabies.
- In an unvaccinated dog or cat that has been exposed, recommend immediate euthanasia for examination of tissues. If euthanasia is not allowed by the owner, strict isolation is required for 6 months with vaccination either at entry or 1 month before release. If illness suggestive of rabies develops during isolation, immediate euthanasia and testing for rabies is required.

Prevention in Humans

Approximately 15% of humans untreated after a bite from a known rabid animal become infected. Once signs develop in a human, rabies is almost always fatal; thus, prevention is essential.

Pre-Exposure Prevention

- For pre-exposure prevention in humans in high-risk situations (e.g., veterinarians and their employees), immunization with human diploid cell vaccine (HDCV) or another vaccine approved by the Food and Drug Administration is recommended. Contact your state health department for specific recommendations.

Animal Bites to Humans:

For management of animals that bite humans, follow the Compendium of Animal Rabies Prevention and Control, published annually by the National Association of State Public Health Veterinarians (available at www.nasphv.org).

▼ ***Key Point*** Immediately notify local public health authorities when an animal bite to a human has occurred or whenever there is the possibility of contact with a rabid animal.

- When a healthy pet dog or cat has bitten a human, the owners must confine and observe the animal for 10 days. During confinement, the animal must be isolated from contact with other animals and confined in an escape-proof enclosure or building except for leash walking under owner control. Any signs of illness in the confined animal must be reported to local public health authorities.
- When a wild animal or a feral or stray dog or cat with unknown vaccination status has bitten a human, regard the animal as potentially rabid and sacrifice it immediately for laboratory examination of tissues under the guidance of local public health officials.
- Vigorously cleanse the wounds of an exposed human with copious amounts of soap and water to reduce virus in the wound. Ethanol (70%) and benzalkonium chloride (1–4%) are acceptable rabicidal disinfectants. Depending on the circumstances, public health authorities will decide immediately whether postexposure prophylaxis is indicated. Previously immunized humans generally receive two doses of vaccine (on days 0 and 3), whereas non-immunized humans are given five doses of vaccine (on days 0, 3, 7, 14, and 28) and rabies immunoglobulin.

PSEUDORABIES

Etiology

- Pseudorabies is a herpesvirus that predominantly infects pigs (also called Aujeszky's disease and mad itch). Most mammals are susceptible (but not humans), and infections are seen sporadically in dogs and cats in areas where the disease is enzootic in pigs.
- Pseudorabies in dogs and cats is almost always a direct result of ingestion of contaminated raw pork. Direct contact with pigs shedding virus in nasal secretions and saliva is rarely a source of infection.
- The virus invades nerve endings in the pharynx and travels by way of nerve fibers to the brain, where it causes acute fatal panencephalitis.

Clinical Signs

Pseudorabies in dogs and cats causes an acute disease that is almost always fatal within 3 to 5 days of exposure. Initial signs may include depression and inactivity or anxiety and restlessness. The most characteristic sign (but not seen in every case) is intense pruritus, especially involving the head and neck regions, that leads to excoriation and self-mutilation. Other signs may include fever, diarrhea, vomiting, copious hypersalivation, various cranial neuropathies, ataxia, and seizures. Progressive depression, dyspnea, coma, and death follow shortly thereafter. Death occurs within 48 hours from the onset of clinical signs.

▼ ***Key Point*** Suspect pseudorabies in a dog or cat with acute onset of violent, frantic scratching and self-mutilation around the face, head, neck, and ears, especially if there is a history of exposure to pigs or of ingestion of raw pork in an endemic area.

Diagnosis

- The clinical presentation of pseudorabies is indistinguishable from rabies and is similar to other forms of encephalitis.
- It is virtually impossible to make a definitive antemortem diagnosis of pseudorabies in dogs and cats. Routine hematologic and serum chemistry evalua-

tions are normal. Cerebrospinal fluid may show nonspecific increases in protein and mononuclear cells suggestive of viral encephalitis. The serologic tests used in pigs are not diagnostically useful in dogs and cats.

- Postmortem diagnosis is based on specialized testing of unfixed brain tissue for virus using immunofluorescent, virus isolation, animal inoculation, or molecular techniques. Routine histopathology may show characteristic viral inclusion bodies.

Treatment

No effective treatment is known.

Prevention

To prevent pseudorabies in dogs and cats in endemic areas, prevent direct contact with pigs and never feed raw pork. An effective vaccine is not available.

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Chapter

16 Miscellaneous Viral Diseases

Robert G. Sherding

INFECTIOUS CANINE HEPATITIS

Etiology

Infectious canine hepatitis (ICH) is caused by canine adenovirus type 1 (CAV-1), a virus related to but distinct from CAV-2 that causes canine infectious tracheobronchitis (kennel cough; see Chapter 12).

Incidence

Dogs, foxes, coyotes, wolves, other wild canids, and bears are susceptible to CAV-1. Because of widespread use of highly effective CAV vaccines, ICH is rare and is seen almost exclusively in unvaccinated dogs. Wild canids are a reservoir for the virus.

Transmission

CAV-1 is acquired through oronasal exposure. The virus is found in all tissues and is shed in all secretions during acute infection. It also is shed for at least 6 to 9 months in the urine after recovery. CAV-1 is highly resistant to inactivation and disinfection, thus enabling spread by fomites and possibly ectoparasites.

Pathogenesis

- After oronasal exposure, CAV-1 causes viremia and disseminates to all tissues, especially targeting hepatocytes and endothelial cells. Hepatocyte injury results in acute hepatic necrosis or chronic hepatitis.
- Endothelial injury can affect any tissue, but CAV-1 is noted particularly for its effects on corneal endothelium (corneal edema, anterior uveitis), renal glomeruli (glomerulonephritis), and vascular endothelium (disseminated intravascular coagulation [DIC]).

Clinical Signs

Peracute Infection

Acutely ill dogs become suddenly moribund and die within hours.

Acute Systemic Infection

- A 5- to 7-day course is characterized by a fever of 103 to 106°F (39.5–41°C), vomiting, diarrhea, abdominal pain, tonsillitis-pharyngitis, cervical lymphadenopathy and edema, cough (pneumonitis), and hemorrhagic diathesis (petechiae, ecchymoses, epistaxis, and melena).
- Central nervous system (CNS) signs (disorientation, depression, stupor, coma, and seizures) may occur as a result of hepatic encephalopathy, hypoglycemia, or non-suppurative encephalitis.

Ocular Infection

Ocular disease can develop during acute infection, after recovery from inapparent infection, or after modified live virus (MLV) CAV-1 vaccines (no longer commercially available). Ocular findings include the following:

- Corneal edema (cloudy cornea; also called hepatitis blue eye)
- Anterior uveitis (blepharospasm, aqueous flare, miosis)
- Secondary glaucoma

Chronic Hepatitis

In infected dogs with partial immunity, a persistent hepatic infection that causes chronic hepatitis, and hepatic fibrosis has been reported.

Diagnosis

Suspect ICH based on clinical signs in unvaccinated dogs, especially young puppies.

Routine Laboratory Evaluations

ICH may cause neutropenia/lymphopenia (early), neutrophilic leukocytosis (later), increased alanine transaminase (ALT) and alkaline phosphatase (ALP) levels, thrombocytopenia and coagulation abnormalities typical of DIC (see Chapter 23), proteinuria, and occasionally hypoglycemia. The abdomen may contain a non-septic exudate.

Definitive Diagnosis

ICH can be confirmed by serologic testing, virus isolation, immunofluorescent studies, or histopathology (centrilobular hepatic necrosis with intranuclear viral inclusions); however, a definitive diagnosis is not needed for instituting supportive treatment measures.

Treatment

Treatment is supportive until recovery from the acute stage of infection and hepatocellular regeneration can occur. This usually requires parenteral fluid therapy using potassium and dextrose-supplemented solutions (see Chapter 5), treatment for DIC using fresh plasma or whole blood transfusion (see Chapter 23), treatment for hepatic encephalopathy (see Chapter 91), and antibiotics for secondary bacterial complications such as pneumonia or pyelonephritis.

Prevention

▼ ***Key Point*** Vaccination is highly effective for preventing CAV-1 infection.

- MLV canine adenovirus vaccines can induce effective immunity against ICH; however, only CAV-2 vaccines are recommended. This is because CAV-2 vaccines produce highly effective immunity against both adenoviruses with minimal side effects, whereas CAV-1 vaccine viruses can localize in the kidney and produce mild nephritis and urine shedding of virus or may localize in the eyes and produce anterior uveitis (in approximately 0.4% of vaccinates). The cloudy cornea is usually transient but sometimes irreversible.
- Vaccinate puppies using CAV-2 at 6 to 8 weeks, 9 to 11 weeks, and 12 to 14 weeks of age. Give the first booster 1 year later and additional boosters every 3 years thereafter (see Chapter 7 for comprehensive vaccination recommendations).

CANINE ACIDOPHIL CELL HEPATITIS

Etiology

A transmissible form of hepatitis has been described in dogs in Great Britain. Although the etiologic agent has not been identified, evidence strongly suggests that it is a virus and that it is distinct from CAV-1 and CAV-2.

Clinical Signs

Clinical forms of the disease, which may represent stages of progression, include acute hepatitis, chronic hepatitis, cirrhosis, and occasionally hepatocellular carcinoma. Early signs, such as anorexia, vomiting, and occasional fever, are nonspecific. Later signs reflect progressive hepatic failure (ascites, hepatic encephalopathy).

Diagnosis

Laboratory findings are nonspecific and typical of those found in other types of acute and chronic liver disease. Increased serum ALT and ALP activities are the most consistent abnormalities. Diagnosis depends on liver biopsy to identify hepatitis associated with characteristic acidophil cells.

Treatment and Prevention

Specific measures for treatment and prevention are unknown; however, supportive treatment for liver failure in general and specific treatment used in other forms of hepatitis and cirrhosis may be applicable (refer to Chapter 71).

CANINE HERPESVIRUS

Etiology

Canine herpesvirus (CHV) infects only canids. Its biologic behavior is similar to herpesviruses of other species. Infected dogs remain latent carriers for life. CHV is inactivated relatively easily outside the host.

Incidence

CHV is widespread in the canine population; however, it causes clinical disease almost exclusively in newborn puppies during the first 3 weeks of life.

Transmission

Perinatal infection is acquired before, during, or soon after birth. Transmission can occur in utero, during passage through the birth canal, or by direct oronasal contact with infectious secretions from the infected mother, littermates, or fomites. Respiratory and venereal transmission may occur in adults.

Clinical Signs

▼ ***Key Point*** Overt clinical signs of CHV occur almost exclusively in puppies from 3 weeks before birth until 3 weeks after birth. This is manifested as a reproductive failure in infected bitches or a highly fatal systemic disease in newborn puppies.

Fetal Infection

- Reproductive failure in infected bitches results from early fetal resorption, late-term abortion, or stillbirth associated with in utero CHV infection.

Neonatal Systemic Infection

- Infection at birth until 2 to 3 weeks of age leads to viremia and virus dissemination to all tissues, resulting in a fatal generalized form of disease. The incubation period is 3 to 6 days.

- The susceptibility to this form of CHV is related to the narrow temperature range of 35°C to 36°C needed for optimal growth of CHV, which coincides with the low body temperatures and lack of febrile responsiveness found in neonates in the first week of life.
- Neonatal infection causes multifocal lesions of necrosis and hemorrhage (DIC) in many organs, including the kidneys, adrenal glands, liver, spleen, gastrointestinal tract, lungs, and CNS.
- Signs include depression, refusal to nurse, incessant crying, subnormal body temperature, yellow-green diarrhea, abdominal pain, nasal discharge, petechial hemorrhages on mucosal surfaces, skin papules, and CNS signs (coma, opisthotonus, and seizures). Nursing ceases and death usually occurs within 24 to 72 hours.
- This form is seen mostly in neonates born to an infected but seronegative mother. Subsequent litters produced by the dam rarely are infected because of protective maternal antibodies transferred in colostrum.

Adult and Older Puppy Infections

- Marked resistance to CHV develops abruptly in animals after 1 to 2 weeks of age because of higher body temperature and better immune function; thus, infection beyond 2 weeks of age results only in mild or inapparent infection confined to the respiratory and genital tracts.
- Transient, mild respiratory signs and conjunctivitis with episodic shedding can occur.
- The primary manifestation in adults is lymphofollicular lesions on the vaginal or preputial mucosa, with or without mild hyperemia and discharge. Local genital infection may be a source of venereal transmission between adult animals and of vaginal transmission to neonates during birth.

Diagnosis

- *For infected neonates:* The age of onset and clinical signs are characteristic. Necropsy lesions are usually diagnostic. Virus isolation, immunohistochemistry, and polymerase chain reaction (PCR) on tissues are confirmatory. Positive serologic titers (virus neutralizing antibody) in the dam and surviving pups provide additional presumptive evidence.
- *For adult carriers:* Virus isolation from the oropharynx or genital lesions confirms the diagnosis.

Treatment

There is no effective treatment for CHV. Treatment of the neonatal form probably is not warranted because it is almost always fatal, and the few puppies that do recover often have irreversible neurologic sequelae (e.g., cerebellar dysfunction).

Prevention

- In breeding kennels, promote proper husbandry practices and maintain warm ambient temperatures for neonates.
- In kennels with CHV problems, consider isolating infected bitches and their litters; disinfect the premises (CHV is susceptible to most detergents and disinfectants); and administer hyperimmune antiserum (harvested from seropositive bitches that recently have produced CHV-infected litters), 1 to 2 ml, intraperitoneally, for prophylaxis in newborn puppies.
- An effective vaccine for CHV is unavailable.

CANINE VIRAL PAPILLOMATOSIS

Etiology

The canine papillomavirus causes mucocutaneous tumors that are benign and self-limiting. Virus-induced papillomas are multiple (often 50–100 separate tumor nodules) and occur in young dogs, in contrast to noninfectious papillomas, which are solitary and usually affect older dogs. Transmission appears to be by direct viral contact with oral mucosa. The incubation period is 1 to 2 months.

Clinical Signs

The three forms of infectious papillomatosis in dogs are oral, ocular, and cutaneous.

- *Oral papillomatosis* is by far the most common form and usually affects dogs younger than 2 years of age. Lesions begin as smooth, white mucosal elevations that develop into cauliflower-like warts on the lip margins, oral mucosa, tongue, palate, pharynx, and epiglottis. They usually increase in number and size for 4 to 6 weeks and then begin to regress. Common presenting signs are halitosis, ptyalism, reluctance to eat, and oral bleeding.
- *Ocular papillomatosis* is uncommon; it affects dogs 6 months to 4 years of age and is characterized by papillomas on the conjunctiva, cornea, and eyelid margins.
- *Cutaneous papillomatosis* is rare (see Chapter 30).

Diagnosis

The history and physical appearance of the lesions are adequate for diagnosis of oral and cutaneous papillomatosis. In the ocular form of the disease, confirmatory excisional biopsy is advisable to exclude other ocular tumors that may have a similar physical appearance. Immunohistochemical and PCR assays can be used to identify the presence of papillomavirus in tumor tissue.

Treatment

- For the oral form, treatment is not necessary because viral oral papillomas usually regress spontaneously within 3 months once immunity develops. There have been rare reports of failure to regress for more than 2 years. Ocular and cutaneous forms take longer to regress, often 6 to 12 months.
- Removal by surgical excision, cryosurgery, or electrosurgery is indicated for ocular papillomas and for oral lesions that interfere with eating or that bleed and discharge excessively. Submit tissues for biopsy to confirm the diagnosis. Removal of some of the tumors often triggers regression of the remaining ones.
- When regression fails to occur, remission can be induced in some dogs with weekly single-agent chemotherapy using vincristine or cyclophosphamide at the usual doses (see Chapter 26). Autogenous vaccines have also been used.
- Recovered animals and dogs older than 2 years of age usually are immune to papillomavirus.

FELINE VIRAL PAPILLOMATOSIS

An uncharacterized papillomavirus has been identified in a few cats with papillomas. Feline papillomas are located on the head, neck, dorsal thorax, and abdomen. They appear as slightly raised verrucous plaques rather than typical warts. Most affected cats have been on immunosuppressive drugs or infected with feline immunodeficiency virus. The diagnosis is based on tumor histopathology and immunohistochemistry or electron microscopy to document the presence of papillomavirus. Treatment has not been evaluated.

FELINE POXVIRUS

Etiology

Cowpox virus *(Orthopoxvirus)* causes disease in cats more often than in any other species, including cows, but has been recognized only in Europe and Asia. Poxvirus causes widespread skin lesions with occasional systemic involvement. The source of infection is contact with other infected cats (rare) or endemic rodent reservoirs, mainly through contaminated skin wounds. Cats have also been infected with *Parapoxvirus* and uncharacterized poxviruses.

Clinical Signs

- The initial inoculation site or skin wound (usually a bite wound on the head, neck, or forelimb) is called the primary lesion.
- Then, 1 to 3 weeks later, after a period of viremia and sometimes mild systemic signs (low fever, anorexia, depression, and mild upper respiratory signs), widespread secondary pox lesions develop. These lesions begin as multiple, small (1 mm) skin nodules that progress and increase in number over 2 to 4 days to become well-circumscribed ulcers covered with scabs. Most cats have more than 10 of these pox lesions. Buccal ulcers are seen occasionally.
- The scabs dry and fall off in 4 to 6 weeks, revealing underlying healing skin. Some lesions result in permanent bald patches.
- Susceptibility and severity of disease are increased by immunosuppressive conditions, such as feline leukemia virus or feline immunodeficiency virus infections or glucocorticoid therapy. Rarely, fatalities occur because of secondary bacterial infection.

Diagnosis

- Suspect feline cowpox virus in rural cats that hunt rodents in endemic areas, especially cats with typical secondary pox lesions after a recent history of a primary skin wound lesion.
- Confirmation is based on detection of virus in the scabs by fluorescent antibody staining (preferred method), PCR, electron microscopy, or virus isolation. Presumptive diagnosis is based on serologic assay for poxvirus-specific antibodies (indirect fluorescent antibody or enzyme-linked immunosorbent assay) or identification of the characteristic histopathologic abnormalities in skin biopsies.

Treatment

There is no specific treatment for poxvirus infections, but the disease is self-limiting and skin lesions regress in 4 to 6 weeks. Antibiotics and topical cleansing help control secondary bacterial infection of skin lesions, but take proper precautions (e.g., wear rubber gloves when handling cats) because cowpox virus is potentially transmissible to humans as a zoonotic disease. Corticosteroids are contraindicated.

RARE AND EMERGING VIRUSES

The following viral infections have been identified in dogs and cats, but the clinical significance is not yet established.

West Nile Virus

West Nile virus (WNV) is a flavivirus found worldwide in endemic bird populations and is transmitted by mosquitoes to birds, humans, horses, and occasionally other species such as dogs and cats. West Nile virus causes life-threatening meningoencephalitis in birds, humans, and horses. Experimental infection of dogs and cats produces viremia with little or no illness; however, sporadic naturally occurring cases of fatal acute encephalitis in dogs in the United States caused by WNV have been

confirmed by postmortem PCR assay of brain tissue. The seroprevalence in dogs and cats in endemic areas of North America appears to be low. Oral transmission of West Nile virus can occur in cats through ingestion of infected rodents.

Bornavirus

Bornavirus is a neurotropic virus that mostly infects horses and sheep, but it also causes a rare but fatal neurologic disease in cats and dogs, especially in central Europe and Japan. Non-suppurative meningoencephalomyelitis (especially gray matter) causes progressive neurologic signs of ataxia, circling (dogs), paresis, behavior changes, salivation, hyperesthesia (cats), loss of vision, and seizures. The diagnosis is based on postmortem demonstration of *Bornavirus* in brain tissue using PCR. The reservoir of infection is unknown, but transmission is presumed to be vector-borne. Human infections also occur.

Other Vector-Borne Viruses

Dogs and cats are susceptible to several viruses that are transmitted by arthropods, such as mosquitoes and ticks. In most cases these viruses target other host species; dogs and cats are merely incidental hosts that seroconvert after subclinical infection. Examples of vector-borne viruses that can infect dogs and/or cats include equine togaviruses (Eastern, Western and Venezuelan equine encephalitis), flaviviruses (St. Louis encephalitis, louping ill, yellow fever, and others), bunyaviruses (e.g., Rift Valley fever), and orbiviruses (African horse sickness and blue tongue).

Influenza Viruses

The avian influenza virus strain H5N1 that has caused fatal human infections in Asia also can infect cats and cause fatal pneumonia. Infection occurs through contact with or ingestion of infected poultry. Under experimental conditions, horizontal cat-to-cat transmission has been shown. Zoonotic cat-to-human transmission has not been ruled out.

Paramyxoviruses

Hendra virus in horses in Australia and Nipah virus in pigs in Malaysia are fatal zoonotic respiratory diseases that can be experimentally transmitted to cats. Fruit bats are the endemic reservoirs for these paramyxoviruses. Antibodies to human mumps paramyxovirus have been found in dogs, but experimental inoculation of dogs with mumps virus have been inconclusive.

Hantavirus in Cats

Hantavirus is endemic worldwide in rodent reservoirs. Serologic evidence of *Hantavirus* infection in cats has been found in North America, Europe, and Asia, and the virus has been demonstrated in lung and kidney tissue of cats. However, the clinical significance of this virus in cats is not yet known. Most if not all infections in cats appear to be subclinical. In humans, *Hantavirus* is a life-threatening zoonotic infection that causes hemorrhagic fever, renal syndrome, or pulmonary syndrome, depending on the strain of virus. The virus is transmitted in aerosolized rodent excrement and rarely by rodent bites.

Feline Foamy Virus

This feline *Spumavirus* is in the retrovirus family and was formerly known as feline syncytium-forming virus. Infection with this virus is very common in cats, with seroprevalence as high as 90% in some cat populations. This feline retrovirus is ubiquitous and has been studied for over 3 decades, but it has yet to be associated with clinical disease in cats except for early studies that found a statistical link to feline chronic progressive polyarthritis.

Feline Spongiform Encephalopathy

Feline spongiform encephalopathy (FSE) is a fatal neurologic disease that has primarily been seen in cats in Great Britain and a few other European countries since the 1990s concurrently with the European outbreak of bovine spongiform encephalopathy (BSE). The etiology of FSE is considered to be the same prion, or self-replicating protein, that causes BSE in cattle or scrapie in sheep. Cats are probably infected through ingestion of table scraps or prepared cat foods that contain prion-infected meat from cattle, sheep, or goats. After a prolonged incubation period, cats with FSE develop neurologic signs (e.g., behavior changes, ataxia, tremors, salivation, and hyperesthesia) that slowly progress to death. There is no effective treatment. The diagnosis is based on distinctive gray matter vacuolation and fibril deposits in the brain at necropsy. The occurrence of FSE is expected to decline now that strict regulations are in place for control of BSE and scrapie.

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Chapter 17

Rickettsiosis, Ehrlichiosis, Anaplasmosis, and Neorickettsiosis

Robert G. Sherding

Microbial genetic analyses have recently led to the extensive taxonomic reclassification and renaming of several animal pathogens that are now found in the genera of *Rickettsia*, *Ehrlichia*, *Anaplasma*, and *Neorickettsia*. Pathogens in these four genera are obligate intracellular bacteria that are vector-transmitted by tick bites *(Rickettsia*, *Ehrlichia*, *Anaplasma)* or parasitized trematodes and aquatic insects that are ingested *(Neorickettsia)*. The geographic distribution of vectors determines regional prevalence of each infectious agent. In general, serologic cross reactivity is common among organisms within each genus, but minimal between genera.

The full scope of disease caused by many of these agents is still being defined. In high-prevalence areas with a heavy tick population, such as the southeastern United States, dogs are frequently infected with multiple tick-transmitted pathogens simultaneously; for example, dogs infected with *Ehrlichia* spp. and *Anaplasma* spp. may be co-infected with *Bartonella vinsonii (berkhoffii)*, *Borrelia burgdorferi*, or *Babesia* spp. Breitschwerdt has observed that the synergistic effects of these polymicrobial infections may lead to an unpredictable variety of chronic disease manifestations not seen with single-agent infections.

ROCKY MOUNTAIN SPOTTED FEVER

(Rickettsia rickettsiae)

Rocky Mountain spotted fever (RMSF) is a tickborne rickettsial disease of dogs and humans that is most prevalent in the Southeast, Midwest, and Great Plains regions of the United States. Because of its acute nature, most cases of canine RMSF occur during tick season, between April and October.

Etiology

Canine RMSF is a tick-transmitted infection caused by *R. rickettsii*, one of several rickettsial species included in the spotted fever group.

Transmission

- The main vectors for *R. rickettsii* are the American dog tick *(Dermacentor variabilis),* found primarily east of the Great Plains and in parts of the west coast, and the wood tick *(Dermacentor andersoni),* found in an area from the Rocky Mountains to the Cascades. These are three-host ticks; the permanent hosts are humans, dogs, and cats, and the reservoirs are rodents.
- Ticks usually acquire the organism through feeding on infected animals, although vertical transmission in tick populations also can occur.
- Ticks usually do not infect the hosts until they have been attached for a minimum of 5 to 20 hours. This infection also can be transmitted iatrogenically through blood transfusions.

Pathogenesis

- Once inoculated into the host via a tick bite, the organism quickly invades and replicates in vascular endothelial cells, resulting in widespread necrotizing vasculitis, altered vascular permeability, edema, platelet aggregation, and multi-organ damage (e.g., skin, brain, heart, lung, liver, and kidneys). The incubation period varies from 2 to 14 days.
- Only an acute form of clinical disease is recognized in dogs. The clinical illness lasts 7 to 14 days, with high mortality rate in untreated animals. In contrast to most other tickborne infections in dogs, *R. rickettsii* has not been associated with chronic or recurrent disease, and it does not persist in a chronic carrier form.

Clinical Signs

Exposure to *R. Rickettsii* can lead to either subclinical infection or an acute, rapidly progressive disease of short duration. Most dogs with acute RMSF present between April and October, coinciding with the tick season. The clinical signs and laboratory abnormalities are highly variable. Because of the acute course, ticks

may still be found on the dog (or may have been recently removed by the owner); however, a negative tick history by no means excludes RMSF.

Clinical findings in dogs with acute RMSF can include any of the following:

- **General signs:** Fever, anorexia, lethargy, vomiting/diarrhea, weight loss, and generalized lymphadenopathy.
- **Polyarthritis:** Poorly localized joint and muscle pain and lameness.
- **Ocular signs:** Schleral and conjunctival hyperemia and petechiae; retinal vasculitis and hemorrhages; and anterior uveitis and hyphema.
- **Neurologic signs:** Hyperaesthesia, tetraparesis, ataxia, vestibular signs, stupor, and seizures.
- **Cutaneous vasculitis:** Hyperemia, edema, and petechial-to-ecchymotic hemorrhages (face, distal extremities, scrotum, ventral abdomen); and skin necrosis and gangrene in severe cases.
- **Pneumonitis:** Cough, tachypnea, dyspnea, and exercise intolerance.
- **Myocarditis:** Cardiac arrhythmias or sudden death.
- **Other signs:** Icterus, orchitis, bleeding (epistaxis, melena, and hematuria), or oliguric renal failure.

Laboratory Findings

- Frequent hematologic findings include mild-to-moderate thrombocytopenia (>80% of cases), leukocytosis with a left shift, toxic granulation of neutrophils, monocytosis, and mild anemia. Rare findings are transient leukopenia (early) and overt disseminated intravascular coagulation (DIC) (late). Anti-platelet antibodies have been demonstrated in natural and experimental canine RMSF infections.
- Biochemical abnormalities, which reflect vascular injury and organ damage, can include hypoalbuminemia, increased serum liver enzymes, hyperbilirubinemia, azotemia, hyponatremia, hypochloremia, hypercholesterolemia, and metabolic acidosis.
- Synovial fluid is typical of neutrophilic polyarthritis, and cerebrospinal fluid has a mild increase in protein and cells (neutrophils).

Diagnosis

Suspect RMSF in dogs residing in endemic areas that present with an acute, rapidly progressive febrile illness and a recent history of tick infestation. The diagnosis of RMSF can be confirmed by serum antibody titers and polymerase chain reaction (PCR) assays that are readily available to practicing veterinarians through the Vector Borne Disease Diagnostic Lab at North Carolina State University. Submission requirements and forms are available at www.cvm.ncsu.edu/docs/tickbornediseaselab.html.

- Using the indirect fluorescent antibody (IFA) serologic test, a serum titer of >1:128 is presumptive evidence of RMSF; however, dogs often have a negative titer when tested early in the disease (first 5 days). A definitive diagnosis is established by a fourfold rise in paired titers (2–3 weeks apart); or based on a single titer of >1:1024 at 7 days or more after the onset of clinical signs.
- The prevalence of seropositivity is higher than the prevalence of the clinical disease and must be considered when interpreting titers. This is due in part to cross reactivity with nonpathogenic tickborne *Rickettsia* spp. High titers can persist for up to 1 year after successful treatment or recovery from the disease, which also must be considered.
- Rapid confirmation of the diagnosis can be established by PCR identification of rickettsial DNA in an EDTA blood sample or in tissues. Prior antibiotics can cause a false-negative PCR result.
- The direct immunofluorescence test can confirm the diagnosis by detecting rickettsial antigens in fresh or paraffin-embedded tissues, especially skin, as early as 3 to 4 days post-inoculation. Skin biopsies obtained with local anesthetic and a biopsy punch can be used. A positive result is highly specific for RMSF; however, false-negative results occur in up to 30% to 40% of cases (low sensitivity).

Treatment

- Doxycycline (5–10 mg/kg, PO or IV, q12h) for 14 days is the drug of choice for treating dogs with RMSF. Tetracycline (22 mg/kg PO q8h), enrofloxacin (3 mg/kg, SC or PO, q12h), or chloramphenicol (15–25 mg/kg, PO, IM, or IV, q8h) given for 14 days have also been effective for treating dogs with RMSF.
- Initiate supportive therapy as needed, but use extreme caution with fluid therapy because vascular damage predisposes the patient to severe edema.

▼ ***Key Point*** Do not delay treatment of dogs suspected of having RMSF. Initiate doxycycline while awaiting confirmatory diagnostic tests to prevent development of complications such as fatal central nervous system (CNS) disease, cardiovascular collapse, oliguric renal failure, or gangrene.

Prognosis

The prognosis is good when treatment is instituted promptly. Clinical response should occur within hours of initiating appropriate drug administration. The mortality rate is high if an ineffective antibiotic is used or treatment is delayed until the disease is advanced. Dogs with severe CNS signs may die within hours, before treatment takes effect.

Prevention

- Prevention of RMSF in dogs depends on minimizing tick exposure, using an effective tick preventative product on a regular basis, and routinely checking dogs for ticks and removing them promptly. Dogs that recover from RMSF are immune to re-infection.
- RMSF is one of the most important rickettsial diseases in humans. Dogs are not reservoirs or chronic carriers for *R. rickettsiae*, and thus dogs are considered minimal zoonotic risk. However, take precautions (i.e., wear gloves) when removing ticks or handling blood from a potentially infected dog.
- A confirmed diagnosis of RMSF in a dog is an indication that *R. rickettsiae* is endemic in the local tick population. Dogs can thus serve as sentinels for the potential risk of human exposure in a geographic area.

CANINE EHRLICHIOSIS

Canine ehrlichiosis is a tick-transmitted infectious disease of dogs caused by various species of *Ehrlichia*, a genus comprised of obligate intracellular gram-negative cocci that have a tropism for leukocytes. This intracellular location facilitates chronic persistence and resistance to antimicrobial therapy. Feline ehrlichiosis is discussed at the end of this chapter under Feline Ehrlichia-Like Diseases.

Etiology and Transmission

Ehrlichia organisms are transmitted to dogs through the saliva of an attached tick, and ticks become infected when they feed on the blood of an infected host. *Ehrlichia* species are distributed worldwide according to the geographic distribution of specific vector ticks. *Ehrlichia* organisms can also be transmitted iatrogenically through transfusion of contaminated blood.

- ***Ehrlichia canis*** is transmitted primarily by *Rhipicephalus sanguineous,* the common brown dog tick, and infection occurs worldwide in tropical and temperate climates. *E. canis* infections have been reported year-round throughout the United States, most frequently in the Southeast.
- ***Ehrlichia ewingii*** is transmitted by *Amblyomma americanum*, the lone-star tick, and probably other ticks (e.g., *Dermacentor variabilis*, *Rhipicephalus sanguineous*). Infection occurs predominantly in the Southern and Central United States, including Missouri, during tick season (spring and summer).
- ***Ehrlichia chaffeensis*** is transmitted by *Amblyomma americanum*, and infection occurs in the Southern United States.

Clinical Signs and Laboratory Findings

E. canis and *E. chaffeensis* most frequently infect circulating monocytes and mononuclear phagocytic cells in lymph nodes, spleen, liver, and bone marrow, resulting in widespread lymphoreticular hyperplasia, organomegaly (lymphadenomegaly, splenomegaly, and hepatomegaly), and hematologic abnormalities. *E. ewingii* infects granulocytes.

After a transient acute phase of infection, dogs either clear the infection, or in the case of *E. canis* infection, they enter a prolonged subclinical phase that can extend for months to years until they finally develop clinical signs of chronic-phase disease. Most dogs with *E. canis* infection are diagnosed in the chronic phase.

Acute Phase of Infection

The acute phase of canine ehrlichiosis begins 1 to 3 weeks after the bite of an infected tick. The clinical signs vary from mild to severe and last 2 to 4 weeks. The clinical presentation of acute ehrlichiosis can resemble RMSF (see previous section).

- Acute-phase infection causes transient fever, anorexia, lethargy, oculonasal discharge, generalized lymphadenopathy, splenomegaly, hepatomegaly, and moderate-to-severe thrombocytopenia.
- Less frequent manifestations that are seen in severe cases include neurologic signs due to meningoencephalitis (ataxia, paresis, hyperaesthesia, twitching, cranial nerve deficits); anterior uveitis and chorioretinitis; dyspnea or exercise intolerance due to pneumonitis; edema of the limbs and scrotum; and petechial and ecchymotic hemorrhages due to thrombocytopenia or platelet dysfunction.
- *E. ewingii* most frequently causes acute neutrophilic polyarthritis with lameness, stiffness, and joint pain and swelling. It also can cause acute meningoencephalitis and a variety of neurologic signs (ataxia, paresis, etc.).
- Laboratory findings during the acute-phase include thrombocytopenia (due to peripheral destruction of platelets), leukopenia, mild to severe anemia, hypercellular bone marrow cytology (especially megakaryocytic hyperplasia), mild hyperglobulinemia, and mild elevation of serum liver enzyme activities.

▼ ***Key Point*** Thrombocytopenia is the most consistent hematologic abnormality found in all stages of canine ehrlichiosis.

- Antibody titers may be negative during the acute phase because it takes 2 to 4 weeks to develop a significant titer.

Chronic Phase of Infection

After apparent recovery from the transient acute phase followed by a prolonged subclinical phase lasting

months to years, dogs with persistent *E. canis* infection develop a variety of chronic vague illnesses accompanied by lymphoreticular hyperplasia and bone marrow dysfunction.

- Clinical signs can be mild or severe, and may include weight loss, fever, spontaneous bleeding (petechiae and ecchymoses, epistaxis, melena, hematuria, hyphema), pallor due to anemia, generalized lymphadenopathy, splenomegaly, hepatomegaly, uveitis (anterior uveitis, chorioretinitis, retinal hemorrhages or detachments), meningoencephalomyelitis (ataxia, paresis, seizures, stupor, vestibular signs, etc.), polyarthritis, and intermittent limb edema.
- Chronic-phase ehrlichiosis may be more severe in German shepherds and Doberman pinschers.
- Hematologic findings can include nonregenerative anemia, thrombocytopenia, leukopenia, or all three (pancytopenia), due to bone marrow hypoplasia; lymphocytosis (occasionally composed of atypical or large granular lymphocytes); bone marrow and splenic plasmacytosis; and occasional Coombs'-positive hemolytic anemia.
- Other laboratory findings include hyperglobulinemia caused by polyclonal (or less often monoclonal) gammopathy; hypoalbuminemia; proteinuria; and a positive test for anti-nuclear antibodies (ANA). In some cases severe protein-losing nephropathy is associated with immune-complex glomerulonephritis.

▼ ***Key Point*** Clinical signs, physical findings, and laboratory abnormalities in dogs with chronic ehrlichiosis may resemble multiple myeloma or chronic lymphocytic leukemia.

Diagnosis

Canine ehrlichiosis must be differentiated from various other infectious and immune-mediated diseases that can present with similar clinical signs. The diagnosis of canine ehrlichiosis can be confirmed by cytologic visualization of organisms in blood or cytology specimens, and by serum antibody titers and PCR assays that are available to practicing veterinarians through the Vector Borne Disease Diagnostic Lab at North Carolina State University. Submission requirements and forms are available at www.cvm.ncsu.edu/docs/tickbornediseaselab.html. Blood culturing for *Ehrlichia* is not available except in research labs because it is difficult and expensive and growth takes up to 8 weeks.

▼ ***Key Point*** A confirmed diagnosis of *Ehrlichia* is a marker for exposure to ticks and the infectious agents they transmit. Consider using a serologic tick panel to test for other concurrent tick-transmitted infections, such as *Anaplasma*, *Rickettsia*, *Bartonella*, *Borrelia*, and *Babesia*.

Serology by Indirect Fluorescent Antibody

Serologic testing for *E. canis* antibodies using IFA is highly sensitive and reliable for presumptive diagnosis of canine ehrlichiosis.

- Antibody titers >1:64 are considered indicative of prior or active infection.
- Diagnostic titers may not be detected until 2 to 4 weeks after infection; thus, some dogs develop clinical signs before developing a positive titer. Most dogs with clinical signs are seropositive.
- Antibodies to one *Ehrlichia* species may or may not cross react with other species. *E. canis* titers are positive in most dogs with *E. chaffeensis* infection, but only half of dogs with *E. ewingii* infection.
- *Ehrlichia* antibody titers do not confer protection against reinfection. Titers persist for at least 9 to 12 months after treatment or recovery.

Serology by Enzyme-Linked Immunosorbent Assay

An ELISA-based test kit (SNAP 3Dx; IDEXX) for detecting *E. canis* antibodies is available as a rapid point-of-care screening test for canine ehrlichiosis. This tests simultaneously for heartworms and *Borrelia burgdorferi*, hence the name "3Dx".

- The SNAP 3Dx is calibrated to be positive at an IFA titer of >1:500. Limited studies have shown good correlation with IFA testing; the reported sensitivity is 71% to 95%, and the specificity is 99%.
- This assay is intended for *E. canis* and does not detect other *Ehrlichia* infections.

Polymerase Chain Reaction Testing

PCR for detection of *Ehrlichia* DNA in EDTA blood can be used to definitively diagnose canine ehrlichiosis and to identify the infecting *Ehrlichia* species. Always use PCR in conjunction with serologic testing, not in place of it.

- False-negative PCR blood tests can occur, especially in animals treated recently with antibiotics.
- In some dogs, splenic and bone marrow aspirates have been PCR positive when blood was PCR negative.

Cytology

Identification of intracellular *Ehrlichia* organisms (morulae) in peripheral blood leukocytes (buffy coat smears) is confirmatory; however, this is a time-consuming and highly insensitive means of diagnosis.

- Morulae can also be seen in bone marrow cells, cerebrospinal fluid leukocytes, joint fluid leukocytes, or fine-needle aspirates of the spleen or lymph nodes.
- Plasmacytosis also is frequently prominent in cytologic specimens from dogs with ehrlichiosis.

▼ ***Key Point*** Morulae within circulating monocytes are consistent with *E. canis* or *E. chaffeensis* infection, and morulae within circulating neutrophils are consistent with *E. ewingii* or *Anaplasma phagocytophilum* infection.

Treatment

- Doxycycline (5–10 mg/kg, PO, q12h for 28 days) is the drug of choice for treating canine ehrlichiosis. Tetracycline (22 mg/kg PO q8h for 21–28 days) is also effective. Alternatives include minocycline or chloramphenicol. Enrofloxacin does not effectively eliminate infection.
- Imidocarb dipropionate (2 doses of 5 mg/kg, IM, 2 weeks apart), a drug used to treat babesiosis, has been effective for resolving the clinical signs of ehrlichiosis; however, recent studies suggest that imidocarb is not efficacious for eliminating *E. canis* infection.
- Institute supportive therapy (e.g., blood or blood products, fluids) as needed.
- In selected cases, corticosteroids may be useful for immune-mediated complications, such as refractory thrombocytopenia, polyarthritis, vasculitis, or meningitis.

Monitoring of Treatment

- Clinical signs usually improve within 48 hours in acute-phase or mild chronic-phase cases.
- The platelet count should begin to increase within 2 to 7 days, and normalize by day 14. The platelet count should remain normal at 4 and 8 weeks after treatment if infection has been eliminated.
- Hyperglobulinemia should gradually resolve over 6 to 9 months.
- Most dogs become seronegative 6 to 9 months after elimination of *Ehrlichia* infection. Some clinically recovered dogs maintain high titers for years, suggesting either continued infection or persistence of antibodies. Reevaluate PCR in these cases.
- PCR should be negative at 2 weeks after successful treatment and remain negative at a 2-month recheck.

Prognosis

The prognosis for canine ehrlichiosis is good with appropriate treatment, unless the bone marrow is severely hypoplastic.

- Clinical response usually begins within 48 hours after initiation of doxycycline, but in the chronic form may take up to 3 to 4 weeks. Reevaluate the diagnosis in dogs that fail to improve within 1 to 2 weeks.
- Dogs with severe chronic disease with pancytopenia or aplastic anemia may take months to achieve full hematologic recovery. In some cases severe pancytopenia is fatal.

Prevention

Prevention of ehrlichiosis in dogs depends on minimizing tick exposure, using an effective tick preventative on dogs living in endemic areas (e.g., fipronil, imidacloprid/permethrin, or amitraz), and routinely checking dogs for ticks and removing them promptly.

- Dogs that recover from *Ehrlichia* infection are not immune against reinfection.
- Daily low doses of doxycycline (3 mg/kg PO q24h), tetracycline (6.6 mg/kg PO q24h), or repositol oxytetracycline (200 mg IM twice weekly) have been used successfully for prevention of ehrlichiosis in military dogs in highly endemic areas; however, this is not routinely advocated for pets because it might foster antimicrobial resistance.

Public Health

Infected ticks can transmit *Ehrlichia* spp. to humans on rare occasions. However, there is no evidence of direct zoonotic transmission from infected dogs or cats to people. Pets may carry infected tick vectors into an environment shared with people. The prolonged chronic carrier state of *Ehrlichia* spp. in dogs suggests that dogs have the potential to be reservoir hosts for infecting ticks that subsequently transmit infection to people. Pets also may serve as sentinels for the potential risk of human exposure in a geographic area.

ANAPLASMOSIS

(Anaplasma phagocytophilum)

Etiology

Anaplasmosis is caused by *A. phagocytophilum* (formerly, *E. equi*), an infectious agent that is transmitted by *Ixodes* ticks to dogs, cats, wildlife, horses, small ruminants, and humans. The white-footed mouse serves as the natural reservoir of infection. The highest prevalence of infection in the United States is in the Northeast, upper Midwest, and Pacific coast of California. Feline anaplasmosis is discussed under Feline Ehrlichia-Like Diseases.

Clinical Signs and Laboratory Findings

Most cases are identified in acutely infected animals; however, dogs can be chronically infected for at least 6 months.

- Clinical signs are nonspecific and often mild, such as fever, lethargy, and reluctance to move (arthralgia, myalgia, or polyarthritis).
- Lab findings are lymphopenia, thrombocytopenia, elevated alkaline phosphatase, and hypoalbuminemia.
- Intracellular organisms (morulae) may be visualized in neutrophils and appear identical to *E. ewingii*.

Diagnosis

Confirmation is based on finding granulocytic morulae, demonstrating a rising serum antibody titer in paired sera, or PCR detection of *A. phagocytophilum* DNA (available through the Vector Borne Disease Diagnostic Lab at North Carolina State University; www.cvm.ncsu.edu/docs/tickbornediseaselab.html).

Treatment

Dogs with anaplasmosis respond rapidly to doxycycline (5–10 mg/kg, PO, q12h for 14–21 days) or tetracycline (22 mg/kg PO q8h for 21 days).

Prevention and Public Health

Prevention of *A. phagocytophilum* depends on minimizing tick exposure, using an effective tick preventative product on a regular basis, and routinely checking dogs for ticks and removing them promptly. Infected ticks can transmit *A. phagocytophilum* to humans, but there is no evidence of direct transmission of *Anaplasma* infection from animals to people.

CANINE CYCLIC THROMBOCYTOPENIA

(Anaplasma platys)

Etiology

Canine cyclic thrombocytopenia is cause by *A. platys* (formerly *E. platys*), a bacterial organism that only replicates in platelets.

- It is presumed that *A. platys* is transmitted by ticks, but the specific tick species are not known. Experimentally the brown dog tick, *Rhipicephalus sanguineous*, did not transmit *A. platys*.
- In the United States, *A. platys* infection is reported most frequently in the Southeast and Gulf Coast states. One study of dogs in Louisiana found a seroprevalence of 40% in thrombocytopenic dogs and 50% in healthy kennel dogs.

Clinical Signs and Laboratory Findings

A. platys appears to be minimally pathogenic and is not associated with clinical signs in most dogs. Thrombocytopenia develops at 10 to 14 day intervals in association with cyclic *A. platys* bacteremia. Thrombocytopenic episodes are generally incidental findings in seemingly healthy dogs. Uveitis was reported in one infected dog.

- Thrombocytopenia is moderate to severe, with a nadir as low as 20,000 to 50,000 platelets/µl. Platelet aggregation is also impaired. However, signs of spontaneous bleeding are rare.
- Other laboratory findings can include mild normochromic-normocytic nonregenerative anemia, leukopenia, hypoalbuminemia, and hyperglobulinemia.

Diagnosis

The diagnosis is based on serology, PCR, or blood cytology. See Chapter 22 for a discussion of the differential diagnosis of thrombocytopenia. *A. platys* and *E. canis* often infect dogs concurrently; thus, consider evaluating dogs for both agents.

- Serologic testing by IFA detects antibodies against *A. platys* after 2 to 3 weeks. *A. platys* does not cross react serologically with *E. canis*, *A. phagocytophila*, or *N. risticii*.
- PCR detection of *A. platys* DNA is confirmatory. PCR is available through the Vector Borne Disease Diagnostic Lab at North Carolina State University; www.cvm.ncsu.edu/docs/tickbornediseaselab.html.
- *A. platys* organisms (morulae) are occasionally visualized within platelets as blue inclusions in Giemsa-stained blood smears; however, this is too insensitive to be used as the only diagnostic test.

Treatment

E. platys infection is effectively eliminated by doxycycline (5–10 mg/kg, PO, q12h for 14 days) or tetracycline (22 mg/kg PO q8h for 14 days).

Prevention

Prevention of *A. platys* infection depends on minimizing tick exposure, using an effective tick preventative product on a regular basis, and routinely checking dogs for ticks and removing them promptly.

NEORICKETTSIOSIS

(Neorickettsia risticii)

Etiology

Neorickettsia risticii, the agent that causes equine Potomac Horse Fever (formerly *E. risticii*), can also infect dogs and cats, but its clinical importance and the extent of its pathogenicity is not yet known. Feline neorickettsiosis is discussed under Feline Ehrlichia-Like Diseases.

- The vectors that transmit *N. risticii* infection are trematodes (flukes) that use snails and aquatic insects as intermediate hosts. Dogs and cats are presumably infected by ingesting free-living trematode stages in standing water, or by ingesting snails or aquatic insects that are parasitized by *N. risticii*-infected trematode metacercariae.
- *N. risticii* has a tropism for monocytes and enterocytes.
- Experimentally, inoculation of *N. risticii* induces subclinical infection or mild clinical illness in dogs and cats.

Clinical Signs and Laboratory Findings

- The clinical signs associated with *N. risticii* infection in dogs have included lethargy, intermittent vomiting, petechial hemorrhages and bleeding, arthralgia (polyarthritis), dependent edema, and posterior paralysis; however, a causative role for *N. risticii* is unproven.
- Laboratory findings have included anemia, thrombocytopenia, and coagulopathy.

Diagnosis

Infected dogs have positive antibody titers against *N. risticii*, and they do not cross react on serologic tests for *Ehrlichia* spp. Researchers have detected this neorickettsial infection in dogs by culture and PCR.

Treatment

The recommended treatment is doxycycline (5 mg/kg PO q12h) or tetracycline (22 mg/kg PO q8h) for 21 to 28 days, but efficacy may be variable.

Prevention

Prevention depends on minimizing exposure to the trematode vector by not allowing dogs to drink from standing bodies of water.

SALMON POISONING DISEASE

(Neorickettsia helminthoeca)

Salmon poisoning disease is a vector-borne neorickettsial infection that is only found in dogs in the Pacific Northwest. The vector that transmits this infection to dogs is a species of intestinal trematode (fluke) rather than ticks.

Etiology

Salmon poisoning disease is caused by *N. helminthoeca* and the Elokomin fluke fever agent (likely a variant strain of *N. helminthoeca*). These agents are closely related to *Ehrlichia* spp.

Transmission

Dogs acquire salmon poisoning disease after ingesting raw salmon (or other fish or salamanders) that contain the metacercariae of the fluke *Nanophyetus salmincola* infected with the causative *N. helminthoeca* organisms. These flukes require three hosts to complete their life cycle: a snail, a fish, and a fish-eating mammal or bird. The limited geographic distribution of the snail intermediate host explains why *N. helminthoeca* only occurs in dogs in the Pacific Northwest.

Pathogenesis

- Within 5 to 7 days after a dog ingests raw fish parasitized with infected fluke metacercariae, the flukes mature and attach to the dog's intestinal mucosa, thereby inoculating the *N. helminthoeca* organisms. The *Neorickettsia* infect the intestinal epithelium and mononuclear cells, and then disseminate to the mononuclear phagocyte system (MPS) organs (e.g., lymph nodes, spleen, liver), and to other areas such as the CNS and the lungs.
- The incubation period ranges from 5 to 21 days.
- Cats are not susceptible to salmon poisoning disease.

Clinical Signs and Laboratory Findings

- Clinical signs and physical examination findings in dogs with acute salmon poisoning include high fever (104–107.6°F) followed by hypothermia, anorexia, persistent diarrhea (usually hemorrhagic), vomiting, profound weight loss, mild serous naso-ocular discharge, and generalized lymphadenopathy, which can be marked.
- Because of the acute onset of fever and GI signs, salmon poisoning disease can resemble canine parvovirus infection.
- Laboratory abnormalities are nonspecific, but leukocytosis or leukopenia, thrombocytopenia, elevated serum alkaline phosphatase, and hypoalbuminemia are common findings.

Diagnosis

- Operculated trematode ova are usually found on direct fecal smears or by standard sugar flotation or fecal washing-sedimentation techniques; however, the presence of fluke infection does not necessarily confirm *N. helminthoeca* infection.
- Giemsa-stained fine-needle aspirates of enlarged lymph nodes usually reveal reactive lymph node hyperplasia with intracytoplasmic rickettsial bodies (pleomorphic, coccobacillary, purple staining) in macrophages.

Treatment

- Give doxycycline (5–10 mg/kg PO or IV, q12h) or tetracycline (22 mg/kg PO q8h) for 21 days. Because of the severe vomiting and diarrhea that occur in this disease, begin with parenteral doxycycline or oxytetracycline (7 mg/kg IV q8h) for the first 3 to 5 days. The response to tetracyclines is rapid, whereas untreated infections are often fatal.
- Give praziquantel (Droncit), at one dose of 10 to 30 mg/kg, PO or SC, to eliminate flukes.
- Use supportive treatment (e.g., fluid therapy, antiemetics, antidiarrheals, nutritional support) as needed.
- The prognosis is good with appropriate treatment.

Prevention

- To prevent the disease, keep dogs from feeding on raw infected fish. Keep dogs away from areas where fresh-caught salmon are being eviscerated and cleaned.
- Freezing (–20°C for 24 hours) or thoroughly cooking fish destroys the metacercariae and rickettsiae.

FELINE EHRLICHIA-LIKE DISEASES

Etiology and Transmission

Current evidence suggests that cats can be infected naturally with *E. canis*, *N. risticii*, and *A. phagocytophilum*. This is based on serology, PCR, and the visualization of *Ehrlichia*-like morulae within mononuclear cells and granulocytes of cats with doxycycline-responsive illness resembling the canine forms of these diseases.

The source of infection in cats is unknown, but transmission involving tick vectors is likely for *Ehrlichia* and *Anaplasma*. *Neorickettsia* is transmitted by ingestion of trematode vectors found in water, aquatic insects, snails, or possibly transport host prey (e.g., rodents).

Clinical Signs and Laboratory Findings

- The most frequent clinical signs are fever, lethargy, inappetance, gastrointestinal signs, weight loss, pallor, hyperaesthesia, and joint pain (neutrophilic polyarthritis). Splenomegaly, lymphadenopathy, and dyspnea due to interstitial pneumonitis have also been observed. Experimental infections in cats have generally been asymptomatic or resulted in mild illness.
- Laboratory abnormalities can include nonregenerative anemia, leukocytosis or leukopenia, thrombocytopenia, or pancytopenia. Hyperglobulinemia (polyclonal gammopathy) and the presence of anti-nuclear antibodies is reported.

Diagnosis

Feline *Ehrlichia*, *Anaplasma*, or *Neorickettsia* infections have been confirmed by visualization of organisms (morulae) in blood, serologic testing for the presence of antibodies, and PCR testing to detect organism DNA. Some cats have been serologically positive and PCR negative, while others have been PCR positive and serologically negative; thus, until these infectious agents are better understood in cats, both confirmatory testing methods should be used together.

Treatment

Cats suspected of *Ehrlichia*, *Anaplasma*, and *Neorickettsia* infection have responded to doxycycline (5–10 mg/kg PO q12h for 21 days), tetracycline (22 mg/kg PO q8h for 21 days), or imidocarb diproprionate (2 doses at 5 mg/kg IM, given 2 weeks apart).

Prevention and Public Health

Prevention of ehrlichiosis and related infections in cats depends on minimizing tick exposure, using an effective tick preventative product approved for use in cats, and routinely checking cats for ticks and removing them promptly.

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Chapter 18

Borreliosis (Lyme Disease)

Robert G. Sherding

Lyme borreliosis is a polysystemic, tickborne disease caused by the spirochete *Borrelia burgdorferi*. The disease has been associated with polyarthritis in dogs, cattle, horses, and humans. Infection is widespread in the United States, and is endemic in the northeastern coastal states and the upper Midwest. Infection also occurs worldwide and is prevalent in areas of Europe. Borreliosis is transmitted to animals and people by deer ticks.

ETIOLOGY

Lyme borreliosis in dogs and humans is caused by at least 6 subspecies of the *Borrelia burgdorferi sensu lato* complex. The strain that primarily causes borreliosis in North America is *Borrelia burgdorferi senso stricto*. These eubacteria are spiral-shaped, flagellated, gram-negative spirochetes that are related to *Leptospira*, except they do not survive as free-living organisms outside of the host.

B. burgdorferi is easy to isolate from vector ticks but not from clinically affected patients. The organisms are microaerophilic and have special growth requirements. The outer membrane of the spirochete can undergo antigenic variation during the course of infection, which enables the organism to evade the host's immune response and cause persistent infection. Antigenic variation may limit the effectiveness of vaccines.

Dogs in endemic areas are commonly co-infected with other tickborne agents, especially *Anaplasma phagocytophila* (see Chapter 17), and mixed infections may contribute to the pathogenesis and severity of disease in some cases.

Prevalence

▼ ***Key Point*** The risk of *Borrelia burgdorferi* infection correlates with the prevalence of infected ticks in an area and the likelihood of being bitten by a vector tick.

- Borreliosis commonly affects dogs that have recreational exposure to tick-infested vegetation in endemic areas, especially outdoor sporting and hunting dogs.
- In the United States, over 90% of clinically affected dogs are found in the northeastern coastal states and Wisconsin and Minnesota. Within endemic regions, there are focal areas of high and low prevalence. The seroprevalence in dogs in highly endemic areas commonly reaches 50% to 90%, and 60% to 80% of the ticks in these areas may harbor *Borrelia* spirochetes. The seroprevalence in Southern and Western states is less than 4%.
- 95% of seropositive dogs are asymptomatic.

Transmission

Dogs are infected through the bite of an infected tick. The primary vectors of Lyme borreliosis are *Ixodes* spp. ticks, also called black-legged or deer ticks. These hard ticks are small (2–3 mm) 3-host ticks that have a 2-year life cycle with larval, nymph, and adult stages.

- In the Northeast, Southeast, and Midwest regions of the United States, *Borrelia burgdorferi* is carried by *Ixodes scapularis* (formerly designated *I. dammini*). In California and other western states, *I. pacificus* is the carrier. Various other *Ixodes* ticks are involved in Europe and Asia. Other species of ticks and biting insects such as flies and mosquitoes can carry *Borrelia* spirochetes, but these are not a significant source of transmission.
- Deer support the adult stage of *I. scapularis* but are not usually infected by the spirochete. Mice and other small rodents are the main reservoirs of borreliosis because they maintain the larval and nymphal stages of *I. scapularis* and can become infected with the spirochete. Migratory birds may be important reservoirs because they have the ability to transmit ticks and spirochetes over long distances. Dogs are incidental hosts.
- Western *I. pacificus* ticks are less efficient as vectors because they prefer to feed on lizards that contain borreliacidal factors.
- Direct transmission between dogs is unlikely. Uninfected dogs housed with infected carrier dogs for 1 year did not become infected. In utero transmission is not likely. Iatrogenic transmission by blood transfusion is a possibility.

▼ ***Key Point*** Transmission of *Borrelia* infection requires at least 48 hours of attachment and feeding by a vector tick.

- Once inside the animal host, *Borrelia* spirochetes live intercellularly in the skin and spread through connective tissue migration rather than hematogenously. A small area of erythematous skin around the tick bite may be seen in the first week.

CLINICAL SIGNS

▼ ***Key Point*** In endemic areas, most dogs in the population have serologic evidence of exposure to *Borrelia*, but never develop clinical signs, indicating that subclinical infection is common.

Most dogs develop persistent subclinical infection that may lifelong. Seroconversion occurs within 3 to 6 weeks after exposure. Clinical disease develops in only 5% of infected dogs, depending on age, immune status, strain of *Borrelia*, and dose of exposure (number of ticks). In experimental infections, clinical signs develop 2 to 5 months after tick exposure.

Polyarthropathy

Acute, chronic, or intermittent shifting-leg lameness due to polyarthritis is the most common clinical sign.

- Systemic signs can include fever, anorexia, lethargy, lymphadenopathy, and weight loss; however, many animals show no clinical signs other than lameness.
- Swelling and pain in one or more joints may be evident. Arthritis usually occurs first in the joint closest to the tick bite. The carpi are the most frequently affected joints.
- Chronic, progressive, non-erosive arthritis may develop in persistently infected dogs.
- Radiographically, affected joints may have joint effusion, but usually show little or no evidence of degenerative joint disease.
- Synovial fluid analysis reveals neutrophilic (suppurative) inflammation with leukocyte counts ranging from 2,000 to 100,000 nucleated cells per µl, similar to findings in idiopathic immune-mediated polyarthritis.

Renal Disease

A unique syndrome of protein-losing glomerulonephropathy and acute progressive renal failure ("Lyme nephropathy") has been associated with canine borreliosis, especially in Labrador retrievers and golden retrievers. *Borrelia* is not the proven cause, and mixed infections or an unrecognized co-infection by another tickborne agent could play a role.

- Renal lesions include immune-mediated glomerulonephritis, renal tubular necrosis, and lymphocytic-plasmacytic interstitial nephritis.
- Clinical findings can include acute vomiting, hypertension, edema, ascites, azotemia, hypoalbuminemia, hypercholesterolemia, proteinuria, and tubular casts in the urine. Most cases progress rapidly over 1 to 2 weeks and die despite therapy.

Other Manifestations

Meningitis, encephalitis, uveitis, and myocarditis with cardiac arrhythmias are seen rarely in association with canine borreliosis, but the relationship of these to *Borrelia* infection is uncertain.

Feline Borreliosis

Naturally-occurring clinical disease is not well documented in cats; however, many healthy cats are seropositive for *Borrelia* infection and experimentally infected cats develop polyarthritis, meningitis, pneumonitis, and lymphadenopathy.

DIAGNOSIS

Consider borreliosis in dogs from endemic areas with typical clinical signs, especially if there is a history of exposure to a wooded environment or tick-infested area. The diagnosis depends on finding the organism or antibodies directed against the organism. Serologic testing provides a presumptive diagnosis; however, in endemic areas many healthy dogs have been exposed and are seropositive, leading to a tendency to overdiagnose the disease. Definitive diagnosis requires identification of the *Borrelia* spirochetes by culture or polymerase chain reaction (PCR) assay, but these are not routinely available to the clinician.

In endemic areas, the differential diagnosis is challenging because other doxycycline-responsive tickborne infectious diseases are often prevalent as well, many of which cause clinical signs that overlap with borreliosis; such as infections caused by *Anaplasma*, *Ehrlichia*, *Rickettsia*, and *Bartonella* (see Chapters 17 and 19). Lyme borreliosis also is difficult to distinguish from immune-mediated polyarthritis (see Chapter 124).

▼ ***Key Point*** A positive *Borrelia* antibody titer is a marker for exposure to ticks and the infectious agents they transmit. Consider the potential for other tickborne diseases in any seropositive dog.

Serologic Tests for Borrelia Antibodies

Serologic tests for the presence of antibodies to *Borrelia* are widely available and used as indirect evidence of exposure. The traditional serologic tests are based on whole-cell enzyme-linked immunosorbent assay

(ELISA) or immunofluorescent antibody (IFA) techniques. These do not differentiate between antibodies from natural exposure and vaccination. The C6 antibody test and Western blot analysis are more specific for natural exposure.

ELISA and IFA Antibody Titers

The antibody titer detected by ELISA or IFA increases by 4 to 6 weeks after exposure, which is almost always before the onset of clinical signs; thus, ELISA or IFA titers are acceptable screening tests for Lyme borreliosis in unvaccinated dogs. Unfortunately, reliability and reproducibility of results vary between different commercial laboratories.

▼ ***Key Point*** Routine ELISA or IFA serologic testing does not differentiate between dogs with active Lyme disease and those with persistent antibodies from earlier exposure or vaccination.

Positive Titer

- In an endemic area, a positive titer can be an incidental finding resulting from prior infection. Antibody titers after natural exposure persist for years. Other causes of positive titers include prior vaccination, crossreactivity to other noncausative organisms (e.g., nonpathogenic *Borrelia* strains, *Leptospira* spp., oral spirochetes), and nonspecific reactions seen in other inflammatory conditions.
- Positive titers have a low predictive value for the development of clinical disease. In one study seropositive dogs were observed for 20 months, and less than 5% developed clinical joint disease.

▼ ***Key Point*** A positive *Borrelia* antibody test indicates exposure, but it does not prove that the clinical signs are caused by borreliosis.

- Paired titers (to identify a rising titer) are not helpful, and high titers can persist for years, even after treatment.
- Because dogs do not develop clinical disease before the rise in immunoglobin G (IgG) antibody, differentiation of immunoglobin M (IgM) and IgG is not useful. In addition, IgM titers persist for many months and do not indicate recent exposure.
- In cases suspected of neuroborreliosis, a high cerebrospinal fluid (CSF)-to-serum antibody titer ratio has been suggested as an indicator of central nervous system (CNS) antibody production and active neural infection.

Negative Titer

- False-negative antibody titer results are rare; thus, a negative titer in an animal with clinical signs rules out Lyme borreliosis with high probability.
- Evaluate animals with a negative titer and clinical signs suggesting borreliosis for immune-mediated causes of polyarthritis (see Chapter 124).

▼ ***Key Point*** Routine ELISA and IFA tests are highly sensitive screening tests, but they have poor specificity and thus are not suitable as confirmatory tests.

C6 Antibody Test

This test uses a synthetic C6 peptide as the antigen for detecting C6 antibodies against the highly conserved invariable region 6 (IR_6) of the outer surface protein (Osp) of *B. burgdorferi*. C6 antibodies are formed in response to natural exposure, but not in response to vaccination.

- The C6 antibody test is highly specific (99% specificity) for *B. burgdorferi*. The test does not crossreact with antibodies from prior Lyme vaccination or nonspecific antibodies against other spirochetes (e.g., *Leptospira*), thus eliminating the major causes of false-positives seen with traditional whole-cell ELISA and IFA tests.
- The C6 antibody test is more sensitive than traditional whole-cell ELISA for detecting early infections, detecting infections even as early as 3 weeks post-exposure, before clinical signs develop. This test may also be more sensitive for detection of certain strains of *Borrelia*, such as those found in Europe.

▼ ***Key Point*** The C6 antibody test (SNAP 3Dx) distinguishes between natural exposure and vaccine-induced antibodies.

- An ELISA-based test kit for C6 antibodies (SNAP 3Dx; IDEXX) is available as an in-office screening test for Lyme borreliosis. The kit simultaneously tests for heartworms and *Ehrlichia canis*, hence the name "3Dx". The manufacturer recommends a two-tiered testing approach, first using the in-office SNAP 3Dx test kit as the *qualitative* screening test for C6 antibodies. Positive results are then further characterized with a *quantitative* C6 antibody test on a serum sample sent to a reference laboratory.
- The quantitative C6 antibody test correlates with *Borrelia* load. In seropositive healthy dogs, a high level of C6 antibody may help to determine if treatment is warranted, although additional studies are needed to confirm this.
- In seropositive dogs with clinical borreliosis, the quantitative C6 antibody level can be measured prior to treatment and then used to monitor response to the therapy. The C6 antibody level usually declines by 3 months after successful antibiotic treatment. Current recommendations are to reevaluate the test at 3 and 6 months after treatment.

Western Blot Assay

The Western blot assay detects a pattern of antibodies against the Osp of the *Borrelia* spirochete that specifically indicates *B. burgdorferi* infection and excludes false positives caused by prior vaccination or nonspecific crossreactions to other organisms. In unfed infected ticks and during vaccine processing, OspA is prominently expressed by the spirochete, but in infected dogs OspC is most prominent. Western blot assay results that show a strong OspC response are specific for *B. burgdorferi* infection; whereas a strong OspA response indicates an antibody response to vaccination. The Western blot test provides similar diagnostic information as the C6 antibody test, but it is more cumbersome and expensive, and thus less useful for clinical situations.

Tests to Identify Borrelia Organisms

PCR and culture are specialized confirmatory tests used to identify *B. burgdorferi* organisms.

Polymerase Chain Reaction

PCR is highly specific but not yet routinely available. The fluid or tissue specimen chosen for PCR must contain *Borrelia* DNA for the result to be positive. False negatives are common because the location of the spirochetes in infected dogs is highly variable. *Borrelia* organisms do not usually spread hematogenously, so blood is not useful for PCR. The most reliable specimen is a skin biopsy near the tick bite site, or near the first joint affected. Joint fluid or synovium from affected joints may be used. Urine also can be tested. CSF testing is useful in cases with neurologic signs. PCR may not differentiate between viable spirochete organisms and nonviable remnants. It may take months following treatment or recovery for these non-infective remnants to clear and the PCR to become negative.

Culture

B. burgdorferi has fastidious growth requirements, and attempts to culture spirochetes from blood, joints, or tissues is often unrewarding. The highest isolation rate is from skin at the tick bite site. Synovium can also be cultured. *Borrelia* are rarely cultured from the blood. Although a positive culture is definitive confirmation of infection, culturing is difficult and not readily available for routine clinical diagnosis.

TREATMENT

Healthy Seropositive Dogs

Asymptomatic seropositive dogs do not need to be treated; however, they should be monitored for clinical signs of borreliosis, especially lameness, and given treatment if these occur. Monitoring for proteinuria and microalbuminuria as early indicators of Lyme nephritis has been suggested, but studies are needed to validate this approach.

▼ ***Key Point*** Treatment is rarely indicated for healthy seropositive dogs in the absence of clinical signs.

Dogs with Clinical Borreliosis

Treat dogs that have clinical signs compatible with Lyme borreliosis and a positive C6 antibody test. Use one of the following antibiotics.

- Doxycycline; 10 mg/kg q12h PO, for 4 weeks.
- Amoxicillin; 22 mg/kg q8h PO, for 4 weeks.
- Azithromycin; 5 mg/kg q12h PO, for 4 weeks, for refractory cases.
- Ceftriaxone; 25 mg/kg q24h, IV, for 4 weeks, for CNS involvement (rarely).

▼ ***Key Point*** Doxycycline is the treatment of choice for Lyme borreliosis.

- The response to antibiotic therapy is typically rapid (24 to 48 hours), especially in early infections.
- Some dogs remain persistently culture-positive and PCR-positive after antibiotics. Prolonged antibiotic therapy (weeks to months) may be required in these chronic, established infections.

▼ ***Key Point*** In longstanding infections the responsiveness to treatment may be inversely proportional to the duration of clinical signs.

- If the initial response to therapy is poor, reevaluate the diagnosis and look for concurrent diseases. Consider a diagnostic "tick panel" to exclude other concurrent tickborne infections, such as *Ehrlichia*, *Anaplasma phagocytophila*, *Rickettsia*, *Babesia*, and *Bartonella*.
- Use nonsteroidal anti-inflammatory drugs to control joint pain during episodes of recurrent arthritis.
- Avoid immunosuppressive doses of corticosteroids that can exacerbate *Borrelia* infection.
- Treat protein-losing glomerulopathy and acute renal failure with the measures described in Chapter 77.

PREVENTION

Vaccination

Killed whole-cell bacterins and recombinant OspA vaccine products are marketed for immunizing dogs against Lyme borreliosis using an initial series of 2 doses, 2 to 4 weeks apart, followed by annual revaccination. Recombinant vaccines may have less risk of adverse effects and are preferred by the author.

▼ ***Key Point*** Do not routinely vaccinate all dogs for Lyme borreliosis. Limit vaccination to high-risk dogs (e.g., outdoor, hunting, and field trial dogs) residing in tick-infested areas with a high prevalence of borreliosis.

- Crossprotectivity of vaccines against the multiplicity of *Borrelia* strains is uncertain.
- Vaccination of infected dogs has no known therapeutic benefit. The benefits as well as risks of vaccinating healthy seropositive dogs are unknown.
- A disadvantage of vaccination is that it causes false-positive results on routine serologic tests (see "Diagnosis").

Vector Control

▼ ***Key Point*** Tick bite avoidance is an important aspect of prevention.

Fipronil, permethrin, and amitraz are highly effective against ticks and for preventing *Borrelia*. Use one of these regularly for dogs residing in tick-infested areas. Always follow the label directions.

- Fipronil/methoprene monthly topical medication (Frontline Plus; Merial) is for both dogs and cats.
- Imidacloprid/permethrin monthly topical medication (Advantix; Bayer) is for dogs only, and is toxic in cats.
- Amitraz-impregnated collars (Preventic collar; Virbac) are effective for dogs, but lose activity when wet and can be toxic if ingested.
- Reduce the risk of exposure of animals by limiting their access to tick-infested areas.
- Periodically check animals for ticks and promptly remove them to decrease exposure to *B. burgdorferi*.

PUBLIC HEALTH

Human *B. burgdorferi* infections result from outdoor activities associated with exposure to tick vectors. In the United States, human Lyme borreliosis has been reported in nearly all states; however, 85% of cases occur in the Northeast and in Wisconsin, and Minnesota.

- Human Lyme disease begins several days after a tick bite as an expanding, annular, non-pruritic, erythematous rash (erythema chronicum migrans), and progresses to fever, flu-like symptoms, polyarthritis, meningitis, myocarditis, and uveitis.
- Infected dogs and cats do not directly transmit *Borrelia* to humans. Pets may occasionally transport infected ticks into the household on their haircoat, but this is a rare source of human infection.
- Transmission requires prolonged tick attachment (48 hours); therefore, measures that reduce tick exposure are the best means of preventing human infection. In tick-infested areas, the tick repellant N,N-diethyl-meta-toluamide (DEET) is recommended for exposed skin.

SUPPLEMENTAL READING

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Chapter 19

Systemic Bacterial Infectious Diseases

Robert G. Sherding

A large number of bacteria can infect dogs and cats. This chapter focuses on leptospirosis, brucellosis, and bartonellosis. Chapter 18 is devoted to Lyme borreliosis. Other infectious diseases caused by bacteria are summarized in Table 19-1, and most are described in the respective organ-system chapters. *Bordetella bronchiseptica* is associated with the canine infectious tracheobronchitis (see Chapter 12). *Mycoplasma haemofelis* and *Mycoplasma haemominutum* are hemotropic infections (see Chapter 22). Mycobacterial infections are associated with chronic skin disease (see Chapter 39). Actinomycosis and nocardiosis are causes of pyothorax (see Chapter 164). Tetanus and botulism cause severe neuromuscular dysfunction (see Chapters 128 and 130, respectively). Salmonellosis, campylobacteriosis, yersiniosis, and *Clostridium perfringens* and *Cl. difficile* primarily involve the intestinal tract (see Chapter 69).

LEPTOSPIROSIS

Etiology

Leptospira are filamentous, motile, spirochete bacteria that infect many wild and domestic animals and humans. Over 200 leptospiral serovars have been described. A universal feature of pathogenic serovars is the ability to colonize the proximal renal tubules resulting in a prolonged renal carrier state and urine shedding.

In North America, canine leptospirosis is most frequently caused by serovars of *Leptospira interrogans* (serovars *L. icterohaemorrhagiae, L. canicola, L. pomona,* and *L. bratislava*) and *Leptospira kirschneri* (serovar *L. grippotyphosa*). Serovar *L. autumnalis* may also be emerging in some regions.

Transmission

▼ ***Key Point*** Infection is spread by recovered animals that shed *Leptospira* organisms in their urine for months to years after infection.

- Wild animal populations serve as reservoirs of infection that persistently shed *Leptospira* organisms and contaminate the environment. Suburban "backyard" wildlife such as raccoons, skunks, squirrels, voles, and other rodents may be especially important sources of infection.
- Exposure usually occurs by mucocutaneous contact with *Leptospira* organisms in the environment, most importantly contaminated surface water, but also food, bedding, soil, vegetation, or fomites. The organisms penetrate mucosa or abraded skin. In addition, transplacental, venereal, and bite-wound transmission can occur.

Prevalence

Canine leptospirosis appears to be a reemerging disease with increasing prevalence, especially involving serovars *L. grippotyphosa* and *L. pomona*. Middle-aged, male, large-breed outdoor dogs that live in peri-urban areas are most commonly affected; however, all dogs are at risk. The incidence is highest in late summer and early fall. Infection rates increase after wet periods of rainfall and flooding.

Pathogenesis

Leptospiremia occurs 4 to 12 days post-infection. The primary targets in leptospirosis are the kidneys and the liver. Vasculitis and disseminated intravascular coagulopathy (DIC) may result from widespread acute endothelial injury.

- *Leptospira* preferentially infect renal tubule epithelium, often causing acute tubular injury and renal failure. Renal colonization and urine shedding are prolonged, continuing for months to years after clinical recovery.
- *Leptospira* can injure hepatocytes, resulting in hepatocyte dysfunction, cholestasis, acute hepatic necrosis, jaundice, and occasionally chronic hepatitis and hepatic fibrosis (especially *L. grippotyphosa*).
- Infection typically is subclinical in vaccinated (immune) dogs and in nearly all cats.

Table 19-1. BACTERIAL DISEASES OF DOGS AND CATS

Disease	Etiology (Source)	Clinical Signs	Diagnosis	Treatment
Leptospirosis	*Leptospira interrogans* serovars: *canicola, icterohaemorrhagia, pamona, bratislava, grippotyphosa* (urine shedding)	Acute renal failure, acute hepatic failure, chronic hepatitis, vasculitis, DIC, anorexia, depression, fever, myalgia,	Serology (MA, ELISA); PCR	Penicillin, ampicillin, or amoxicillin, followed by doxycycline
Borreliosis (Lyme disease)	*Borrelia burgdorferi* (tickborne)	Fever, polyarthritis, acute renal disease	Serology (IFA, ELISA, C6 antibody); PCR	Doxycycline; tick control
Brucellosis	*Brucella canis* (aborted tissues, vaginal discharges, semen, urine)	*Male:* infertility, orchiepididymitis, scrotitis *Female:* abortion, infertility *Male and female:* lymphadenopathy	Serology (slide test, tube test, AGID), blood culture	Minocycline or doxycycline plus dihydrostreptomycin or gentamicin; spay or neuter
Bartonellosis	*Bartonella henselae* (in cats and dogs; flea vector); *B. vinsonii* (in dogs; tickborne)	*Cat:* subclinical, transient fever *Dog:* endocarditis, granulomatous and immune diseases, epistaxis *Human:* cat scratch disease, etc	Serology, blood culture, PCR	*Acute:* amikacin plus amoxicillin, *Chronic:* azithromycin, enrofloxacin, doxycycline *Prevention:* flea and tick control
Bordetellosis (kennel cough)	*Bordetella bronchiseptica* (respiratory secretions)	Acute tracheobronchitis (cough); rhinitis	Culture (airways)	Doxycycline, amoxicillin-clavulanate, or azithromycin
Botulism	*Clostridium botulinum* (neurotoxin in contaminated food)	Ascending neuromuscular paralysis	Clinical signs; toxin assay	Type C antitoxin; respiratory support
Tetanus	*Clostridium tetani* (neurotoxin in contaminated wounds)	Muscle rigidity, stiff gait, tetanic spasms, trismus, seizures	Clinical signs	Tetanus antitoxin; penicillin G or metronidazole; sedatives
Campylobacteriosis	*Campylobacter jejuni* (feces)	Watery mucoid diarrhea or subclinical carrier	Fecal culture, fecal microscopy	Erythromycin, neomycin, clindamycin, or fluoroquinolone
Salmonellosis	*Salmonella typhimurium, S. enteritidis* (feces)	Acute gastroenteritis: fever, vomiting, diarrhea, bacteremia; subclinical carrier	Fecal culture	Enrofloxacin, trimethoprim sulfa, or chloramphenicol
Yersiniosis	*Yersinia enterocolitica* (feces)	Diarrhea (rare) or subclinical carrier	Fecal culture	Cephalosporins, tetracyclines, etc.
Tyzzer disease	*Clostridium piliforme* (rodent feces)	Acute hepatic necrosis, necrotizing ileocolitis	Necropsy lesions, cell culture isolation	None (100% fatality)
Plague	*Yersinia pestis* (rodent fleas and rodent ingestion)	*Cat:* lymph node abscess, high fever, pneumonia, fatal septicemia *Dog:* mild fever or no signs	Lymph node cytology, culture, and IFA; serology; PCR	Gentamicin, doxycycline; flea control
Tularemia	*Francisella tularensis* (tickborne; ingestion of rabbits or rodents)	Fever, oral ulcers, lymphadenopathy, draining abscesses, fatal bacteremia	Serology (agglutinating antibody titer), culture	Gentamicin, doxycycline, or fluoroquinolones; tick control
Actinomycosis	*Actinomyces* spp. (oral flora migration, bitewounds)	Subcutaneous abscesses, draining fistulous tracts, pyothorax, osteomyelitis	Cytology (gram-positive filamentous rods), culture of exudate	Penicillin, clindamycin; debride wounds; drain and lavage pyothorax
Nocardiosis	*Nocardia* spp (soil via wounds, plant awns, inhalation)	Subcutaneous abscesses, draining fistulous tracts, pyothorax, pneumonia	Cytology (gram-positive filamentous rods); biopsy; culture of exudate	Trimethoprim-sulfa; debride wounds; drain and lavage pyothorax
Tuberculous mycobacteriosis	*Mycobacterium tuberculosis, M. bovis, M. avium* (*Dog:* inhalation) (*Cat:* ingestion of milk, meat, offal)	*Dog:* granulomatous pneumonia, hilar lymphadenopathy *Cat:* granulomatous enteritis, mesenteric lymphadenopathy	Cytology or biopsy (acid-fast bacteria); culture (slow-growing); PCR	For *M. tuberculosis* or *M. bovis*: euthanasia because of public health risks For *M. avium*: triple combination of rifampin, enrofloxacin, azithromycin
Feline leprosy	*M. lepraemurium* (contact with rats)	Ulcerating cutaneous nodules	Cytology or biopsy (acid-fast bacteria); PCR	Surgical excision; clofazimine alone, or with clarithromycin or rifampin (see Ch. 39)
Opportunistic (atypical) mycobacteriosis	*M. fortuitum, M. chelonei, M. smegmatis,* (skin contact with contaminated soil and water)	Ulcerating dermal nodules; nonhealing wounds; spreading subcutaneous fistulous tracts; panniculitis	Cytology or biopsy (acid-fast bacteria); culture	Enrofloxacin alone, or with azithromycin; for *M. cheloni* use clarithromycin (see Ch. 39)

AGID, agar-gel immunodiffusion; DIC, disseminated intravascular coagulation; ELISA, enzyme-linked immunosorbent assay; IFA, indirect fluorescent antibody; MA, microscopic agglutination; PCR, polymerase chain reaction.

Clinical Signs

- **Systemic signs**: This can include acute onset of anorexia, depression, fever, vomiting, dehydration, stiff gait and reluctance to move (generalized myalgia), and congested mucous membranes. Vascular collapse and peracute death are seen in some animals.
- **Acute renal failure**: Systemic signs combined with renal pain and polyuria-polydipsia (mild cases), oliguria, or anuria (severe cases).
- **Acute hepatic failure**: Systemic signs combined with jaundice and DIC.
- **Acute vasculitis and DIC**: Systemic signs combined with widespread tissue edema and petechial and ecchymotic hemorrhages, hematemesis, melena, hematochezia, and epistaxis.
- **Chronic hepatitis and hepatic fibrosis**: Signs of chronic liver failure develop; e.g., weight loss, ascites, jaundice, and hepatic encephalopathy.
- **Other findings**: Less frequent manifestations include uveitis, meningitis, myocarditis (arrhythmias), acute pulmonary hemorrhage and interstitial pneumonitis (cough, dyspnea), and abortion or stillbirths.

Diagnosis

Complete Blood Count (CBC)

- Leukopenia (early response to leptospiremia)
- Neutrophilic leukocytosis with left shift (at time of presentation)
- Thrombocytopenia; severe cases may have coagulation abnormalities of DIC (see Chapter 23)

Urinalysis

- Proteinuria, pyuria, cylindruria, bilirubinuria, glucosuria, and isosthenuria
- Darkfield microscopy of urine is unreliable and not recommended.

Serum Chemistries

- Azotemia—increased blood urea nitrogen (BUN), serum creatinine, and serum phosphorus
- Increased serum concentrations of liver enzymes (ALT, AST, ALP), bilirubin, and bile acids
- Increased serum creatine kinase (myopathy)
- Electrolyte imbalances reflecting renal and gastrointestinal effects

Diagnostic Imaging

- Kidney size can be normal or enlarged. Ultrasonographically, kidneys show increased cortical echogenicity in 75% of cases and pyelectasia in nearly 50% of cases. Some dogs have a distinctive echogenic demarcation of the corticomedullary border ("medullary rim sign"). Perinephric effusion may be seen.
- Liver ultrasonography is usually unremarkable. Nonspecific changes in echogenicity may be seen.
- Thoracic radiographs may show patchy alveolar, reticulonodular, or generalized pulmonary interstitial infiltrates with dorsocaudal distribution indicative of pneumonitis, vasculitis, or pulmonary hemorrhage.

Serology

▼ ***Key Point*** *Leptospira* organisms are fastidious, slow-growing, and difficult to culture, and they are difficult to identify in fluids or tissues; thus, the combination of serology and clinical signs is the most practical means of diagnosis.

Microscopic Agglutination Titer

▼ ***Key Point*** The presence of microscopic agglutination (MA) antibodies can indicate current infection, past infection, or prior leptospiral vaccination.

The MA test is the standard method for presumptive clinical diagnosis of leptospirosis. MA titers become positive after 1 week, peak at 3 to 4 weeks, and remain positive for several months after either natural infection or vaccination.

- Although single titers do not definitively diagnose current active infections, MA titers at 1:400 or greater are suggestive, and at 1:800 or greater they are highly indicative of leptospirosis. However, booster vaccines given in the preceding 2 to 3 months can produce titers that overlap with these values. Most post-vaccinal titers are 1:100 to 1:400, but rarely titers as high as 1:3,200 can occur within 3 months of vaccination. The magnitude of the MA titer can be blunted by early antibiotic therapy.

▼ ***Key Point*** The presumptive diagnosis of leptospirosis is based on a single high MA titer (≥1:800) with compatible clinical signs, or a 4-fold rise in MA titer in paired sera.

- MA titers can be negative in the first week of acute illness, requiring a second titer 2 to 4 weeks later for diagnosis. Use paired MA titers during acute illness and recovery (convalescence) to demonstrate a 4-fold rise in titer as a criterion to distinguish current infection from previous infection or vaccination. Because the timing of the titer peak varies, take a convalescent titer 2 to 3 weeks after acute illness, and possibly another 1 to 2 weeks later.
- Ideally, the lab will test for the various serovars listed in the Etiology section, and potentially others known to occur in the geographic region. The serovar with the highest titer is interpreted to be the infecting serovar and other serovars with lower titers are considered to represent nonspecific

crossreactivity and/or background titers from prior vaccination.

Combined Immunoglobulin Titers

Combined immunoglobulin M (IgM)-immunoglobulin G (IgG) enzyme-linked immunosorbent assay (ELISA) titers differentiate the early IgM antibody response of acute infection from the later IgG response that is seen with recovery, prior infection, or vaccination. Although the combined IgM-IgG ELISA helps to identify natural infection in vaccinated dogs, it does not distinguish between different serovars. The ELISA test is not as readily available as the MA test.

- The IgM titer becomes positive within the first week of infection (before the MA test) and peaks at 2 weeks.
- The IgG titer becomes positive 2 to 3 weeks after infection and persists for months.

Identification of Leptospiral Organisms

Leptospirosis can be confirmed by identification of *Leptospira* organisms by microscopy and culture. These tests are most useful for confirming positive serologic tests, and only positive results are meaningful. Because of low detection rates, negative results never exclude the possibility of leptospirosis. In addition, antibiotics rapidly eliminate the organisms from blood and urine so they will be undetectable by culture. Polymerase chain reaction (PCR) identification of leptospiral DNA may be a more reliable means of documenting infection.

Microscopic Identification

- Darkfield microscopy is used to detect leptospires on a wet mount of fresh urine. Accuracy is highly operator dependent, and the high rate of false positives and false negatives makes this an unreliable test.
- *Leptospira* organisms can sometimes be identified in urine or in tissues (e.g., by kidney and liver biopsy or cytology specimens) using Giemsa or silver stains, immunohistochemical staining, or fluorescent antibody techniques.

Culture

Culture for *Leptospira* is technically difficult and has a low detection rate; thus, it is rarely used for clinical diagnosis. The organisms are fastidious and may take several weeks to grow. The preferred specimen is fresh urine taken by cystocentesis prior to administration of antibiotics. In hydrated dogs, a low dose of furosemide (0.5 mg/kg, IV) prior to urine collection may optimize the recovery rate. Collected urine must be alkalinized to >pH 8 and transported in special media.

Polymerase Chain Reaction Test

PCR detection of leptospiral DNA in blood, urine, or tissues is highly sensitive and specific. It detects infection earlier than serology, and may be useful for identifying subclinical urine shedding. Unfortunately, validated PCR assays are not yet readily available to the clinician.

Treatment

Effective treatment requires general supportive therapy, treatment of the leptospiremic phase of infection, followed by treatment of the leptospiruric carrier phase of infection. With intensive management, survival rates of 75 to 90% can be expected. Most dogs recover completely, but residual chronic renal failure is a potential outcome.

- **For supportive care**: Administer intensive fluid and electrolyte therapy (see Chapter 5) and, depending on clinical findings, initiate appropriate treatment for acute renal failure (see Chapter 77), acute hepatic failure (see Chapter 71), and DIC (see Chapter 23), as recommended in other chapters in this book. Oliguric renal failure and fulminant DIC are life-threatening complications of leptospirosis that often need the most immediate attention and intensive care.

▼ ***Key Point*** The antibiotics of choice are penicillin derivatives for terminating leptospiremia, and doxycycline for eliminating leptospiruria.

- **For leptospiremia**: Initially give parenteral antibiotics, such as penicillin G (25,000–40,000 units/kg IV, q12h) or ampicillin (22 mg/kg IV, q6–8h). Once vomiting resolves, switch to oral amoxicillin (22 mg/kg PO, q8–12h) and continue treatment for 2 weeks.
- **For leptospiruria**: To eliminate the renal carrier state once amoxicillin treatment has been completed, give doxycycline (5 mg/kg PO q12h) for 2 weeks. Other alternatives for treating the carrier state include macrolides (erythromycin, azithromycin), fluoroquinolones, or aminoglycosides (avoid in dogs with renal impairment).
- For caretaker precautions, see the "Public Health" section.

Prevention

Because wild animal reservoirs harbor and shed leptospiral organisms that contaminate the environment, prevention of exposure is not a realistic expectation. Routine vaccination for leptospirosis helps to decrease the incidence and severity of canine leptospirosis and to reduce the zoonotic risks to pet owners.

- Bivalent *Leptospira* bacterins *(L. canicola* and *L. icterohaemorrhagiae)* have been widely used for routine

canine vaccination since the 1970s. Bivalent vaccines have reduced the incidence of infections caused by *L. canicola* and *L. icterohaemorrhagiae*, but they do not crossprotect against other serovars that now account for most leptospiral infections in dogs.
- Use multivalent vaccines that contain the serovars *L. pomona*, *L. grippotyphosa*, *L. canicola* and *L. icterohaemorrhagiae* to give a broader spectrum of protection.
- Vaccinate dogs over 12 weeks of age in high-prevalence areas or high-risk situations with at least 3 doses, 3 to 4 weeks apart, for primary immunization, followed by annual revaccination (see Chapter 7).
- Anaphylactic reactions (facial edema, pruritus, hypotension, or dyspnea) occur with leptospiral bacterins, and the incidence may be increased in small breeds and puppies less than 9 weeks of age. Newer improved vaccines derived from *Leptospira* antigenic subunits will likely cause fewer allergic reactions.

Public Health

Leptospirosis is a widespread and potentially fatal zoonotic infection. Most humans are infected through outdoor recreational activities in and around water, but animal caretakers and veterinarians are considered at risk because direct contact of mucous membranes or damaged skin with the urine of infected animals is a potential source of infection. Therefore, caretakers and pet owners must take proper precautions and maintain strict sanitation when treating dogs with leptospirosis. Consider the following preventive measures.

- Regard urine-contaminated objects as biological hazards.
- Require latex gloves for caretakers and handlers of dogs with leptospirosis.
- Avoid spray washing of contaminated cages or kennels, because it could aerosolize urine. Use protective goggles and face masks during cage cleaning.
- Use iodophor as a disinfectant for urine-contaminated areas.
- Treat all known and suspected shedders with doxycycline.
- Eliminate rodent infestations.

CANINE BRUCELLOSIS

Etiology

Canine brucellosis is caused by *Brucella canis,* a gram-negative aerobic coccobacillus. In addition, rare infections caused by *B. abortus*, *B. suis*, and *B. melitensis* have been reported in dogs in contact with livestock. Cats can be infected with *B. canis* experimentally, but are resistant and do not develop clinical signs. Rare zoonotic *B. canis* infections are seen in humans in contact with infected dogs.

Transmission

B. canis is transmitted by infected semen (venereal), vaginal discharges (at estrus, breeding, and post-abortion), aborted fetal tissues, and urine. Infection occurs by penetration of oronasal, conjunctival, and genital mucous membranes.

Pathogenesis

Brucella canis is an intracellular pathogen that can persist for years within the mononuclear phagocytes of the host. Brucellosis is characterized by a prolonged leukocyte-associated bacteremia that begins 1 to 4 weeks after infection, and can last from 6 months to over 5 years. Spontaneous recovery after 1 to 5 years depends on cell-mediated immunity. *Brucella* organisms most often localize in the following areas.

- Lymphoid and mononuclear phagocyte systems (resulting in lymphoreticular hyperplasia and occasional splenomegaly)
- Prostate and testes of male dogs (resulting in orchiepididymitis and infertility)
- Gravid uterus of female dogs (resulting in infertility, abortion, or stillbirth)
- Rarely, the eye (anterior uveitis), kidney (glomerulonephritis), or intervertebral discs (diskospondylitis).

Clinical Signs

Most infected animals have no overt clinical signs. Generalized lymphadenopathy, splenomegaly, and reproductive failure are the principal manifestations. Diskospondylitis and uveitis are less common. Fever and systemic illness are rare.

Male Reproductive Failure

Brucellosis causes infertility and physical findings of scrotal swelling, scrotal dermatitis, enlarged epididymides (epididymitis), and testicular atrophy. Various semen abnormalities result in sterility (see "Diagnosis" section).

Female Reproductive Failure

Brucellosis causes abortion of dead, partially autolyzed fetuses at 40 to 60 days of gestation without any other signs of illness; persistent discharge for 1 to 6 weeks after abortion; and failure to conceive (because of early fetal resorption).

Other Uncommon Forms of Brucellosis

- **Diskospondylitis**: This causes spinal pain progressing to paresis and ataxia with spinal cord compression. The radiographic appearance of diskospondylitis is distinctive, but other bacteria also can cause this.
- **Uveitis**: This manifests as anterior uveitis (aqueous flare, hyphema, secondary glaucoma, corneal edema)

or chorioretinitis (vitreal haze, retinal lesions or detachment).
- **Meningoencephalitis**: This is very rare and not well characterized.
- **Glomerulonephritis**: This is seen as subclinical proteinuria without azotemia.

Diagnosis

▼ ***Key Point*** Consider brucellosis in all canine infertility evaluations and bitches with late-term abortion.

- Routine CBC, urinalysis, and serum chemistries are normal except for occasional hyperglobulinemia.
- Lymph node cytology reveals nonspecific reactive hyperplasia.
- Semen abnormalities—more than 80% of sperm are morphologically abnormal (immature sperm, deformed acrosomes, swollen midpieces, detached tails, head-to-head agglutination); increased semen leukocytes; and aspermia in advanced cases.

Serology

▼ ***Key Point*** The diagnosis of brucellosis is a 2-step process. First, use a screening serologic test for presumptive diagnosis, then confirm positives with a high-specificity serologic test, a blood culture, or, ideally, both.

Because other bacteria elicit antibodies that crossreact with *B. canis*, false-positive results are common with agglutination tests. Hemolysis (hemoglobin) also causes false-positive results. False-negative titers are rare, but can result from sequestration of infection or recent antibiotics. In recent infections, it can take up to 4 weeks to seroconvert; thus, when screening dogs for entry into a breeding kennel, a negative test result on day 1 and again after 4 weeks is required.

Rapid Slide Agglutination Test

The rapid slide agglutination test (RSAT) (D-Tec CB; Synbiotics) is an inexpensive, in-office screening test that is used to identify suspects that need further testing. The RSAT detects antibodies to *B canis* cell-wall antigen. This highly sensitive screening test has an accurate negative predictive value, but false positives are common. Nearly 99% of negatives are true negatives. Only one half to two thirds of positives are confirmed to be truly infected; thus, all RSAT positives must be confirmed by a more specific serologic test, a blood culture, or, ideally, both.

Tube Agglutination Test

The tube agglutination test (TAT) is used to provide quantitative titer confirmation of positive RSAT results. The TAT titer is more specific than the RSAT, but because of false positives the TAT is not considered definitive (titers 1:50 to 1:100 are suspicious; titers ≥ 1:200 are highly suggestive).

Agar Gel Immunodiffusion

The agar gel immunodiffusion (AGID) is a sensitive and specific test for antibodies to either cell wall or cytoplasmic antigens of *B. canis*. The cytoplasmic-antigen AGID has the best specificity and is the preferred serologic confirmatory test for diagnosis of brucellosis. AGID is available at some commercial and state diagnostic laboratories.

Other Serologic Tests

Indirect fluorescent antibody (IFA) and ELISA titers for *B. canis* have high specificity and are used as confirmatory tests (titers of 1:50 to 1:100 are suspicious; titers ≥ 1:200 are diagnostic).

Bacterial Culture

- A positive *Brucella* culture is definitive evidence of infection. Whole blood is the preferred culture specimen because of the characteristically prolonged bacteremia of brucellosis. Urine, semen, vaginal discharges, and aborted fetal tissues also can be cultured.
- Negative cultures never rule out brucellosis because the bacteremia can be intermittent or transiently suppressed by antibiotics. Use a serologic test such as the RSAT to screen for infection, and then use blood cultures for confirmation.

▼ ***Key Point*** Although positive serologic tests are indicative of active brucellosis, a positive blood culture is the gold standard for definitive diagnosis and should be used whenever possible for confirmation.

Treatment

Brucella organisms are refractory to antibiotics because of their intracellular location. This is compounded by poor penetration of antibiotics into protected sites such as the testes, prostate, eyes, and the central nervous system (CNS). Always treat with at least two synergistic antibiotics. Single antibiotic therapy is not effective.

- The traditional antibiotic regimen is: minocycline (12.5 mg/kg, PO, q12h for 4 weeks) combined with dihydrostreptomycin (10 mg/kg, IM, q12h for 7 days, on weeks 1 and 4). Doxycycline (5–10 mg/kg, PO, q12h) is an alternative to minocycline, and gentamicin (5 mg/kg SC q24h for 7 days) is usually substituted for the dihydrostreptomycin, but is less effective. For refractory cases, a fluoroquinolone

or rifampin can be added as a triple antibiotic regimen.
- Bacteremia often recurs weeks to months after cessation of treatment; thus, three or more repeated courses of antibiotics guided by follow-up titers and blood cultures are often required.

▼ ***Key Point*** Eradication of *Brucella* with antibiotics is difficult and highly unpredictable. Cure may not be possible in some dogs.

- Recommend spay or neuter of infected dogs.
- Recommend caution for people in contact with *Brucella*-positive dogs because there have been rare cases of human infection with *B. canis*. Canine brucellosis is regarded as a low-level public health risk.

Prevention

▼ ***Key Point*** Eliminate all *Brucella*-positive dogs from breeding programs.

- Test all breeding stock for *Brucella* two times at a 4-week interval before entry into a breeding program and, ideally, test before each breeding in females and once or twice yearly in sexually active male dogs.

BARTONELLOSIS

Bartonella species are fastidious, aerobic, pleomorphic, gram-negative bacteria that infect dogs and cats through vectors such as fleas and ticks. *Bartonella* are considered to be hemotropic. They cause persistent bacteremia in mammalian reservoir hosts by localizing intracellularly in erythrocytes and vascular endothelium. This intracellular location of *Bartonella* organisms promotes (1) persistence in the blood, (2) efficient transmission by arthropod vectors, and (3) resistance to antibiotics and attack from the host immune system. Dogs and cats are infected by several species of *Bartonella*, and the list is growing. *Bartonella* bacteria have worldwide importance as causes of zoonotic infections in humans.

Feline Bartonellosis

Etiology

Cats are infected by at least 4 *Bartonella* species. Cats serve as the main reservoir host for *B. henselae*, a ubiquitous infection in cats that is transmitted by fleas and causes cat scratch disease and other conditions in humans (see "Public Health" section). Cats are also a reservoir for the less prevalent *B. clarridgeiae*, another cause of cat scratch disease. *B. koehlerae*, and *B. bovis* (formerly *B. weissii*) have been isolated sporadically from cats, but their clinical significance is unknown.

Transmission

▼ ***Key Point*** *Bartonella* infection is transmitted from cat to cat by fleas.

- *B. henselae* replicates in fleas and survives for days in flea feces. Feces from fleas feeding on bacteremic cats may be the main infective source of *B. henselae*.
- Direct horizontal transmission does not occur between infected and uninfected cats that co-habit in a flea-free environment.
- Vertical (in utero) and lactogenic transmission to kittens has not been shown.
- Transmission can occur through contaminated blood transfusions or injection needles.

Prevalence

- Cats are the main reservoir for *B. henselae*, and infection is common in cats worldwide. Seroprevalence indicating exposure varies by region, but ranges from 4% to 80% in the United States, and exceeds 50% of pet cats in warm, humid coastal and southern regions of the United States where fleas thrive. Up to 33% of pet cats are bacteremic (i.e., actively infected) in these high-prevalence areas.
- In a U.S. regional comparison in 271 young pet cats (age < 2 years), the prevalence of seroconversion/bacteremia varied from 67%/33% in Florida, to 62%/28% in Southern California, to 28%/12% in Washington, D.C. to only 12%/6% in Chicago.
- Factors associated with increase risk of infection include young age (<1 year), flea infestation, indoor-outdoor lifestyle, and origination from a shelter or stray situation.
- *B. clarridgeiae* accounts for 10% of *Bartonella*-infected cats in the United States, but over 30% in parts of Europe and Asia.

Pathogenesis

Most cats infected with *Bartonella* spp. are healthy carriers with chronic bacteremia. Experimental inoculation of cats with *B. henselae* results in bacteremia within 1 to 2 weeks coinciding with seroconversion, and transient signs of fever, lethargy, anorexia, regional lymphadenopathy, and occasional neurologic signs. Most infected cats maintain a persistent or episodic bacteremia for months to years.

Clinical Signs

Natural infections with *Bartonella henselae* are only rarely associated with recognizable clinical disease in cats. Most bacteremic cats are clinically healthy carriers. *Bartonella* infection has been associated with fever, lymphadenopathy, anterior uveitis, gingivitis/stomatitis, endocarditis, neurologic disease, and reproductive failure. Because so many healthy cats are carriers, it is

possible that the *Bartonella* isolated from cats with these conditions is coincidental rather than causative, or it may be a cofactor with other infections.

Diagnosis

Blood culture, blood PCR, and serologic testing can be used to evaluate the *Bartonella* infection status of cats, and these diagnostic procedures are readily available to practicing veterinarians through the Vector Borne Disease Diagnostic Lab at North Carolina State University. Submission requirements and forms are available at www.cvm.ncsu.edu/docs/tickbornediseaselab.html.

▼ ***Key Point*** Diagnostic testing is only indicated in cats suspected of clinical bartonellosis. Routine testing of healthy cats for *Bartonella* infection is not currently recommended.

Serology merely indicates exposure and the possibility of infection. Only culture and PCR can prove active infection. Most cats that have negative results on these tests are not actively infected. In some cats, however, bacteremia can be intermittent, resulting in occasional false negatives with culture and PCR.

Serology

Serologic testing is based on IFA or ELISA procedures for detection of antibodies against *B. henselae*. Serology has limited diagnostic value because a positive titer (>1:64) does not distinguish between prior exposure and active infection. In cats with acute illness (i.e., recent infection), paired titers over 2 to 3 weeks may be required to document seroconversion. Pre-adoption serologic testing of kittens and young cats may be useful, especially when the prospective owner is immunocompromised, because seronegative cats are unlikely to be infected. However, some false negatives occur with serology (up to 10% of seronegative cats may have bacteremia).

Blood Culture

Isolation of *Bartonella* spp. from bacteremic cats is much easier than in dogs or humans; thus, blood culture is a good confirmatory test for feline *Bartonella* infection. *Bartonella* cultures are slow growing, so results can take up to 8 weeks to obtain. False negatives occur when bacteremia is intermittent or suppressed by prior antibiotics, or with improper sample collection. Always obtain *Bartonella* cultures prior to administering antibiotics. Contact the laboratory for specific instructions on sample collection and submission.

PCR Assay

PCR detection of *Bartonella* DNA in blood is a confirmatory test that is comparable to culture in reliability, with the advantages of quicker results and speciation of the positives. False negatives are uncommon except when bacteremia is transiently suppressed by prior antibiotics. False positives are rare.

Treatment

The optimal treatment for eliminating *Bartonella* infection in cats has not been established. Infection is extremely refractory to antibiotics because of the intracellular location of the bacteria. In most cats, antibiotics transiently suppress the bacteremia without curing the infection. Relapse of bacteremia typically occurs several weeks after discontinuation of antibiotics. Thus, treatment is only indicated for cats with clinical disease attributable to bartonellosis.

▼ ***Key Point*** Treatment of healthy *Bartonella*-infected cats is not recommended and usually ineffective.

The following antibiotics have been suggested for clinical bartonellosis in cats. Use one or more antibiotics for a minimum of 6 weeks (after informing the owner of the uncertainty of antibiotic efficacy). Following treatment, evaluate blood cultures at 4- to 8-week intervals for at least 3 to 4 months to detect relapse.

- Macrolides (e.g., azithromycin, 7.5–10 mg/kg PO q12h)
- Fluoroquinolones (e.g., enrofloxacin, 2.5 mg/kg q12h PO; *caution*: higher doses can cause retinal degeneration and blindness in cats); can be used alone or in combination with amoxicillin
- Doxycycline (10 mg/kg PO q12h), or amoxicillin-clavulanate (15 mg/kg PO q12h), have also been used, but are considered less effective options.

Prevention

▼ ***Key Point*** Rigorous flea control is the most effective prevention against *Bartonella* infection in cats.

Use an integrated flea control program to reduce the risk of exposure to *Bartonella* (see Chapter 45 and Table 45-1 for a complete discussion of flea control options). For rapid killing of fleas on a cat that is already infested, use oral nitenpyram (Capstar, Novartis) or topical pyrethrin. Do not use permethrin; it is highly toxic in cats. For routine control of fleas, and thus prevention of *Bartonella* infection, use one of the following long-acting topical flea control products at least monthly.

- Fipronil/methoprene (Frontline Plus; Merial)
- Imidocloprid (Advantage; Bayer)
- Selamectin (Revolution; Pfizer)

▼ ***Key Point*** All cats used as blood donors should be seronegative and either culture-negative or PCR-negative for *Bartonella*.

Public Health

Domestic cats are the primary reservoirs for zoonotic human infections with *B. henselae* and *B. clarridgeiae*. Both agents cause cat scratch disease in healthy people, characterized by a small erythematous skin papule (inoculation granuloma) at the entry site after 7 to 12 days, followed in 1 to 2 weeks by variable malaise and benign regional lymphadenopathy that is usually self-limiting within 2 to 3 months.

Serious atypical manifestations of *B. henselae* develop most frequently in immunocompromised people, and can include bacillary angiomatosis, parenchymal bacillary peliosis, endocarditis, encephalopathy, neuroretinitis, arthritis, osteomyelitis, and relapsing fever with bacteremia. *Bartonella* is isolated from 3% of human endocarditis patients and 18% of febrile HIV-infected patients.

Transmission and Risk Factors in Humans

Most human infections occur through contamination of cat scratches and cat bites with flea excrement. Approximately 90% of the cats owned by people with cat scratch disease are bacteremic with *B. henselae*. Young, flea-infested cats are the greatest zoonotic risk.

- Cats under 1 year of age are most likely to infect people. Owners of kittens are 15 times more likely to develop cat scratch disease than owners of adult cats.
- The highest prevalence in people in the United States is in coastal and southern regions, especially in summer and fall, coinciding with the time of greatest flea activity.
- Seroprevalence is 3% to 6% in the general population, but 7% to 15% in veterinary health-care providers.

Prevention of Bartonellosis in Immunocompromised Pet Owners

Recommend that immunocompromised people avoid cats less than 1 year of age and cats with a history of flea infestation. Flea-free adult cats kept in a flea-controlled environment are least likely to infect people. Acquisition of a new cat from a private owner or breeder is preferable to adoption of a stray or shelter cat. In addition, seronegative cats are less likely to have bacteremia and thus are less of a potential risk, although not all seronegative cats are free of infection (see "Serology" section). Immunocompromised people should consider the following recommendations.

- House cats indoors to lessen the potential for flea exposure.
- Use flea control products regularly (see "Prevention" section).
- Wash hands after handling cats.
- Avoid rough play to reduce accidental cat scratches.
- Cleanse cat-inflicted skin wounds immediately, and seek medical advice.
- Do not restrain cats or pull cats from cat carriers.

Canine Bartonellosis

Etiology

Dogs can be infected by several *Bartonella* species, most commonly by *B. henselae* and *B. vinsonii* (ssp. *berkhoffii*), and sporadically by various others (e.g., *B. clarridgeiae, B. elizabethae, B. washoensis*). The most seroprevalent *Bartonella* species in dogs is *B. henselae*; however, *B. vinsonii* (*berkhoffii*) is the species most frequently associated with clinical disease.

Bartonella vinsonii (berkhoffii)

▼ ***Key Point*** Canine *B. vinsonii* (*berkhoffii*) infection is transmitted by ticks.

- *B. vinsonii* (*berkhoffii*) is transmitted by *Rhipicephalus sanguineous* ticks and possibly others (e.g., *Amblyomma americanum*, *Dermacentor* spp., and *Ixodes* spp). Coyotes serve as a major reservoir host of *B. vinsonii* (*berkhoffii*) infection in some areas (in California, 35% of coyotes are seropositive and 28% are bacteremic).
- Serosurveys have found *B. vinsonii* (*berkhoffii*) worldwide in dogs. The seroprevalence in the United States ranges from 1% to 3% of healthy pet dogs to 3% to 5% of sick dogs. The prevalence is much higher in dogs diagnosed with other tickborne infections.
- Risk factors include heavy tick exposure, living in a rural environment, and a free-roaming lifestyle.
- Coinfection with other tickborne infections is common, especially *Ehrlichia canis* (Chapter 17) and *Babesia canis* (Chapter 22).

Bartonella henselae and Other Species

- *B. henselae* and other *Bartonella* spp. in dogs are transmitted primarily by fleas. Cats are the primary reservoir host for *B. henselae* and *B. clarridgeiae*; rodents are the main reservoir for *B. elizabethae*, and squirrels for *B. washoensis*.
- The seroprevalence of *B. henselae* in dogs is highest in the flea-dense southeastern United States (10% of healthy pet dogs and 28% of sick dogs), but only 1% to 2% of dogs in many other areas.

Clinical Signs

Dogs experimentally infected with *B. vinsonii* (*berkhoffii*) develop persistent bacteremia and immunosuppression, but they have minimal clinical signs except for transient fever. Dogs with natural infection can be persistent subclinical carriers for months to over a year.

Various clinical conditions are emerging in association with canine bartonellosis, and this list is expanding. Most of these have been implicated by serologic and PCR evidence, but a definitive causative relationship is unproven. Some of these conditions may be the result of mixed infections with multiple tickborne pathogens.

- Valvular endocarditis (especially aortic valve) and myocarditis, mostly in large breed dogs, leads to arrhythmias, murmurs, syncope, sudden death, congestive heart failure, and systemic thromboembolism. The mortality rate is high.
- Prolonged or intermittent fever of unknown origin
- Granulomatous rhinitis; epistaxis; mucopurulent nasal discharge
- Granulomatous lymphadenitis
- Granulomatous hepatitis
- Granulomatous meningoencephalitis
- Anterior uveitis; chorioretinitis
- Peliosis hepatis is characterized by vascular proliferation and multifocal, blood-filled cystic spaces in the liver. This distinctive lesion has also been seen in immunocompromised humans with disseminated bartonellosis.
- Immune-mediated diseases
  - Immune-mediated hemolytic anemia
  - Immune-mediated thrombocytopenia
  - Polyarthritis
  - Protein-losing nephropathy
  - Cutaneous vasculitis
  - Positive anti-nuclear antibody (ANA) test

▼ ***Key Point*** Consider *Bartonella* infection in dogs with aortic valve endocarditis, unexplained granulomatous disease, unexplained epistaxis, or immune-mediated disease.

Diagnosis

The diagnosis of canine bartonellosis is based on serology and PCR assay in dogs with compatible clinical findings.

Nonspecific Clinical Findings

- **Hematologic findings** in dogs with clinical bartonellosis may include anemia, thrombocytopenia (in half of cases), eosinophilia (in one third of cases), monocytosis, and neutrophilic leukocytosis. Some dogs have proteinuria.
- **ANA tests** are positive in 10% of dogs infected with *B. vinsonii* (*berkhoffii*) alone, and in 45% of dogs with *B. vinsonii* (*berkhoffii*) combined with *Ehrlichia canis* or other tickborne pathogens.
- **Diagnostic imaging** can detect some of the lesions listed under "Clinical Signs." In particular, echocardiographic aortic valve lesions are found consistently in dogs with *Bartonella* endocarditis.
- **Aspiration cytologies and biopsies** may occasionally reveal intracellular bacteria that stain positive with silver stain within macrophages and lymph nodes.

Serology and PCR Assay

The diagnosis of canine bartonellosis is based on serum antibody titers and PCR assays that are readily available to practicing veterinarians through the Vector Borne Disease Diagnostic Lab at North Carolina State University. Submission requirements and forms are available at www.cvm.ncsu.edu/docs/tickbornediseaselab.html.

- *B. vinsonii* (*berkhoffii*) antibody titers of >1:64 indicate exposure and potentially active infection. Because the seroprevalence of *B. vinsonii* (*berkhoffii*) in the general dog population is low (<5% of dogs), clinically sick dogs with significant titers are presumed to be actively infected and are treated. Dogs with *Bartonella* endocarditis usually have very high titers (>1:512).
- Isolation of *Bartonella* spp. from blood cultures in dogs is rarely successful; thus, PCR detection of *Bartonella* DNA is the preferred confirmatory test for canine bartonellosis. PCR testing can be done on blood or fresh, frozen, or paraffin-embedded tissue specimens.

▼ ***Key Point*** Mixed tick-transmitted infections are common in dogs residing in high-prevalence areas. Consider testing all *Bartonella*-positive dogs for other tickborne infections, such as *Ehrlichia*, *Anaplasma*, *Rickettsia*, *Babesia*, and *Borrelia burgdorferii*.

Blood Culture

B. vinsonii (*berkhoffii*) is very difficult to culture from infected dogs compared with *B. henselae* in cats; thus, blood cultures are unreliable for diagnosing most dogs with clinical bartonellosis.

Treatment

Initiate antibiotic therapy in seropositive and/or PCR-positive dogs with clinical signs attributable to *Bartonella* infection. The optimal treatment for canine bartonellosis has not been established, but antibiotics that achieve high intracellular levels are recommended. In dogs, bacteremia is not as persistent or as likely to relapse as in cats. Effective treatment is indicated by a drop in the *Bartonella* titer after 3 to 6 months.

- **Treat severe or life-threatening clinical disease** (e.g., endocarditis or meningoencephalitis) with an initial combination of a parenteral aminoglycoside (e.g., amikacin) and a penicillin derivative (e.g., amoxicillin or ampicillin). After 1 to 2 weeks, continue for an additional 4 weeks with one of the antibiotics below.
- **Treat less severe or chronic disease** with a macrolide (e.g., azithromycin) or a combination of a fluoroquinone and amoxicillin. Doxycycline can also be used, but is not considered as effective. Continue antibiotics for at least 4 to 6 weeks.
  - Azithromycin (7.5–10 mg/kg PO q12h)
  - Enrofloxacin (5 mg/kg q12h PO) plus amoxicillin-clavulanate (15 mg/kg PO q12h)

- Doxycycline (10 mg/kg PO q12h)
- Rifampin can be added in refractory cases

Prevention

▼ ***Key Point*** Rigorous flea and tick control is the most effective prevention against *Bartonella* infection in dogs.

Reduce the risk of exposure to *Bartonella* spp. by limiting access to tick-infested areas. Use an effective long-acting topical flea and tick preventative at least monthly on dogs residing in flea and tick-infested areas, such as one of the following:

- Fipronil/methoprene (Frontline Plus; Merial)
- Imidacloprid/permethrin (Advantix; Bayer); for dogs only (permethrin is toxic in cats).
- Amitraz tick collar (Preventic; Virbac) plus topical permethrin for fleas

▼ ***Key Point*** Do not use dogs that are seropositive for *Bartonella* spp. as blood donors.

Public Health

Dogs have very rarely been implicated as the source of human *Bartonella* infections; however, dogs are capable of carrying ticks or fleas that could transmit *Bartonella* spp. to people.

MYCOBACTERIOSIS

The categories of mycobacterial infection in dogs and cats are (1) the systemic or tuberculous form, (2) the opportunistic form, and (3) the lepromatous form (feline leprosy). Each of these is caused by a different variety of mycobacterial species. This section describes systemic tuberculous mycobacteriosis. Chapter 39 is devoted to opportunistic mycobacterial infections and feline leprosy, which are primarily cutaneous infections characterized by ulcerating skin nodules and draining fistulous tracts.

Etiology

Mycobacteria are environmentally resistant, non-spore–forming, aerobic, acid-fast, gram-positive bacteria that infect a wide range of animals worldwide, including dogs, cats, and humans. Mycobacteria cause persistent intracellular infection leading to chronic granulomatous inflammation. Systemic tuberculous mycobacteriosis (i.e., classic tuberculosis) in dogs and cats is usually caused by infection with *M. tuberculosis*, *M. bovis*, or *M. avium*, with sporadic reports of *M. microti*, *M. microti*-like, and *M. simiae*.

- *M. tuberculosis* infection is an inverse zoonosis transmitted from infected humans to pets through inhalation of aerosolized sputum. Dogs are infected more than cats. Pulmonary infection is most common.
- *M. bovis* infection results from ingestion of unpasteurized milk, uncooked meat, or offal from infected cattle or wildlife such as deer. Cats are infected more commonly than dogs. The intestinal tract and abdominal viscera are usually involved.
- *M. avium* is ubiquitous in the environment, and infection results from contaminated water and soil, or infected poultry feces or carcasses. Siamese cats and basset hounds seem to have a genetic predisposition, and immunosuppression may play a role in some animals.
- *M. microti* and *M. microti*-like are rodent pathogens that occasionally infect cats that hunt prey.

Clinical Signs

Clinical signs are usually chronic and reflect the site of granulomatous lesions.

- **Cutaneous**: Dermal nodules and non-healing wounds with draining fistulous tracts, and regional lymphadenopathy.
- **Pulmonary**: Occurs mostly in dogs with *M. tuberculosis*. Granulomatous pneumonia and hilar lymphadenopathy cause signs of fever, weight loss, and chronic cough.
- **Intestinal**: Occurs mostly in cats with *M. bovis*. Granulomatous transmural enteritis and mesenteric lymphadenopathy cause anorexia, vomiting, diarrhea, weight loss, blood loss anemia, and peritoneal effusion.
- **Disseminated**: This is typical of *M. avium* infections that cause widespread granulomatous lesions in lymph nodes, liver, spleen, other abdominal viscera, thorax, CNS, eyes (uveitis), and bone.

Diagnosis

- Leukocytosis and hyperglobulinemia may be seen.
- Diagnostic imaging may identify granulomatous abdominal masses, pulmonary lesions, effusions, internal lymphadenopathy, or bone lesions.
- A presumptive diagnosis is established by finding acid-fast bacteria in cytologies or biopsies of lesions. Intracellular bacteria with clubbed shape and beaded appearance are typical and most abundant in *M. avium* infections.
- Definitive diagnosis and speciation require culture or PCR. Mycobacteria that cause systemic mycobacteriosis are slow-growing and culturing may take up to 6 weeks. The advantage of PCR is more rapid results.

▼ ***Key Point*** Intradermal tuberculin testing is inconsistent and unreliable in dogs and cats.

Treatment

Generalized systemic or tuberculous mycobacteriosis is resistant to treatment and has a poor prognosis.

Treatment requires a minimum of 6 months of multidrug therapy, and some cases require lifelong therapy. Drug toxicity and expense are often limiting factors.

▼ ***Key Point*** Euthanasia rather than treatment is generally recommended for dogs and cats infected with *M. tuberculosis* or *M. bovis* because of the poor prognosis and public health concerns.

- For *M. avium* infections, treat the animal for at least 2 months with triple therapy, using a combination of rifampin (10 mg/kg PO q12h), enrofloxacin (5 mg/kg PO q24h), and azithromycin (10 mg/kg PO q12h), followed by another 4 months of dual drug therapy using rifampin plus either azithromycin or enrofloxacin. Because of poor prognosis, euthanasia rather than treatment may be appropriate in many cases.
- Surgical excision and debulking of focal lesions or masses may increase the effectiveness of medical therapy.

Public Health

- *M. tuberculosis:* The potential risk of pet-to-human transmission is unlikely but possible, thus, euthanasia is recommended.
- *M. bovis:* Dogs and cats may transmit the infection to humans through their feces and can contribute to enzootic spread of infection on farms; thus, euthanasia is recommended.
- *M. avium:* Dogs and cats are unlikely to transmit infection to humans; thus, the zoonotic risk is considered minimal and treatment is an option, except in households with an immunocompromised person. The source of human infections with *M. avium* is contaminated soil and water rather than animals.

TULAREMIA

Tularemia is an arthropod-borne bacterial zoonosis caused by *Francisella tularensis*, a pleomorphic, gram-negative coccobacillus. Ticks, rodents, and rabbits are the primary reservoir hosts, but a wide variety of animal species are susceptible, including cats, dogs, livestock, and humans. Tularemia is seen throughout temperate regions of North America, Europe, and Asia. In the United States high-prevalence areas are Arkansas, Missouri, Oklahoma, and South Dakota.

Transmission

F. tularensis is considered highly infectious by several routes, including bites from tick and deerfly vectors, scratches and bites from infected animals (especially cats), inhalation of aerosolized organisms, and ingestion of contaminated food, carrion, or water. Infected animals develop intracellular infection of macrophages and hematogenous dissemination.

Clinical Findings

Cats are more susceptible to clinical disease than dogs, which can range from mild illness with transient fever to fatal overwhelming sepsis. Infected dogs develop mild self-limiting febrile illness or subclinical infection with seroconversion.

- Clinical signs in cats vary and can include anorexia, depression, fever, lymphadenopathy, draining abscesses, oral ulcers, pneumonia, hepatosplenomegaly, multifocal hepatic necrosis, and jaundice.
- Laboratory findings can include a high or low white blood cell (WBC) count with a left shift, thrombocytopenia, elevated serum liver enzymes, and hyperbilirubinemia.

Diagnosis

The diagnosis is based on serology and culture (consult state health department or Centers for Disease Control and Prevention, Atlanta, GA). PCR assay may also be useful when available.

- Serologic testing (by tube agglutination, microagglutination, or ELISA) is available through state diagnostic laboratories. Antibodies may not be detected until after 2 to 3 weeks; thus, the serologic diagnosis is based on a 4-fold increase in paired serum titers, 2 to 4 weeks apart.
- The preferred culture specimens are aspirates of bone marrow or lymph nodes, although *F. tularensis* can also be isolated from blood, exudates, and others tissues. Cultures are a human biohazard and must be done at a Biological Safety Level II or III (BSL-2 or 3) laboratory, such as certain state diagnostic labs.

Treatment and Prevention

Tularemia is a serious public health threat and infected pets can transmit infection to people; thus, notify local and state health authorities prior to treating an animal with this disease. Infected pets can be treated with gentamicin or enrofloxacin for a minimum of 10 days, or doxycycline for a minimum of 14 days. Use tick control on pets for prevention in high-prevalence areas.

FELINE PLAGUE

Plague is a flea-transmitted bacterial zoonosis caused by *Yersinia pestis*, a gram-negative, bipolar coccobacillus. Rodents are the primary reservoir hosts for *Y. pestis*, and rodent fleas transmit the infection to various other animal species including cats, dogs, and humans.

Plague is found worldwide except in Australia. In the United States, infections occur in the western states, especially New Mexico, Arizona, Colorado, and California, where the principal reservoirs are rabbits, prairie dogs, ground squirrels, woodrats, and mice.

Transmission

Cats are more susceptible to plague than dogs, and are mainly infected by bites from wildlife fleas, or from hunting and eating rodents and rabbits. Cats with the pneumonic form of infection can also directly transmit infection to people by aerosol droplets.

Clinical Findings

The incubation period is 1 to 4 days and the clinical course is rapidly progressive. Infected cats can develop the 3 classic clinical forms of plague: bubonic (lymph nodal), pneumonic, and septicemic. Clinical illness in infected dogs is rare; most dogs develop subclinical infection with seroconversion, or, rarely, transient fever with self-limiting submandibular lymphadenitis.

- **Bubonic plague**, the most common form in cats, is characterized by fever, malaise, and regional necrosuppurative lymphadenitis most often affecting submandibular lymph nodes. Affected lymph nodes become enlarged and painful, and may abscess and drain. Without adequate treatment, the bubonic form can rapidly progress to the septicemic form.
- **Pneumonic plague** can be from primary inhalation of infectious organisms from another animal with pneumonic infection, or it can be from secondary spread of bubonic or septicemic infection to the lungs. Pulmonary lesions include diffuse interstitial pneumonia with coalescing areas of necrosis and abscessation in the lung. Cats with pulmonary involvement pose a serious public health risk. Inadequately treated pneumonic infection can rapidly progress to septicemia.
- **Septicemic plague** is characterized by widespread hematogenous dissemination to many organs leading to systemic inflammatory response of sepsis, acute respiratory distress, septic shock, DIC, multiple organ failure, and death.

Diagnosis

Finding a homogeneous population of gram-negative coccobacilli in exudate from a lymph node abscess is presumptive evidence of feline plague in endemic areas. The diagnosis is confirmed by immunofluorescence detection of *Y. pestis* antigen, serology (single high titer or four-fold rise in paired titers), or culture. Confirmatory testing requires a state public health laboratory or the Centers for Disease Control and Prevention (Atlanta, GA). Consult the destination lab for specimen collection and submission requirements.

Treatment and Prevention

Feline plague is a serious public health threat and infected cats can directly transmit infection to people via oral secretions and aerolized respiratory secretions; thus, notify local and state health authorities when feline plague is suspected.

- To prevent risk to the owner, do not discharge infected cats to the care of the owner. Isolate the cat within a veterinary hospital. Veterinary personnel should use precautions when treating a cat with plague (gown, mask, eye protection, and gloves).
- Initiate antibiotic therapy immediately after diagnostic specimens have been collected; while awaiting for confirmation. Parenteral gentamicin (10 days) is the drug of choice for treating infected pets. Oral doxycycline (3 weeks minimum) can also be used as an alternative, or as a follow-up to gentamicin.
- For prevention in high-prevalence regions, use flea control on cats and restrict cats from roaming and hunting of prey.

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Chapter 20

Systemic Mycoses

Robert G. Sherding

The four classical systemic mycoses of dogs and cats are histoplasmosis, blastomycosis, coccidioidomycosis, and cryptococcosis.

▼ ***Key Point*** Systemic mycoses are not contagious diseases. Infection results from contact with organisms in the environment, especially through inhalation.

Fungal infections with a predilection for individual organ systems are discussed elsewhere; thus, for deep cutaneous fungal infections see Chapter 40, for dermatophytosis see Chapter 42, for intestinal pythiosis see Chapter 69, and for nasal aspergillosis see Chapters 160 and 163.

▼ ***Key Point*** Histoplasmosis, blastomycosis, and coccidioidomycosis are endemic to defined regions of North America (Fig. 20-1).

HISTOPLASMOSIS

Etiology

- Histoplasmosis is caused by *Histoplasma capsulatum,* a dimorphic soil-dwelling fungus found in many temperate and subtropical regions of the world. In North America, the disease is most prevalent in the river valley regions of the central United States, especially in areas bordering the Mississippi, Ohio, and Missouri Rivers and their tributaries (see Fig. 20-1). Both dogs and cats are susceptible.
- At ambient temperatures, soil enriched by decomposing nitrogenous matter (e.g., bird feces or bat guano) provides an ideal growth medium for the mycelial phase of *Histoplasma.* The principal route of infection is by inhalation of airborne spores (conidia) and mycelial fragments in windblown soil; however, intestinal infection via ingestion also may occur. At body temperature (37°C), *Histoplasma* organisms transform into a yeast phase that causes a facultative intracellular infection of macrophages.

Pathogenesis

- Histoplasmosis primarily invades the lung and then spreads to the mononuclear phagocyte system (liver, spleen, etc.). The incubation period is 12 to 16 days. Widespread hemolymphatic dissemination can occur to virtually any tissue or organ system. Infection causes a granulomatous response.
- The outcome of infection is influenced by level of exposure; host cell-mediated immunity; age of the host (clinical disease is most common in young animals <4 years of age); breed (highest prevalence in sporting and hound breeds because of higher exposure risk); and immunosuppressive factors (corticosteroids may enhance dissemination).

Clinical Signs

Inapparent subclinical infections are common. The clinical forms of histoplasmosis are pulmonary, intestinal, and disseminated (multisystemic).

Subclinical Infection

An inapparent, self-limiting infection confined to the respiratory tract is the most common outcome of natural infection. The aftermath of this form is sometimes identified radiographically as multiple, discrete, calcified interstitial foci in the lungs (inactive encapsulated or healed lesions). Calcified tracheobronchial lymph nodes are seen less often.

Acute Pulmonary Infection

Acute pulmonary histoplasmosis is characterized by severe fulminant granulomatous pneumonia with signs of cough, tachypnea, dyspnea, abnormal lung sounds, fever, and severe malaise. Death from hypoxemia may occur despite treatment. The radiographic findings are diffuse or nodular interstitial pulmonary infiltrates, often with patchy coalescing alveolar densities and moderately enlarged tracheobronchial lymph nodes.

Chronic Pulmonary Infection

Chronic pulmonary histoplasmosis is more common than the acute form and is characterized by chronic

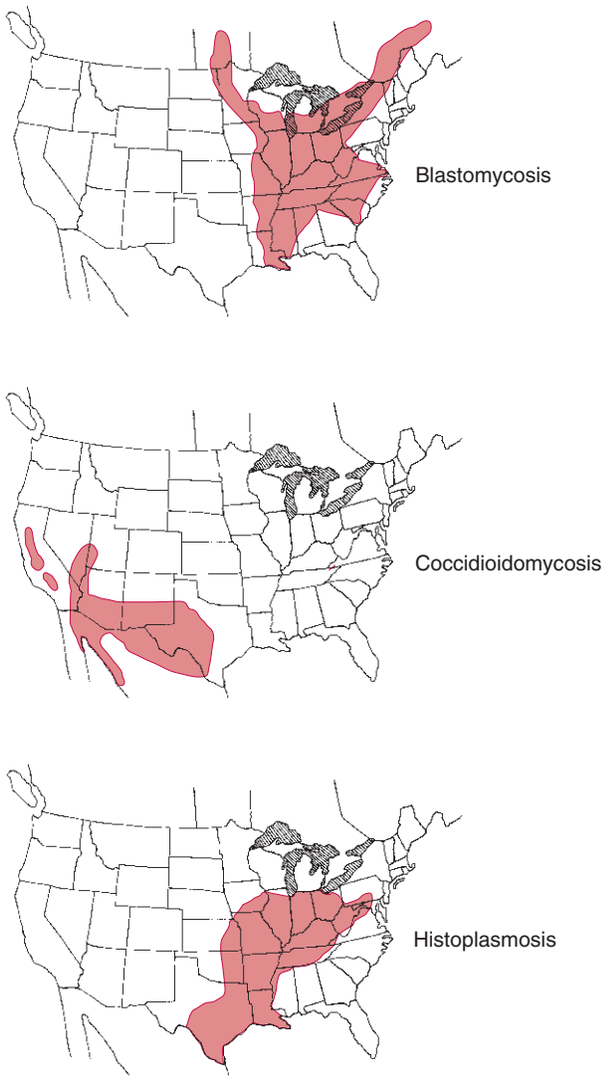

Figure 20-1. Geographic distribution of blastomycosis, coccidioidomycosis, and histoplasmosis in North America.

granulomatous pneumonia (diffuse or multifocal) with marked perihilar tracheobronchial lymphadenopathy that compresses the bifurcation of the trachea and mainstem bronchi. Clinical signs include chronic cough, exercise intolerance, and mild dyspnea with variable weight loss and fever. Radiographically, massive enlargement of the perihilar tracheobronchial lymph nodes and variable linear or nodular interstitial infiltrates are seen.

Intestinal Infection

Intestinal histoplasmosis is a common extrapulmonary form in dogs but not cats, and it may represent primary infection by ingestion. The colon, the small intestine, or a combination of both can be affected by extensive granulomatous thickening of the bowel wall and mucosal ulceration, often accompanied by mesenteric and visceral lymphadenopathy. Intractable diarrhea and progressive weight loss are the most consistent clinical signs. Other signs may include anorexia, lethargy, fever, anemia, vomiting, and abdominal effusion.

- ***Granulomatous colitis*** causes bloody-mucoid large bowel diarrhea with urgency and sometimes tenesmus. If the rectum is involved, mucosal proliferations may be detected by digital palpation of the rectum.
- ***Granulomatous enteritis*** causes intractable small bowel diarrhea, malabsorption, weight loss, palpably thickened intestines, and sometimes protein-losing enteropathy.

Disseminated Infection

Extrapulmonary dissemination causes a variety of clinical signs depending on the organs involved. Most cats develop this disseminated form of histoplasmosis. The mononuclear phagocyte system is a common site of dissemination. Manifestations can include anorexia, depression, fever, weight loss, and pulmonary involvement combined with any of the following:

- ***Bone marrow***—Nonregenerative anemia
- ***Lymph nodes***—Peripheral or abdominal lymphadenopathy
- ***Liver***—Hepatomegaly, icterus, ascites
- ***Spleen***—Splenomegaly
- ***Peritoneum***—Omental masses, mesenteric adhesions, nodular or granular serosal surfaces
- ***Eyes***—Exudative anterior uveitis, multifocal granulomatous chorioretinitis, optic neuritis
- ***Central nervous system (CNS)***—Ataxia, seizures
- ***Skin***—Cutaneous and subcutaneous nodules that ulcerate or fistulate, drain or crust over
- ***Bone***—Lameness and bone pain associated with proliferative or lytic bone lesions (osteomyelitis)
- ***Oral cavity***—Oral and lingual ulcers

Diagnosis

Consider histoplasmosis on the basis of clinical signs in animals from endemic areas. The results of routine laboratory evaluations are variable and nonspecific. Radiographic findings in the pulmonary form are often highly suggestive of a mycotic disease such as histoplasmosis. Identification of the *Histoplasma* organisms by cytology, biopsy, or culture is necessary for definitive diagnosis. Serology is unreliable.

Hematology

- Normocytic-normochromic nonregenerative anemia frequently results from chronic inflammation, dissemination of *Histoplasma* into the bone marrow, intestinal blood loss, or hemolysis.
- Neutrophilic leukocytosis or neutropenia with a left shift and monocytosis can be seen, and occasionally

pancytopenia in cats. *Histoplasma* organisms are occasionally seen within circulating monocytes or neutrophils on routine blood smears, especially if 1,000 cells are examined in differential cell counts or if buffy coat smears are examined.
- Mild to moderate, subclinical thrombocytopenia is common. Platelet counts of less than 50,000/µl are seen occasionally in association with macroplatelets in the circulation and increased megakaryocytes in the bone marrow, suggesting platelet consumption or destruction.

Serum Chemistry Evaluations

- Mild hypoalbuminemia, with or without concomitant hyperglobulinemia is common in intestinal and disseminated forms. Severe panhypoproteinemia occasionally occurs in dogs with protein-losing enteropathy.
- Hypercalcemia is reported in histoplasmosis.
- Elevated serum liver enzymes and bilirubin are seen with hepatic dissemination.
- Intestinal function tests may be abnormal in intestinal histoplasmosis (see Chapter 69).

Radiography and Ultrasonography

Thoracic Radiography

- Perihilar density around the tracheal bifurcation related to tracheobronchial lymphadenopathy (especially in dogs).
- Diffuse linear or nodular ("miliary") interstitial pulmonary infiltrates.
- Coalescing patchy alveolar infiltrates (especially in cats).
- Calcified pulmonary interstitial nodules (healed lesions), and calcified tracheobronchial lymph nodes indicate inactive lesions.

Other Diagnostic Imaging

- Hepatosplenomegaly; ultrasonography may show nodularity and abnormal echogenicity.
- Abdominal or thoracic effusions.
- Osteolytic and periosteal proliferative bone lesions.
- Barium contrast gastrointestinal (GI) radiography and GI ultrasonography may show diffuse irregularity and thickening of the intestinal wall, indicative of a diffuse infiltrative lesion.

Serology

- Serologic tests for histoplasmosis are unreliable; thus, every effort should be made to confirm infections through identification of the *Histoplasma* organisms.
- Complement fixation titers of 1:16 or greater or positive agar-gel immunodiffusion (AGID) (precipitin) tests are suggestive of histoplasmosis; however, false positives and false negatives are common.

Cytology

Exfoliative and fine-needle aspiration cytology generally are the most practical and high-yield methods for definitive diagnosis of histoplasmosis. Wright-Giemsa or Diff-Quik stains are ideal for identification of *Histoplasma* in cytology preparations. The organisms are found most often intracellularly within the cytoplasm of macrophages as round to oval yeast bodies, 2 to 4 µm in size, surrounded by a characteristic clear halo or "pseudocapsule" that results from shrinkage of the cytoplasm from the cell wall during fixation. The best source of cytologic specimens with potential diagnostic benefit depends on dissemination sites as indicated by clinical signs.

▼ ***Key Point*** Definitive diagnosis of histoplasmosis requires identification of *Histoplasma* organisms in cytology, biopsy, or culture specimens.

Respiratory Cytology

Use bronchoalveolar lavage, tracheobronchial washings, or fine-needle lung aspirates.

Intestinal Cytology

Use smears of rectal mucosal scrapings, impression smears of endoscopic biopsies, and ultrasound-guided fine-needle aspirates of abdominal lymph nodes or intestinal masses. Consider endoscopy of the colon and duodenum for the collection of diagnostic cytology or biopsy specimens. Histoplasmosis lesions appear endoscopically as areas of irregular mucosal thickening and proliferation that produce a corrugated or cobblestone appearance, with or without mucosal hemorrhage and ulceration.

Other Cytology Specimens

- Liver, spleen, or lymph node aspirates
- Bone marrow aspirates and buffy coat smears of blood
- Abdominal or thoracic effusions
- Skin lesion impression smears
- Oculocentesis cytology

Histopathology

Biopsies of affected tissues reveal granulomatous inflammation, but organisms are usually sparse and do not stain well with H&E stain. Detection of organisms in biopsies may be facilitated by the use of special fungal stains such as periodic acid-Schiff (PAS), Gomori methenamine silver (GMS), or Gridley stain.

Culture

Most specimens for cytologic or biopsy identification of *Histoplasma* are also suitable for culture. The *Histoplasma* mycelial phase grows on Sabouraud's dextrose at room temperature in 7 to 10 days, and the yeast phase

grows on blood agar from 30°C to 37°C. Use a diagnostic laboratory instead of in-clinic culturing, because fungal growth is potentially infectious for humans and poses a biohazardous risk to personnel.

Treatment

Refer to the "Antifungal Therapy" section at the end of this chapter for specific treatment regimens and drug dosages.

- ***Itraconazole*** is the treatment of choice for histoplasmosis that is not immediately life-threatening. Treat for a minimum of 4 to 6 months and at least 1 to 2 months beyond clinical resolution.
- ***Itraconazole plus amphotericin B*** is preferred for treating severe, rapidly progressive infections, preferably using lipid-complexed amphotericin to allow higher doses with less toxicity. Combined therapy is followed by azole therapy alone for 2 to 4 months and at least 1 to 2 months beyond clinical resolution.
- ***Fluconazole*** may not be as effective as itraconazole, but it can be used for refractory ocular and neurologic infections because of its better penetration of the eyes and CNS.
- ***Ketoconazole*** is less effective than itraconazole (especially in cats), and it has more side effects; however, it can be used if other antifungal drugs are cost prohibitive for the owner. It also can be combined with amphotericin B.
- ***Corticosteroids*** can be used with antifungal therapy to reduce perihilar lymphadenopathy when it is causing significant tracheobronchial obstruction. Only use if needed, and do not use for prolonged periods because corticosteroids can worsen fungal infections or facilitate dissemination.

BLASTOMYCOSIS

Etiology

- *Blastomyces dermatitidis* is a dimorphic soil-dwelling fungus with a geographic distribution in the central, mid-Atlantic, and southern Great Lakes regions of the United States, especially areas bordering the Mississippi River and its tributaries and along the St. Lawrence River region of the United States and Canada (see Fig. 20-1). The organisms reside in sandy, acidic soil near water. Most infected dogs live within ¼ mile of water.
- Inhalation of airborne spores (conidia) is the primary source of infection and leads to mycotic pneumonia. In addition, focal skin infection can occur from direct cutaneous inoculation through a wound. In tissues the fungi become budding yeast. Extrapulmonary dissemination is common in blastomycosis, especially involving lymph nodes, skin, eyes, bones, and CNS (cats). The incubation period is 1 to 3 months.
- Dogs are considered highly susceptible to blastomycosis, and the canine infection rate in endemic areas is 10 times the human infection rate. Young (<5 years) male, large-breed dogs are infected most frequently, especially pointers, hounds, and other sporting breeds, probably because of increased exposure through outdoor activities. Blastomycosis is rare in cats.

Clinical Signs

Pulmonary and disseminated forms of infection are seen. Nonspecific signs of fever, anorexia, weight loss, and depression are common. Signs may be acute (days) or chronic (weeks to months).

Pulmonary Infection

Lung lesions are present in 85% of cases. Cough, tachypnea, and dyspnea are typical presenting signs. Respiratory manifestations can include the following:

- Diffuse interstitial pyogranulomatous pneumonia
- Perihilar tracheobronchial lymphadenopathy
- Alveolar infiltration and consolidation
- Solitary mediastinal or lung masses
- Pleural effusion

Disseminated Infection

Extrapulmonary dissemination is common in blastomycosis, especially to the peripheral lymph nodes (50% to 60% of cases), skin (40%), eyes (40%), bone (20%), and to a lesser extent CNS, male genitalia, oral cavity, nasal cavity, and abdominal viscera.

- ***Cutaneous:*** Solitary or multiple circumscribed, raised ulcerating pyogranulomas; fistulas that drain pus or bloody fluid; deep abscesses (cats); paronychia; and regional lymphadenopathy
- ***Ocular:*** Anterior uveitis, chorioretinitis, retinal detachment, panophthalmitis, lens rupture, cataracts, secondary glaucoma, and blindness
- ***Bone:*** Osteomyelitis of distal limbs, with lameness and adjacent soft tissue swelling
- ***CNS:*** Most often in cats as seizures, dementia, blindness, or ataxia
- ***Genital:*** Pyogranulomatous orchitis and epididymitis in 16% of intact male dogs; also prostatitis

Diagnosis

Consider blastomycosis on the basis of clinical signs in animals from endemic areas. The results of routine laboratory evaluations are variable and nonspecific. Radiographic findings in the pulmonary form are often highly suggestive of mycotic infection. Serology provides a presumptive diagnosis, but identification of *Blastomyces* organisms is necessary for definitive diagnosis, usually by cytology.

Hematology and Serum Chemistries

- Typical findings are neutrophilic leukocytosis, monocytosis, lymphopenia, and mild nonregenerative anemia.
- Serum chemistries are usually unremarkable except for mild hypoalbuminemia, hyperglobulinemia, and occasional hypercalcemia (10% of cases).

Diagnostic Imaging

Radiography, ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI) are useful for evaluating the lungs and suspected dissemination sites and for guiding collection of cytology and biopsy specimens.

Thoracic Radiography

- Diffuse interstitial infiltrate or nodular pattern (often miliary) in 70% of canine cases.
- Perihilar tracheobronchial lymphadenopathy (30% of canine cases).
- Less frequent findings are alveolar infiltrates, lobar consolidation, solitary lung masses, mediastinal masses, pleural effusion, and cavitary lesions.

Other Diagnostic Imaging

- Radiography can identify lytic bone lesions with variable periosteal proliferation, most often in the distal limbs.
- Ultrasonography can identify involvement of abdominal viscera, testes, and prostate.
- CT and MRI can identify CNS lesions.

Serology

Serology can provide a presumptive diagnosis of blastomycosis when repeated attempts to identify organisms by cytology have failed. The highest titers are seen in dogs with disseminated disease. The AGID test is most reliable (90% sensitivity and specificity). Complement fixation is not as reliable as AGID, but a titer of 1:32 or greater is suggestive of blastomycosis.

Cytology and Biopsy

Identification of *Blastomyces* organisms by cytology, biopsy, or culture provides a definitive diagnosis. The best site and method for procuring specimens depends on the location of the lesions.

- Cytologies most often diagnostic for blastomycosis include skin impression smears, lymph node aspirates, pulmonary cytology (tracheobronchial washing, bronchoalveolar lavage, fine-needle lung aspirate), and vitreal aspirates; however, any affected tissue can be sampled. Organisms are also found in fluid specimens such as urine, prostatic washes, cerebrospinal fluid (CSF), or pleural effusion. Any routine cytology stain can be used.
- *Blastomyces* in tissues appear as thick-walled, extracellular yeast bodies (5–20 µm) with broad-based budding.

▼ ***Key Point*** *Blastomyces* organisms are usually plentiful and easily identified in lesions by cytology; thus, cytology is the initial confirmatory test of choice.

- The inflammatory pattern in blastomycosis is pyogranulomatous (macrophages and non-degenerate neutrophils). Special stains such as PAS, GMS, and Gridley may be used to identify fungal organisms.

Culture

Specimens for culture can be collected in a similar manner as for cytology. Mycelial growth occurs on Sabouraud's dextrose agar at 37°C after 1 to 4 weeks, and yeast will grow on blood or brain-heart infusion agar at 25°C in 1 to 2 weeks. Use a diagnostic laboratory instead of in-clinic culturing because fungal growth is potentially infectious for humans and poses a biohazardous risk to personnel.

▼ ***Key Point*** Human blastomycosis infection can result from accidental inoculation of infective material from animal patients (e.g., needle-stick injury and cuts from contaminated surgical or necropsy instruments).

Treatment

Refer to the "Antifungal Therapy" section at the end of this chapter for specific treatment regimens and drug dosages.

- ***Itraconazole*** is the treatment of choice for blastomycosis that is not immediately life threatening and does not involve the CNS. Treat for at least 2 to 3 months and until 1 month beyond clinical resolution. The cure rate with itraconazole is 75%.
- ***Itraconazole plus amphotericin B*** is the treatment of choice for life-threatening, rapidly progressive infections, preferably using lipid-complexed amphotericin B to allow higher doses with less toxicity. Combination therapy is followed by an additional 2 months of azole therapy.
- ***Amphotericin B*** is also effective by itself. It has a more rapid onset of action than azole drugs, but it has the disadvantages of parenteral administration and nephrotoxicity. Lipid-complexed forms are best but expensive.
- ***Fluconazole*** is generally less effective and more expensive than itraconazole for blastomycosis, but it is indicated for refractory ocular, neurologic, and prostatic

infections because of its better penetration of these sites.

- ***Ketoconazole*** is less effective than itraconazole for treating blastomycosis (the response rate is less than 50%, the relapse rate is higher, the duration of therapy is longer, and toxicity is more frequent); however, ketoconazole can be used if other antifungal drugs are cost prohibitive for the owner. It also can be combined with amphotericin B.
- ***Ancillary treatment:*** Use appropriate topical ophthalmic treatment in animals with uveitis and monitor for secondary glaucoma (see Chapters 136 and 137). Castration is indicated in intact males with testicular or prostatic infection.

Prognosis

Treatment is successful in 75% of cases. Dogs that live through the first 10 days usually do well.

- Treatment failures are most likely in dogs with severe hypoxemic pulmonary disease, CNS involvement, or widespread dissemination involving three or more organ systems.
- Irreversible blindness is a frequent complication of ocular blastomycosis.
- Relapses can occur in up to 20% of apparently recovered cases after several months and up to a year or more. Fortunately, most of these relapses can be successfully re-treated.

COCCIDIOIDOMYCOSIS

Etiology

- Coccidioidomycosis ("valley fever") is caused by *Coccidioides immitis,* a soil-dwelling dimorphic fungus found in the dry, desert-like, lower Sonoran regions of the southwestern United States, Mexico, and Central and South America (see Fig. 20-1). In the soil, *Coccidioides* fungi grow mycelia during periods of rainfall, and then arthrospores form when the soil dries. These fungal spores then become airborne in dry, windy conditions.
- Infection occurs by inhalation of windblown spores. An infectious dose in dogs may be as few as 10 spores. The incubation period is 1 to 3 weeks. Cutaneous inoculation may occur, but rarely. In body tissues, *Coccidioides* forms large spherules (20–100 µm) that release hundreds of endospores. Young, male, medium and large outdoor dogs are most often affected. *Coccidioides* is not contagious.

Clinical Signs

Coccidioides can cause subclinical, pulmonary, or disseminated infection.

Subclinical Infection

Self-limiting, subclinical pulmonary infection is the most common outcome of natural infection in healthy animals.

Pulmonary Infection

Clinically apparent pulmonary coccidioidomycosis is characterized by acute or chronic granulomatous pneumonia and perihilar tracheobronchial lymphadenopathy, associated with cough, fever, malaise, and occasionally dyspnea.

Disseminated Infection

Extrapulmonary dissemination is usually chronic (months to years) and insidious. Fever, anorexia, lethargy, and weight loss are common. Bone involvement is most common in dogs, whereas skin lesions are the predominant finding in cats.

- ***Bones and joints:*** Chronic lameness associated with painful bone swellings (osteoproliferative bone reaction), head and neck pain
- ***Skin:*** Ulcerated nodules and draining fistulas, frequently over bone lesions
- ***Regional lymphadenopathy:*** Associated with bone and skin lesions
- ***Abdomen:*** Granulomatous lesions of spleen, liver, lymph nodes, omentum, or kidneys
- ***Heart and pericardium:*** Myocarditis, pericarditis, congestive heart failure
- ***CNS:*** Behavior changes, hyperesthesia, seizures, etc.
- ***Eyes:*** Uveitis, retinal detachment, blindness

Diagnosis

Consider coccidioidomycosis on the basis of clinical signs in animals from endemic areas. The results of routine laboratory evaluations are variable and nonspecific. The radiographic lesions in the lungs and bones are often highly suggestive of the disease. The presumptive diagnosis is based on clinical findings combined with serology. Identification of *Coccidioides* organisms is necessary for definitive diagnosis; however, the organisms are generally sparse and difficult to find in cytology or biopsy specimens, so serology is more sensitive. Cultures are biohazardous for humans and not routinely used.

Hematology and Serum Chemistries

Findings may include a variable leukocytosis, monocytosis, and mild nonregenerative anemia. Hyperglobulinemia and hypoalbuminemia are common in chronic cases.

Radiography

- Thoracic radiographs often show a diffuse or nodular pulmonary interstitial pattern and perihilar lym-

phadenopathy. In cases with cardiac involvement, pericardial effusion or pulmonary edema may be seen.
- Dissemination to bone is common in dogs, especially to the distal aspects of long bones, resulting in multifocal osteoproliferative and, less often, lytic lesions. The spine can also be involved.

Serology

A reasonably reliable presumptive diagnosis can be based on the detection of antibodies against *Coccidioides*. The tube precipitin test, which detects the early immunoglobulin M (IgM) response, and the complement fixation test, which detects the later and sustained immunoglobulin G (IgG) response, are the traditional serologic tests. The newer immunodiffusion (AGID) and enzyme-linked immunosorbent assay tests for detecting *Coccidioides*-specific IgM and IgG are more reliable.

- The early IgM response becomes positive 2 weeks post-exposure and persists for 4 to 6 weeks. However, in some dogs, IgM titers may persist for months and can be detected simultaneously with high IgG titers, usually indicating dissemination or recrudescence.
- The later IgG response is detected after 8 to 12 weeks. High IgG titers (≥1:64) usually indicate severe pulmonary or disseminated disease.

Polymerase Chain Reaction

A sensitive and specific polymerase chain reaction (PCR) for detecting *Coccidioides* DNA is expected to facilitate the diagnosis of this disease once the test becomes available for clinical use.

Cytology and Biopsy

Definitive diagnosis depends on identifying the large *Coccidioides* spherules (20–200 µm) in affected tissues using cytology or biopsy; however, spherules are often sparse and difficult to find. Lesions show pyogranulomatous inflammation.

Culture

Coccidioides can be cultured on routine fungal media; however, special facilities are required because *Coccidioides* spores are a serious biohazard for humans and pose a substantial risk to laboratory personnel.

Treatment

Refer to the "Antifungal Therapy" section at the end of this chapter for specific treatment regimens and drug dosages.

▼ ***Key Point*** Disseminated coccidioidomycosis is difficult to cure, especially when bones are involved, and lifelong azole therapy may be required to prevent relapses.

- Treat with one of the oral azoles (ketoconazole, itraconazole, or fluconazole) for at least 8 months and a minimum of 4 months beyond clinical resolution. Use fluconazole to treat animals with CNS involvement.
- Amphotericin B lipid complex is indicated for fulminant infections and animals that do not tolerate azole drugs.
- Lufenuron, a chitin synthesis inhibitor licensed for control of fleas in dogs and cats, does not appear to be an effective antifungal agent despite initial anecdotal reports.

CRYPTOCOCCOSIS

Cryptococcosis is the most common systemic fungal disease of cats and is more prevalent in cats than in dogs.

Etiology

- Cryptococcosis is caused by *Cryptococcus neoformans*, a saprophytic yeast found in many regions of the world and throughout North America or by *C. gattii* in Australia and various subtropical regions. High concentrations of *Cryptococcus* can be found in pigeon droppings and in areas where pigeons and other birds roost. Infection is acquired by inhalation of the yeast organisms or basidiospores from the environment.
- The organisms are budding yeasts (4 to 7 µm) that possess a uniquely prominent polysaccharide capsule. This thick capsule is essential to the pathogenicity of *Cryptococcus* because it inhibits plasma cell function, phagocytosis, leukocyte migration, and complement. The capsule also allows the organisms to stand out in stained cytology preparations for easy identification and is the basis for the cryptococcal capsular antigen diagnostic test (see the related "Diagnosis" section).
- Dissemination from the nasal cavity can occur by hematogenous spread or by direct extension through the cribriform plate to the CNS or through the nasal bones to the paranasal soft tissues and skin.

Clinical Signs

Cryptococcosis can cause localized nasal infection or disseminated infection. Anorexia and depression are common, but fever occurs infrequently (<25% of the cases); in fact, temperatures exceeding 37°C inhibit *Cryptococcus*.

▼ ***Key Point*** In cats, *Cryptococcus* has a predilection for the nasal cavity, where the inhaled organisms initially deposit and cause granulomatous rhinitis and sinusitis.

Nasal Infection

Chronic upper respiratory signs are seen in up to 80% of cats with cryptococcosis and up to 50% of dogs.

- Common signs include sneezing, sniffling, and unilateral or bilateral mucopurulent nasal discharge, which may contain blood.
- Obstructing mucinous or granulomatous polyp-like masses often occur in the nostrils or nasal passages of cats and obstruct nasal airflow.
- Firm swellings over the bridge of the nose may cause nasal or facial deformity.
- Nasopharyngeal masses may cause stertorous breathing, inspiratory dyspnea, and voice change.

Disseminated Infection

▼ ***Key Point*** The preferred sites for cryptococcal dissemination are the skin, CNS, and eyes.

- ***Skin and subcutis***—(40% of cats; 20% of dogs) can have firm nodules that rapidly enlarge and then ulcerate and drain, mostly in the head and face area, often near the nostrils and planum nasale.
- ***CNS***—(25% of cats; 75% of dogs) hematogenous spread or local extension through the cribriform plate results in diffuse or mass-like granulomatous meningoencephalitis or myelitis. Signs may include behavior changes, seizures, circling, head-pressing, blindness, dementia, ataxia, paresis, head tilt, and cranial nerve (CN) deficits (CN II, VII, VIII).
- ***Eyes***—(25% of cats; 40% of dogs) often accompanies CNS dissemination; may include granulomatous chorioretinitis, exudative retinal detachment, optic neuritis, anterior uveitis, and blindness.
- ***Lungs***—Up to 50% of cats and dogs have subclinical cryptococcal lung infection at necropsy, but overt signs of lower respiratory tract disease are uncommon, especially in cats.
- ***Other dissemination sites***—May include peripheral lymph nodes (especially the submandibulars), pharynx and oral cavity, bone marrow, kidneys (30% of patients have renal granulomas at necropsy), liver, spleen, heart, and skeletal muscle.

Diagnosis

Consider cryptococcosis on the basis of clinical signs, especially in cats. The results of routine laboratory evaluations and radiography are variable and nonspecific. Serology provides a presumptive diagnosis, but identification of *Cryptococcus* organisms by cytology, biopsy, or culture is required for definitive diagnosis. In most cases cytology is a quick and easy way to confirm the diagnosis.

Hematology

The complete blood count is usually normal, except for occasional neutrophilia or eosinophilia.

Radiography

Nasal radiographs and nasal CT may show increased soft tissue density within the nasal cavity and frontal sinuses, turbinate destruction, and nasal bone destruction or expansion. Thoracic radiographs may show diffuse or nodular interstitial pulmonary infiltrates.

Serology

Serologic testing provides a presumptive diagnosis based on detection of cryptococcal capsular antigen in serum, CSF, or urine using latex agglutination. This is an antigen test that indicates the presence of cryptococcal organisms; it is not a test for an antibody response as with other fungal serologic tests.

- Positive titers in infected cats range from 1:10 to 1:100,000, with a median of 1:1,000.
- Commercial capsular antigen test kits have good sensitivity and specificity; however, false negatives occasionally occur in localized (non-disseminated) disease.
- False positives are rarely caused by interfering substances, such as in patients treated recently with hetastarch and in CSF contaminated with talc particles from latex gloves.
- The capsular antigen titer can also be used to monitor treatment response, a persistent titer indicating unresolved infection.

Cytology and Biopsy

Definitive diagnosis requires identification of the *Cryptococcus* organisms in cytologies (e.g., nasal exudate, CSF, skin exudate or impressions, lymph node aspirates, oculocentesis specimens, or urine sediment) using Gram's, PAS, new methylene blue, DiffQuik, or Wright-giemsa stains or in biopsies using mucicarmine, H&E, PAS, GMS, or Gridley stains. Cryptococcal yeast are usually numerous and easy to identify by their characteristic budding and prominent unstained capsule.

Culture

Cryptococcus can be cultured on Sabouraud's dextrose agar from the same specimen sources as cytology; however, growth can take from a few days up to 6 weeks, thus limiting the diagnostic usefulness of cultures.

Treatment

See the following section on "Antifungal Therapy" for dosages and additional details.

- ***Fluconazole*** is the treatment of choice for cryptococcosis. It is effective but costly. It has excellent penetration into the CNS and eyes, which are the preferred cryptococcal dissemination sites.
- ***Itraconazole*** is effective in most cases. It is slightly less effective, but more affordable than fluconazole.
- ***Ketoconazole*** is not as effective as either of the other azole drugs, and side effects are more frequent.
- ***Amphotericin B*** is highly effective for cryptococcosis, but it is inconvenient (parenteral route) and has more adverse effects (especially nephrotoxicity). Oral flucytosine can be given concurrently.

▼ ***Key Point*** Monitor treatment response with the cryptococcal capsular antigen test.

- Continue azole therapy for 6 to 12 months and at least 2 months beyond clinical resolution. The titer should become negative or drop to a low residual titer level in response to treatment. Reevaluate the capsular antigen test at 3 and 6 months after discontinuing treatment to assess for relapse.

Prognosis

- The prognosis is generally good for cats without CNS involvement. Cats with CNS involvement and dogs with any form of the disease have a guarded prognosis.
- Progressive decrease in the capsular antigen titer tenfold over 2 months is a good prognostic indicator.
- Cats with concurrent feline leukemia virus or feline immunodeficiency virus infection are less likely to respond to treatment.

UNCOMMON MYCOTIC INFECTIONS

A variety of opportunistic deep mycotic infections can occasionally lead to disseminated infection. These are summarized in Table 20-1. Many of these are described in greater detail in Chapter 40.

ANTIFUNGAL THERAPY

Most systemic mycotic infections in dogs and cats are successfully treated with an oral azole drug, parenteral amphotericin B, or a combination of both. Antifungal drugs are expensive, the treatment protocols are prolonged, and adverse side effects are considerable.

The duration of antifungal therapy is variable but should extend at least 1 to 2 months beyond clinical resolution. Relapses can occur 1 year or more after therapy is discontinued. If recrudescence occurs, reinstitute a full course of therapy or switch to another drug.

▼ ***Key Point*** The oral triazole, itraconazole, is the single-agent treatment of choice for most systemic fungal infections that are not immediately life threatening.

Fluconazole has the best penetration of the CNS, eyes, and prostate and thus may be the preferred treatment when these areas are involved, especially in cryptococcosis.

▼ ***Key Point*** Regardless of the treatment regimen, the unpredictable response in the disseminated forms of mycotic disease requires a guarded prognosis, especially if the CNS is involved.

Amphotericin B

Amphotericin B is a potent, broad-spectrum antifungal agent with rapid onset of action, but it must be given parenterally and is frequently nephrotoxic.

▼ ***Key Point*** The most effective treatment for severe fungal infections is lipid-complexed amphotericin B combined with an oral azole drug.

Indications

- As a single drug, amphotericin B is most effective for treatment of blastomycosis and histoplasmosis. It is moderately effective for coccidioidomycosis and cryptococcosis and occasionally effective for systemic candidiasis, zygomycosis, and pythiosis.
- In life-threatening, rapidly progressing cases of blastomycosis and histoplasmosis, combine amphotericin B for its rapid onset of action with an azole drug for an initial 2- to 4-week induction phase of therapy and then follow with long-term azole therapy.
- Amphotericin B is preferred over oral azoles if oral absorption might be impaired by vomiting or severe GI disease (e.g., intestinal histoplasmosis).

Pharmacology

Amphotericin B (AMB) is a polyene antibiotic for IV use that has both fungicidal and fungistatic actions. It binds to ergosterol in the fungal cell membrane, damaging the cell membrane and leading to fungal cell death. AMB also has beneficial stimulatory effects on host macrophages.

- AMB is not absorbed orally, so it must be given parenterally.
- AMB distributes well into most tissues, except for the CNS and eyes.
- AMB is cumulatively nephrotoxic, and azotemia during the course of therapy is common (see the "Adverse Effects" section).

Table 20-1. UNCOMMON DISSEMINATED MYCOTIC INFECTIONS

Disease	Etiology	Source	Location	Clinical Signs	Diagnosis	Treatment
Aspergillosis	*Aspergillus* spp.	Inhalation	Worldwide	Fever, draining tracts, lymphadenopathy, uveitis, chorioretinitis, dissemination to bone, kidney, liver, spleen, CNS, etc.	German shepherds; cytology (septate hyphae); culture	Itraconazole plus ABLC
Sporotrichosis	*Sporothrix schenckii*	Puncture wounds, bites, scratches	Worldwide	Draining skin/subcutis pyogranulomas; lymphadenopathy; dissemination to abdomen, lung, eyes, CNS, etc.	Cats > dogs; cytology (oval or cigar-shaped yeast); culture	Itraconazole (note: zoonotic considerations)
Pythiosis	*Pythium insidiosum*	Waterborne (warm); cutaneous or GI inoculation	Gulf Coast U.S., South America, Southeast Asia, Australia	*Cutaneous form:* Non-healing wounds, invasive ulcerated and draining skin/subcutis masses, nasopharyngeal lesions (cats) *GI form:* Chronic vomiting and diarrhea, GI bleeding, transmural granulomatous GI masses, GI obstruction, mesenteric lymphadenopathy	Dogs > cats; young, male large-breed working dogs; eosinophilia, anemia, hyperglobulinemia; abdominal imaging (masses); serum ELISA; biopsy (GMS+ stain, broad poorly septate hyphae) with culture, PCR, and immunohistochemistry	Aggressive surgical resection followed by itraconazole plus terbinafine
Lagenidiosis	*Lagenidium* spp.	Waterborne (warm); cutaneous inoculation (damaged skin sites)	Gulf Coast and southeast U.S.	Multifocal skin/subcutis nodular lesions with ulcers and draining tracts, lymphadenopathy, hind limb edema; lesions in aorta, vena cava, lung, mediastinum	Young large-breed dogs; biopsy (GMS+ stain, broad poorly septate hyphae) with culture, PCR, and immunohistochemistry	Aggressive surgical resection followed by itraconazole plus terbinafine
Zygomycosis	*Basidiobolus* spp.; *Conidiobolus* spp.	Cutaneous inoculation (damaged skin sites); inhalation	Ubiquitous saprophytes	*Conidiobolus:* Ulcerative nasal, nasopharynx, and palate lesions; multifocal skin and subcutis draining nodules *Basidiobolus:* ulcerative draining skin lesions with GI and lung lesions	Biopsy (GMS+ stain, broad poorly septate hyphae) with culture	Aggressive surgical resection followed by itraconazole
Phaeohyphomycosis	Numerous (see Chapter 40)	Traumatic implantation	Ubiquitous saprophytes	Granulomas of skin, subcutis, nasal, CNS, etc.	Biopsy (septate hyphae with melanin)	Surgical resection or itraconazole
Candidiasis	*Candida albicans*	Commensal mucosal yeasts; proliferate with immunosuppression, mucosal damage	Ubiquitous commensals	Fever, neutropenia, non-healing oral and GI mucosal ulcers, skin lesions, myositis, osteomyelitis, nephritis, microabscesses, signs referable to organs affected	Cytology (oval yeasts); culture; biopsy of tissue invasion	Itraconazole plus ABLC; correct underlying predisposing factors

ABLC, amphotericin B lipid complex; CNS, central nervous system; ELISA, enzyme-linked immunosorbent assay; GI, gastrointestinal; GMS, Gomori methenamine silver stain; PCR, polymerase chain reaction.

- Avoid concurrent use of other potentially nephrotoxic medications with AMB.
- Always follow the package insert instructions for reconstituting and handling AMB products.
- AMB is available in its original formulation as deoxycholate suspension and in three newer lipid-based and liposomal formulations.

▼ ***Key Point*** Lipid-based formulations of amphotericin B minimize the risk of nephrotoxicity, thus allowing higher doses and increased efficacy.

Dosage and Administration

Amphotericin B protocols are designed as a series of three infusions per week until a cumulative dose is achieved, with interruption of therapy if azotemia occurs. Amphotericin B therapy is combined and followed with long-term oral azole therapy in most cases.

Amphotericin B Deoxycholate

- ***IV in dogs:*** Give amphotericin B (Fungizone, ER Squibb) at dosages of 0.5 to 1.0 mg/kg, IV, q48h (3 times weekly), to a total cumulative dose of 6 to 10 mg/kg. Each dose can be given as a 10-minute bolus; however, infusion in 5% dextrose over 2 to 6 hours is preferred to reduce nephrotoxicity (see "Renoprotective Measures").
- ***IV in cats:*** Give amphotericin B at dosages of 0.25 to 0.50 mg/kg, IV, q48h (3 times weekly), to a total cumulative dose of 4 to 8 mg/kg. Infuse as for dogs.
- ***Subcutaneous protocol:*** A daily dose of 0.5 to 0.8 mg/kg is added to 0.45% saline with 2.5% dextrose solution (400 ml for cats, 500 ml for dogs <20 kg, and 1,000 ml for dogs >20 kg) then given SC q48h (3 times weekly) to a total cumulative dose of 10 to 20 mg/kg.
- ***Combination protocol:*** When amphotericin B is used with itraconazole or other azole, use the low end of the daily and cumulative dosage ranges for amphotericin B.

Lipid-Complexed Amphotericin B

- Lipid-complexed amphotericin B reduces the risk of nephrotoxicity up to 10-fold. Preferential uptake of lipid complexes by phagocytic cells delivers high concentrations of drug to target sites of inflammation and organs such as the liver, spleen, and lung, while renal uptake is decreased; thus, higher doses can be used with less risk of renal injury.
- Formulations include lipid complexed (Abelcet, Enzon), colloidal dispersion (Amphotec, Sequus), and liposome encapsulated (AmBisome, Fujisawa). Of these, amphotericin B lipid complex (ABLC) has been used most often in dogs and cats and is the least expensive.
- ***For dogs:*** Give ABLC at dosages of 2 to 3 mg/kg, IV, q48h (3 times weekly), for a total of 9 to 12 treatments to a total cumulative dose of 24 to 27 mg/kg. Dilute in 5% dextrose to a concentration of 1 mg/ml and infuse over 1 to 2 hours.
- ***For cats:*** Give ABLC at 1 mg/kg, IV, q48h (3 times weekly), for a total of 12 treatments to a total cumulative dose of 12 mg. Dilute and infuse as for dogs.

Renoprotective Measures

- Evaluate a urinalysis and renal function (serum creatinine, blood urea nitrogen [BUN]) before initiating AMB therapy, and monitor these frequently during treatment (once or twice weekly). In general, the earliest evidence of a renal effect is decreased urine-specific gravity. This is followed by abnormal numbers of renal cells and casts in fresh urine sediment, and eventually azotemia may develop.

▼ ***Key Point*** If BUN exceeds 50 mg/dl or serum creatinine exceeds 2.5 mg/dl during amphotericin therapy, suspend treatment until azotemia resolves. Azotemia is reversible in most cases.

- Always ensure that the patient is well hydrated prior to each dose of AMB.
- Consider the slow IV infusion method whenever possible. Give AMB diluted in 250 to 500 ml of 5% dextrose solution by slow IV infusion over a period of 2 to 6 hours.
- Other measures used less often to enhance renal blood flow and glomerular filtration rate include pretreatment sodium diuresis (0.9% sodium chloride, 10 to 20 ml/kg, IV, over 1 to 3 hours prior to AMB); concurrent administration of mannitol (0.5–1.0 g/kg, IV); furosemide (2 mg/kg, IV); or dopamine (3 to 10 µg/kg/min, by constant-rate IV infusion).

Adverse Effects

- The major adverse effect of AMB is dose-related nephrotoxicity caused by a combination of reduced renal blood flow (arteriolar vasoconstriction) and direct renal tubular injury. Although there is considerable individual variation in susceptibility to nephrotoxicity, most animals treated with AMB show some degree of renal dysfunction and azotemia. Nephrotoxicity is less of a risk with lipid-complexed AMB but still is a possibility.
- Other side effects of AMB include thrombophlebitis (local irritant effect), fever, anorexia, nausea or vomiting, hypokalemia, hypomagnesemia, distal renal tubular acidosis, cytopenias, cardiac arrhythmias, and perivascular irritation if extravasated. For infusion-associated nausea and fever, pretreat with an antihistamine such diphenhydramine.
- Local irritation and sterile abscesses occasionally occur with the subcutaneous protocol, especially if the AMB concentration is >20 mg/L.

Oral Azole Drugs

The azoles include the imidazole drug, ketoconazole, and the triazole drugs, itraconazole and fluconazole. These fungistatic drugs inhibit the biosynthesis of ergosterol in fungal cell membranes, thus inhibiting growth.

▼ ***Key Point*** The initial onset of clinical response to azole therapy has a lag time of up to 2 weeks.

Ketoconazole and itraconazole require an acidic environment for maximal absorption; the concurrent use of antacid drugs impairs absorption; and bioavailability is increased when taken with food. Fluconazole is not affected by gastric pH or by feeding. Fluconazole readily passes the blood-brain, blood-prostate, and blood-ocular barriers and thus achieves high concentrations in CSF, prostatic, and ocular fluids, as well as urine. Ketoconazole has the most dose-related side effects, and itraconazole has the least.

Itraconazole

Itraconazole is the initial treatment of choice for most dogs and cats with histoplasmosis, blastomycosis, cryptococcosis, and coccidioidomycosis if the infection is not immediately life threatening and the CNS is not involved. Itraconazole is more effective than ketoconazole with fewer side effects, but it is more costly.

Pharmacology

- Itraconazole requires an acidic pH for optimal absorption; thus, avoid concurrent use of antacids. Bioavailability is increased when given with food or cola beverages. Oral suspension is absorbed more consistently than capsules, especially in cats.
- Itraconazole does not penetrate the CNS, eyes, prostate, or urine as well as fluconazole does. Despite this, itraconazole is effective for treating most cases of fungal meningitis, uveitis, and prostatitis.

Dosage and Administration

The lag time between start of the drug and clinical response is 1 to 2 weeks. To shorten this, use a higher loading dose for the first 3 to 5 days. Sporanox oral suspension (10 mg/ml) is absorbed better than capsules, especially in cats. Treat for 1 to 2 months beyond clinical resolution.

- ***For dogs:*** Give itraconazole (Sporanox, Janssen), at dosages of 5 to 10 mg/kg, PO, q24h or divided bid, with food.
- ***For cats:*** Give itraconazole at dosages of 10 mg/kg, PO, q24h or divided BID, with food.
- ***Combination protocol:*** In animals with severe disease, combine amphotericin B with itraconazole as initial therapy for the first 2 to 4 weeks, then follow with long-term itraconazole therapy.

Adverse Effects

- Itraconazole causes less liver and GI side effects than ketoconazole, and it does not affect adrenal and testicular steroidogenesis. Anorexia occurs occasionally. Mild subclinical elevation of serum liver transaminases occurs in half the cases but does not usually require modifying treatment unless accompanied by anorexia, depression, and vomiting.
- Overt hepatotoxicity is rare, but if it occurs, stop treatment until appetite returns and liver enzymes return to normal (usually 2 weeks), then reinstitute treatment at one-half dose and monitor serum liver enzymes every 2 weeks.
- Cutaneous vasculitis with localized ulcerative dermatitis and limb edema is a rare side effect of itraconazole. This appears to be dose dependent and resolves when the drug is discontinued.

Fluconazole

The major advantage of fluconazole over other azoles is its excellent penetration of the CNS for treatment of fungal meningitis. It also is well absorbed on an empty stomach or in anorexic animals. The disadvantage of fluconazole is that it is expensive.

▼ ***Key Point*** Fluconazole is primarily indicated for mycotic infections of the CNS or eye that are refractory to itraconazole, and it is specifically indicated for cryptococcosis.

Dosage and Administration

Treat for 1 to 2 months beyond clinical resolution. Fluconazole is excreted by the kidney; thus, reduce the dose or use an alternative drug in animals with renal insufficiency.

- ***For dogs:*** Give fluconazole (Diflucan, Pfizer) at dosages of 2.5 to 5.0 mg/kg, q12–24h, PO or IV. Use twice the recommended daily dosage for the first day as a loading dose.
- ***For cats:*** For CNS involvement in cats, give fluconazole at dosages of 10 to 15 mg/kg, q12–24h, PO or IV, or 50 mg total dose, q12–24h.

Adverse Effects

Adverse effects are infrequent but can include GI intolerance, hepatotoxicity, and cutaneous eruption.

Ketoconazole

Ketoconazole has been used successfully to treat histoplasmosis, blastomycosis, and coccidioidomycosis when the more effective antifungal drugs are cost prohibitive for the owner. It is less effective against *Cryptococcus*. Ketoconazole is not usually effective against ocular and CNS mycoses.

Pharmacology

- Ketoconazole depends on hepatobiliary metabolism and excretion, and it is distributed widely except in the CNS, eye, prostate, and testes.
- Acidity is required for optimal absorption of ketoconazole; thus, avoid concurrent use of drugs such as H_2 blockers that inhibit gastric acid secretion.
- Bioavailability is increased and nausea and vomiting are minimized when ketoconazole is given with food.

Dosage and Administration

The oral dosage of ketoconazole (Nizoral, Janssen), ranges from 10 to 30 mg/kg/day. Divide this total daily dose into two or three doses for better GI tolerance. Give with food. Continue ketoconazole for at least 1 to 2 months beyond clinical resolution.

- ***For dogs:*** Give 10 to 15 mg/kg, q12h, PO with food.
- ***For cats:*** Give 5 to 10 mg/kg, q12h, PO with food, or a total dose of 50 mg, q24h. Cats generally are more susceptible to the side effects of ketoconazole. If tolerance is a problem in a cat, administer a dosage of 20 mg/kg on alternate days or switch to a different drug.
- ***Combination protocol:*** For severe infections, use amphotericin B in combination with ketoconazole for the first few weeks or use itraconazole.

Adverse Effects

- The most common immediate side effects of ketoconazole are anorexia, vomiting, and diarrhea. Minimize these GI side effects by dividing the daily dose and administering the drug with food.
- Longer-term side effects may include hepatotoxicity (hepatomegaly, elevated serum liver enzymes, icterus), weight loss, and haircoat changes (lightening of color, alopecia). Because of hepatic effects, it is advisable to monitor serum liver enzymes monthly during treatment. The liver, GI, and haircoat reactions are usually reversible with reduction in dose.
- Ketoconazole inhibits adrenal and testicular steroidogenesis. In dogs, but not cats, ketoconazole diminishes serum testosterone and cortisol while increasing serum progesterone. Ketoconazole is embryotoxic and teratogenic and thus should not be used in pregnant animals.

Newly Emerging Azole Drugs

A new generation of triazole antifungal drugs with greater potency and broader spectrum of activity is being developed for resistant fungal pathogens in humans. These drugs have not yet had clinical evaluation for treatment of mycotic infections in dogs and cats. New triazole drugs are costly, but they will likely have a future role for treatment of fungal infections in dogs and cats that are refractory to other available treatments.

Voriconazole

Voriconazole (Vfend, Pfizer) is a derivative of fluconazole with greater potency and broader spectrum of activity against many fungal pathogens, including invasive aspergillosis. It has excellent oral and IV bioavailability.

Posaconazole

Posaconazole (Noxafil, Schering-Plough) is a derivative of itraconazole with greater potency and broader spectrum of activity against aspergillosis and molds.

Ravuconazole

Ravuconazole (Bristol-Myers Squibb) is a fluconazole derivative with extended half-life.

Flucytosine

Flucytosine (Ancobon, Roche) is an antimitotic, antifungal drug used exclusively for its synergism with amphotericin B in the treatment of cryptococcosis. Flucytosine is most useful for CNS involvement, because it attains 60% to 80% of serum concentration in CSF. Use this drug only in combination with amphotericin B because fungal resistance develops rapidly if it is used alone.

- The dosage in dogs and cats is 25 to 50 mg/kg, PO, q6–8h.
- Side effects are common, including anorexia, vomiting, diarrhea, cytopenias caused by bone marrow suppression, and mucocutaneous drug eruptions (in dogs).

Terbinafine

Terbinafine (Lamisil, Sandoz) is an allylamine drug that blocks synthesis of ergosterol in the fungal cell membrane. The main indication is for treatment of dermatophytosis and cutaneous fungal infections. It has not been well evaluated in systemic mycoses of dog and cats. Terbinafine (5 to 10 mg/kg, PO, q24h) combined with itraconazole has reportedly been beneficial in some dogs and cats with pythiosis and lagenidiosis (see Chapter 40). Potential side effects include GI, hepatic, and cutaneous reactions.

Chitin and Glucan Inhibitors

These drugs inhibit the synthesis of either chitin or beta-glucan, two structural components of the cell walls of fungi that are not found in mammalian cells.

- ***Chitin inhibitors*** such as the nikkomycins and lufenuron have a limited spectrum, but they have been of interest for treatment of coccidioidomycosis. However, Lufenuron (Program, Novartis), a chitin synthesis inhibitor licensed for monthly flea control in dogs and cats, has not been an effective antifungal

agent for *Coccidioides* and other systemic mycoses despite initial anecdotal reports of its use in dogs.

- ***Beta-glucan inhibitors*** include echinocandins and pneumocandins, for example, caspofungin (Cancidas, Merck), micafungin, and anidulafungin. These are potent broad-spectrum antifungal drugs with activity against *Aspergillus, Candida,* and *Pneumocystis carinii.* These agents are very costly and considered investigational only at this time. Future indications for use of these drugs in dogs and cats will need to be determined.

PREVENTION

Because the principal source of systemic mycotic infection is airborne fungal elements from the soil, there is no practical means of prevention in endemic areas. High concentrations of *Histoplasma* can be found in chicken and bat excreta, and *Cryptococcus* is found in high concentrations in pigeon excreta; thus, exposure to these sources should be avoided. Systemic mycoses are not contagious diseases between animals.

Although humans can be infected from the same environmental point sources as animals, zoonotic transmission from animals to humans does not occur except very rarely by direct inoculation of an open wound with infected material from an animal. Vaccination for these mycoses is not available.

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Chapter 21

Toxoplasmosis and Other Systemic Protozoal Infections

Robert G. Sherding

The protozoa that infect dogs and cats can be classified broadly into those that disseminate and cause systemic disease and those that primarily live in the intestinal tract. This chapter describes toxoplasmosis, the most important systemic protozoal infectious disease in North America, and other emerging systemic protozoal infections—neosporosis, hepatozoonosis, and leishmaniasis. These and other systemic protozoal infections are summarized in Table 21-1, including trypanosomiasis, babesiosis, cytauxzoonosis, encephalitozoonosis, acanthamebiasis, and pneumocystosis.

Protozoa that parasitize erythrocytes, such as *Babesia* spp. and *Cytauxzoon felis,* are discussed in Chapter 22. Enteric protozoal infections (coccidiosis, giardiasis, tritrichomoniasis, amebiasis, and balantidiasis) are discussed in Chapter 69.

TOXOPLASMOSIS

Etiology

Toxoplasma gondii is an obligate intracellular protozoan parasite with worldwide distribution. The feline species is the definitive host for this coccidium, but most warm-blooded animals can be infected as intermediate hosts, including dogs and humans. Only cats complete the coccidian life cycle with intestinal replication and passage of oocysts in the feces.

- Serologic surveys estimate that over 30% of cats and humans are seropositive and presumed infected.
- Seroprevalence in cats increases with age, and it is higher in male and domestic shorthaired cats.

Routes of Transmission

Warm-blooded vertebrates can be infected by ingestion of any of the three life stages of the parasite (see the next section) or transplacentally.

Ingestion of Tissue Cysts

Cats are mainly infected through the ingestion of meat and animal tissues (carnivorism) that contain dormant *Toxoplasma* cysts (bradyzoites). Sources include uncooked meat (or meat scraps scavenged from garbage) or hunted prey (mice, birds).

- Ingestion of raw or undercooked meat (especially pork) is an important source of toxoplasmosis in dogs and humans.
- Ingestion of tachyzoites passed in milk can cause lactogenic infection in nursing kittens. Ingestion of tachyzoites in raw (unpasteurized) milk, especially from goats, is a rare source of infection.

Ingestion of Fecal Oocysts

Food, water, and soil contaminated with cat feces containing sporulated *Toxoplasma* oocysts are potentially important sources of infection for intermediate hosts such as humans, dogs, livestock, and rodents.

- Compared with carnivorous feeding, this is a relatively minor source of infection in the primary host, the cat.
- Oocysts can be transported from defecation sites in soil by cockroaches, flies, and earthworms.

Transplacental Infection

When a pregnant animal or human becomes infected during gestation, *Toxoplasma* tachyzoites can cross the placenta and infect the unborn fetus, resulting in severe or fatal disease (see under "Public Health Considerations").

- For this reason, toxoplasmosis has major public health significance in humans.
- In dogs and cats, congenital toxoplasmosis is uncommon, but it is a potential cause of abortion, stillbirth, and neonatal mortality.

Stages of Infection

The three stages of *Toxoplasma* infection are (1) intestinal replication (cats only), (2) acute dissemination and intracellular replication, and (3) chronic tissue encystment.

Table 21-1. SYSTEMIC PROTOZOAN INFECTIONS OF THE DOG AND CAT

Diseases	Etiology (Source)	Endemic Locations	Clinical Signs	Diagnosis	Treatment
Leishmaniasis	*Leishmania infantum* (sand fly vector, bloodborne)	Endemic in North American foxhounds, Mediterranean region, Central and South America, Asia, Africa	*Disease primarily in dogs:* Chronic diffuse skin hyperkeratosis (dry scaling), dry brittle haircoat, skin nodules, mucocutaneous ulcers, fever, muscle atrophy, weakness, cachexia, anorexia, inactivity, vomiting, diarrhea, lymphadenopathy, splenomegaly, uveitis, conjunctivitis, bleeding (epistaxis, melena), glomerulonephritis, polyarthritis	*General:* Origin from endemic country or U.S. foxhound kennel; hyperglobulinemia, hypoalbuminemia, proteinuria, azotemia, elevated serum liver enzymes, anemia *Specific:* —Identify organisms by cytology (e.g., bone marrow) —PCR assay —*Serology:* Not as sensitive or specific	*Caution:* Zoonotic (indirectly) *See text for dosages* —Sodium stibogluconate (from CDC) —Meglumine antimonite —Allopurinol —Amphotericin B *Prognosis:* Fair to good for remission but poor for cure
American trypanosomiasis (Chagas disease)	*Trypanosoma cruzi* (reduviid "kissing" bug vector, bloodborne)	Southern U.S. (rarely), Central and South America	*Disease primarily in dogs:* Acute myocarditis (fever, weakness, sudden collapse, fatal tachyarrhythmias), chronic cardiomyopathy (after 1–3 years, heart failure, ascites, pleural effusion, edema), lymphadenopathy, splenomegaly, meningoencephalitis	*General:* Endemic region, abnormal cardiac evaluations (radiography, ECG, echocardiography) *Specific:* —Identify organisms in blood (direct or buffy coat smear) or lymph node aspirates —*Serology:* Exposure or active —PCR assay	*Caution:* Zoonotic (indirectly) *Investigational per CDC:* —Nifurtimox (Lampit, Bayer): 2–7 mg/kg POq6h for 3–5 mo —Benznidazole (Ragonil, Roche): 5 mg/kg PO q24h for >2 mo *Prognosis:* Good in acute cases; poor in chronic cases
Hepatozoonosis	*Hepatozoon americanum* (U.S only) (tickborne), *Hepatozoon canis* (worldwide) (tickborne)	U.S. (Gulf Coast states, Texas, Oklahoma), Brazil, Europe, Asia, Africa	*Disease primarily in dogs:* Episodic fever, cachexia, chronic myositis and periosteal bone proliferation (reluctance to move, general muscle pain, atrophy), bloody diarrhea, ocular discharge	*General:* Endemic region, mild anemia, severe neutrophilic leukocytosis, widespread periosteal bone proliferation *Specific:* Identify organisms in blood smear (in WBC) or in muscle biopsy (most reliable test)	*For H. americanum* (see text): —Clindamycin —Trimethoprim-sulfadiazine —Pyrimethamine —Decoquinate *For H. canis* (see text): —Imidocarb dipropionate *Prognosis:* Good for remission but poor for cure
Babesiosis	*Babesia canis, Babesia gibsoni,* etc. (tick vector, bloodborne)	*Dog: B. canis, B. gibsoni* (U.S. and worldwide) *Cat: B. felis,* etc. (Africa, Asia, South America)	Hemolytic anemia (pallor, depression, weakness, jaundice, hemoglobinuria, fever, splenomegaly), weight loss, subclinical carrier	*General:* Regenerative anemia (often Coombs' positive), thrombocytopenia *Specific:* —Identify organisms in Giemsa-stained smears of capillary blood (from ear or toenail) or splenic aspirate —*Serology:* IFA titer > 1:80 is positive —PCR assay	*Dogs:* —Imidocarb dipropionate (Imizol, Glaxo Wellcome): 5.0–6.6 mg/kg SC or IM, two doses 14 days apart —Phenamidine isethionate (Oxopirvedine, Merial): 15 mg/kg SC q24h × 2 days —Diminazene aceturate (Berenil 10%, Ganaseg): 3.5 mg/kg IM once, then repeat in 14 days

Table 21-1. SYSTEMIC PROTOZOAN INFECTIONS OF THE DOG AND CAT—cont'd

Diseases	Etiology (Source)	Endemic Locations	Clinical Signs	Diagnosis	Treatment
					Cats: —Primaquine phosphate: 0.5 mg/kg IM once *Prognosis:* Good but relapses are common
Cytauxzoonosis	*Cytauxzoon felis* (tick vector, blood-borne)	U.S. (south-central and southeastern states)	*Disease in cats only:* Anorexia, depression, high fever, anemia, jaundice, congestion and edema (of lungs, spleen, liver), shock, death in less than 1 week	*General:* Free-roaming in a wooded area *Specific:* —Identify organism in blood smear (ring-shaped RBC inclusions) or cytology of bone marrow, lymph node, or spleen —PCR assay	—Imidocarb dipropionate (Imizol): 5 mg/kg IM, two doses 14 days apart —Diminazene aceturate (Berenil): 2 mg/kg IM, two doses 7 days apart *Prognosis:* Poor No treatment known
Encephalitozoonosis	*Encephalitozoon cuniculi* (oronasal exposure to urine spores or ingestion of infected tissues)	U.S. (rarely), Europe, South Africa	*Neonatal disease in kennels:* Stunted growth, acute nephritis (renal failure) and encephalitis (depression, muscle spasms, ataxia, seizures, blindness, aggression, paralysis)	*General:* Nonregenerative anemia, azotemia, pyuria, hematuria, elevated CSF protein and mononuclear cells *Specific:* —Identify spores in gram-stained urine sediment —Serology and PCR	
Acanthamebiasis	*Acanthamoeba* species (water, sewage, soil)	U.S. (very rare; epizootics seen in greyhounds)	*Disease in dogs only:* Pneumonia (fever, cough, dyspnea, nasoocular discharge), encephalitis (ataxia, seizures), mimics canine distemper	Leukopenia; no diagnostic test available (identify organisms in lung biopsies)	—No established treatment protocol —Trimethoprim-sulfonamide: 30 mg/kg PO q12h
Pneumocystosis	*Pneumocystis carinii* (airborne)	—Worldwide (rare in dogs and cats) —Predisposition in miniature dachshunds with immunodeficiency syndrome	*Dogs (mostly miniature dachshunds):* Acute or chronic pneumonia in immunocompromised dogs (non-febrile, exercise intolerance, dyspnea, dry cough, weight loss)	*General:* Neutrophilic leukocytosis, diffuse radiographic alveolar and interstitial lung densities *Specific:* Identify organisms in lung cytology or biopsies (Giemsa and methenamine silver stains)	—Trimethoprim-sulfadiazine: 15–30 mg/kg PO q8–12h for 2–3 weeks —Pentamidine isethionate (Lomidine, Merial): 4 mg/kg IM q24h for 2–3 weeks *Prognosis:* Fair to guarded

CDC, Centers for Disease Control and Prevention; IFA, immunofluorescent antibody; PCR, polymerase chain reaction; RBC, red blood cell; WBC, white blood cell.

Intestinal Replication and Oocyst Shedding

This is also called the *sporozoite stage*. When cats ingest the meat of an infected intermediate host, the encysted *Toxoplasma* bradyzoites are liberated by the cat's digestive enzymes and invade the intestinal epithelial cells. Replication within the intestinal epithelium results in fecal excretion of millions of oocysts beginning 3 to 10 days after exposure and continuing for 1 to 3 weeks. Except for occasional transient diarrhea, clinical signs are usually absent until after oocyst shedding is over and the cat enters the next stage of infection.

- Infection by oocyst ingestion is a less important source in cats, but when it does occur, subsequent shedding of oocysts is delayed for 3 weeks or more and is much less pronounced.
- Excreted oocysts are oval-shaped, $10 \times 12\,\mu m$ in size, and unsporulated (uninfective). To become infec-

tious, oocysts first must sporulate, which takes 1 to 5 days in the environment.
- These sporulated oocysts are environmentally resistant and can remain infectious in the environment for months to years.

▼ ***Key Point*** Intestinal replication and fecal excretion of *Toxoplasma* oocysts, which can contaminate soil, water, and food and can infect other animals, only occurs in cats, the definitive host.

- Intestinal immunity lasting up to 6 years after the first exposure prevents significant oocyst production upon reinfection.

Dissemination and Intracellular Replication

This is also called the *tachyzoite stage*. Simultaneous with intestinal replication in cats, or after infection by ingestion or transplacental transfer in non-feline species, *Toxoplasma* disseminates to extraintestinal tissues via blood and lymph. These rapidly multiplying tachyzoite forms can parasitize almost any cell in any tissue. The tachyzoites eventually rupture and destroy infected cells, releasing organisms to infect new cells and thus producing foci of necrosis and inflammation.

- In a small percentage of animals, these lesions become extensive enough to cause overt clinical disease, with the signs dependent on which tissues are damaged most severely.
- In most animals, this rapid replication stage is brief, and, as immunity develops and before signs occur, aggregates of these organisms encyst and become dormant.

Chronic Tissue Encystment

This is also called the *bradyzoite stage*. Coincident with the onset of immunity, slowly multiplying bradyzoite forms develop and form large (10 to 50 µm) tissue cysts, especially in muscle, brain, and visceral organs.

- There is minimal host response to these cysts, and they can persist in this dormant form for the life of the chronic carrier animal.
- Encysted *Toxoplasma* usually do not cause any clinical signs except in rare instances when cysts rupture within the central nervous system (CNS) or eye or when the infection is reactivated to an acute stage because of loss of host immune competence.

▼ ***Key Point*** In carnivores such as the cat, the principal source of infection is ingestion of *Toxoplasma* organisms encysted in the meat of chronically infected food-producing animals, small mammals, and birds.

Clinical Signs

Clinical toxoplasmosis is recognized more frequently in cats than in dogs, but the spectrum of signs is similar for both species. Clinical signs depend on the location and extent of tissue damage that results from extraintestinal dissemination and rapid intracellular replication of tachyzoites. The most commonly affected organs are lung, eyes, liver, and pancreas, as well as CNS and skeletal muscle. Organ-specific clinical signs are usually accompanied by anorexia, depression, and fever (often >104°F and unresponsive to antibiotics).

- Clinical signs can occur at the time of initial infection (acute or primary toxoplasmosis) or from reactivation of encysted infection (chronic or secondary toxoplasmosis) caused by an underlying immunosuppressive condition.
- Clinical toxoplasmosis is most severe and often fatal in neonatal kittens infected transplacentally or through milk.

▼ ***Key Point*** Most animals with toxoplasmosis are asymptomatic and have only serologic evidence of infection. Up to 30% of cats in the United States have *Toxoplasma* antibody titers and are presumed infected, with the highest prevalence in free-roaming and feral cats that hunt for their food.

Ocular Signs

Ocular toxoplasmosis (uveitis) is one of the most common forms of the disease. Blindness may result.

- Anterior uveitis causes aqueous flare, keratic precipitates, hypopyon, glaucoma, and lens luxation (see Chapter 136).
- Chorioretinitis causes retinal detachment, hyporeflective lesions in the tapetal fundus, and white fluffy infiltrates in the non-tapetum (see Chapter 138).

Respiratory Signs

Acute necrotizing interstitial and alveolar pneumonia is common and can cause progressive dyspnea.

Neuromuscular Signs

- Encephalomyelitis can cause behavior changes, seizures, ataxia, circling, tremors, paresis or paralysis, and cranial nerve deficits, depending on location of the lesions within the CNS.
- Myositis can cause hyperesthesia, stiff gait, muscle atrophy, and weakness.

Hepatic and Digestive Tract Signs

- Diffuse necrotizing hepatitis and cholangiohepatitis can cause anorexia, vomiting, diarrhea, jaundice, and ascites.
- Pancreatitis can cause anorexia, vomiting, abdominal pain, and jaundice.

- Enterocolitis can cause vomiting and diarrhea.
- Mesenteric lymphadenitis can cause palpable abdominal lymph nodes.

Cardiac Signs

Myocarditis can cause cardiac arrhythmias, sudden death, or heart failure.

Reproductive Signs

Transplacental infection can cause birth of stillborn kittens or kittens that die of neonatal toxoplasmosis of the lung, liver, and CNS.

Laboratory and Radiographic Findings

Abnormalities found on routine diagnostics are varied and nonspecific.

Hematology and Serum Chemistries

- Hematologic findings are variable and may include leukopenia with degenerative left shift (in acute disease) or neutrophilic leukocytosis, mild nonregenerative anemia, lymphocytosis, or eosinophilia.
- Hepatitis can cause elevated serum bilirubin, liver enzymes, and bile acids.
- Pancreatitis can cause increased pancreatic lipase immunoreactivity in cats or serum amylase and lipase dogs.
- Myositis can cause elevated muscle enzymes (e.g., creatine kinase [CK] and aspartate aminotransferase [AST]).

Radiography

- Pulmonary toxoplasmosis can cause generalized coalescing, patchy alveolar and interstitial lung infiltrates, and mild pleural effusion.
- Involvement of abdominal viscera can cause peritoneal effusion and hepatomegaly.

Cerebrospinal Fluid Analysis

- Cerebrospinal fluid (CSF) protein may be normal or increased.
- CSF nucleated cell count is usually mildly increased with a predominance of small mononuclear cells.
- CSF can also be evaluated by serology and polymerase chain reaction (PCR) (see the next section).

▼ ***Key Point*** Clinical toxoplasmosis can be an opportunistic disease associated with immunosuppression; thus, consider underlying concurrent infections such as feline immunodeficiency virus, feline leukemia virus, and feline infectious peritonitis in cats and canine distemper in dogs. Immunosuppressive drugs (glucocorticoids, cyclosporine, or antitumor therapy) may also predispose to clinical toxoplasmosis.

Diagnosis

The diagnosis of clinical toxoplasmosis is usually based on the combination of clinical findings and serologic and PCR testing of blood, CSF, and aqueous humor. PCR assays and serologic tests for immunoglobulin M and G (IgM and IgG) are available to the practicing veterinarian through the Veterinary Diagnostic Laboratory (College of Veterinary Medicine, Colorado State University, Fort Collins, CO 80523) and other reference labs.

- Visual identification of tachyzoites in cytology or biopsy specimens is only possible in a small fraction of the animals with toxoplasmosis, but in those cases it establishes a definitive diagnosis.
- Visual identification of *T. gondii* oocysts in the feces of clinically healthy cats is possible during the brief intestinal replication stage, but this is not useful for diagnosis of clinical toxoplasmosis.

Serology

Enzyme-linked immunosorbent assay (ELISA) methods are generally most reliable for determining *Toxoplasma*-specific antibody titers. Positive IgG and IgM antibody titers document previous or current infection. The IgM titer reflects the early immune response and has the best correlation with clinically active toxoplasmosis.

▼ ***Key Point*** The presence of antibodies against *T. gondii* indicates previous or current infection but does not prove clinical disease as a result of infection; thus, only use serology in conjunction with other clinical information.

Immunoglobulin M Antibody Titer

The IgM titer rises initially 1 to 2 weeks after exposure, typically coinciding with the onset of signs; it peaks after 3 to 6 weeks and dissipates by 12 weeks in most cats, thus paralleling clinical disease activity.

- *Interpretation:* IgM titer ≥ 1:64 suggests active or recent infection.
- The IgM titer may persist up to 1 year in some cats when there is reactivation of chronic infection or delayed antibody class shift from IgM to IgG caused by concurrent feline immunodeficiency virus infection or glucocorticoid therapy.

▼ ***Key Point*** The serum IgM *Toxoplasma* antibody titer is the serologic test of choice for presumptive diagnosis of active or recent infection.

Immunoglobulin G Antibody Titer

The IgG titer rises initially 2 to 4 weeks after exposure and persists for years to life; thus, a single positive IgG titer does not distinguish previous infection from current active infection.

- *Interpretation:* A fourfold rise in the IgG titer in paired specimens over a 2- to 3-week period is indicative of active infection. Both specimens must be measured together in the same test run to avoid assay variation.

▼ ***Key Point*** A single, high serum IgG *Toxoplasma* antibody titer is *not* diagnostic of active infection, no matter how high the titer level.

Antibody Titers in Cerebrospinal Fluid and Aqueous Humor

The diagnosis of CNS and ocular toxoplasmosis is aided by evaluating the local production of *Toxoplasma*-specific IgG and IgM antibodies in CSF or aqueous humor using the calculated antibody coefficient (C-value), which distinguishes true local production of *Toxoplasma* antibodies from inflammatory leakage. This can be combined with PCR assay for *Toxoplasma* DNA in CSF or aqueous humor. Specimens must be collected prior to glucosteroid therapy. Aqueous humor and CSF assays are available at the Veterinary Diagnostic Laboratory (College of Veterinary Medicine, Colorado State University, Fort Collins, CO 80523).

$$\text{C-value} = \frac{\left[\begin{array}{c}T.\,gondii \text{ antibody (aqueous or CSF)} \\ \times \text{ Total antibody (serum)}\end{array}\right]}{\left[\begin{array}{c}T.\,gondii \text{ antibody (serum)} \\ \times \text{ Total antibody (aqueous or CSF)}\end{array}\right]}$$

- C-value of 1 to 8 is suggestive of ocular or CNS toxoplasmosis.
- C-value of >8 is conclusive evidence of local ocular or CNS antibody production.

▼ ***Key Point*** The combination of antibody titers (especially IgM) and PCR assay on aqueous humor or CSF is the most accurate way to diagnose ocular or CNS toxoplasmosis.

Polymerase Chain Reaction and Antigen Assays

- PCR assay can be used to detect *T. gondii* DNA in blood, CSF, or aqueous humor. The PCR assay in blood can be positive in cats with and without clinical disease; thus, a positive PCR by itself does not confirm clinical toxoplasmosis.
- Toxoplasma antigen can be detected in cats initially 1 to 4 weeks after exposure and then intermittently for up to 1 year. This does not distinguish active from past infection and thus has no advantage over antibody titers.

Identification of Toxoplasma Organisms

Detection of Tachyzoites

Characteristic intracellular inclusions are occasionally identified in aspirate and impression smear cytologies stained routinely or in biopsies.

- Specimens to consider (depending on sites of involvement) include lung bronchoalveolar lavage (BAL), liver aspirates, lymph node aspirates, body cavity fluids, CSF, and aqueous humor by oculocentesis.
- *Disadvantage:* Tachyzoites are often sparse and difficult to find; thus, sensitivity of detection is generally low. However, in experimentally infected cats, BAL was a reasonably effective method of diagnosis.

Detection of Oocysts in Feces

Fecal oocysts are rarely detected because most cats are past the transient stage of oocyst shedding by the time clinical signs occur (see under "Stages of Infection"); thus, this is not a suitable method for diagnosis of clinical toxoplasmosis.

- *Procedure:* Use Sheather's sugar centrifugation-flotation (Sheather's solution: 500 g of table sugar, 320 ml of distilled water, and 6.5 g of phenol crystals melted in a hot water bath). Make a fecal suspension with 5–10 g of feces and water, then centrifuge one part fecal suspension with two parts Sheather's solution for 10 minutes at 1000 g and examine one to two drops from the meniscus.
- *Disadvantages:* Oocysts are small, easily overlooked, and morphologically indistinguishable from certain other coccidia (*Hammondia* spp., *Besnoitia* spp.) without specialized animal inoculation studies. Nevertheless, assume coccidian oocysts 10 × 12 µm in size in feline feces to be *Toxoplasma* until proved otherwise.

▼ ***Key Point*** Detection of fecal oocysts is not a reliable diagnostic test for clinical toxoplasmosis because oocyst shedding occurs only briefly and usually ends before clinical signs begin.

Treatment

Toxoplasmosis can be treated with clindamycin, trimethoprim-sulfonamide, or azithromycin. Localized ocular infection is most responsive. Approximately 60% of animals with generalized toxoplasmosis recover with treatment; thus, the prognosis is guarded. Mortality rate is highest in neonates and in animals that are severely immunosuppressed.

▼ ***Key Point*** Clindamycin is the initial drug of choice for treating clinical toxoplasmosis, and it penetrates the blood-brain and blood-eye barriers. It also reduces oocyst shedding.

- Clindamycin (Antirobe, Upjohn): 12.5 mg/kg PO or IM q12h for 28 days.
- Trimethoprim-sulfadiazine: 15 mg/kg PO q12h for 28 days.
- Azithromycin (Zithromax): 10 mg/kg PO q12h for 7 days.

- For uveitis, use 1% prednisone drops topically every 6 to 8 hours for 2 weeks.

Prevention in Cats

Prevent cats from ingesting tissue cysts in meat and prey animals.

- Do not feed cats raw meat, viscera, or bones, and do not allow them to scavenge these from garbage.
- Do not allow cats to ingest raw (unpasteurized) milk, especially from goats.
- Do not allow cats to roam free where they can hunt prey (mice, birds) for food.
- Do not allow cats to eat transport vectors (cockroaches, flies, earthworms).

Public Health Considerations

Toxoplasmosis is an important zoonosis in humans. Infection in immunocompetent people is inapparent or causes a self-limiting, flu-like illness. Infection during pregnancy can cause fetal toxoplasmosis, leading to stillbirth or severe ocular or CNS disease. Approximately 10% of people with AIDS develop toxoplasma encephalitis from reactivation of encysted bradyzoites.

Preventive Measures in Humans

Prevention of human infection is based on avoiding ingestion of sporulated oocysts in the environment or tissue cysts in undercooked meat. Contaminated drinking water has caused some outbreaks.

▼ ***Key Point*** Pregnant women and severely immunocompromised people should avoid contact with soil, cat feces, litter boxes, and raw meat.

- Do not eat raw or undercooked meat. Cook meat to 160°F to kill tissue cysts.
- Use good kitchen hygiene. Wash hands, cutting boards, sink tops, and utensils that come in contact with raw meat.
- Change the litter box daily to remove oocysts before they have 24 hours to become infective. Disinfect with boiling or scalding water.
- Wear gloves while gardening, or wash hands after gardening to prevent exposure to oocysts in soil.
- Wash fruits and vegetables thoroughly before eating to remove soil particles with oocysts.
- Boil or filter surface water before drinking if contamination is possible.
- Keep sandboxes covered when not in use so that cats cannot defecate in them.

Risks of Owning an Infected Cat

Direct contact with cats is highly unlikely to pose a risk of human infection. Oocysts shed in cat feces are the only means of transmission from cat to human. Exposure to oocysts is very unlikely from petting cats or from cat licks, bites, and scratches.

▼ ***Key Point*** Because of the way cats defecate, bury their feces, and keep their haircoats clean, transmission of *Toxoplasma* oocysts to humans by touching and caring for a pet cat is very unlikely.

- The question often is raised, how dangerous is a healthy pet cat with a positive *Toxoplasma* antibody titer? Most seropositive cats and cats with clinical toxoplasmosis have completed oocyst shedding by the time they develop a positive titer. Repeat exposure of a seropositive cat results in little or no shedding.
- Most cats that are shedding infective oocysts are seronegative and preclinical. Seronegative cats are non-immune and would be more likely to shed oocysts if exposed, thus posing a greater risk to its owner than a seropositive cat.

▼ ***Key Point*** Serologic testing of healthy cats for *Toxoplasma* antibodies has little public health benefit and is not recommended.

Environmental Control Measures

- Control the stray cat population to reduce contamination of the environment, soil, and water with oocysts. Cats that defecate in the soil are likely to be the same cats that must hunt for their food and thereby have a high risk of infection.
- To reduce entry of *Toxoplasma* into the food chain, prevent cats from roaming where food-producing animals and livestock feed are kept. Pork is the most likely source of cyst ingestion in people in the United States.

NEOSPOROSIS

Etiology

Neosporosis is a protozoan disease of dogs caused by *Neospora caninum,* a coccidian parasite that resembles the appearance of *Toxoplasma* and has a similar life cycle. Dogs and wild canids are definitive hosts, and other animals (especially cattle) are intermediate hosts.

- Dogs are infected by ingesting meat infected with tissue cysts containing bradyzoites or by transplacental transmission.
- Rapidly replicating tachyzoites disseminate and produce necrotizing lesions in many tissues or cause transplacental infection of a developing fetus. Clinical disease in dogs primarily reflects neuromuscular infection.
- As the definitive host, the dog completes the life cycle in its intestines and sheds fecal oocysts that become infective in the environment within 24 hours of passage.

- Clinical disease has not been seen in cats, but experimentally infected kittens develop encephalomyelitis and polymyositis.
- *N. caninum* has worldwide economic importance as a major cause of abortion in dairy cattle.

Clinical Signs

Multifocal, progressive neuromuscular signs predominate as a result of non-suppurative encephalomyelitis, polyradiculoneuritis, and fibrosing polymyositis.

- Clinical signs can include hind-limb paresis and ataxia progressing to ascending paralysis, hind-limb extensor rigidity, and muscle atrophy and contracture. Dysphagia and masticatory muscle involvement can be seen.
- Less common manifestations include myocarditis (arrhythmias), pneumonia (fever, dyspnea, cough), ulcerative or pruritic dermatitis, chorioretinitis, and multifocal intra-abdominal dissemination (hepatitis, pancreatitis).

▼ ***Key Point*** Subclinically infected bitches can transmit *Neospora* in utero to successive litters of puppies. Congenital neosporosis is particularly severe and often leads to in utero or neonatal puppy mortality.

Laboratory and Radiographic Findings

- Muscle involvement may cause increased serum levels of muscle enzymes (CK, AST) and abnormal electromyographic findings.
- CSF shows a moderately increased protein (20 to 150 mg/dl) and increased leukocytes (10 to 100 cells/μl) composed of a mixture of small and large mononuclear cells and neutrophils.
- Thoracic radiographs may show interstitial and alveolar infiltrates.

Diagnosis

- Presumptive diagnosis is based on the combination of compatible clinical signs and a *Neospora* antibody titer of >1:200 using immunofluorescent antibody (IFA) or ELISA. Serologic crossreactivity with *Toxoplasma* is minimal.
- Rarely, the diagnosis can be confirmed by identification of *Neospora* tachyzoites in cytologies of CSF, skin lesions, or BAL or in biopsies of infected tissues (e.g., muscle). Oocysts can be detected by fecal flotation or PCR, but oocyst shedding is not found in dogs with overt clinical disease. *Neospora* organisms can be distinguished from *Toxoplasma* by PCR, immunohistochemistry, or electron microscopy.

Treatment

Neosporosis is treated similar to toxoplasmosis using one or a combination of both of the following regimens.

- Clindamycin (15 mg/kg PO q12h) for 28 days
- Trimethoprim-sulfadiazine (15–20 mg/kg PO q12h) combined with pyrimethamine (0.5 mg/kg PO q12h) for 28 days

Treat all littermates of infected puppies. The prognosis for dogs with severe neurologic involvement is grave, and animals that recover usually have residual neurologic deficits.

Prevention and Public Health

- Do not breed dogs with a history of whelping infected puppies.
- Avoid glucocorticoids in seropositive dogs because of the potential for activating encysted infection.
- *Neospora* is seroprevalent in white-tailed deer; thus, do not let dogs have access to deer carcasses.
- Do not allow dogs to have access to bovine placental tissues (afterbirth) or aborted fetuses.
- Because *Neospora* infection has a large economic impact as a cause of bovine abortion, prevent dog feces from contaminating livestock feed and water.
- *Neospora caninum* antibodies have been detected in people, but it is not yet clear whether *Neospora* is a cause of zoonotic disease.

HEPATOZOONOSIS

Etiology

Hepatozoonosis is a tick-transmitted protozoan disease of dogs caused by *Hepatozoon americanum* or *Hepatozoon canis*. Ticks become infected during feeding on an infected dog. The infection is then transmitted to a new canine host when the tick is ingested, not by the tick bite.

- *H. americanum* is most common in North America and is transmitted by the Gulf Coast tick, *Amblyomma maculatum*. Infection is endemic in southern states in the Gulf Coast region (Texas, Oklahoma, Louisiana, Mississippi, Alabama, Florida, and Georgia).
- *H. canis* is transmitted by the brown dog tick, *Rhipicephalus sanguineous*, and occurs in Southern Europe, the Middle East, Africa, and Asia.

▼ ***Key Point*** *H. americanum,* the etiology of American hepatozoonosis, causes a more severe form of clinical disease than *H. canis,* which usually causes subclinical or mild disease.

- Uncharacterized *Hepatozoon* spp. have been reported sporadically in cats.

Pathogenesis

After an infected tick is ingested, *H. americanum* organisms disseminate widely and form numerous distinctive tissue cysts, especially in the muscles. The organisms

replicate until cysts rupture, eliciting a severe pyogranulomatous inflammatory response and disseminating more organisms to form new cysts.

▼ ***Key Point*** American hepatozoonosis is a chronic debilitating illness characterized by waxing and waning fever, extreme leukocytosis, polymyositis, proliferative periosteal bone lesions, and severe cachexia.

In contrast, *H. canis* has relatively low pathogenicity; clinical signs are absent or mild in many infected dogs. Severe disease is mostly limited to dogs with concurrent disease or immunosuppression. Muscle and periosteal involvement do not occur with *H. canis,* but organisms are frequently seen in circulating leukocytes.

Clinical Signs

Clinical signs begin within 4 weeks of ingesting an infected tick and continue to wax and wane as more organisms are released into muscle tissue, exacerbating myositis, muscle pain, and fever.

- Fluctuating fever (>104°F) and lethargy
- Myalgia, stiffness, lameness, painful gait, reluctance to move
- Hyperesthesia over the paraspinal muscles
- Progressive weight loss, weakness, and muscle atrophy
- Mucopurulent ocular discharge with each flare-up
- Transient bloody diarrhea
- Possible protein-losing glomerulonephropathy (due to immune complex glomerulonephritis or amyloidosis) in advanced cases

Laboratory and Radiographic Findings

The presumptive diagnosis of hepatozoonosis in dogs from endemic areas is based on the combination of typical clinical signs (fever, pain, and muscle wasting), extreme leukocytosis, typical serum chemistry abnormalities, and characteristic periosteal bone lesions on radiographs.

- The most characteristic hematologic finding is extreme neutrophilic leukocytosis (mean 75,000 to 85,000/µl; range 20,000 to 200,000/µl), consisting of mostly mature neutrophils with a mild left shift. Mild normocytic-normochromic nonregenerative anemia is also common. The platelet count is usually normal to increased. Dogs with thrombocytopenia should be evaluated for other concurrent tick-borne infections (see Chapter 17).
- Common serum chemistry abnormalities are increased alkaline phosphatase, hypoglycemia (in vitro artifact of high white blood cell count), hypoalbuminemia, and hyperglobulinemia.
- Radiographically, most dogs infected with *H. americanum* develop diffuse periosteal bony proliferations, most pronounced on the pelvis, long bones of the limbs, and vertebrae. The periosteal lesions may appear as smooth, lamellar thickening of the bone or irregular proliferations.

Diagnosis

▼ ***Key Point*** Muscle biopsy is the most reliable means of confirming American hepatozoonosis.

- Definitive diagnosis is based on visual identification of tissue stages of *H. americanum* organisms, which are most reliably found in skeletal muscle biopsies and rarely in circulating leukocytes on Giemsa-stained blood smears. In contrast, blood smears are usually diagnostic for *H. canis* infection.
- An ELISA-based serologic test for *H. americanum* has a sensitivity of 93% and specificity of 96%.

Treatment

No treatment has been found to effectively eliminate *H. americanum* from infected tissues in dogs. However, the following treatment has been shown to prolong survival and control clinical signs for extended periods, even years. Pain and fever improve within 48 hours of initiating treatment.

- For *H. americanum,* use the combination of clindamycin (Antirobe) (10 mg/kg PO q8h), trimethoprim-sulfadiazine (Tribrissen or Ditrim) (15 mg/kg PO q12h), and pyrimethamine (Daraprim) (0.25 mg/kg PO q24h) for 2 weeks to establish remission; and follow this with decoquinate (Deccox, Alpharma) (10–20 mg/kg PO q12h, mixed with food) for 2 years and possibly lifelong to maintain remission and prevent relapses. Decoquinate, an anticoccidial livestock feed additive, decreases recurrences by inhibiting development of the organisms released from tissue cysts, thereby preventing repeated cycles of reinfection and illness.
- Use nonsteroidal anti-inflammatory drugs as needed for pain and fever.
- Avoid corticosteroids because they can worsen the disease.
- For *H canis,* imidocarb dipropionate (Imizol) (5–6 mg/kg IM or SC, two doses 2 weeks apart) is highly effective and considered the drug of choice. It may be effective for *H. americanum.* Pretreatment with atropine (0.04 mg/kg SC), 30 minutes prior to imidocarb injections, reduces the parasympathomimetic side effects of imidocarb.

Prevention and Public Health

- Prevention depends on minimizing tick exposure, using an effective tick preventative product on dogs in endemic areas, and routinely checking dogs for ticks and removing them promptly.

- Zoonotic transmission from dogs to people does not appear to occur.

LEISHMANIASIS

Etiology

Leishmania spp. are flagellated protozoan parasites that cause vector-transmitted cutaneous and visceral diseases in dogs, humans, and other mammals. In most areas of the world, rodents and dogs serve as reservoir hosts, and infection is transmitted by sand fly vectors. Leishmaniasis occurs worldwide and is endemic in the Mediterranean region of Europe and South America. *Leishmania infantum,* a member of the *Leishmania donovani* complex, is the most frequently reported cause of visceral leishmaniasis in dogs.

▼ ***Key Point*** Visceral leishmaniasis is endemic in North American foxhounds and foxhound kennels.

- Other dog breeds have also been infected sporadically in North America. The source of infection in most of these cases has been traveling or living in an endemic country or importation from an endemic country.
- Cats are usually subclinically infected or only develop cutaneous leishmaniasis.
- Infection can also be transmitted iatrogenically by transfusion of contaminated blood.

Clinical Signs

Sand flies transmit infection during feeding on the host. Intracellular organisms (amastigotes) are disseminated by macrophages and cause cutaneous lesions, polysystemic vasculitis, lymphoreticular hyperplasia, hyperglobulinemia, and immune complex disease of the kidneys and joints. Dogs have subclinical infection for months to several years before developing clinical signs. Visceral leishmaniasis with cutaneous involvement is the most common form of disease in dogs.

- Fever, chronic weight loss, muscle wasting (despite normal appetite)
- Vomiting, diarrhea, melena
- Hepatosplenomegaly, generalized lymphadenopathy
- Ulcerative or granulomatous dermatitis characterized by non-pruritic facial alopecia, hyperkeratosis, scaling, mucocutaneous ulcers, and intradermal nodules on the muzzle, pinnae, ears, and foot pads
- Elongated brittle toe nails
- Anterior uveitis, conjunctivitis, blepharitis
- Cough; sneezing (rhinitis), epistaxis
- Neutrophilic polyarthritis (lameness, swollen painful joints)
- Glomerulonephritis, polyuria-polydipsia, renal failure
- Icterus

Laboratory Findings

- Hematologic findings are thrombocytopenia, anemia, lymphopenia, leukocytosis with a left shift, and occasional positive Coombs test.
- Other lab findings are polyclonal hyperglobulinemia (sometimes monoclonal), hypoalbuminemia, proteinuria, azotemia, increased serum liver enzymes, and the presence of antinuclear antibodies (ANAs).

Diagnosis

Presumptive diagnosis of leishmaniasis is based on clinical signs, international travel history, breed (foxhound), and antibody titer. Confirmation is based on cytologic identification of organisms (especially bone in marrow), detection of *Leishmania* DNA by PCR assay, or protozoal culture.

- Antibody titers develop 2 to 4 weeks after infection and decline 1 to 3 months after treatment. Infections are considered persistent; thus, a positive IFA antibody titer (≥1:64) is indicative of current "active" infection. Dogs occasionally have false-negative titer results. Trypanosoma causes crossreacting antibodies.
- Definitive diagnosis can be established in some dogs by cytologic identification of organisms (amastigotes; 2.5 to 5 µm × 1.5 to 2 µm) in aspirates of bone marrow (60% of cases), lymph nodes (30% of cases), or spleen; in impressions of skin lesions; or by the presence of organisms in biopsies of skin or infected organs.
- Confirmation can also be based on PCR detection of *Leishmania* DNA in aspirates of bone marrow (the specimen of choice), lymph nodes, or spleen. Blood PCR is useful but less reliable than bone marrow. Both antibody titers and PCR assay are available to practicing veterinarians through the Vector Borne Disease Diagnostic Lab at North Carolina State University. Submission requirements and forms are available at *http://www.cvm.ncsu.edu/docs/tickbornediseaselab.html.*
- The U.S. Centers for Disease Control, Division of Parasitic Diseases (CDC, Atlanta, GA; telephone: 770-488-4475) also provides diagnostic confirmation, including protozoal culture using bone marrow or lymph node aspirates.

Treatment

▼ ***Key Point*** Treat leishmaniasis with an antimonial drug plus allopurinol for inducing remission, followed by long-term allopurinol to prevent relapse.

Leishmania infection can often be controlled with medical therapy, but it is usually not curable in dogs. Since the organisms are not eliminated by treatment, relapses are common a few months after treatment is stopped. The prognosis for remission is variable. Dogs

with renal disease have a poor prognosis. The following drug regimens are recommended:

- *Allopurinol* (Zyloric, Glaxo): 15 to 20 mg/kg PO q12–24h, initially combined with sodium stibogluconate or meglumine antimonite, then continued alone for several months to maintain remission.
- *Sodium stibogluconate* (Pentostam, Wellcome): 30 to 50 mg/kg IV or SC q24h, combined with allopurinol, for 3 to 4 weeks or until resolution of signs and lab abnormalities; available in the United States through the CDC at *http://www.cdc.gov/ncidod/srp/drugs/drugservice.html.*
- *Meglumine antimonite* (Glucantime, Merial; available in Europe): 100 mg/kg IV or SC q24h, combined with allopurinol, for 4 weeks or until resolution of signs and lab abnormalities.
- *Amphotericin B lipid complex* (ABLC) (Abelcet, Enzon) at 3 mg/kg IV q48h (3 times weekly) for a minimum of five treatments. ABLC can be used as an alternative to antimonials in animals with good renal function. Dilute in 5% dextrose to a concentration of 1 mg/ml and infuse over 1 to 2 hours (see Chapter 20). Liposome-encapsulated amphotericin (AmBisome, Gilead Sciences) is a more expensive alternative.

Prevention and Public Health

- In endemic regions, avoid sand flies, especially at night when they feed, and use insecticides as premise sprays and topical applications to dogs. Deltamethrin collars are highly effective. Permethrin spray is also effective.
- Screen potential blood donors to prevent iatrogenic transmission.
- Direct contact with infected dogs is unlikely to pose a risk of human infection; however, dogs serve as a reservoir for infection of sand flies that can transmit infection to people. In highly endemic countries, control of canine infections is key to reducing leishmaniasis in people.

OTHER PROTOZOAL INFECTIONS

Other systemic protozoal infections are summarized in Table 21-1.

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Section

3 Hematology/Oncology

Janet L. Peterson

Chapter

22 Erythrocytes, Leukocytes, and Platelets

Rose E. Raskin

ERYTHROCYTE DISORDERS

Anemia: Overview

Anemia is characterized by a reduction in the overall erythrocyte content, number of erythrocytes, or hemoglobin concentration. It is one of the most frequent hematologic abnormalities encountered in practice. Anemia is not a disease but rather the reflection of a disease state. Causes of anemia may be divided into three general categories: blood loss, hemolysis, and decreased erythrocyte production.

▼ ***Key Point*** Determine the cause of the anemia before giving supportive treatment.

Clinical Signs

- Primary signs of anemia relate to the reduction in oxygen-carrying capacity of the blood. The patient may present with lethargy, weakness, anorexia, heart murmur, tachypnea, and pale mucous membranes.
- Occasionally, the animal may appear normal, but routine blood evaluation before an elective surgical procedure may uncover the abnormality. Sedentary animals, especially cats, often have moderate anemia that goes unnoticed for long periods.
- Secondary signs of anemia often relate to the effects of increased blood cell destruction, such as icterus, splenomegaly, and hepatomegaly from extravascular hemolysis or extramedullary hematopoiesis and discolored urine from the effects of hemoglobin or excess bilirubin excreted.

Principles of Diagnosis

Several tests can be used to document and characterize the anemia morphologically or etiologically.

History and Physical Examination

Use the history and physical examination to determine the following:

- Occurrence of trauma or surgery
- Drug, chemical, or toxin exposure
- Underlying infectious, parasitic, or neoplastic disease
- Duration of disease, sites of blood loss, and presence of organomegaly

Complete Blood Count (Table 22-1)

- Packed cell volume (PCV) is the most accepted and least expensive method of documenting anemia. Spin microhematocrit tubes 5 minutes at a rate of 12,000 to 15,000 $\times g$ and measure the proportion of the concentrated cell population of the total plasma volume. Evaluate the plasma color after centrifugation. Alternatively, the hematocrit (Hct) can be calculated by multiplying the number of the erythrocytes in mil-

Table 22-1. HEMATOLOGY REFERENCE RANGES FOR DOGS AND CATS*

Parameter	Canine	Feline
PCV or Hct (%)	37–55	30–45
Hemoglobin (g/dl)	12–18	8–15
RBCs ($\times 10^6$/µl)	5.5–8.5	5–10
MCV (fl)	60–75	40–55
MCHC (g/dl)	32–36	30–36
Reticulocytes ($\times 10^3$/µl)	<80	<60 aggregate
Platelets ($\times 10^3$/µl)	200–900	300–700
WBCs ($\times 10^3$/µl)	6–17	6–18
Segmented neutrophils ($\times 10^3$/µl)	3–12	3–12
Band neutrophils (/µl)	0–300	0–300
Lymphocytes (/µl)	1000–5000	1500–7000
Monocytes (/µl)	150–1350	50–850
Eosinophils (/µl)	100–1250	100–1500
Basophils (/µl)	<100	<100
Plasma protein (g/dl)	6.0–8.0	6.0–8.0
Fibrinogen (mg/dl)	200–400	150–300

*These values are only meant as a guide; individual laboratories may vary in their ranges, depending on instrumentation and regional differences in animal populations.
Hct, hematocrit; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; PCV, packed cell volume; RBCs, red blood cells; WBCs, white blood cells.
Source: Purdue University, Veterinary Clinical Pathology Laboratory.

lions by the mean cell volume divided by 10. There may be 1 to 3 percentage units increased in PCV over Hct related to trapped plasma.

- Determine plasma protein or total solids by refractometer.
- Erythrocyte, or red blood cell (RBC), count usually is performed by an automated cell counter. This value is necessary for calculation of the erythrocyte indices.
- Hemoglobin (Hgb) concentration in grams per deciliter is determined most accurately by the cyanmethemoglobin method, using a colorimeter or spectrophotometer. Artifactual increases may occur with gross lipemia or an excessive number of Heinz bodies, both of which produce light interference.
- Mean cell or corpuscular volume (MCV) may be determined directly by the automated cell counters, or it may be calculated as follows: MCV (femtoliters) = PCV × 10 divided by RBC (10^6/µl).
- MCV reflects erythrocyte size and may be categorized as *macrocytic,* suggesting increased red cell turnover; *microcytic,* suggesting defective cell growth; or *normocytic,* unchanging cell size. Note that Akita and Shiba dogs normally have microcytic erythrocytes, while some toy and miniature poodles, as well as greyhounds, may have macrocytic erythrocytes.
- Other erythrocyte indices such as mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) help classify the types of anemia into *normochromic* and *hypochromic.* Decreased levels reflect the presence of reticulocytes or abnormal hemoglobinization. Increased levels occur artifactually from hemolysis. MCH may be calculated by dividing Hgb by RBC (10^6/µl) and multiplying this by 10, but it provides no additional value than MCHC, which is calculated by dividing Hgb by PCV and multiplying by 100.
- Blood smear evaluation involves quantitation of changes in size *(anisocytosis),* shape *(poikilocytosis),* and color *(polychromasia).* The presence of immature nucleated forms and basophilic stippling often signals abnormal erythropoiesis or defective circulation of erythrocyte precursors. Infectious parasites and Heinz bodies often require careful examination of the smear.

▼ ***Key Point*** The most important part of the complete blood count (CBC) is an evaluation of the blood smear for morphologic abnormalities.

Reticulocyte Count

This is the most accurate method to evaluate regeneration. Perform reticulocyte counts when the PCV falls below 30% in dogs and 20% in cats.

- Incubate equal volumes of blood and 0.5% new methylene blue stain together for 15 to 20 minutes; then make a routine blood smear and count the number of aggregate and punctate forms per 1000 erythrocytes. Absolute numbers of reticulocytes per microliter are calculated by the following formula:

$$\text{Absolute reticulocyte count/µl} = \text{Reticulocyte percentage} \times \text{RBC/µl}$$

- Dogs normally have 0% to 1% reticulocytes (0–80,000/µl). In healthy cats, aggregated reticulocytes range from 0% to 0.4% (0–60,000/µl) and punctate reticulocytes are less than 5% (<500,000/µl). Aggregate reticulocytes represent the most active or recent form of regeneration in the dog and cat. Punctate reticulocytes in cats, which do not stain as polychromatophilic cells, represent regenerative attempts that occurred 2 to 4 weeks previously.
- By using the PCV instead of the erythrocyte count, a corrected reticulocyte percentage may be calculated as follows:

$$\text{Corrected \% reticulocytes} = \text{\% Reticulocytes} \times \{\text{Patient's PCV/Normal PCV}\}$$

- Normal PCV is considered 45% for dogs and 35% for cats. A corrected percentage for a reticulocyte value greater than 1% indicates increased RBC regeneration. Once initiated at the bone marrow level, regeneration may take at least 3 days before reticulocytes appear in the circulation.

Fecal Examination and Urinalysis

These tests are performed to determine sources of blood loss and function of the kidney.

Biochemical Profile

Biochemical profiles may reveal organic disease that can affect the ability to regenerate erythrocytes.

Bone Marrow Evaluation

Bone marrow evaluation is necessary whenever regenerative attempts appear diminished. Hemolytic conditions do not warrant marrow examination unless the response is less than normally expected. Results always must be compared with a concurrent CBC to determine the current status of regeneration.

▼ ***Key Point*** Perform bone marrow evaluation by obtaining both aspirate and core biopsies together because each provides different information.

- This is a sterile procedure that may be performed with only local anesthesia, sedation with reversible analgesia, or general anesthesia.
- Sites frequently used in dogs include the dorsal ilium, humerus (best for obese animals), and femur (small dogs or puppies). Sites frequently used in cats include the femur and dorsal ilium by a transilial or perpendicular approach.

Bone Marrow Aspiration Biopsy Technique

1. Use an Illinois sternal disposable needle, 15 to 18 gauge, 1 to 2 inches long (Cardinal Health, Dublin, OH).
2. Pass the needle with the stylet through the cut skin and subcutaneous tissues and into the bone a few millimeters until it is firmly embedded.
3. Place a 12-ml syringe containing 0.5 ml of 5% ethylenediaminetetraacetic acid (EDTA) solution onto the biopsy needle and collect 1 to 2 ml of bloody material.
4. Place the marrow material on a plastic Petri dish and pick up the glistening particles with a glass pipette.
5. Gently expel this material out of the pipette onto a glass slide. Make a squash preparation by laying a second slide on the first and sliding them horizontally apart.

Bone Marrow Core Biopsy Technique

1. Use a Jamshidi aspiration biopsy disposable needle, 11 to 13 gauge, 2 to 4 inches long (Cardinal Health, Dublin, OH).
2. Pass the needle with the stylet through the cut skin and subcutaneous tissues.
3. Remove the stylet while advancing the needle 0.5 to 1.5 cm into the bone, depending on the size of the animal.
4. Twist the instrument sharply to cut the sample, and withdraw the needle slowly.
5. Remove the core sample and roll it onto a glass slide for cytologic examination; then place the sample in 10% buffered formalin for histologic fixation.

Principles of Transfusion Therapy

Therapy depends on the etiology of the anemia. Rapid decreases in PCV warrant replacement of whole blood. However, slow daily decreases in PCV of 1% to 3% may not cause clinical signs of dyspnea or weakness. Whole blood transfusion is discussed here, and blood component therapy is discussed in Chapter 23.

Cross-matching

Perform cross-matching before transfusion. The procedure, which involves collection of erythrocytes and serum or plasma from the donor and the patient, is as follows:

- Wash erythrocytes and pellet 3 times in 0.9% saline.
- Make a 4% cell suspension by adding 4.8 ml of saline to 0.2 ml of cells.
- Measure compatibility between donor and patient optimally at three temperatures: 37°C, 20°C, and 4°C.

▼ ***Key Point*** Perform cross-matching prior to all blood transfusions to prevent incompatibility reactions.

- Donors are incompatible if any agglutination or hemolysis occurs in the major cross-match. The types of cross-match are defined as follows:
  - *Major:* 100 µl donor cells + 100 µl patient serum/plasma
  - *Minor:* 100 µl patient cells + 100 µl donor serum/plasma
  - *Donor or patient controls:* 100 µl of donor or patient cells to 100 µl of donor or patient serum/plasma, respectively
- Under emergency conditions, donors may be used if mild agglutination occurs in the minor cross-match.

Cross-matching Procedure:

- After 15 minutes of incubation, centrifuge tubes at 280 ×*g* for 1 minute.
- Note any hemolysis in supernatant and gross agglutination of resuspended cells.
- Place a small drop on glass slide and examine for microscopic agglutination.

Whole Blood Transfusion

- In dogs, this procedure is best performed using animals negative for the dog erythrocyte antigen DEA-1 and DEA-7 blood types.
- Although most cats have type A blood, it is best to cross-match blood, because as little as 1 ml of mismatched blood can cause a fatal transfusion reaction in cats.
- Estimated dosage is 10 to 20 ml/kg in dogs or cats, with a maximum of 40 ml in an adult cat. A more specific guideline for the amount of donor blood in anti-

coagulant (ml) is as follows: kg × 80 (dog) or 60 (cat) × (desired PCV – patient PCV) divided by donor PCV.
- When performing whole blood transfusion, use appropriate filters and administration sets to retain clotted blood or debris.
- Warm blood before administration.
- For the first 30 minutes, keep the initial rate of administration slow (0.25 ml/kg) to observe any incompatibility reactions (recommended rate of whole blood infusion in general is 10 ml/kg/hour). The rate of infusion depends on the hydration status of the patient.
- Evaluate the hematocrit before and after transfusion to document relative improvement and to screen for hemolysis as an indicator of incompatibility.

Blood Loss Anemia

Large volumes of blood must be lost before appreciable changes occur in the numbers of erythrocytes or PCV. The immediate loss of blood results in little or no change to the PCV owing to the concurrent loss of erythrocytes and plasma fluids. Over the course of several hours to days, redistribution of fluids occurs, resulting in a lowered PCV and plasma protein. Depending on the amount of blood lost and the time period over which it is lost, regenerative responses may range from moderate to extremely weak. Chronic blood loss causes decreased iron stores, resulting in decreased erythrocyte production.

Etiology

Causes of blood loss include the following:

- Trauma
- Surgery
- External and internal parasitism
- Gastric ulcers
- Tumors of the gastrointestinal (GI) and urinary systems
- Splenic rupture
- Coagulation abnormalities

Treatment

Administer cross-matched whole blood for *acute* hemorrhage when the PCV drops to 20% to 25% in the dog or cat. Also consider autotransfusion if hemorrhage has occurred recently in a body cavity and the blood is not contaminated with bacteria or neoplastic cells.

Hemolytic Anemia

Causes of hemolytic anemia include congenital abnormalities, immune-mediated destruction, infections, chemical or toxic agents, mechanical fragmentation, and hypophosphatemia. The net effect of hemolytic loss of erythrocytes is often a very strong to moderate regenerative response (Fig. 22-1). However, in some cases, the anemia may occur so rapidly that the animal may have too little time to mount a regenerative response by the time the condition is recognized.

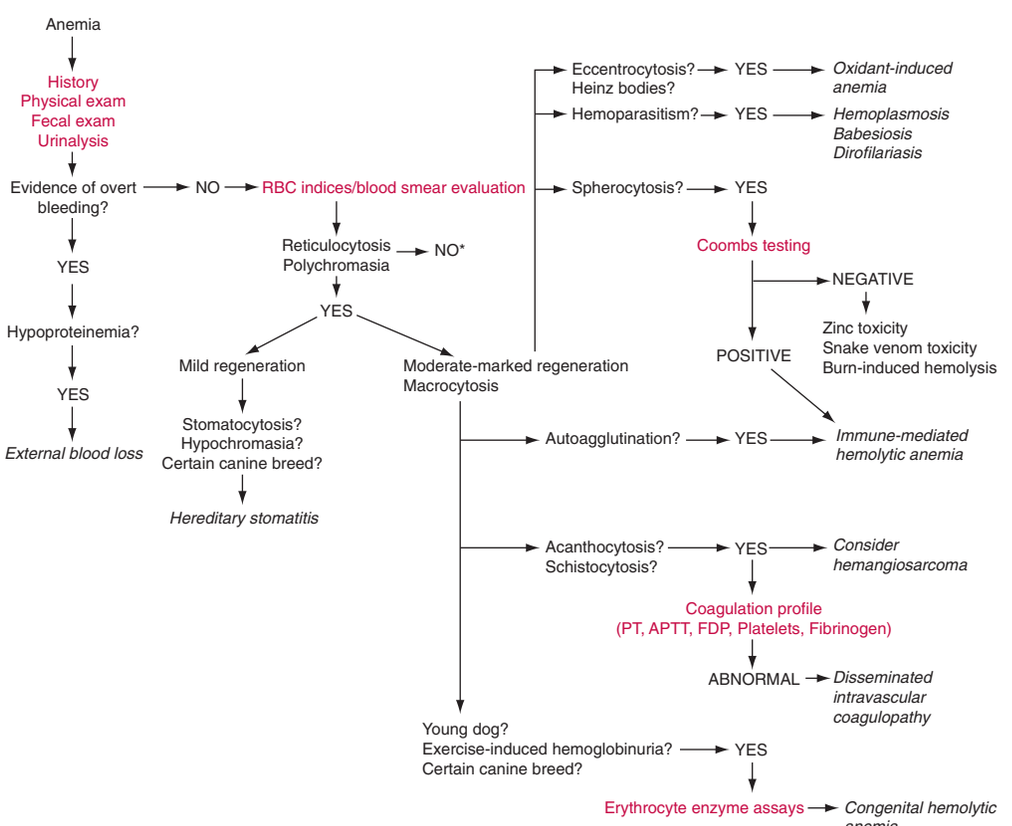

Figure 22-1. Diagnostic approach to common regenerative anemias in dogs and cats.* See Figures 22-2 and 22-3. (APTT, activated partial thromboplastin time; FDP, fibrin degradation product; PT, prothrombin time.)

▼ ***Key Point*** A period of 2 to 3 days is necessary for erythrocyte maturation and reticulocytosis once the stimulation from hypoxia or severe erythrocyte depletion has occurred.

- Depending on the severity or acuteness of the destruction and the conjugating ability of the liver, icterus may or may not be present.
- Plasma protein concentrations usually are normal.

Congenital Erythrocyte Abnormalities

Pyruvate Kinase Deficiency

Pyruvate kinase deficiency is an erythrocyte enzyme deficiency associated with an autosomal recessive inheritance. During anaerobic glycolysis, pyruvate kinase is necessary for the production of adenosine triphosphate (ATP), which erythrocytes need to maintain their integrity and viability.

- The condition has been documented in several dog breeds, including the basenji, beagle, West Highland white terrier, Cairn terrier, American Eskimo dog, miniature poodle, Chihuahua, and pug.
- It has been reported in Abyssinian, Somali, and domestic shorthaired cats.

Clinical Signs

- Young animals usually present with anemia, exercise intolerance, tachycardia, and splenomegaly. The outcome of the disease is usually death by 4 years of age.
- Myelofibrosis and osteosclerosis may occur, resulting in reduced hematopoiesis.
- Frequent erythrocyte destruction may lead to hemosiderosis and failure of organs such as the liver.

Diagnosis

This disease is suggested clinically by the presence of an intense reticulocytosis (15–50%), along with frequent nucleated red cells in a young dog. Echinocytosis or erythrocytes with sharp projections unrelated to crenation may be seen in circulation.

- Polymerase chain reaction (PCR) based genetic tests are currently available for the basenji, West Highland white terrier, and Cairn terrier to detect affected and carrier animals.
- Definitive diagnosis for other breeds requires a special erythrocyte assay for the enzyme.

Phosphofructokinase Deficiency

Phosphofructokinase deficiency has been identified in English springer and American cocker spaniels as an autosomal recessive inheritance. This glycolytic enzyme deficiency causes a decrease in 2,3-diphosphoglycerate (2,3-DPG) concentration, resulting in an increase in intracellular pH. Erythrocytes from affected animals are especially fragile under alkaline conditions.

- Intravascular hemolysis may occur during hyperventilation-induced alkalemia, resulting in periodic bouts of hemoglobinuria and sometimes bilirubinuria.
- A constant state of hypoxia is produced by the low levels of 2,3-DPG, with subsequent increased oxygen binding to hemoglobin.
- The result is persistent reticulocytosis (10–30%) even though the PCV is normal or mildly decreased, except during hemolytic episodes.

Clinical Signs. The clinical signs may involve lethargy, pale or icteric mucous membranes, mild hepatosplenomegaly, myopathy, and fever. Dogs may have a normal life span if properly managed.

Diagnosis. The enzyme deficiency is diagnosed by specialized erythrocyte assays in homozygous and heterozygous animals. A PCR-based test is available to screen for affected and carrier animals of any age.

Hereditary Stomatocytosis

Hereditary stomatocytosis is an autosomal recessive trait in Alaskan malamutes associated with chondrodysplasia. The defect may involve abnormalities of the cell membrane or of ion transport, leading to increased water content and a larger cell size (96 fl). Morphologically, some erythrocytes appear to have a slit-like or mouth-like area of central pallor.

- Dwarfism is recognized clinically in affected Alaskan malamutes, and there is a mild hemolytic anemia and slight reticulocytosis (2%). Erythrocyte numbers are reduced, but the PCV remains normal because of enlarged erythrocytes.
- Other breeds associated with congenital stomatocytosis include Drentse Patrijshonds and miniature and giant schnauzers.

Feline Porphyria

Feline porphyria is an infrequent inheritable trait that results in an enzyme deficiency affecting heme synthesis.

- Clinical signs include pink urine, pinkish-brown teeth, and severe anemia resulting from the deposition of red non-heme pigments and the lysis of erythrocytes when exposed to sunlight. Skin photosensitization can occur; therefore, exposure to sunlight should be avoided.
- Discolored teeth often display red fluorescence under ultraviolet light.
- The disease can be prevented by not breeding carrier animals.

Hereditary Non-spherocytic Hemolytic Anemia

Hereditary non-spherocytic hemolytic anemia is recognized in two breeds: poodles and beagles. In both

breeds, erythrocytes are morphologically normal and enzyme activities are not affected.

Poodles. Poodles develop an autosomal dominant condition that resembles pyruvate kinase deficiency, but decreases in this enzyme are not demonstrable. Affected animals have a persistent macrocytic hypochromic anemia (PCV of 13–31%) with moderate reticulocytosis. It is clinically evident by 1 year of age and fatal by 3 years of age. Myelofibrosis, osteosclerosis, and hemosiderosis are present at death.

Beagles. In beagles, the condition presents with chronic anemia and moderate reticulocytosis. The mode of inheritance is likely autosomal recessive. The disease is less severe in beagles than in poodles, and the disorder can remain subclinical for up to 4 years in affected dogs. The short erythrocyte life span in beagles may be caused by an unidentified membrane abnormality.

Immune-Mediated Hemolytic Anemia

See the chapter on systemic immune-mediated diseases (Chapter 24).

Infectious Causes of Hemolysis

Hemoplasmosis

Hemoplasmosis or hemotrophic mycoplasmosis, previously known as hemobartonellosis, is caused by a mycoplasma organism that infects the erythrocytes of dogs *(Mycoplasma haemocanis)* and cats *(M. haemofelis* and *"Candidatus M. haemominutum").* It can be transmitted by ticks and fleas or by queens to their newborn kittens in the absence of blood-sucking arthropods. Splenectomy (especially in the dog), immunosuppression caused by glucocorticoid therapy, or stress in cats with latent *M. haemofelis* infection predispose to the development of clinical disease in the animal infected by the organism.

Clinical Signs. Clinical signs include those generally observed with anemia. Weight loss may occur if the anemia develops slowly, whereas acute, severe anemia produces sudden depression and icterus. Splenomegaly often is noted.

Diagnosis. Laboratory findings generally reflect a strong regenerative response in the CBC. The absence of marked anisocytosis or polychromasia in confirmed cases of feline hemoplasmosis may suggest peracute infections with too little time to respond or concurrent infection with feline leukemia virus (FeLV) or feline immunodeficiency virus (FIV).

- Thin smears, made directly without anticoagulant, assist in finding the epicellular organisms. Blood films should be well stained without precipitate to minimize any confusion in identifying the parasite.
- Cats often have coccoid or ring shapes, whereas dogs mostly have linear chain forms.
- A positive Coombs test result may be associated with feline hemoplasmosis, presumably because of erythrocyte membrane alteration.
- PCR-based assays are available for the diagnosis of hemoplasma infections in cats.

Treatment

- Consider whole blood transfusion if the anemia is severe.
- Prednisolone (2 mg/kg PO q12h) may be necessary initially to suppress the severe immune-mediated destruction of erythrocytes.
- Doxycycline (5 mg/kg PO q12h for 4 weeks) is preferred for dogs and cats.
- Enrofloxacin (5 mg/kg PO q24h for 14 days) can be used in cats intolerant of doxycycline.
- Cats who recover may become latent carriers.

Babesiosis

Babesiosis is a tick-borne protozoal disease affecting erythrocytes of dogs *(Babesia canis, B. gibsoni). B. canis* is common in kennel conditions and is associated especially with greyhounds. *B. gibsoni* has been associated with pit bull and American Staffordshire terriers. *Babesia felis* has not been reported in North American cats but is reported in Africa and southern Asia. Concurrent infections with other tick-borne agents such as *Ehrlichia canis* are common.

Clinical Signs. Clinical signs in babesiosis range from an acute hemolytic crisis to an unapparent subclinical form. Signs of the acute disease include splenomegaly, icterus, anemia, thrombocytopenia, hemoglobinuria, and fever.

Diagnosis. Initial diagnosis is made by examination of a blood smear.

- A large, clear, teardrop-shaped trophozoite organism in erythrocytes, sometimes seen in pairs, is representative of the three subtypes of *B. canis.*
- A much smaller, signet ring–shaped form occurring singularly and more frequently suggests subtypes of *B. gibsoni* or a Californian isolate genetically similar to *Theileria* species.
- An indirect fluorescent antibody (IFA) serum test is available but may be negative in early infections or display crossreactivity.
- A nested PCR test is most sensitive and can distinguish among canine babesial subtypes.
- A Coombs test is frequently positive in dogs with severe anemia related to a secondary immune-mediated disease.

Treatment. Treat babesiosis with one of the following drugs. The only drug approved in the United States is imidocarb. In general, the small *Babesia* species infections are considered more resistant to treatment and often develop a chronic carrier state.

- Imidocarb dipropionate (Imizol, Schering-Plough) (6.6 mg/kg SC or IM given twice 2 weeks apart)
- Diminazene aceturate (Berenil, Hoechst) (3.5 mg/kg SC or IM given once)
- Phenamidine isethionate (15 mg/kg SC q24h for 2 days)

Leptospirosis

Leptospira serovars can cause kidney disease, liver disease, hemolysis, icterus, and coagulopathies. Toxins released from proliferating organisms interfere with cellular metabolism and damage cells. The clinical findings, diagnosis, and treatment are discussed in Chapter 19.

Chemical or Toxic Injury of Erythrocytes

Oxidant-Induced (Heinz Body) Anemia

Heinz body anemia is produced by oxidant agents that cause precipitation of hemoglobin. Oxidative injury to the iron moiety of hemoglobin (methemoglobinemia) is discussed in a separate section later in this chapter. Accelerated red cell destruction involves intravascular fragmentation or extravascular phagocytosis by the spleen.

Etiology. Chemicals, drugs, or plants associated with Heinz body formation include acetaminophen, methylene blue, onions, vitamin K_3, dl-methionine, zinc, topical benzocaine (e.g., Cetacaine) sprayed on the larynx to aid intubation, and propylene glycol. Heinz body formation in cats also has been associated with ketoacidosis in diabetic cats, hyperthyroidism, and lymphoma.

▼ ***Key Point*** Cats are predisposed to oxidant damage and Heinz body formation because of their hemoglobin structure.

Clinical Signs. Acute hemolysis causes depression, hemoglobinemia, hemoglobinuria, moderate to severe anemia, and occasional icterus.

Diagnosis. Diagnosis is made by observation of a single, large, pale-staining area in erythrocytes of Romanowsky-stained blood smears. They also may appear as a single blunt projection by the Heinz body bulging from the membrane surface. These structures appear as dark blue spots when stained with new methylene blue in a direct wet mount procedure or after incubation of the stain with the blood.

- *Erythrocyte refractile bodies* are similar to Heinz bodies but are smaller, infrequent, and present in normal cats without presence of anemia. Contrast these to many large Heinz bodies with signs of a regenerative response.
- *Eccentrocytosis* is another erythrocyte change associated with oxidative damage resulting in hemolysis, which occurs from fusion of the erythrocyte membrane, producing a thin, colorless portion or hemighost on one side of the cell and a dense, hemoglobin portion on the opposite side. This has been associated with onion and garlic ingestion in dogs.

Treatment

- Remove the source of oxidant exposure. Use emetics if recent ingestion has occurred.
- Give blood transfusions or other forms of supportive care, as indicated.
- For acetaminophen-induced toxicity, give acetylcysteine (Mucomyst, Roxane Laboratories), 140 mg/kg of a 5% solution diluted with saline given IV as a loading dose, then give 70 mg/kg of a 5% solution every 4 hours for three to five treatments.

Snake Venom Toxicity

Snake venom toxicity has been recognized as a cause of hemolysis. Toxins, such as those produced from coral snakes, may be associated with spherocyte formation, in addition to neurologic and coagulation abnormalities.

- Diagnosis is based on the presence of a regenerative anemia and a bite wound with a history supporting recent exposure to a snake.
- For both coral snake and rattlesnake envenomation in dogs, a transient erythrocyte shape change of echinocytosis has been observed.
- Treatment involves use of a specific venom antidote and supportive care.

Zinc Toxicity

Zinc toxicity can produce intravascular hemolysis in dogs. Sources of the zinc include ingestion of galvanized wire or kennel cage nuts and pennies produced since 1983.

- Diagnosis involves the presence of a regenerative anemia and proof of zinc exposure. Spherocytosis and Heinz bodies have been noted in some cases on blood smear evaluation.
- Radiograph the abdomen to identify metallic foreign bodies in the GI tract and remove the source of zinc via surgery or endoscopy.

Mechanical Fragmentation of Erythrocytes

Heartworm Disease

Dirofilariasis may produce anemia after intravascular hemolysis as large numbers of adult heartworms *(Dirofilaria immitis)* obstruct blood flow, causing turbulence that mechanically disrupts erythrocytes.

- Clinical signs reflect the organs affected, such as the lungs, liver, or kidneys.
- Postcaval syndrome results from obstruction of the caudal vena cava causing, in addition to hepatic failure, erythrocyte fragmentation (schistocytosis), hemoglobinemia, and hemoglobinuria.

- Definitive diagnosis is based on detection of circulating microfilaria in the blood or on serologic detection of circulating antigens or antibodies (see Chapter 152).

Disseminated Intravascular Coagulopathy

Disseminated intravascular coagulopathy may cause a microangiopathic hemolytic anemia because of fibrin deposition that result from damage to small blood vessels. Mechanical fragmentation of erythrocytes appears in blood smears as schizocytes or spherocytes.

- Etiology involves a variety of conditions, such as neoplasia, infections, necrosis, toxins, and immune complex formation. These can lead to massive tissue destruction and activation of clotting pathways.
- Diagnosis is based on consumption of platelets (thrombocytopenia), reductions in clotting factors (prolonged prothrombin time [PT], activated partial thromboplastin time [APTT], hypofibrinogenemia), and increased amounts of fibrin degradation products (see Chapter 23).
- Treatment is aimed at the inciting condition (see Chapter 23).

Hypophosphatemia

Cases of feline diabetes mellitus and hepatic lipidosis have been associated with hypophosphatemia-induced hemolysis. Heinz body formation may play a role in the development of hemolytic anemia in these cases.

Nonregenerative Anemia

Nonregenerative anemia generally is related to direct toxicity of erythroid precursors in the bone marrow or secondary suppression of erythropoiesis (Fig. 22-2). Often neutrophils and platelets also are affected (Fig. 22-3).

- Reduction in erythrocytes, leukocytes, and platelets in circulation is termed *pancytopenia.*
- The term *aplastic anemia* is used to describe bone marrow failure involving the three cell lines that leads to peripheral pancytopenia. The bone marrow in this condition is severely hypoplastic, with total or near complete replacement of hematopoietic elements by adipose tissue.
- In contrast, crowding from abnormal cellular infiltrates can suppress hematopoiesis, producing *myelophthisis.*

▼ ***Key Point*** Chronic, nonregenerative anemias may not require blood transfusion until the PCV falls below 15% in the dog and 12% in the cat.

Causes of nonregenerative anemia include infectious agents, nutritional disturbances, organic disease, endocrine abnormalities, toxic agents, myelophthisis, irradiation, and immune-mediated destruction.

Infectious Agents

Feline Leukemia Virus

FeLV-associated anemia is usually normochromic and normocytic to macrocytic. Nonregenerative anemia results from bone marrow suppression caused by both primary infection of hematopoietic stem cells and infection of the supporting stromal cells.

- Severe red cell hypoplasia is most common and is associated with depletion and arrest of maturation of erythroid precursors in the bone marrow.
- Approximately 10% of the cases are hemolytic with regeneration related to immune destruction of erythrocytes.
- One type of virus-induced anemia is associated with erythrocyte macrocytosis and is thought to be related to a defect in mitosis during erythrocyte maturation.

Diagnosis. Diagnosis is based on positive enzyme-linked immunosorbent assay (ELISA) or IFA test results (see Chapter 8). Bone marrow aspirate smears or core biopsy sections indicate decreased cellularity with increased fat infiltration when the infection is not associated with a proliferative leukemia.

Treatment. Treatment varies depending on concurrent conditions such as neoplasia, hemoplasmosis, FIV, or feline infectious peritonitis (FIP). Supportive care, in the form of blood transfusions (see "Principles of Transfusion Therapy"), antibiotics, appetite stimulants, and anabolic steroids, is often necessary (see Chapter 8 for additional information on FeLV).

Other Viruses

Other viruses, such as FIP, FIV, feline panleukopenia virus, canine parvovirus, and canine distemper virus, have been associated with suppression of erythropoiesis. The anemia is often mild to moderate and nonresponsive. Other cell lines, such as granulocytes or lymphocytes, are affected more severely. Diagnosis usually is determined by exposure history, clinical signs, virologic or serologic tests, characteristic histopathologic lesions, and identification of viral particles or inclusions within affected cells. In canine distemper virus, erythrocytes or leukocytes may contain one or more pale blue spots in the cytoplasm with Romanowsky-type stains. However, these inclusions stain a deep purple color with aqueous-based Wright stains (e.g., Diff-Quik).

Ehrlichiosis and Anaplasmosis

Ehrlichia spp. and *Anaplasma* spp. are tick-transmitted rickettsial infections that produce chronic polysystemic disease in dogs and cats associated with hyperglobulinemia, thrombocytopenia, mild to moderate nonregenerative anemia, and sometimes leukopenia or pancytopenia in the later stages. The epidemiology,

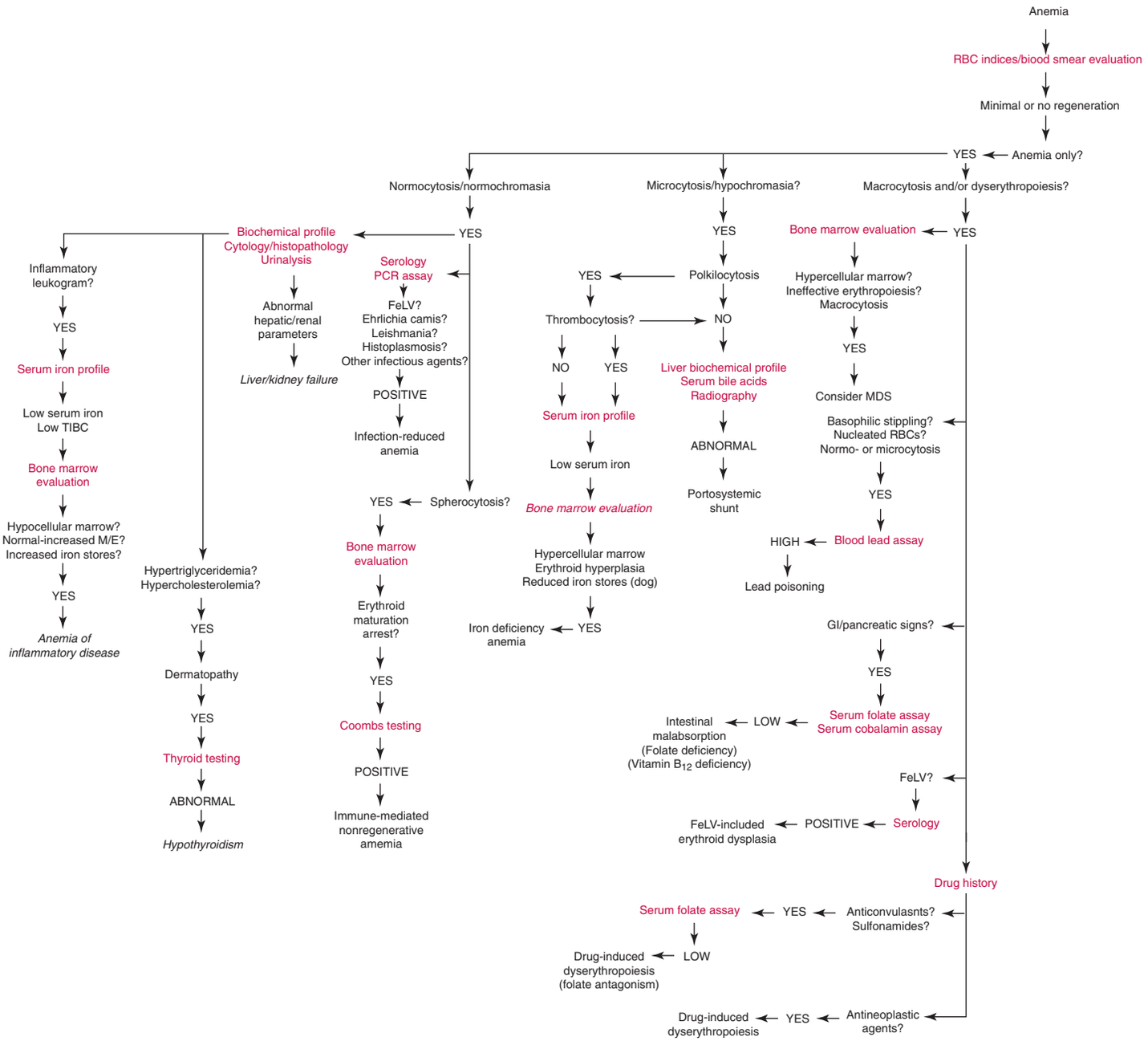

Figure 22-2. Diagnostic approach to common nonregenerative anemias in dogs and cats when only the erythrocyte line is involved. (FeLV, feline leukemia virus; MDS, myelodysplastic syndrome; M/E, myeloid-to-erythroid ratio; PCR, polymerase chain reaction; TIBC, total iron-binding capacity.)

clinical manifestations, diagnosis, and treatment of these infections are described in Chapter 17.

- Intracytoplasmic morulae are found infrequently in mononuclear cells *(E. canis, Ehrlichia chaffeensis)* or granulocytes *(Ehrlichia ewingii, Anaplasma phagocytophilum),* during the acute stage of the disease. Bone marrow, at this time, is often normocellular to hypercellular with increased numbers of megakaryocytes and plasma cells.
- In the chronic or late stages of monocytic ehrlichiosis, bone marrow cellularity decreases severely, with fat replacing hematopoietic elements.

Leishmaniasis

Leishmaniasis is an infrequent protozoal disease in dogs caused by *Leishmania* spp. The parasite, transmitted by sand flies, produces visceral or cutaneous manifestations. Organisms are present in macrophages of the

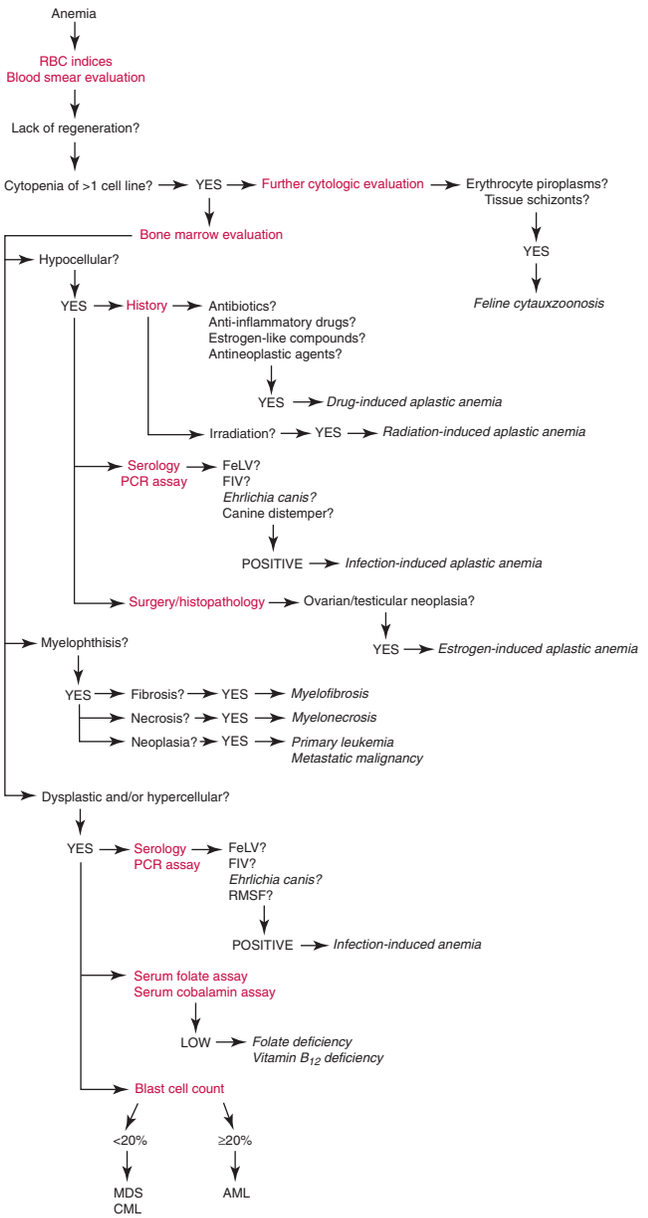

Figure 22-3. Diagnostic approach to common nonregenerative anemias in dogs and cats when multiple cytopenias are present. (AML, acute myeloid leukemia; CML, chronic myeloid leukemia; FeLV, feline leukemia virus; FIV, feline immunodeficiency virus; MDS, myelodysplastic syndrome; PCR, polymerase chain reaction; RMSF, Rocky Mountain spotted fever).

bone marrow, lymph nodes, spleen, and liver. The clinical signs, diagnosis, and treatment are discussed in Chapter 21.

- Leishmaniasis is endemic in many North American foxhound kennels. In other dogs, the history usually indicates travel outside the United States to endemic countries such as Greece, Spain, or Italy.
- Hyperglobulinemia and a mild to moderate normocytic, normochromic anemia may occur.

Cytauxzoonosis

Cytauxzoonosis is a highly fatal protozoal disease of cats caused by *Cytauxzoon felis*. It is a tick-borne infection, most prevalent in the wooded areas of the southern United States. The bobcat is the natural reservoir host.

Clinical Signs. Initial clinical signs include anorexia, dehydration, and lethargy, with gradual development of fever. This progresses rapidly to icterus, moderate anemia, leukopenia, thrombocytopenia, and splenomegaly. Cats usually die within a week after clinical signs are recognized.

Diagnosis. The diagnosis is generally made postmortem by histologic identification of large schizonts in endothelial cells of the lungs, liver, bone marrow, or spleen. Terminally, blood films may contain small (1 to 2 µm in diameter) ring or "safety pin" structures within erythrocytes.

Treatment. Treatment is usually unsuccessful despite the use of antibiotics and supportive care. Most reported cases have been fatal, except for several suspected to be infected with a less virulent strain of the organism.

Nutritional Deficiencies

Iron Deficiency

Iron deficiency produces a poorly regenerative anemia caused by deficient hemoglobin synthesis. It occurs with increased iron utilization, such as during growth or pregnancy, from decreased intestinal absorption of iron, and most commonly, when iron stores are reduced through hemorrhage or blood loss.

Etiology. Iron deficiency anemia is caused by neoplasia with tissue necrosis, trauma, internal or external parasites (hookworms, fleas), coagulopathies, and various GI diseases that cause hematemesis, melena, or hematochezia.

Diagnosis. Diagnosis is based on history and low serum iron levels.

- Erythrocytes in blood smears may appear normal in size but lighter in color, with increased central pallor (hypochromasia). Electronic cell counters report an MCV of less than 60 fl (microcytosis) in dogs.
- Poikilocytosis may be prominent in the form of schistocytes, keratocytes, codocytes, and elliptocytes.
- Thrombocytosis occurs in 50% of canine cases.
- Iron profiles have normal to increased level of transferrin (total iron-binding capacity) and decreased serum iron level (in cats <60 µg/dl, in dogs <8 µg/dl). The percentage of saturation of transferrin in iron-deficient animals is often less than 19% (normal is about 33%).
- Bone marrow examination is necessary to determine iron storage amounts, especially in the dog. It is less helpful in the cat, which typically lacks stainable iron in the bone marrow. Aspirate and core biopsies of the

bone marrow indicate hypercellularity with marked erythroid proliferation.

Treatment. Correct the inciting cause and treat with iron supplementation. Give ferrous sulfate at a dosage of 4 to 6 mg of iron per kilogram per day PO in divided doses. Continue therapy for several weeks to months until the PCV and MCV return to normal.

Cobalamin Deficiency

Cobalamin (vitamin B_{12}) deficiency may occur through acquired disorders such as small intestinal disease, exocrine pancreatic insufficiency, or bacterial overgrowth in dogs (see Chapter 69).

- Selective malabsorption of vitamin B_{12} has been described in giant schnauzers having an autosomal mode of inheritance. Clinical signs include weight loss, decreased appetite, and failure to thrive at 3 months of age.
- Laboratory findings involve chronic normocytic, normochromic, nonregenerative anemia with occasional erythroid dysplasia in peripheral blood or bone marrow.
- Serum cobalamin levels can be measured to determine affected animals (for normal values and additional information, see Chapter 69).
- Resolution of clinical and hematologic effects occurs with parenteral administration of cobalamin (initially 1 mg IM daily).

Folate Deficiency

Folate deficiency may produce macrocytic anemia in animals with neoplasia, intestinal malabsorption, liver disease, dietary imbalance, and severe anorexia or starvation. Drugs such as anticonvulsants (phenobarbital, primidone), sulfonamides (sulfasalazine, trimethoprim-sulfadiazine), and antineoplastic agents (methotrexate) may act as folate antagonists by impairing its absorption or production.

- Diagnosis is based on a history of drug exposure or concurrent disease. Serum folate levels can be measured to confirm the deficiency (for normal values and additional information, see Chapter 69).
- The hemogram may indicate a normochromic anemia with macrocytosis and megaloblastic changes in erythroid precursors.
- Treatment is aimed at the inciting cause, along with oral folate supplementation (5 mg/day in dogs, 2.5 mg/day in cats).

Inflammatory Disease

Anemia of inflammatory disease is a frequent cause of nonregenerative anemia. The mechanism may involve increased macrophage activity with cytokine release leading to decreased erythropoiesis, reduced iron availability through sequestration in macrophages, and decreased RBC survival. Primary infections and neoplasia are most often responsible for chronic inflammation. The animal may present with prolonged anorexia, weight loss, and weakness. Other clinical signs reflect the actual source of chronic inflammation or organ systems affected.

- Laboratory findings indicate a normocytic, normochromic anemia, inflammatory leukogram, low serum iron, low total iron-binding capacity, and increased bone marrow stores of iron.
- The bone marrow is usually hypocellular with a normal to increased myeloid-to-erythroid ratio.
- Treatment depends on the original cause. Iron supplementation does not effectively reverse this form of anemia.

Organic Disease

Kidney Disease

Chronic kidney disease may be associated with normocytic, normochromic, nonregenerative anemia.

- The mechanisms involved include reduced erythropoiesis, decreased erythrocyte survival, and blood loss.
- Diagnosis of renal failure involves the presence of azotemia and an abnormal urinalysis. For pathogenesis, diagnosis, and treatment, see Chapter 77.

Liver Disease

Chronic liver disease may be associated with normocytic, nonregenerative anemia. Blood smears often reveal poikilocytosis (acanthocytes, budding fragmentation). Pathogenic mechanisms include concurrent inflammation with iron sequestration, reduced erythropoiesis, and decreased erythrocyte survival.

- Blood loss may occur from coagulopathies related to decreased synthesis of clotting factors.
- Portosystemic shunts may develop erythrocyte microcytosis and poikilocytosis, with or without anemia, possibly related to a relative decrease in iron availability.
- Laboratory findings suggestive of hepatic disease include elevated serum liver enzymes (ALT, SAP, GGT), increased serum bile acid levels, hypoalbuminemia, and hyperbilirubinemia. Liver disease is discussed in Chapter 71.

Endocrine Disease

Hypothyroidism

Hypothyroidism may present with mild anemia in one-third of cases. Pathogenetic mechanisms include reduced tissue oxygen demand and depressed erythropoiesis at the stem cell level. Diagnosis is based on history, dermatologic signs, and hormone assay results (see Chapter 31).

Hyperestrogenism

Hyperestrogenism is associated with endogenous production by tumors (e.g., testicular Sertoli cell or ovarian granulosa cell) or exogenous administration of estrogenic compounds (see Chapters 51, 86, and 90). The mechanism of reduced erythropoiesis is thought to occur at the level of DNA transcription.

- Moderate to severe anemia may be accompanied by thrombocytopenia and leukopenia.
- Diagnosis of an estrogen-producing tumor may be confirmed by surgical removal with subsequent recovery of the cell lines.
- Supportive care, such as blood transfusion and anabolic steroids, may be necessary.

Hypoadrenocorticism

Hypoadrenocorticism may be a cause of nonregenerative anemia in a small percentage of cases. The anemia usually is discovered after fluid replacement for volume deficits associated with the disease (see Chapter 33).

Drug and Toxin-Induced Disease

Drug-Induced Anemia

Drugs (e.g., estrogens, phenylbutazone, antineoplastic agents, thiacetarsamide, quinidine, meclofenamic acid, and trimethoprim-sulfadiazine) are associated with reduced erythropoiesis and aplastic anemia in dogs.

- An idiosyncratic toxicosis caused by griseofulvin administration resulting in a nonregenerative pancytopenia has been reported in a cat.
- Exogenous estrogens are toxic in the dog, depending on the dose given and age of the animal (worse in older dogs). Initially, anemia and thrombocytopenia occur with leukocytosis, which is an inflammatory neutrophilia. Later, pancytopenia develops. After drug cessation, recovery begins in 1 month, starting with leukocytosis and followed by the return of the other cell lines.
- Chloramphenicol administration in cats causes a dose-dependent, reversible marrow suppression involving the erythroid series primarily. Dogs are much less sensitive to chloramphenicol.
- Treatment for drug-induced aplastic anemia often includes supportive care, such as blood transfusions (see "Principles of Transfusion Therapy"), anabolic steroids, and antibiotics in severe cases, once the drug has been stopped.

Lead Toxicity

Lead poisoning causes a mild anemia in some cases, possibly because of increased erythrocyte fragility and abnormal erythropoiesis. Lead primarily affects heme synthesis, causing defective maturation. Other clinical signs involve GI and neurologic disturbances.

Diagnosis

- The diagnosis of lead toxicity often is based on a history of exposure to lead in paint or automobile batteries. Heparinized blood samples are used to determine lead levels. Affected animals have levels greater than 0.06 mg/dl.
- The hemogram strongly suggests lead poisoning when large numbers of nucleated erythrocytes are present with a normal or slightly decreased PCV. The anemia is often normocytic and normochromic but may be microcytic and hypochromic.
- Basophilic stippling is best seen with Romanowsky-stained blood films prepared without EDTA anticoagulant. Polychromasia generally is rare.
- Bone marrow aspirates or core biopsies are characterized by maturation arrest at the metarubricyte stage.

Treatment. Treat lead toxicity in dogs and cats with calcium EDTA (100 mg/kg) diluted to 10 mg/ml in 5% dextrose and given SC, in four divided doses, daily for 5 days.

Myelophthisis

Neoplasia

Neoplasia of the bone marrow can occur with primary hemolymphatic tumors or metastatic tumors. Mild infiltrates or focal lesions within the bone marrow produce minimal peripheral blood changes. Cytopenias occur if the involvement is diffuse and severe. Approximately 57% of dogs with multicentric lymphoma have metastasis to the bone marrow at the time of diagnosis. Only half of these have evidence of abnormal cells in circulation. Diagnosis requires bone marrow examination by both aspirate and core biopsies (see discussion under "Leukemic Disorders").

Myelofibrosis

Myelofibrosis usually occurs as a result of marrow damage produced by inflammation, necrosis, neoplasia, and toxic agents and may be seen in the terminal stages of pyruvate kinase deficiency.

- Pancytopenia is observed in severe cases, along with poikilocytosis in the form of dacryocytes and schistocytes.
- Bone marrow aspiration attempts usually produce "dry taps" (i.e., blood alone without marrow particles). Bone marrow core biopsy evaluation is necessary to diagnose myelofibrosis.
- Myelofibrosis also is associated with myelodysplastic syndrome and acute myelogenous leukemia in cats (see discussion of dysplastic and leukemic disorders).
- Supportive care, including antibiotics, blood transfusions, anabolic steroids, and glucocorticoids, often is required in severe cases. Myelofibrosis may be reversible under some conditions.

Myelonecrosis

Myelonecrosis is an uncommon cause of nonregenerative anemia. It often is associated with neoplasia but may be related to infections or toxic agents. The mechanism likely involves occlusion of microcirculation or direct injury to endothelium.

- Diagnosis is based on bone marrow examination. Aspirate biopsies may contain peripheral blood, degenerative cells, increased macrophage activity, and amorphous stringy material representing necrotic bone marrow particles. Focal to diffuse regions of necrosis appear on histologic sections of bone marrow.
- Treatment includes removal of the inciting cause, along with supportive care. Prognosis is often poor.

Osteopetrosis

Osteopetrosis is an uncommon inheritable condition affecting the normal development of bone. It causes obliteration of the marrow cavities by bone and may be associated with refractory anemia, or pancytopenia in immature or young adult dogs.

- Clinical signs usually are related to anemia.
- Diagnosis is established by the inability to obtain bone marrow material on aspiration and by distinctive radiographic findings. Increased bone density is present and cortices are thickened, leaving a narrow medullary region. Histologic examination of medullary bone reveals thickened trabeculae, reduced marrow cavities, and an absence of osteoclasts.
- Despite supportive care, the prognosis is poor.

Irradiation

Irradiation acts as a local cytotoxic agent for cancer therapy. It also is used to treat hemolymphatic malignancies and genetic defects before bone marrow transplantation. High doses produce irreversible pancytopenia and aplastic bone marrow. Supportive care (e.g., blood transfusions, antibiotics, and immunosuppressive drugs) often is given after transplantation.

Immune-Mediated Destruction (Pure Erythrocyte Aplasia)

This uncommon condition is characterized by severe reduction of erythroid stem cells without affecting granulocytic or megakaryocytic lines. Both congenital and acquired forms have been reported in dogs. The myeloid-to-erythroid ratio is usually 10:1 to 20:1. Coombs testing has been positive in a few dogs. The mechanism is considered immune-mediated because the disease often responds to prednisolone and/or cyclophosphamide therapy (also see Chapter 24).

Polycythemia

Relative Polycythemia

Increase in erythrocytes (erythrocytosis) in relative polycythemia generally is related to fluid depletion (e.g., dehydration or hemoconcentration). However, excitement or fear may cause splenic contraction and a transient rise in PCV. Greyhounds normally have a high PCV of 60%.

- Clinical signs include dark red mucous membranes with slow capillary refill time.
- Diagnosis is based on a history of stress or fluid loss, elevated PCV, and increased erythrocyte and plasma protein concentrations. The erythrogram returns to normal after fluid replacement.
- If splenic contraction is suspected, the PCV should be retaken after the patient has relaxed.

Absolute Polycythemia

The erythrocytosis in absolute polycythemia may be primary or secondary, with a sustained increase in the circulating erythrocyte mass, based on erythropoietin production.

- *Primary erythrocytosis,* or *polycythemia vera,* has low serum erythropoietin that suggests the increased erythrocyte numbers are derived from an intrinsic stem cell defect (see "Leukemic Disorders").
- *Secondary erythrocytosis* involves overproduction of erythropoietin. Causes of secondary erythrocytosis include hypoxia (e.g., caused by high altitude, chronic pulmonary disease, or cardiac disease with right-to-left shunting), tumors that produce erythropoietin (e.g., renal lymphoma, renal carcinoma, and renal fibrosarcoma), and renal disease (e.g., pyelonephritis).

Diagnosis

Diagnosis of hypoxia is based on history and evidence of lung disease or right-to-left shunting heart disease. Renal disease, benign or malignant, can be excluded by urinalysis, radiography, ultrasonography, or biopsy. Serum erythropoietin levels currently are measured by radioimmunoassay and ELISA methods.

Treatment

Treatment of secondary erythrocytosis often involves removal of the inciting cause (e.g., nephrectomy).

Methemoglobinemia

Methemoglobinemia occurs from the oxidation of iron in hemoglobin. This form of oxidized hemoglobin is unable to bind and carry oxygen, producing a state of relative hypoxia. Clinically, the mucous membranes appear blue-gray or cyanotic if methemoglobin levels

exceed 30%. The patient is often dyspneic, weak, and ataxic.

Diagnosis

The appearance of dark red or chocolate-colored blood, even after exposure to air, is diagnostic for the condition. The color change, from dark to bright red in normal blood, is readily visible by a spot test on filter paper. The blood of affected animals shows no such color change if the methemoglobin content exceeds 15%.

- Severe disease is produced from oxidant drugs and chemicals, similar to those mentioned in the previous section on Heinz body formation. Both conditions present together, but methemoglobinemia tends to occur before Heinz bodies appear.
- Several breeds of dog and a domestic shorthaired cat were reported to have a rare enzyme (NADH-methemoglobin reductase) deficiency with a mild to moderate form of the disease.
- Quantitative measurement of methemoglobin content is performed by spectrophotometry at specialized laboratories.

Treatment

Treatment is similar to Heinz body anemia. In addition, methylene blue (1 mg/kg IV, as a 1% solution), if carefully administered, has been used to treat the condition caused by oxidant drugs. Caution is necessary to avoid potentiating a hemolytic crisis. Therapy usually is not required for animals with the reductase enzyme deficiency.

▼ ***Key Point*** A mild secondary polycythemia may develop in animals with methemoglobin reductase deficiency.

LEUKOCYTE DISORDERS

Congenital Disorders

Pelger-Huët Anomaly

Pelger-Huët anomaly is an inherited disorder in dogs and cats involving granulocyte maturation. Leukocyte function in dogs is not impaired, and there is no predisposition to infection or immunodeficiency. Chondrodysplasia has been recognized in a cat with a homozygous form of this disorder.

- Diagnosis is based on the appearance of mature leukocytes in blood that have nuclei with condensed, coarse, and patchy chromatin-lacking segmentation. The nuclear shapes often resemble those of bands, metamyelocytes, and myelocytes. The cytoplasm undergoes normal maturation. Abnormalities frequently are found during routine preoperative screening and may be mistaken as a severe left shift. Inflammatory conditions should be ruled out.
- No treatment is necessary.

Feline Chédiak-Higashi Syndrome

This is a rare, inheritable disorder seen in blue-smoke Persian cats with yellow eye color. Pathogenesis involves abnormal and enlarged lysosomal granule formation in granulocytes and monocytes. Affected cats may be photophobic with cataract formation. There is increased bleeding time because of platelet granule defects. With Romanowsky stains, neutrophils contain characteristic large, pink to magenta cytoplasmic inclusions that stain positive with peroxidase and Sudan black B. These cats do not exhibit an increased susceptibility to infection although neutropenia may occur.

Lysosomal Storage Diseases

Mucopolysaccharidosis and Gangliosidosis

These are inheritable lysosomal storage diseases reported in cats and dogs caused by an enzyme deficiency. Mucopolysaccharidosis (MPS) types VI and VII have been reported in cats and dogs and present with skeletal and ocular lesions. In cats with GM_2-gangliosidosis, neurologic deficits and corneal opacification are displayed.

- In all these diseases, neutrophils may contain coarse, red-purple granules when stained with Wright-Giemsa or toluidine blue. Cells must be distinguished from toxic neutrophils.
- A urine spot test is used to screen for glycosaminoglycans, whereas a cell enzyme activity test is diagnostic.
- Experimentally, bone marrow transplantation has been used to treat some of these disorders. Affected animals should not be bred.

Other Lysosomal Storage Diseases

Other lysosomal storage diseases in dogs and cats that present with progressive neurologic dysfunction or skeletal lesions involve a distinctive lymphocyte vacuolation abnormality. The specific lysosomal storage diseases that may display lymphocyte vacuolation include GM_1- and GM_2-gangliosidosis, Niemann-Pick disease, alpha-mannosidosis, MPS (types I, VI, and VII), and alpha-fucosidosis.

- Affected lymphocytes have multiple punctate cytoplasmic vacuoles on blood films. These vacuoles should not be confused with the artifactual changes seen with prolonged storage of blood in EDTA.
- These different diseases may be distinguished by special tests for enzyme activity from blood and/or affected tissues.
- Recently, genetic tests have been used for diagnosis.

Abnormal Granulation Syndrome in Birman Cats

This is a genetic anomaly recognized in Birman cats without associated clinical disease. Diagnosis is based on the presence of fine, pinkish-purple granules within the cytoplasm of neutrophils. These lysosomal granules have normal morphology, and neutrophil function is unaffected.

Neutrophilia

Neutrophilia is defined as more than 11,500 neutrophils per microliter in the dog and more than 12,500 neutrophils per microliter in the cat. Neoplastic neutrophilic conditions are discussed in the section on leukemic disorders.

Physiologic Neutrophilia

Epinephrine release as the result of stress, fear, or strenuous muscular exertion causes demargination of leukocytes, producing a rapid rise in neutrophils and lymphocytes. Within 30 minutes, the cell counts return to normal. The effect is more common and greater in cats than in dogs.

Corticosteroid-Induced Neutrophilia

Neutrophilia may be related to exogenous administration or endogenous release of glucocorticoids. Cells are released from marginating pools and bone marrow storage pools. The magnitude and duration of the effect depends on the type of corticosteroid given.

- Diagnosis is determined by the history and by the presence of concurrent lymphopenia, eosinopenia, or monocytosis, without a left shift.
- Neutrophil hypersegmentation is common because of a prolonged life span.

Inflammatory Neutrophilia

Evidence of inflammation is an increase in non-segmented forms of neutrophils, termed a *left shift*.

Etiology

Etiology involves infectious or non-infectious sources.

- *Infectious agents* include bacteria, systemic fungi, protozoa, or rickettsiae (see Section 2).
- *Non-infectious conditions* involve tissue necrosis, such as necrotizing pancreatitis, neoplasia, thrombosis, and burns.
- *Certain malignancies* (e.g., metastatic fibrosarcoma or renal tubular carcinoma) are reported to induce a leukemoid response, presumably as a paraneoplastic disorder, rather than come from tissue necrosis alone. Leukemoid counts range from 50,000 to 100,000 leukocytes per microliter with a left shift back to bands, metamyelocytes, and myelocytes.
- *Severe abscessation* (e.g., pyometra) can also cause this extreme degree of leukocytosis.
- *Immune-mediated reactions*, such as systemic lupus erythematosus, can result in a left shift with neutrophilia.
- *Granulocytopathy syndrome* in Irish setters is a congenital cause of inflammatory neutrophilia. Neutrophils appear morphologically normal but have impaired bactericidal activity related to a deficiency of adhesion proteins. Affected dogs have recurrent bacterial infections with extreme leukocytosis that can mimic chronic granulocytic leukemia (see "Leukemic Disorders").

Diagnosis

Diagnosis of inflammatory neutrophilia is based on a careful history and a CBC evaluation. A regenerative left shift requires a simultaneous neutrophilia.

- A left shift without neutrophilia is considered degenerative, especially if there is neutropenia (see the next section), or if more non-segmented forms are present compared with mature neutrophils.
- In addition to a significant shift toward immaturity (bands >1000/µl), neutrophils may exhibit toxicity. Toxins released from bacteria are mostly responsible for the focal or diffuse cytoplasmic basophilia and vacuolation found in mature or immature neutrophils.
- Antibiotic responsiveness suggests a bacterial cause.
- Tests for specific infectious agents and immune-mediated disorders may be indicated.

Treatment

Treatment depends on the inciting cause.

▼ ***Key Point*** Animals possessing neutrophil function defects present with neutrophilia and persistent and recurrent infections.

Neutropenia

Neutropenia is defined as less than 3000 neutrophils per microliter in the dog and less than 2500 neutrophils per microliter in the cat.

Congenital Cyclic Neutropenia

Cyclic neutropenia or cyclic hematopoiesis is an inherited disorder of gray collies. It is characterized by periodic fluctuations in neutrophils and, to a lesser extent, in monocytes, platelets, and reticulocytes as a result of the intrinsic bone marrow stem cell defect. Neutropenic cycles recur at 12-day intervals.

Clinical Signs

Clinical signs during neutropenic episodes include lethargy, pyrexia, anorexia, arthritis, keratitis, and respiratory or GI infections.

Diagnosis

Diagnosis is based on history, clinical signs, and cyclic decreases in cell counts. Carrier animals can be determined only by test mating.

Treatment

Antibiotics and supportive care are necessary during neutropenic cycles. Most affected dogs die within 6 months, after chronic recurrent infections. Experimental treatments involve bone marrow transplantation and administration of lithium carbonate (21–26 mg/kg/day) or recombinant canine granulocyte-colony stimulating factor (5 µg/kg/day).

Infectious Neutropenia

Consumption of neutrophils during severe systemic inflammation often produces neutropenia with an increase of immature forms, termed a *degenerative left shift*.

- Gram-negative bacteria usually are involved, as with septicemia, severe enteritis, or other severe bacterial infections.
- Systemic mycoses and protozoal infections (e.g., *Toxoplasma*) also can cause neutropenia.
- Reduced granulopoiesis may be associated with such viruses as FeLV, FIV, feline panleukopenia virus, and canine parvovirus. FeLV is associated with a cyclic neutropenia that may respond to lithium and prednisone.
- *E. canis* also may cause bone marrow suppression. Diagnosis of infectious causes is based on the history, CBC, and bone marrow findings, in addition to specific serologic or bacterial culture results.
- Neutropenia without a marked left shift may indicate peracute consumption without adequate time for bone marrow response. The lack of a left shift, if persistent, suggests an absolute reduction of neutrophilic precursors or myeloid hypoplasia of the bone marrow.

Drug- and Toxin-Induced Neutropenia

Drugs that cause neutropenia due to myelotoxicity include estrogens, antimicrobials, and cancer chemotherapeutic agents (see "Nonregenerative Anemia"), among others. Treatment requires cessation of the drug and supportive care, particularly antibiotics. The use of recombinant canine granulocyte colony-stimulating factor has shown promise in reducing the severity of drug-induced myelosuppression.

- *Antimicrobials* include chloramphenicol, trimethoprim-sulfadiazine, cephalosporins, and griseofulvin.
- *Antineoplastic agents* include cyclophosphamide, chlorambucil, busulfan, melphalan, cisplatin, cytosine arabinoside, methotrexate, mitoxantrone, doxorubicin, and hydroxyurea.
- *Nonsteroidal anti-inflammatory drugs* occasionally have been associated with myelotoxicity.
- *Endotoxins* from gram-negative sepsis produce a transient neutropenia. Mechanisms involve a shift of neutrophils from the circulation to the marginating pools and a shortened circulating half-life (normal is approximately 5.5–7.5 hours).

Immune-Mediated Neutropenia

Destruction of antibody-coated neutrophils by macrophages is a mechanism of neutropenia considered to occur in animals. As in immune-mediated hemolysis, the disorder may involve antibody directed against surface antigens of the cell itself or antibody directed toward drug antigens attached to neutrophils.

- Drugs responsible for suspected immune-mediated blood cell destruction include antithyroid drugs (e.g., thiouracil and methimazole) and cephalosporins.
- Definitive diagnosis requires detection of antineutrophil antibodies on the cells or in serum; however, such assays are not currently available for clinical usage.
- The bone marrow is expected to show myeloid hyperplasia, with a marked decrease in late-stage forms.
- In one suspected case in a dog, immunosuppressive doses of prednisone produced a positive response.

Paraneoplastic Syndrome

Neutrophilia was found to be associated with the presence of a benign rectal polyp in a dog. In a case of lung carcinoma in a dog and dermal adenocarcinoma in a cat, extreme neutrophilia occurred without clinically detectable inflammatory foci. In these two animals, hematopoietic growth factors or colony-stimulating factor concentrations were increased as demonstrated by PCR assays.

Myelophthisis

See the section on nonregenerative anemia.

Irradiation

See the section on nonregenerative anemia.

Monocytosis

Corticosteroid-Induced Monocytosis

Monocytosis, particularly in the dog, can be induced by glucocorticoid administration. Diagnosis is based on the history, but when it is unavailable, the presence of concurrent lymphopenia, eosinopenia, and mature neutrophilia should suggest the effects of corticosteroids.

Inflammatory Monocytosis

Acute and chronic inflammatory diseases that cause a high demand for macrophages may produce monocytosis. These include immune-mediated disorders, tissue necrosis, foreign body reactions, and mycobacterial or fungal infections. Diagnosis is based on the history, physical examination, immunologic testing, cytology, and histopathology.

Neoplastic Monocytosis

See the section on leukemic disorders.

Eosinophilia

Parasitic Eosinophilia

Peripheral eosinophilia may result from infiltration of the skin, respiratory tract, and alimentary tract by such parasites as *Ancylostoma* spp, *Trichuris vulpis, Toxocara canis, Dirofilaria immitis, Dipetalonema reconditum,* lungworms (*Aelurostrongylus abstrusus, Capillaria* spp., *Filaroides* spp.), and *Paragonimus kellicotti.* Definitive diagnosis of parasitism is determined by positive fecal examinations, tracheobronchial washes, thoracic radiographs, and heartworm serologic or concentration techniques.

Allergic and Inflammatory Eosinophilia

Hypersensitivity reactions can occur owing to the effects of fleas, food, grasses, and nonspecific allergens. The production of immunoglobulin E (IgE) causes mast cell degranulation and release of chemical mediators that attract eosinophils. Peripheral eosinophilia commonly is found in these conditions. The skin, respiratory, GI, and genitourinary systems often are affected.

- The history, physical examination, skin or food testing, and tracheobronchial lavage help locate the type of allergen and the system most affected.
- Eosinophilic granuloma is a localized infiltration of the dermis by eosinophils that occurs in the oral cavity or skin of dogs and cats. Impression smears and histopathology confirm the lesion. Clinical findings, underlying causes, and treatment are discussed in Chapter 53.
- Treatment usually involves elimination of the allergen, along with antihistamine and glucocorticoid administration.

Tumor-Associated Eosinophilia

Tumor-associated eosinophilia is a reported paraneoplastic syndrome in dogs with fibrosarcoma, anaplastic mammary carcinoma, and mast cell tumors. In cats, mast cell tumors and T cell lymphoma are the neoplasms most commonly associated with eosinophilia, although it may occur in other malignancies. Diagnosis depends on normalization or reduction of the eosinophil count in response to removal of the tumor.

Feline Hypereosinophilic Syndrome

Hypereosinophilic syndrome is an uncommon form of peripheral eosinophilia accompanied by severe infiltration of eosinophils into many organs, often including the GI tract (see Chapter 69), liver, spleen, lymph nodes, and lung. It resembles leukemia of well-differentiated eosinophils resulting from an apparent involvement of the bone marrow and may in fact be considered part of a continuum of a neoplastic disease. The cause is idiopathic. Clinical signs may include anorexia, weight loss, fever, vomiting, diarrhea, and lymphadenopathy. Death results from organ dysfunction caused by tissue infiltration.

Neoplastic Eosinophilia

See the section on leukemic disorders.

Eosinopenia

Endogenous release or exogenous administration of corticosteroids produces eosinopenia within a few hours. Levels will normalize in 1 day after a single dose is given. Mechanisms implicated are enhanced margination, decreased bone marrow release, and reduced bone marrow production. Absolute reductions in eosinophils or relative decreases from a previous eosinophilia suggest the effects of glucocorticoids. Elevated cortisol levels and an endocrine dermatopathy support hyperadrenocorticism (see Chapter 33).

Basophilia

Basophil granules in dogs and cats normally stain poorly. The cells frequently are mistaken for toxic neutrophils in dogs or faded eosinophils in cats.

Parasitic Basophilia

Heartworm infection, including occult disease, is a frequent cause of basophilia in dogs and cats. Dogs with hookworms also may have basophilia. Diagnosis often involves concurrent eosinophilia and positive proof of parasitic infestation.

Allergic Basophilia

Hypersensitivity reactions cause IgE production in such organs as the skin and lungs. The immune response leads to increased numbers of mast cells and basophils.

Basophilia Associated with Lipemia

Basophilia without eosinophilia has been associated with lipemia and is thought to be related to deficiency of heparin, which is found in basophils and is needed to activate lipoprotein lipase. This enzyme is necessary to clear lipemia. This has been associated with hypothyroidism but is observed infrequently.

Basophilia Associated with Mast Cell Neoplasia

Basophilia was found in 5 of 16 dogs with systemic mastocytosis. It is also reported in a cat with intestinal mastocytoma.

Neoplasia

See the discussion on leukemic disorders.

Lymphocytosis

Epinephrine-Induced Lymphocytosis

A transient rise in lymphocytes occurs with severe exertion or physiologic stress. This is especially significant in the young cat. Transient lymphocytosis that normalizes after a short time suggests epinephrine effects on the leukogram.

Infectious Lymphocytosis

- Lymphocytosis may be the result of antigen stimulation caused by FeLV, *E. canis, Rickettsia rickettsii,* and systemic fungi. In particular, lymphocytosis involving granular lymphocytes has been associated with *E. canis* infection in dogs.
- Modified live vaccines also may produce lymphocytosis, along with the morphologic appearance of reactivity, about 1 week after immunization.
- Slightly enlarged lymphocytes with deeply basophilic cytoplasm resembling plasma cells support the diagnosis of reactivity from antigen stimulation.
- Hyperglobulinemia due to a polyclonal gammopathy and plasma cell infiltration of tissues also may occur.

Neoplastic Lymphocytosis

Lymphocytosis resulting from metastatic lymphoma occurs in 20% of dogs and cats with lymphoma. Acute or chronic lymphoid leukemia often is characterized by lymphocytosis and atypical or immature lymphoid cells. However, rare blast cells may be found in non-neoplastic conditions such as immune-mediated hemolytic anemia and canine ehrlichiosis. Persistent hematologic abnormalities must be present to consider neoplasia and should be evaluated further with bone marrow aspiration and core biopsies (see Chapter 27).

Lymphopenia

Corticosteroid-Induced Lymphopenia

Endogenous or exogenous corticosteroids produce an absolute lymphopenia or a normal value reduced from a previous lymphocytosis. It is transient because cell counts return to normal within 1 to 3 days of drug withdrawal. Lymphopenia also may relate to redistribution of lymphocytes to other tissues (see "Neutrophilia"). Lymphopenia often accompanies the stress of many acute diseases.

Infectious Lymphopenia

Viral agents, such as canine distemper virus, FeLV, FIV, and canine or feline parvoviruses, may cause lymphopenia because of direct lymphocytolysis or lymphoid tissue destruction.

Lymphopenia in Lymphatic Injury

Rupture or malformation of lymphatic vessels (e.g., chylothorax or protein-losing enteropathy from lymphangiectasia) can cause lymphopenia because of a loss of lymph fluid into the pleural cavity or gut lumen, preventing recirculation (see Chapters 164 and 69). Destruction of normal lymph node architecture or blockage of lymph drainage, as in lymphoma, may also lead to lymphopenia (see Chapter 27).

Congenital Lymphopenia

Combined immunodeficiency of T and B lymphocytes occurs in basset hounds. It is associated with severe bacterial infections within the first few weeks of life. Diagnosis is based on the presence of low Ig levels, depressed T cell function, and histologic evidence of lymphoid cell depletion, as well as peripheral lymphopenia. Supportive therapy with antibiotics is suggested, but death may occur in severe cases.

Mastocytosis or Mastocythemia

See Chapter 28.

PLATELET DISORDERS

Thrombocytopenia: Overview

Platelets may be decreased in number through immune-mediated injury, increased consumption or utilization, sequestration, and decreased production. Clinical disease may not be present in certain dog breeds that may have a reference range for platelet numbers lower than that for other breeds, such as the cavalier King Charles spaniels and greyhounds.

Clinical Signs

- Petechial or ecchymotic hemorrhages involving the mucous membranes or skin are common manifestations of thrombocytopenia.
- Epistaxis, melena, hematuria, hyphema, or prolonged bleeding from venipuncture sites or wounds often occurs.
- Evidence of inciting conditions, such as infection, neoplasia, or splenomegaly, may be present.

General Diagnostic Considerations

- The history should determine the occurrence of trauma, surgery, drug or toxin exposure, and neoplasia, as well as the time period involved.

- Physical examination discloses sites of hemorrhage, presence of hepatosplenomegaly, and concurrent infections or neoplasia.
- Use CBC to screen for hematologic abnormalities including the adequacy of the platelet numbers.
- Perform platelet counts on fresh samples (within 1–2 hours). Thrombocytopenia is considered less than 100,000 platelets per microliter. However, clinical signs of bleeding are not expected until there are less than 20,000 platelets per microliter.
- Include both aspirate and core biopsies in bone marrow evaluation to check for adequate megakaryocyte numbers.
- Perform clotting profile, including fibrinogen, PT, and APTT or activated clotting time (ACT), to help rule out other coagulopathies (as described in Chapter 23). ACT may be slightly prolonged if platelet counts are less than 10,000/µl.
- Perform a von Willebrand factor assay if the breed and clinical signs suggest a deficiency (see Chapter 23).
- Bleeding time, a platelet function test, may be prolonged because of low platelet numbers.

▼ ***Key Point*** Examine the blood smear carefully, especially at the feathered edge, before making a diagnosis of thrombocytopenia.

Treatment

Supportive therapy may include fresh blood transfusions (administered within 8 hours of collection) if both platelets and erythrocyte numbers are low. If only platelets are needed, administer platelet-rich plasma (see Chapter 23).

Immune-Mediated Platelet Injury

This is one of the most frequent and important causes of thrombocytopenia manifested by clinically significant bleeding. The clinical findings, diagnosis, and treatment are discussed in Chapter 24.

Increased Platelet Consumption or Utilization

Infectious Agents

Thrombocytopenia produced by such agents as *E. canis, E. ewingii, Anaplasma platys,* and *A. phagocytophilum* presumably is the result of increased consumption and the presence of antiplatelet antibodies.

- Thrombocytopenia is the most frequent hematologic finding in canine ehrlichiosis. Bone marrow evaluation during the acute course of *E. canis* infection indicates megakaryocytic hyperplasia. The diagnosis of ehrlichiosis is based on a history of tick exposure and serologic and PCR tests (see Chapter 17).
- *A. platys* infection produces a cyclic thrombocytopenia occurring in 2-week cycles that may be diagnosed by direct observation of morulae within platelets or by serologic and PCR tests (see Chapter 17).

Modified Live Virus Vaccination

Canine distemper virus vaccine may induce thrombocytopenia within 1 week after vaccination. The effect is transient but may persist as long as 3 weeks. It is rarely of clinical significance unless surgery is performed during the platelet count nadir.

Hemorrhage

Bleeding can consume platelets. Consumption of platelets may occur through hemorrhage alone or in association with bacterial or viral infections that produce inflammation. Endotoxemia from gram-negative bacteria leads to endothelial damage and platelet activation.

- Diagnosis is based on history, physical examination, cytology, histopathology, and culture techniques.
- Treatment is aimed at the inciting agent. Whole blood or platelet transfusions may be necessary if thrombocytopenia is severe.

Disseminated Intravascular Coagulation

This condition leads to increased consumption of platelets, as well as clotting factors. It is associated most often with infections, neoplasia, heartworm disease, pancreatitis, and shock.

- Clinical signs involve petechial and ecchymotic hemorrhages. Organ dysfunction usually reflects the effects of the primary disease.
- Diagnosis is based on the findings in tests of coagulation, including hypofibrinogenemia, prolonged PT and APTT, increased fibrin degradation products, and decreased antithrombin III activity (see Chapter 23). Microthrombi formation is found on histopathology.
- Treatment is aimed at the inciting or underlying cause when possible. Supportive care, including fluids, is necessary to prevent shock. Replacement of platelets and coagulation factors using fresh plasma usually is indicated. Heparin rarely is effective, especially if the hemorrhagic stage already has occurred (see Chapter 23).

Platelet Sequestration: Splenomegaly

The spleen normally stores approximately one-third of the body's platelets. With enlargement of the spleen from any cause, there is an increase in blood volume that sequesters more platelets within endothelial passages, resulting in thrombocytopenia. Physical examination of an enlarged spleen without evidence of other conditions that induce thrombocytopenia supports the diagnosis. It is usually of little clinical significance if

associated with benign enlargements of the spleen (see Chapter 25).

Decreased Platelet Production

Congenital Thrombocytopenia

Cyclic hematopoiesis in gray collie dogs may exhibit thrombocytopenia of a cyclic nature (see under "Neutropenia").

Infectious Thrombocytopenia

Canine distemper virus, parvoviruses, FeLV, and *E. canis* may be associated with reduced thrombopoiesis. Approximately 20% of animals with ehrlichiosis have megakaryocytic hypoplasia of the bone marrow, especially in the late stages of the disease.

Drug-Induced Thrombocytopenia

Causes of drug-induced thrombocytopenia are similar to those that produce aplastic anemia (see "Nonregenerative Anemia"). Antineoplastic agents such as cisplatin, cyclophosphamide, chlorambucil, doxorubicin, and hydroxyurea produce significant thrombocytopenia.

Myelophthisic Thrombocytopenia

See the section on nonregenerative anemia.

▼ ***Key Point*** Thrombocytopenia associated with neoplasia occurs through several mechanisms including hemorrhage, microangiopathy, disseminated intravascular coagulation, myelophthisis, immune-mediated destruction, and chemotherapeutic drugs.

Thrombocytosis

Physiologic Thrombocytosis

Increased numbers of platelets are released from the spleen as a result of epinephrine release or during heavy exercise. Pulmonary stores of platelets also may be released during exercise. This is transient and of no clinical significance.

Reactive Thrombocytosis

Conditions associated with reactive or regenerative thrombocytosis include acute blood loss, iron deficiency anemia, trauma, surgery, inflammation, splenectomy, hyperadrenocorticism, and neoplasia.

- *Tumors* that may cause thrombocytosis are mast cell tumor, hemangiosarcoma, osteosarcoma, lymphoid and myeloid leukemias, and some carcinomas.
- *Vincristine* administration produces increased thrombopoiesis and cytoplasmic fragmentation of megakaryocytes because of a reduced maturation time.

Clinical Signs

There are no clinical signs directly related to transiently elevated platelet counts.

Diagnosis and Treatment

Diagnosis is supported by history, physical examination, platelet count greater than 600,000/µl (dog) or greater than 800,000/µl (cat), and mild to moderate megakaryocytic bone marrow hyperplasia without evidence of circulating megakaryoblasts.

- Pseudohyperkalemia can occur because of leakage of potassium from clotted platelets. Therefore, plasma is preferred for measurement of potassium levels in thrombocytotic samples.
- Treatment depends on the inciting cause.

Neoplastic Thrombocytosis

See the section on leukemic disorders.

DYSPLASTIC DISORDERS

Congenital Dysplasia

Inherited Erythrocyte Macrocytosis

An inherited disorder of toy and miniature poodles is associated with abnormal morphology of erythrocytes and their precursors.

- Affected animals present with no clinical signs of anemia, and the dysplastic findings are usually incidental.
- Diagnosis is based on the breed and on findings of a normal hematocrit, presence of macrocytosis (MCV > 80 fl), megaloblastosis in the blood and bone marrow, and absence of polychromasia or reticulocytosis. An asynchrony in maturation between the nucleus and the cytoplasm characterizes the RBC abnormalities. Neutrophil hypersegmentation and giantism also may occur but are less common.
- The condition persists and is not responsive to folate or cobalamin.

Inherited Macroplatelets

Macroplatelets as an inherited disorder have been reported in Cavalier King Charles spaniels without hemorrhages or clinical signs.

Infectious Causes of Dysplasia

Abnormal morphology of erythroid, granulocytic, and megakaryocytic lines occurs in cats infected with either FeLV or FIV.

- Macrocytosis, megaloblastosis, neutrophil giantism, hypersegmentation, and dwarf megakaryocyte for-

mation characterize the dysplastic changes found as a result of viral effects on nuclear development.
- Peripheral cytopenias arise from abnormal maturation of affected cell lines.
- Clinical signs often include concurrent bacterial or protozoal infections, neoplasia, and chronic wasting.
- Definitive diagnosis requires serologic testing.
- Treatment is supportive in nature. The median survival is 12 weeks.

Drug-Induced Dysplasia

Dyserythropoiesis characterized by macrocytosis, megaloblastoid changes, nuclear fragmentation, sideroblastosis, and siderocytosis may occur in animals treated with azathioprine, cyclophosphamide, cytosine arabinoside, vincristine, or chloramphenicol.

- These changes are not associated with folate deficiency.
- Diagnosis is based on blood and bone marrow samples taken during routine post-treatment hematologic evaluations.
- Normal morphology of hematopoietic cells returns several days after cessation of drug therapy.

Nutritional Dysplasia

- Erythroid dysplastic changes and neutrophil hypersegmentation may occur in giant schnauzers with an inherited selective malabsorption of vitamin B_{12} (described in this chapter under "Nonregenerative Anemia").
- A macrocytic nonregenerative anemia is found in acquired folate deficiencies such as intestinal malabsorption, neoplasia, liver disease, dietary imbalance, and severe starvation.
- Drugs such as anticonvulsants, antibiotics, and antineoplastic agents that inhibit folate metabolism produce megaloblastic changes in erythroid precursors (see under "Nonregenerative Anemia").

LEUKEMIC DISORDERS

Lymphoma or Lymphoid Leukemia

See Chapter 27.

Myeloid (Non-lymphoid) Malignancy

The etiology for this group of malignancy is generally unknown, although it is often associated with viral infection (e.g., FeLV), immunologic dysfunction, or irradiation.

Overview of Clinical Signs

Clinical signs include pale mucous membranes (except in polycythemia vera), fever, lethargy, weight loss, chronic infections, hepatosplenomegaly, mild lymphadenopathy, and hemorrhagic tendencies.

Diagnostic Principles

Myeloid leukemias are suggested by the history (e.g., FeLV infection), clinical signs of unexplained or frequent infections, and hematologic abnormalities that affect multiple cell lines. Definitive diagnosis is made from bone marrow aspirate and core examinations.

- *Acute myeloid leukemia* has been defined in the past as subtypes M_1 to M_7, which have blast cells in the bone marrow equal to or exceeding 30% of non-erythroid cells. However, to follow the current human classification, the percentage of myeloblasts may be defined as greater than 20% of non-erythroid cells. In general, survival involves weeks to months for patients with acute myeloid leukemia.
- *Chronic myeloid leukemia* subtypes have increased numbers of blast cells, but these cells account for less than 20% of non-erythroid cells of the bone marrow. A longer survival of months to years is expected for patients with chronic myeloid leukemia.
- Cytochemical staining or immunocytochemistry of blast cells from blood and bone marrow smears may be performed on unfixed slides submitted to special laboratories to determine the cell type primarily involved.
- Alternatively, flow cytometry may be helpful in some cases to define the cell type.

Treatment Principles

Treatment generally consists of supportive care (e.g., antibiotics, blood transfusions, and fluids).

- Antineoplastic agents, including corticosteroids, cytosine arabinoside, chlorambucil, busulfan, and hydroxyurea, have been used with limited success.
- Bone marrow transplantation has been attempted in the cat but is cost prohibitive for clinical application.

Myelodysplastic Syndrome

Myelodysplastic syndrome (MDS) is a clonal expansion of a hematopoietic stem cell abnormality characterized by persistent peripheral cytopenias in one or more hematopoietic cell lines together with features of abnormal maturation. This condition often precedes an overt leukemia by several weeks to months. Cats affected usually are seropositive for FeLV.

Several morphologic types exist relative to the numbers of myeloblasts present (e.g., MDS-RC [refractory cytopenia] or MDS-EB [excess blasts]) and a variant of MDS-RC with erythroid cells present (e.g., MDS-Er [erythroid predominance]). Cases of MDS-EB having 5% or greater marrow myeloblasts demonstrate shorter survival and poor response to treatment.

Clinical Signs

Clinical signs involve chronic infections, lethargy due to anemia, and hemorrhage.

Diagnosis

Despite the cytopenias, the bone marrow is usually hypercellular, with a mild increase in numbers of myeloblasts (<20% of all nucleated cells). Dysplastic changes in the blood or bone marrow include macrocytosis, megaloblastosis, nuclear fragmentation, abnormal cytoplasmic granulation, neutrophil hypersegmentation or hyposegmentation, micromegakaryocyte or macrothrombocyte formation, and cell giantism.

Treatment

Because the condition may persist for long periods without major clinical disease, treatment is usually supportive, including antibiotics and blood transfusions as needed.

- Antineoplastic agents, such as low-dose cytosine arabinoside, have been used to induce normal maturation and prevent conversion to a malignant state. Results with these agents have been mixed and therefore cannot be recommended as treatment.
- Dyserythropoiesis in dogs may respond to prednisone and recombinant human erythropoietin (100 U/kg SC q48h for 10 days).

Acute Myeloid Leukemia

Acute Myeloblastic Leukemia (M_1, M_2)

Acute myeloblastic leukemia (AML) is relatively common among leukemias and often is associated with FeLV in cats. It is characterized by a high percentage of myeloblasts in the bone marrow (>20% of non-erythroid cells). Acute promyelocytic leukemia (M_3) is recognized in people.

- These cells have pale basophilic cytoplasm that may contain several small, red granules. Nuclei are round, with prominent nucleoli. Intermediate- and late-stage forms of neutrophils are present to a variable degree.
- The CBC often indicates a severe nonregenerative anemia and thrombocytopenia. Total leukocyte counts usually are elevated.
- Cytochemical staining of blast cells is variably positive for peroxidase, Sudan black B, chloroacetate esterase, leukocyte alkaline phosphatase, and acid phosphatase.
- The bone marrow that is rebounding from neutropenia, such as that following feline panleukopenia infection, can appear neoplastic because of the presence of circulating myeloblasts. Persistent hematologic abnormalities must occur to confirm leukemia.

Acute Myelomonocytic Leukemia (M_4)

This is a common form of myeloid leukemia in dogs and cats. It involves the common stem cell for both granulocytes and monocytes.

- Cytochemical staining suggests the presence of both monoblasts and myeloblasts.
- The two blast cell types together are >20% of non-erythroid cells in the bone marrow.

Acute Monocytic Leukemia (M_5)

This condition has been reported in both dogs and cats. It is characterized by moderate to marked increases of monoblasts in the bone marrow, which are >20% of non-erythroid cells.

- These cells have basophilic cytoplasm that lacks any obvious granulation. Nuclei exhibit extreme irregularity, which gives the cell a folded appearance. Nucleoli are usually prominent.
- Cytochemical staining of the blast cells is generally positive for nonspecific esterases and acid phosphatase.

Erythroleukemia (M_6)

Erythroleukemia incorporates the varied manifestations of erythroid neoplastic cells. It frequently is associated with FeLV infection in cats.

- Rubriblasts may predominate or accompany neoplastic myeloblasts. Dysplastic changes are frequently prominent, such as megaloblastosis, neutrophil giantism, or hypersegmentation.
- Normochromic macrocytes and nucleated erythrocytes are found in the blood, without regenerative signs of polychromasia or reticulocytosis.
- Over time, this form of leukemia may change in appearance and progress to involve predominantly granulocytic precursors.

Megakaryoblastic Leukemia (M_7)

This is a rare type of leukemia reported in dogs and cats. It may be associated with irradiation in the dog.

- Laboratory findings indicate severe nonregenerative anemia, leukopenia, and often thrombocytopenia, although platelet counts are variable.
- Megakaryoblasts may appear in the circulation, and platelet morphology is often bizarre, characterized by giantism and abnormal granulation.
- Hemolymphatic organs usually are infiltrated by the neoplastic population, which rules out a benign proliferation.
- Immunocytochemical stains are used to determine the megakaryocytic origin of the blast cells.

Chronic Myeloproliferative Diseases

Chronic Granulocytic (Neutrophilic) Leukemia

This disorder is characterized by a low percentage of myeloblasts in the bone marrow (<20% of all nucleated cells), with increased numbers of early forms such as progranulocytes to metamyelocytes in the blood and bone marrow.

- Leukocytes often are elevated markedly (40,000–200,000/µl). Anemia is mild to moderate, and platelet counts are variable.
- The elevated leukocyte count distinguishes this condition from MDS because both conditions have a similar bone marrow presentation. The marrow myeloid-to-erythroid ratio is 4:1 to 25:1.
- This form of leukemia must be differentiated from leukemoid reactions caused by highly suppurative infections such as pyometra (see "Neutrophilia").
- Death often occurs months after detection and may be associated with a blast cell crisis, severe anemia, and thrombocytopenia.

Eosinophilic Leukemia

This type of leukemia is rare, but it has been documented in the cat associated with FeLV infection and in the dog.

- It is characterized by a high eosinophil count (often >50,000/µl) with a shift toward immaturity. A moderate anemia may be present. It may be difficult to differentiate this malignancy from reactive hypereosinophilic conditions (e.g., allergies, parasitism, eosinophilic inflammatory diseases, mast cell tumors, and certain lymphomas) (see "Eosinophilia").
- Leukemic eosinophils spread from the bone marrow and infiltrate other tissues, such as the lymph nodes, liver, and spleen.

Basophilic Leukemia

This disorder is rare, and most cases have been reported in the dog. Mature and immature basophils are increased in the blood or bone marrow, and tissue infiltration may occur. It has been associated with thrombocytosis and anemia.

- Cytochemical staining with omega-exonuclease is helpful in identifying basophil precursors when cytoplasmic granulation is inapparent.
- Basophilic leukemia must be differentiated from mast cell leukemia.
- Treatment is suggested using hydroxyurea (Hydrea, Squibb) at 50 mg/kg/day in dogs for 3 days a week until cell counts are reduced sufficiently. Survival has been reported up to 21 months.

Polycythemia Vera

Polycythemia vera occurs rarely in dogs and cats.

Clinical Signs

Clinical signs differ from other myeloid leukemias because they relate to increased erythrocyte mass and blood hyperviscosity.

- Mucous membranes are dark red because of hematocrits of 65% to 82%. Splenomegaly usually is not present.
- Polyuria, polydipsia, hemorrhage, and neurologic disorders occur in 50% of canine cases.

Diagnosis

Rule out other causes of erythrocytosis (see "Polycythemia"). Arterial blood gas evaluations are normal, with no evidence of hypoxia. Erythropoietin levels are absent or reduced when measured at specialized laboratories. Leukocyte and platelet counts are normal to mildly elevated. Bone marrow examination indicates hyperplasia of the erythroid line, with normal morphology and maturation. Myeloblasts make up less than 20% of nucleated cells.

Treatment

Use phlebotomy for immediate relief (10–20 ml/kg/day).

- Survival of at least 1.5 years is possible with hydroxyurea given at 30 mg/kg/day for 1 week then 15 mg/kg once daily until remission; then taper to the lowest effective frequency of administration based on monitoring hematocrit. Monitor cats more closely because of greater risk of myelotoxicity.
- Radiophosphorus ^{32}P (2.4–3.3 mCi/m^2) has been used with encouraging results.

Primary Thrombocythemia

Primary, or essential, thrombocythemia is a rare neoplastic proliferation of platelets reported in the dog and cat. It is not related to transient or reactive increases (see "Thrombocytosis").

- Clinical signs include splenomegaly and platelet function abnormalities, such as spontaneous bleeding and thromboembolism.
- Platelet counts are persistently greater than 600,000/µl and are usually greater than 1 million/µl. Neutrophilia or basophilia also may be present.
- Treatment may include melphalan (2–4 mg/m^2), hydroxyurea (500 mg/m^2), or radiophosphorus ^{32}P (2.4–3.5 mCi/m^2). Therapy produces a survival of up to 32 months.
- Transformation to chronic myelogenous leukemia has been reported.

Idiopathic Myelofibrosis

This chronic myeloproliferative disease is also known as agnogenic myeloid metaplasia or chronic megakaryocytic-

granulocytic myelosis. It is an uncommon condition that results in intramedullary and extramedullary hematopoiesis accompanied by a reactive or secondary marrow fibrosis late in the course of the disease. The hematopoietic precursors most involved are granulocytic and megakaryocytic forms, which infiltrate the spleen and liver. Some cases may be mistaken for acute myeloid leukemia of megakaryocytic origin.

- The peripheral blood often has concurrent immature granulocytes and erythroid cells, termed a *leukoerythroblastic reaction*. Erythrocytes may display poikilocytosis with a teardrop appearance (dacryocytosis).
- Bone marrow aspiration is often difficult related to the presence of myelofibrosis, so core biopsy is recommended to confirm the diagnosis.
- Survival varies from months to years depending on the response to treatment for the nonregenerative anemia.

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Chapter

23 Coagulation Diseases

Marjory B. Brooks

Coagulation disorders comprise a group of bleeding diatheses caused by dysfunction of the clotting cascade and subsequent failure of fibrin clot formation. Included in this discussion of coagulation disorders are von Willebrand disease and the complex syndrome of disseminated intravascular coagulation. Common bleeding diatheses that are not coagulation disorders include thrombocytopenia and acquired platelet dysfunction (platelet disorders are discussed in Chapter 22). Initial examination should aim to differentiate bleeding caused by localized blood vessel injury or vessel disease from bleeding due to a systemic platelet or coagulation defect.

ETIOLOGY

Categories of bleeding disorders are listed in Table 23-1 and include coagulation factor deficiencies, von Willebrand disease, and disseminated intravascular coagulation.

Coagulation Factor Deficiencies

Acquired Deficiencies

Acquired deficiencies of functional coagulation factors are common disorders and are caused by decreased production of coagulation factors, release of inactive factors, or inhibition of factor activity.

Production Defect

Coagulation factors are proteins synthesized primarily or exclusively in the liver. Clinically significant reduction in these factors most often accompanies acute fulminant necrosis, chronic cirrhosis, and portosystemic shunting diseases; each of these causes severe liver failure and marked reduction in functional hepatic mass.

Inactive Factors

Vitamin K Deficiency

- The prothrombin group of coagulation factors (factors II, VII, IX, and X) require vitamin K for post-translational carboxylation. This modification allows the factors to assume an active conformation and participate in the coagulation cascade.
- The most common vitamin K deficiency state in small animal medicine occurs after ingestion of anticoagulant rodenticides. These poisons prevent intrahepatic vitamin K recycling, which depletes vitamin K from body stores. Potency and duration of effect vary for different poisons. Overdose of the anticoagulant drug warfarin causes bleeding via the same mechanism.
- Posthepatic biliary obstruction and infiltrative bowel disease also cause vitamin K deficiency by reducing its intestinal absorption.
- Occasionally, bleeding due to vitamin K deficiency is seen in neonatal puppies. Typically, these puppies are born prematurely or are delivered by cesarean section.

Factor Inhibition

Heparin

- Heparin inhibits fibrin clot formation by enhancing the activity of the plasma anticoagulant protein, antithrombin III, several thousand-fold.
- Bleeding due to iatrogenic factor inactivation results from overdose of heparin for treatment of thrombotic disorders or excessive heparinization of transfused blood products.
- Release of heparin from mast cell tumor granules often causes local tissue hemorrhage and edema. In rare cases, massive degranulation of disseminated tumor causes systemic anticoagulation.

Pathologic Inhibitors

- High plasma concentration of fibrin(ogen) degradation products can interfere with mature fibrin clot formation.
- Autoantibodies and alloantibodies directed against specific coagulation factors have been reported in human patients and should be included in the differential of acquired coagulopathy in animals.
- Antibodies directed against phospholipid-binding proteins, referred to as “lupus anticoagulants,” cause prolongation of in vitro clotting times but are associated with clinical thrombotic syndromes.

Table 23-1. CLASSIFICATION AND CAUSES OF COAGULATION DISORDERS

Category	Cause
Coagulation factor deficiency	
Acquired (multiple) factor deficiencies	Decreased factor production
	Liver failure (acute necrosis, chronic cirrhosis, portosystemic shunts)
	Decreased factor activation
	Vitamin K deficiency (anticoagulant rodenticide toxicity, biliary obstruction, malabsorption, neonatal)
	Heparin excess (iatrogenic, mast cell tumor)
	Pathologic inhibitors (fibrin degradation products, anti-factor antibodies)
Inherited (single) factor deficiencies	X-linked traits—Males affected
	Hemophilia A—Factor VIII deficiency (most common defect in dogs and cats; German shepherd breed has high prevalence)
	Hemophilia B—Factor IX deficiency (especially Airedale and Bichon, but any purebred and mixed-breed dogs and cats)
	Autosomal traits—Males and females affected
	Dysfibrinogenemia and hypofibrinogenemia (borzoi, French bulldog, DSH cats)
	Prothrombin deficiency (boxer, English cocker)
	Factor VII deficiency—Mild bleeding (beagle), moderate to severe bleeding (malamute)
	Factor X deficiency—Severe bleeding (American cocker spaniel, Jack Russell terrier, DSH cat)
	Factor XI deficiency—Severe bleeding (English springer spaniel, Kerry blue terrier, DSH cat)
	Factor XII deficiency—No abnormal bleeding (common in cats, DSH and purebred)
von Willebrand disease	Inherited—Autosomal trait; 3 subtypes
	Type 1—Variable severity in affected dogs, high prevalence (Doberman pinscher, golden retriever, standard poodle, Pembroke corgi, Bernese mountain dog, miniature pinscher, dachshund, others)
	Types 2 and 3—Severe bleeding in affected dogs (German wirehaired and shorthaired pointer, Scottish terrier, Shetland sheepdog, Chesapeake retriever, others)
Disseminated intravascular coagulation	Factor depletion and systemic fibrinolysis
	Neoplasia (hemangiosarcoma, prostatic and mammary carcinoma, lymphoid tumors)
	Sepsis
	Liver disease
	Pancreatitis
	Intravascular hemolysis
	Severe tissue injury (burns, crush wounds)

DSH, domestic shorthair.

Inherited Deficiencies

Inherited factor deficiencies are caused by mutations in genes coding for specific coagulation proteins or vitamin K recycling enzymes. These defects are typically found in certain lines of purebred dogs and cats and are often propagated when asymptomatic carriers are bred. Hereditary bleeding disorders may also arise from new, spontaneous mutations in previously unaffected families of purebred or mixed-breed animals. Inheritance patterns vary for different factor deficiencies.

X-linked Traits

Hemophilia is by far the most common severe coagulation factor deficiency and is inherited as an X-linked recessive trait. Spontaneous mutations causing hemophilia arise frequently in dogs and cats.

- Males inheriting one abnormal gene from their mother express the trait, whereas females inheriting one abnormal gene from either parent are asymptomatic carriers.
- Mutations in the factor VIII gene cause hemophilia A and arise about 5 times as often as those in the factor IX gene. Hemophilia B is a specific deficiency of factor IX.
- German shepherds, especially those with European dogs in their pedigree, have the highest breed prevalence of canine hemophilia A.

Autosomal Traits

Males and females express these traits with equal frequency.

- Clinically significant bleeding disorders due to inherited deficiencies of factors XI, X, VII, and II and fibrinogen have been described.
- Factor XII deficiency is common in cats but does not cause a clinical bleeding diathesis.
- A combined deficiency of vitamin K-dependent factors (II, VII, IX, and X) has been reported in Devon Rex cats and Labrador retriever dogs.

Von Willebrand Disease

Von Willebrand (vWD) disease is the most common hereditary bleeding disorder in dogs. Bleeding in affected individuals is caused by deficiency or dysfunc-

tion of von Willebrand factor (vWF), a plasma protein critical for normal platelet function in the primary phase of hemostasis.

- The trait is autosomal; both males and females can transmit and/or express vWD.
- Exacerbation of the bleeding tendency of vWD may be seen in association with concurrent thrombocytopenia, infection, hormonal fluctuation, or endocrinopathy (especially thyroid insufficiency). Avoid giving drugs with antiplatelet effects, such as aspirin and other nonsteroidal anti-inflammatory drugs, plasma expanders, and heparin, to vWF-deficient patients.
- Breeds with high prevalence or severe forms of vWD include Doberman pinscher, Scottish terrier, Shetland sheepdog, German wirehair and shorthair pointer, Pembroke Welsh corgi, Chesapeake retriever, and Australian shepherd. The vWD trait can occur in any breed and is occasionally diagnosed in mixed-breed dogs.

Disseminated Intravascular Coagulation

Disseminated intravascular coagulation (DIC) is a dynamic disease process caused by systemic activation of the coagulation cascade. The loss of localized clot formation results in thrombotic occlusion of small and midsize vessels, with compromise to tissue blood supplies and secondary activation of fibrinolytic pathways.

- Disorders that trigger the DIC process cause widespread damage to vascular tissue, platelet aggregation and consumption, or intravascular release of tissue factor.
- DIC most often accompanies severe inflammatory disease syndromes and diseases causing severe tissue injury such as sepsis, neoplasia (especially hemangiosarcoma, hepatic neoplasia, lymphoma, and prostatic and mammary carcinoma), burn or crush wounds, pancreatitis, and intravascular hemolysis.
- Bleeding may develop in patients with DIC as coagulation factors, platelets, and regulatory hemostaticproteins are depleted in the systemic thrombotic process.

CLINICAL SIGNS

Coagulation disorders are characterized by spontaneous hemorrhage and/or excessive bleeding after surgery or trauma. Hemorrhage into the central nervous system (CNS) may cause acute onset of neurologic dysfunction or sudden death. Thrombocytopenia (see Chapter 22), rather than coagulation factor deficiency, is by far the most common cause of petechiae in small animals. Hemorrhagic macules, papules, and ecchymoses are lesions most characteristic of primary or secondary vasculitic diseases and rarely are caused by coagulopathy.

- *Coagulation factor deficiencies* tend to cause spontaneous bleeding into the chest, abdomen, or muscles, and subcutaneous hematoma formation.
- *vWD* is associated most often with spontaneous hemorrhage from mucosal surfaces of oral and nasal cavities or from intestinal and genitourinary tracts. Excessive or prolonged bleeding occurs after injury or surgery.
- *Bleeding in association with DIC* is usually severe and occurs from mucosal surfaces and into body cavities; in addition, signs of the underlying disease are usually present.
- *Bleeding from venipuncture sites* most often accompanies severe deficiencies of multiple coagulation factors or fulminant DIC. Absence of this sign does not rule out a clinically significant coagulation disorder.

DIAGNOSIS

▼ ***Key Point*** The first consideration when evaluating bleeding patients is to differentiate a blood loss due to injury of a single or local group of blood vessels from a systemic bleeding diathesis. This distinction is usually apparent after thorough history, physical examination, and evaluation of quick assessment tests.

History

The history should include specific questions to identify previous episodes of spontaneous bleeding or excessive hemorrhage after surgery or trauma.

- Gingival bleeding from tooth eruption and bleeding from docking or dewclaw removal are common signs of inherited coagulation factor deficiency and vWD. Conversely, history of severe trauma or invasive surgical procedure without excessive hemorrhage rules out an inherited hemostatic defect.
- Patients with histories of hepatic disease or disorders associated with DIC are at risk for acquired coagulation defects and should be further evaluated before invasive procedures.

Physical Examination

Physical examination should define as thoroughly as possible the nature, severity, and precise anatomic source of hemorrhage. In patients with a single obvious site of external blood loss, ophthalmoscopy, digital anorectal examination, careful auscultation, and joint palpation may identify additional sites of hemorrhage that would be suggestive of a systemic hemostatic defect.

Radiographic Examination

Radiography of the thorax and abdomen can detect fluid densities indicative of bleeding in pleural, peritoneal, or retroperitoneal spaces. Intrapulmonary

hemorrhage causes an alveolar pattern on thoracic films. Epistaxis, hematuria, and gastrointestinal hemorrhage may be difficult to differentiate as being signs of local vessel trauma versus signs of systemic coagulation disorder. Contrast radiography, ultrasonography, and computed tomography (CT) scan can non-invasively identify erosive, infiltrative, or mass lesions causing vessel damage. CT scan is especially useful for evaluating the nasal cavity to identify focal lesions early in the disease process before they extend into the CNS.

Quick Assessment Tests

Quick assessment tests (QATs) are useful for identifying hemostatic defects and evaluating hemostatic function prior to performing invasive procedures. Table 23-2 presents additional diagnostic ruleouts and procedures, based on results of QATs, for differentiating coagulation disorders from other hemostatic defects. Table 23-3 lists expected results of the following QATs for categories of common coagulation disorders.

Slide Estimate of Platelet Number

Thrombocytopenia can be ruled out if examination of a stained blood film under oil immersion reveals at least 7 to 10 platelets per field for dogs and 10 to 15 platelets per field for cats.

Activated Clotting Time

Most of the common acquired and inherited coagulation factor deficiencies can be detected by prolongation of activated clotting time (ACT), a functional test of the intrinsic clotting system.

- Procedure
  - Collect 2 ml of whole blood directly into a test tube, maintain the needle (Vacutainer, Becton-Dickinson) in the vein, remove the first tube, and replace it with a second evacuated tube containing siliceous earth (Vacutainer, Becton-Dickinson) to withdraw a second 2-ml sample.
  - Warm the evacuated tube to 37°C before sampling.
  - Immediately after blood collection, gently invert the second tube several times to mix the blood with the siliceous activator then place it in a heating block calibrated at 37°C.
  - After incubation for 45 seconds, remove the tube from the block at 5- to 10-second intervals, gently tilt it, and evaluate for clot formation.
- ACT is the time elapsed from sampling to clot formation.
- Normal range of canine ACT is 60 to 120 seconds; feline range is 60 to 70 seconds.
- ACT may be technically difficult to perform in cats and small dogs.
- Sampling from the jugular vein is not recommended in patients with severe hemorrhagic disorders because iatrogenic hematoma formation and subsequent upper respiratory obstruction might occur.

Bleeding Time Tests

Bleeding time tests are in vivo measures of hemostatic function performed by making a standard wound and timing the interval to cessation of blood flow. These tests should be performed only on patients with platelet counts greater than 100,000/µl because significant thrombocytopenia prolongs bleeding time.

Buccal Mucosa Bleeding Time Test

- Procedure
  - Evert the lip, then hold it in place with gauze that encircles the muzzle and causes the buccal veins to engorge slightly.

Table 23-2. DIAGNOSTIC CHECKLISTS BASED ON RESULTS OF QUICK ASSESSMENT TESTS

QAT	Result; Interpretation	Checklist
Platelet estimate	Low; thrombocytopenia	See Chapter 22
Bleeding time	Prolonged; defect of primary hemostasis	History (drug exposure, familial bleeding) CBC/metabolic profile, endocrine profile Radiography vWF:Ag Fibrin degradation product or D-dimer titer Platelet function testing
Activated clotting time	Prolonged; defect of intrinsic and/or common coagulation system	History (toxin exposure, familial bleeding) Coagulation screening assays Coagulation factor analysis CBC/metabolic profile Liver function Radiography Fibrin degradation product or D-dimer titer Response to vitamin K therapy

CBC, complete blood count; QAT, quick assessment test; vWF:Ag, von Willebrand factor antigen.

Table 23-3. EXPECTED RESULTS OF QUICK ASSESSMENT TESTS FOR COAGULATION DISORDERS

Category	Tests			
	Platelet Count	ACT	TBT	BMBT
Coagulation factor deficiency				
Acquired deficiencies	N	A	A	N
Inherited deficiencies				
Hemophilia (A and B)	N	A	A	N
Dysfibrinogenemia	N	A	A	N/A
Prothrombin and Factor X, XI deficiencies	N	A	A	N
Factor VII deficiency	N	N	N	N
Factor XII deficiency	N	A	N	N
vWD	N	N	A	A
DIC (hemorrhagic phase)	A	A	A	N/A

A, abnormal; ACT, activated clotting time; BMBT, buccal mucosal bleeding time; DIC, disseminated intravascular coagulation; N, normal; QAT, quick assessment test; TBT, toenail bleeding time; vWD, von Willebrand disease.

- Use a template device (Simplate II, Organon Teknika) to make two parallel incisions in mucosa of the upper lip.
- Collect hemorrhage from the wounds on filter paper applied underneath, but not directly to, bleeding sites.

- Buccal mucosa bleeding time (BMBT) is the average time elapsed from triggering the device until blood stops flowing from both incisions.
- Normal BMBT is 2 to 4 minutes for dogs and cats.
- BMBT is prolonged for patients with acquired and inherited platelet dysfunction and vWD but is normal for patients with coagulation factor deficiencies and for some patients with DIC.
- Cats require sedation for BMBT testing, but some dogs tolerate this procedure without chemical restraint.

Toenail Bleeding Time Test

- Procedure
  - Using a guillotine-type toenail clipper, make a clean transection at the tip of the nail cuticle.
  - Allow blood to flow freely from the injury.
- The time from transection until blood ceases to flow is the toenail bleeding time (TBT).
- Normal TBT is 5 to 6 minutes; accuracy depends on technique and immobilization of the patient's digit during the procedure.
- TBT is less specific than BMBT and is prolonged for patients with clinically significant coagulation factor deficiencies, vWD, platelet dysfunction, and bleeding due to DIC.
- The TBT test should only be performed on sedated or anesthetized patients.

Definitive Tests

Definitive tests to diagnose coagulation disorders depend on correct sampling technique and test systems that are validated specifically for canine and feline patients. Table 23-4 lists coagulation factors of the intrinsic, extrinsic, and common pathways, a classification system useful for in vitro diagnosis of bleeding disorders. Table 23-5 presents expected results of diagnostic tests for categories of common coagulation disorders.

Coagulation Screening Assays

These tests measure the time, in seconds, for in vitro fibrin clot formation. Prolongation of screening assay times beyond the laboratory's reference range for the species is indicative of coagulation factor deficiency or inhibition.

- *Activated partial thromboplastin time (aPTT)* is sensitive to deficiencies of intrinsic and common coagulation pathways.

Table 23-4. COAGULATION FACTORS OF THE INTRINSIC, EXTRINSIC, AND COMMON PATHWAYS

Intrinsic	Extrinsic	Common
Contact factors (kininogen, prekallikrein)	Tissue factor	Factor X
Factor XII	Factor VII	Factor V
Factor XI		Factor II (prothrombin)
Factor IX		Factor I (fibrinogen)
Factor VIII		

Table 23-5. DEFINITIVE DIAGNOSTIC TESTS FOR COAGULATION DISORDERS

Category	Tests	Results
Coagulation Factor Deficiency		
Acquired deficiencies		
Liver disease	aPTT, PT, TCT	Prolonged
	Fibrinogen	Low
	Factor assays	Low activity for most factors
Vitamin K deficiency	aPTT, PT	Prolonged
	TCT, Fibrinogen	Normal
	Factor assays	Low factors II, VII, IX, X
Heparin excess	aPTT, PT, TCT	Prolonged (PT least affected)
	Fibrinogen	Normal
	anti-Xa activity	High (>1 U/ml)
Hereditary deficiencies		
Hemophilia	aPTT	Prolonged
	PT, TCT, fibrinogen	Normal
	Factor assays	Low factor VIII (Hemophilia A) or IX (hemophilia B)
Hypo/dysfibrinogenemia	aPTT, PT, TCT	Prolonged
	Fibrinogen	Low
Prothrombin or factor X deficiency	aPTT, PT	Prolonged
	TCT, fibrinogen	Normal
	Factor assays	Low factor II or X
Factor VII deficiency	aPTT, TCT, fibrinogen	Normal
	PT	Prolonged
	Factor assays	Low factor VII
Factor XI or XII deficiency	aPTT	Marked prolongation
	PT, TCT, fibrinogen	Normal
	Factor assays	Low factor XI or XII
von Willebrand Disease		
	aPTT, PT, TCT, fibrinogen	Normal
	Buccal bleeding time	Prolonged
	vWF:Ag	Low (type 1 & 2), absent (type 3)
	vWF collagen binding, multimers	abnormal (type 2)
Disseminated Intravascular Coagulation		
	aPTT, PT, TCT	Normal to marked prolongation
	Fibrinogen	High or normal (thrombotic DIC)
	Platelet count and antithrombin	Low (hemorrhagic DIC)
	FDPs and D-dimer	Low
	Red cell morphology	High
		Schistocytes

aPTT, activated partial thromboplastin time; DIC, disseminated intravascular coagulation; FDP, fibrin or fibrinogen degradation product; PT, prothrombin time; TCT, thrombin clotting time; vWF:Ag, von Willebrand factor antigen.
Reference ranges author's laboratory 2004: Canine: aPTT (10–17 sec); PT (14–18 sec); TCT (5–9 sec); fibrinogen (147–479 mg/dl). Feline: aPTT (14–18 sec); PT (18–22 sec); TCT (5–8 sec); fibrinogen (76–270 mg/dl). Both species: Bleeding time < 4 minutes; vWF:Ag > 50%; antithrombin > 75%; FDP < 5 µg/ml; D-dimer < 250 ng/ml.

- *Prothrombin time (PT)* detects deficiencies in extrinsic and common pathways.
- *Fibrinogen* concentration (mg/dl) is a quantitative measure of plasma fibrinogen.
- *Thrombin clotting time (TCT)* detects both deficiency and dysfunction of fibrinogen.
- Based on the pattern of abnormalities detected in coagulation screening assays, individual clotting factor analyses identify specific single or multiple coagulation factor deficiencies.

Specific von Willebrand Factor Assays

Specific tests must be performed to establish diagnosis of vWD. Clotting time tests, coagulation assays, and platelet count do not detect abnormal vWF. Three subtypes of vWD occur in dogs: Type 1 vWD is a mild to moderate form characterized by low vWF concentration and normal vWF structure. Type 2 vWD causes a severe bleeding diathesis, with low vWF concentration and abnormal structure. Type 3 vWD is a severe form caused by a complete lack of vWF.

- Measurement of vWF antigen is a specific measurement of plasma vWF concentration.
- Patients with vWF below the normal range (established at each testing laboratory) are considered at risk for carrying and/or expressing the vWD trait.
- In addition to low or absent plasma vWF, affected individuals have prolonged *in vivo* bleeding time.

Diagnosis of Disseminated Intravascular Coagulation

Definitive diagnosis of DIC cannot be based on one diagnostic test but depends on a combination of clinical signs and laboratory abnormalities. The DIC process is dynamic, and an early thrombotic or pro-coagulant phase may be followed by later signs of hemorrhage. Serial evaluations are useful to monitor response to therapy and determine prognosis.

- The presence of high plasma concentration of fibrin or fibrinogen degradation products or of cross-linked fibrin fragments (D-dimer) is compatible with ongoing systemic fibrinolysis usually caused by DIC.
- Additional laboratory criteria of DIC include the following:
  - Falling platelet count
  - Low antithrombin activity
  - Low or high fibrinogen
  - Prolongation of coagulation screening assays (aPTT, PT, TCT)
  - Presence of schistocytes on stained peripheral blood smears
  - Elevated values of plasma-soluble fibrin monomer and thrombin-antithrombin complex are believed to be sensitive tests of DIC; however, these assays are not readily available in clinical human or veterinary practice

TREATMENT

▼ ***Key Point*** Successful management of patients with coagulation disorders requires establishing an accurate diagnosis and then administering appropriate transfusion and non-transfusion support. Pretreatment samples are invaluable for establishing definitive diagnosis early in the course of disease.

Transfusion Therapy

Transfusion therapy to supply active factors is required for patients with severe, inherited coagulation factor deficiencies and severe vWD and for patients with acquired disorders that are not responsive to correction of an underlying disease process. Table 23-6 lists blood product(s) and dosages for treating specific coagulation disorders (see Chapter 22 for a description of cross-matching protocol).

- Transfusion of whole blood, administered within 4 to 6 hours of collection, supplies active coagulation factors and vWF, as well as red blood cells (RBCs).
- Transfusion of plasma products (fresh plasma, fresh frozen plasma, plasma concentrate), rather than whole blood, reduces the risk of immunologic transfusion reactions, most importantly RBC sensitization. Plasma components also can be transfused preoperatively and repeatedly in 1 day without causing volume overload.
- Stored whole blood and packed red cells do not contain replacement levels of coagulation factors or vWF, but the administration of red cells is indicated for patients with signs of acute or chronic blood loss anemia. Packed cells, in combination with an appropriate plasma product, are the therapeutic equivalent of fresh whole blood. The use of blood components, rather than fresh whole blood, provides a more convenient, rapid, and often safer means of transfusion support.
- Do not routinely pretreat with antihistamine or corticosteroid before transfusion of any blood product. Acute immune reactions directed against RBCs can be prevented in cats by using donors that are blood type and cross-match compatible with the recipient. Anti-RBC reactions are prevented in dogs by using type-compatible or "universal donor"–type dogs. Dogs negative for dog erythrocyte antigen (DEA) 1 (1.1 and 1.2) and negative for DEA 7 are unlikely to

Table 23-6. GUIDELINES FOR TRANSFUSION*

Product	Volume	Frequency	Indications
Fresh whole blood†	12–20 ml/kg	q24h	Signs of anemia accompanying coagulation factor deficiencies, von Willebrand disease, disseminated intravascular coagulation
Packed red cells	6–10 ml/kg	q12–24h	
Fresh plasma†	6–12 ml/kg	q8–12h	Coagulation factor deficiencies, von Willebrand disease, hemorrhagic disseminated intravascular coagulation
Fresh frozen plasma‡			
Plasma cryoprecipitate§	1 U¶/10 kg	q4–12h (as needed)	Hemophilia A (factor VIII deficiency), fibrinogen deficiency, von Willebrand disease
Cryosupernatant§	6–12 ml/kg	q8–12h	Hemophilia B (factor IX deficiency); Factor VII, X, and XI deficiency; vitamin K deficiency

*Transfuse at a rate of 1–2 ml/min for cats and puppies, 3–6 ml/min for adult dogs.
†Collected in citrate anticoagulant, transfused within 4–6 hours of collection.
‡Frozen within 4–6 hours of collection, stored below –20°C.
§Supernatant remaining after thawing fresh frozen plasma for separation of cryoprecipitate.
¶1 unit = cryoprecipitate produced from 200 ml of fresh frozen plasma.

sensitize recipients and can be considered universal donors.
- Cross-species transfusions of any blood product are contraindicated because fatal anaphylaxis can result.

Nursing Care

Nursing care practices that reduce hemorrhage include the following:

- Confinement to limit activity
- Feeding soft food
- Avoidance of neck leads and intramuscular injections
- Use of peripheral veins for sampling or intravenous catheter placement

Do not give platelet inhibitory drugs, including sulfas and nonsteroidal anti-inflammatory agents.

Wound Management

Good management reduces the need for transfusion in some patients with coagulation disorders and mucosal or cutaneous hemorrhage. The best treatment, for even small wounds, is usually suture and/or pressure bandages. Application of tissue adhesive (Vetbond, 3M Co.) to focal areas of bleeding also can limit local blood loss.

Drug Therapy

Vitamin K Therapy

Vitamin K therapy improves hemostasis only in vitamin K-deficient patients. It often is initiated pending test results, but maintenance of vitamin K therapy is not indicated when diagnosis of inherited factor deficiency, non-obstructive liver disease, vWD, or DIC is made. Anticoagulant rodenticide toxicities are the most common cause of vitamin K deficiency in dogs and cats. Vitamin K reverses the anticoagulant effect of rodenticides over a period of 24 to 48 hours from initiation of therapy.

Treatment for Warfarin Toxicity

Warfarin is a relatively short-acting poison, and treatment for a total of 1 week usually is adequate. Standard treatment is as follows:

- Administer an initial dose of vitamin K_1 (AquaMephyton, Merck, Sharp, Dohme), 2.2 mg/kg subcutaneously (SC).
- Follow with a dose of 1.1 mg/kg SC or by mouth (PO), q12h, until active bleeding subsides.
- Continue therapy with an oral preparation (Mephyton) at the same twice-daily dosage for a total of 1 week.

Treatment for Long-acting Rodenticide Toxicity

The following steps are taken to treat toxicity from second-generation or long-acting rodenticides (diphacinone, pindone, bromadiolone, and brodifacoum):

- Give transfusions for patients with severe anemia, pulmonary, or CNS hemorrhage at presentation (see Table 23-6).
- Initiate parenteral vitamin K_1 as for warfarin (2.2 mg/kg SC).
- Administer vitamin K_1 at 1.1 mg/kg SC, q12h, until the hematocrit value stabilizes and active bleeding subsides.
- Maintain oral vitamin K_1 at 1.1 mg/kg PO, q12h, for a total of 2 weeks.
- Taper the maintenance dose by one-half every 2 weeks during treatment.
- To prevent relapse, continue therapy for 4 to 6 weeks.

▼ ***Key Point*** Subcutaneous injection of vitamin K is the preferred parenteral route of administration because intravenous vitamin K can cause anaphylaxis, and hematomas may form at intramuscular injection sites. Vitamin K_3 (Synkayvite) is not effective for treating rodenticide toxicity because of its delayed onset of action.

Hormonal Therapy

Endocrine imbalance (hypercortisolism or hypocortisolism, hypothyroidism, and hyperestrogenism) can impair hemostasis and complicate the management of acquired or hereditary platelet and coagulation disorders. Diagnosis and correction of the endocrinopathy can prevent or minimize transfusion requirements.

Thyroxin

Thyroid insufficiency (see Chapter 31) is common in many breeds with the vWD trait, including Doberman pinscher, Bernese mountain dog, golden retriever, and standard poodle.

- Treat hypothyroid dogs with L-thyroxine at a standard replacement dosage of 0.02 mg/kg PO q12–24h, with post-pill monitoring to ensure attainment and maintenance of normal T_4 values.

Desmopressin Acetate

Desmopressin acetate (DDAVP, USV Pharmaceutical), a vasopressin analogue, has shown efficacy in transiently improving hemostasis in some dogs affected with type 1 vWD.

- Its activity probably is the result of release of vWF from intracellular stores, and its effectiveness depends on the patient's ability to produce functional vWF protein.
- Duration of action, after a dose of 1 µg/kg SC, is 3 to 4 hours; repeated dosage within 24 hours does not prolong response time. The onset of action is 15 to 30 minutes.
- Desmopressin is often given as preoperative prophylaxis to dogs with mild to moderate type 1 vWD.

Plasma products should be available in case the patient does not respond.

Heparin Therapy

- Unfractionated heparin therapy (100–300 U/kg SC q6–8h) is often used to manage thrombotic DIC and other acute thrombotic syndromes. Because of extensive protein and cell binding, unfractionated heparin (UFH) anticoagulant effect varies widely among patients and requires close monitoring to prevent overdosage and iatrogenic bleeding. Prolongation of aPTT to approximately 1.5 to 2 times the patient's baseline or the assay's mean value is a common therapeutic target.
- Low molecular weight heparins are newer anticoagulant drugs with a more predictable pharmacologic profile than UFH. Safe and effective dosage guidelines have not yet been developed for dogs and cats. The target therapeutic range for high-dose anticoagulant effect in human patients is 0.5 to 1.0 Units of anti-Xa activity per milliliter.
- Transfusion therapy with fresh blood or blood products to replace active coagulation factors, fibrinogen, and platelets is more likely than heparin therapy to benefit patients presenting with severe hemorrhage in association with DIC.

▼ ***Key Point*** The critical factor for successfully managing all patients with DIC is identification and correction of the underlying disorder.

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Chapter 24

Systemic Immune-Mediated Diseases

Michael Stone

Immune-mediated diseases may affect multiple body systems; for example, polyarthritis may be associated with thrombocytopenia or proteinuria. A CBC, platelet count, chemical profile and urinalysis are considered the minimum database for any suspected immune-mediated disease. The diagnosis of "idiopathic immune-mediated disease" remains a diagnosis of exclusion. Infectious/parasitic, neoplastic, and toxic causes must always be excluded with appropriate testing and/or therapeutic trials.

Since many immune-mediated diseases are treated similarly, this chapter begins with a general discussion of treatment and commonly used drugs. This is followed by a discussion of immune-mediated hemolytic anemia, immune-mediated thrombocytopenia, and systemic lupus erythematosus.

TREATMENT OF IMMUNE-MEDIATED DISEASES

Corticosteroids

Corticosteroids are effective immunosuppressive agents. Many animals tolerate their administration with only mild side effects, or the disease goes into remission and the corticosteroid treatment may be stopped. For many animals with immune-mediated disease, single agent therapy with corticosteroids is adequate.

- *Prednisone* is always included initially in immunosuppressive protocols. The dosage is approximately 2.2 mg/kg once daily in most cases; however 1 mg/kg/day may be used in less severe diseases. The dose may be divided into twice daily administration, but there is no obvious benefit from the division. Some dogs are intolerant to prednisone and will develop side effects (polyuria, polydipsia, polyphagia, panting, and/or lethargy) that are unacceptable to the owner.

▼ ***Key Point*** Therapy with an equipotent dose of a different steroid (prednisolone, methylprednisolone, triamcinolone, or dexamethasone) often resolves unacceptable side effects of prednisone (Table 24-1).

▼ ***Key Point*** Some cats do not effectively respond to prednisone. These cats may be "poor converters" that cannot metabolize inactive prednisone to the active form, prednisolone. Thus, when cats don't respond well to prednisone, try using an alternate steroid (see Table 24-1).

- Corticosteroids are generally administered at full doses until the disease is in complete remission. Complete remission may be defined as resolution of signs of disease along with radiographic or laboratory changes that were initially present. After remission is attained the dose is cut, generally in half, for 4 weeks. Reevaluation is then performed, and if signs of disease are absent (on physical or laboratory data), the dose is again halved. This protocol is followed monthly until the animal either relapses or stops medication.

▼ ***Key Point*** The minimum duration of therapy for any immune-mediated disease is 6 months.

- Many patients will experience a relapse as the dose is tapered. Relapse is treated with return to full dose administration, again with monthly tapering, but as the dose is approached that previously allowed relapse, the dosage may then either be held constant or tapered more slowly. If signs of relapse are mild, the dose may instead be increased to the most recently effective dose and held there for a few months before it is tapered again.

Combination Immunosuppression Therapy

Combination immunosuppression therapy is very useful, because the addition of another agent may allow a lower dose of corticosteroid to be used (prednisone-sparing effect). Additional medications may also increase the strength of immunosuppression because they work by different mechanisms. The drug most frequently used in combination with corticosteroids in dogs is azathioprine.

▼ ***Key Point*** Combination immunosuppressive therapy is often more effective and has less side effects than prednisone therapy alone.

Table 24-1. INITIAL IMMUNOSUPPRESSIVE DOSES OF CORTICOSTEROID AND THEIR AVAILABLE STRENGTHS IN THE UNITED STATES

	Available Oral Strengths	Initial Feline Dose (Oral)	Initial Canine Dose (Oral)
Prednisone	1, 2.5, 5, 10, 20, 50 mg tablets; 5 mg/5 ml syrup	10 mg/day	2.2 mg/kg/day
Prednisolone	5, 20 mg tablets; 15 mg/5 ml syrup	10 mg/day	2.2 mg/kg/day
Methylprednisolone	2, 4, 8, 16, 24, 32 mg tablets	8 mg/day	2.2 mg/kg/day
Triamcinolone	4, 8 mg tablets	2–4 mg/day	0.4 mg/kg/day
Dexamethasone	0.25, 0.5, 0.75, 1, 1.5, 4, 6 mg tablets	1–2 mg/day	0.2 mg/kg/day

Azathioprine

- Azathioprine (Imuran) is administered orally. Adverse side effects are infrequent in dogs. The dose is approximately 2.2 mg/kg once daily until remission occurs, then the same dose is administered every other day.
- A potential side effect is bone marrow suppression, and a complete blood count (CBC) should be evaluated after 7 days, and then every 2 weeks while the patient is receiving daily treatment. Once the patient is receiving every other day therapy, a CBC should be evaluated every 3 months, but bone marrow suppression is unusual at this dose.
- Prednisone and azathioprine are frequently used in combination. The drugs are administered together once daily and then tapered after remission is attained. The method of tapering is somewhat arbitrary; if signs of prednisone intolerance are experienced then the prednisone is tapered first; if bone marrow disease is encountered the azathioprine should be tapered or discontinued first. If the disease was difficult to get into remission then only one drug should be tapered at a time; if the disease easily went into remission, then both drugs may be tapered concurrently. Tapering should be performed every 4 weeks, with the minimum duration of therapy being 6 months. It is important to have a therapeutic plan to follow. Notations in the medical record should include the intended date of recheck, with the tests to be performed and the expected decrease of dose if tests return results within normal limits. Relapse is treated with the administration of full dosage of both medications with gradual taper to the lowest effective dose. As the dose that allowed relapse is approached, the dosage may then either be held constant or tapered more slowly.
- Cats often develop life-threatening neutropenia with the use of azathioprine, and its use in this species is not recommended. Instead, the use of chlorambucil is recommended for cats that require immunosuppression in addition to prednisolone.

Chlorambucil

- Chlorambucil (Leukeran) is an oral drug, used in cats at 15 mg/m^2 (4 mg total dose for most cats) once daily for 4 days, repeated every 3 weeks.
- Potential side effects include anorexia and bone marrow suppression. A CBC should be evaluated 5 to 7 days after the last dose. If after two or more evaluations the CBC remains normal (no leukopenia), further monitoring may not be necessary. If leukopenia is detected (absolute neutrophil count < 3,000/µl), the dose of the next administration should be decreased by 25%. Signs of infection (loss of appetite along with fever) during the expected white blood cell count (WBC) nadir (3–10 days after administration) should be aggressively treated. Physical examination, CBC, and treatment with amoxicillin and enrofloxacin are indicated if severe neutropenia (<1,000/µl) and fever are present.
- In cats, the dosage of chlorambucil should be tapered before the dose of prednisolone is tapered.

Monitoring of Immunosuppressive Therapy

Side effects of immunosuppressive medications often lead to significant morbidity; treatment of any immune-mediated disease involves balancing the control of disease against the side effects of immunosuppressive therapeutics. Obesity related to prednisone is very common, and owners should be specifically counseled about its prevention. Body weight should be recorded and weight management discussed at each recheck. Long-term immunosuppressive therapy may also allow the development of asymptomatic infection, especially in the urinary system. Urine culture is recommended

every 3 to 4 months regardless of the absence of clinical signs.

▼ ***Key Point*** Many patients are euthanized due to side effects of prednisone. Strategies to decrease prednisone-induced side effects include: avoidance of obesity, exchanging equipotent doses of an alternate steroid, use of additional immunosuppressive agents, and routinely scheduled monitoring.

IMMUNE-MEDIATED HEMOLYTIC ANEMIA

The diagnosis of immune-mediated hemolytic anemia (IMHA) is suspected upon discovering severe anemia in the presence of normal serum protein levels (Figure 24-1). IMHA may be classified as regenerative or nonregenerative with red cell destruction in the bone marrow prior to the release of reticulocytes. Red cell destruction may be mild (low grade) or rapidly progressive.

Etiology

- Specific causes of IMHA are not known. However, genetic factors may play a role and certain breeds, such as cocker spaniels, poodles, and old English sheep dogs, show higher incidence of IMHA. Initiating events, such as vaccination, stress, or infectious agents can trigger IMHA in patients with the appropriate predisposing genes.
- In animals presenting with hemolytic anemia, IMHA must be differentiated from other causes of hemolytic anemia, both in dogs (Table 24-2) and in cats (Table 24-3). These are described in Chapter 22.

Clinical Signs

- Historical findings may include weakness, collapse, pale gums and/or discolored urine.
- Physical examination may reveal fever, pale or icteric gums, systolic heart murmur, hepatosplenomegaly (sites of red cell phagocytosis), tachycardia and/or tachypnea.

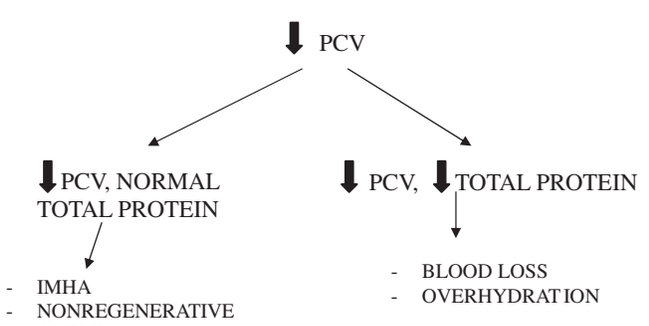

Figure 24-1. Classification of anemia. PCV, packed cell volume; IMHA, immune-mediated hemolytic anemia.

Table 24-2. CAUSES OF HEMOLYTIC ANEMIA IN THE DOG

Hereditary causes (pyruvate kinase deficiency, phosphofructokinase deficiency)
Toxins (onions, zinc, copper)
Babesia canis, B. gibsoni, Mycoplasma hemocanis (formerly *Hemobartonella canis*)
Recent vaccination
Drug reaction (cephalosporins, penicillins, sulfa-drugs, nonsteroidal antiinflammatory drugs, levamisole, Vit K_3)
Neoplasia (hematopoietic, hemangiosarcoma, histiocytic)
Splenic torsion
Hypophosphatemia
Bee sting envenomation
Microangiopathic (disseminated intravascular coagulation, heartworm caval syndrome)
Idiopathic, immune-mediated hemolytic anemia

Table 24-3. CAUSES OF HEMOLYTIC ANEMIA IN THE CAT

Hereditary: pyruvate kinase deficiency (Abyssinian, Somali)
Feline leukemia virus, feline immunodeficiency virus
Mycoplasma hemofelis, Mycoplasma haemiminutum (formerly *Hemobartonella felis*)
Cytauxzoon felis
Toxins (zinc, copper, onion, methylene blue, acetaminophen, D-L-methionine, benzocaine, propylene glycol)
Drug reaction (propylthiouracil, others)
Incompatible blood transfusion
Neonatal isoerythrolysis
Neoplasia (hemangiosarcoma, histiocytic)
Hypophosphatemia
Microangiopathic (disseminated intravascular coagulation)
Idiopathic, immune-mediated hemolytic anemia

Diagnosis

- Perform a CBC with manual differential count, platelet count, reticulocyte count, chemistry profile, urinalysis, thoracic and abdominal radiographs, coagulation profile, Coombs' test and abdominal ultrasonography. Serology for *Babesia canis* and *B. gibsoni* is indicated in endemic areas. Bone marrow cytology is indicated if the anemia is nonregenerative or if infiltration with hemolytic histiocytes is suspected (hemophagocytic syndrome).
- Cats should be tested for feline leukemia virus (FLV) and feline immunodeficiency virus (FIV) as well as hemoplasmosis (microscopic blood examination, polymerase chain reaction).
- Typical CBC findings include anemia, reticulocytosis, spherocytosis, and leukocytosis with left shift. Hemolysis can cause a severe granulocytic response that should not be confused with infection.
- Coombs' (direct antiglobulin) test results are usually, but not invariably, positive, with both false-positive

and false-negative results possible. Spontaneous autoagglutination of red blood cells may occur when blood is placed on a slide, however, rouleaux formation must be excluded. Rouleaux tend to disperse when one drop of anticoagulated blood is diluted in three to four drops of saline, whereas antibody-mediated autoagglutination remains.

▼ ***Key Point*** Spherocytosis is present in most cases of IMHA, and strongly supports the diagnosis of immune-mediated hemolytic anemia.

- Biochemistry may reveal increased liver enzymes (thought to reflect hypoxic damage) and hyperbilirubinemia.
- Coagulation profile results are often abnormal in patients with severe hemolysis. Thromboembolism and disseminated intravascular coagulation are recognized as common complications of hemolytic anemia.
- Consider thoracic radiographs to screen for evidence of neoplasia or pulmonary thromboembolism. Abdominal imaging commonly reveals mild hepatosplenomegaly (representing hyperactivity of the mononuclear-phagocytic cell system), however, consider biopsy for nodular irregularities or lymphadenopathy.

Concurrent Diseases

IMHA may coexist with other immune-mediated disease, the most common of which is immune-mediated thrombocytopenia. Interpretation of test results must be cautious, because low platelets may also indicate systemic thrombosis or disseminated intravascular coagulation.

Treatment

- Intravenous fluids are recommended for most cases and supplemental oxygen is essential for dyspneic patients.
- Red cell transfusion is indicated if the packed cell volume (PCV) drops to less than 15%.
- Due to a high incidence of pulmonary thromboembolism in cases with a rapid rate of hemolysis, use prophylactic therapy with heparin (initially 200 units/kg SC q6h and adjust the activated partial thromboplastin time (aPTT) to 1.5 to 2 times normal values through daily monitoring) or aspirin (0.5–5 mg/kg PO q24h).
- Mild cases with PCV >22% and bilirubin <3 mg/dl: treatment with prednisone alone or prednisone with azathioprine may be effective.
- Aggressive hemolytic cases (PCV rapidly dropping or bilirubin >3 mg/dl): treatment with intravenous fluids, heparin, prednisone or dexamethasone, and azathioprine is indicated. More aggressive therapy may be considered: intravenous human immunoglobulin (0.5g/kg IV once daily for 3 days), cyclosporine (Sandimmune 10 mg/kg IV or PO twice daily; Neoral or Atopica 5 mg/kg PO twice daily), or methylprednisolone sodium succinate pulse therapy (11 mg/kg IV once daily for 3 days).
- Monitor blood counts daily until stabilization occurs, then at least weekly until the PCV is >25%. Full doses of immunosuppressive medications are administered until the hematocrit normalizes, and then they are tapered as discussed in the Treatment section. It is not necessary to normalize the hematocrit to eliminate clinical signs of disease, and in some cases it may be preferable to allow a low grade of anemia to persist in order to decrease medications to tolerable levels. The minimum length of treatment is 6 months.

Prognosis

▼ ***Key Point*** Mild IMHA may respond well to treatment, whereas rapidly progressive cases are associated with a high rate of mortality.

The prognosis is guarded to fair for mild cases and very guarded for aggressively hemolytic cases. Many patients are able to taper completely off medications, however, relapses occur unpredictably. Relapses may be associated with immune stimulation due to vaccination, infection, or stress, and avoidance of these causes may be prudent. Monitoring for control, recurrence, and infection should be performed at least 3 to 4 times per year for the life of the patient.

IMMUNE-MEDIATED THROMBOCYTOPENIA

Immune-mediated thrombocytopenia (IMT) is usually suspected when cutaneous petechiae or bleeding from mucosal surfaces are discovered in an otherwise healthy-appearing animal. Severe thrombocytopenia associated with other causes is more often associated with overt clinical illness.

Etiology

A specific cause of IMT is not known. Many other causes of thrombocytopenia exist (Table 24-4) that must be differentiated from IMT; these are usually associated with less severe thrombocytopenia (>25,000/µl). Any drug the patient is receiving must be considered as a potential cause of hapten-mediated thrombocytopenia and stopped, if possible.

Clinical Signs

- Epistaxis, oral cavity hemorrhage, cutaneous petechiation or ecchymoses, hematuria, hematochezia and/or melena are common presenting complaints. Hematomas, hemothorax, hemoperitoneum and

Table 24-4. CAUSES OF THROMBOCYTOPENIA IN THE DOG AND CAT

Sequestration in spleen (splenic neoplasia, torsion, hematoma, thrombosis/infarction)
Drugs (cytotoxic, antibiotics, estrogen, nonsteroidal antiinflammatory drugs, albendazole, griseofulvin, propylthiouracil, ketoconazole, others)
Neoplasia (hematopoietic, histiocytic, hemangiosarcoma)
Infectious agents (*Ehrlichia canis, E. ewingii, E. chafeensis, Anaplasma phagocytophila, A. platys, Rickettsia rickettsii*, parvovirus, distemper, feline leukemia virus, feline immunodeficiency virus, cytauxzoonsis, systemic mycoses, leptospirosis, *Babesia canis, B. gibsoni*, sepsis, endotoxemia)
Bone marrow disease (myelofibrosis, myelodysplasia, necrosis, myelophthesis)
Recent vaccination
Vasculitis
Disseminated intravascular coagulation/systemic thrombosis (thoracic, abdominal, peripheral)
Hemolytic uremic syndrome
Severe hemorrhage (anticoagulant rodenticide, trauma)
Idiopathic, immune-mediated thrombocytopenia

hemarthroses are more commonly associated with anticoagulant poisonings or hemophilia.

- Physical examination may reveal pale gums, splenomegaly, and cutaneous, mucosal, or ocular hemorrhages. Fever is occasionally present. Fundic examination may reveal retinal hemorrhages. Rectal examination may reveal melena or hematochezia.

Diagnosis

- The presence of severe thrombocytopenia (<25,000/µl) in an otherwise healthy-appearing animal is most likely to be caused by immune-mediated, rather than infectious disease. The diagnosis of infectious thrombocytopenia is more likely if fever or other systemic signs are also present.
- Perform a CBC with manual differential, platelet count, coagulation profile, chemistry profile, urinalysis (voided only to avoid iatrogenic hemorrhage), thoracic radiographs and abdominal ultrasound. Bone marrow cytology may be safely performed despite low platelet counts, but is usually not helpful unless bicytopenia or pancytopenia is found. Tick titers (*Ehrlichia canis, Anaplasma phagocytophila* [formerly *E. equi*], *E. ewingii, Rickettsia rickettsii*) and/or treatment with doxycycline may be indicated.
  - CBC should reveal a platelet count of less than 25,000/µl. If bleeding occurs with platelet counts greater than 25,000/µl, consider other causes (anticoagulant, hemophilia, bleeding neoplasm, vasculitis, thrombopathia).
  - Biochemistry is typically normal. Coagulation profile is typically normal although fibrin degradation products and d-dimers may be mildly elevated due to hemorrhage. Abdominal imaging commonly reveals mild hepatosplenomegaly (representing hyperactivity of the mononuclear-phagocytic cell system).
  - Bone marrow evaluation is not routinely necessary, but may reveal increased or decreased megakaryocytes and mild plasmacytosis. Tests for detection of antiplatelet antibodies are not necessary in most cases.

Concurrent Diseases

IMT may coexist with other immune-mediated diseases. Anemia may be caused by blood loss or concurrent IMHA. The presence of spherocytosis, or severe anemia in the face of normal blood protein levels, is suggestive of concurrent IMHA (see Figure 24-1).

Treatment

- Most cases of IMT respond to immunosuppressive therapy with prednisone alone or with prednisone combined with azathioprine.
- Vincristine (0.5 mg/m^2 IV once weekly) may be administered concurrently. Vincristine is not typically considered to be immunosuppressive, but it appears to work synergistically to raise the platelet count. Vincristine is often administered once and only repeated if relapse or lack of response is seen. Side effects of vincristine are uncommon, however, great care must be used to avoid extravasation.
- Avoid Cyclophosphamide (Cytoxan), since an episode of hemorrhagic cystitis, which may occur after only a single dose, may be fatal.
- Platelet transfusions are impractical, instead, either whole fresh blood (supplying at least some platelets) or packed red cells are administered as needed.
- Monitor platelet counts daily until above 25,000/µl and then weekly. Full doses of immunosuppressive medications are administered until the platelet count normalizes, and then tapered as discussed above. It is not necessary to normalize the platelet count to eliminate clinical signs of disease, and in some cases it may be preferable to allow a low grade of thrombocytopenia to persist in order to decrease medications to tolerable levels. The minimum length of treatment is 6 months.

Prognosis

A guarded prognosis should be given until the platelet count begins to rise. Bleeding into the brain or spinal cord may be fatal. Once the platelet count rises, the prognosis is often good. Many patients are able to taper completely off medications; however, relapses occur unpredictably. Relapses may be associated with immune stimulation due to vaccination, infection, or stress, and avoidance of these factors may be prudent. Monitoring for control, recurrence, and infection should be performed at least 3 to 4 times per year for the life of the patient.

SYSTEMIC LUPUS ERYTHEMATOSUS

Systemic lupus erythematosus (SLE) is an uncommon disease of young to middle aged patients. The disease may affect multiple organs, the most frequently of which are joints, kidneys, and integument. See Chapter 48 for additional discussion of the cutaneous aspects of SLE. A complete diagnostic workup is indicated for patients with waxing and waning signs of illness along with suspicion of immune-mediated disease.

Etiology

- Genetic factors are important and experimental colonies of dogs with SLE have been established.
- SLE patients produce antibodies directed against a broad range of nuclear, cytoplasmic, and cell membrane molecules. Autoantibodies may directly damage tissues or cause damage through the formation of immune complexes. When there is continued production of autoantibody to a self-antigen, overload of the mononuclear phagocyte system may occur. Circulating immune complexes will deposit in walls of blood vessels where there is physiological outflow of fluid, such as glomeruli, synovia, and the choroid plexus.
- Infectious agents and/or environmental triggers (such as sunlight) can worsen SLE in patients with the genetic predisposition.

Clinical Signs

Almost any organ may be affected in SLE, including joints, kidneys, skin, blood cells, muscles, the brain, and the heart (Table 24-5). The most commonly recognized syndrome is immune-mediated polyarthritis, in combination with immune-mediated skin disease, glomerulonephritis, hemolytic anemia and/or thrombocytopenia. Signs may exist concurrently or different manifestations may develop over time.

- Cutaneous manifestations may include erythema, scaling, crusting, depigmentation, and alopecia (see Chapter 48). Ulcers may develop in the skin, mucocutaneous junctions and oral cavity.
- In cats, reported central nervous system (CNS) involvement has included twitching of the ears, tail, and hindlimbs; generalized seizures; hyperesthesia along the dorsum; restless crying; disorientation; ataxia; nystagmus; and ventroflexion of the neck.
- Polymyositis has been suspected in several dogs and cats.
- Neutrophilic myocarditis has been reported in several dogs.

Diagnosis

Criteria for Diagnosis

Patients with SLE must demonstrate at least two separate manifestations of autoimmunity along with positive antinuclear antibody (ANA) test results. Patients with three or more separate manifestations of autoimmunity may also be considered to have SLE despite the absence of detectable ANA. Different manifestations may develop over time. For example, a patient with immune-mediated polyarthropathy and positive ANA that later develops thrombocytopenia, may be considered to have SLE.

Diagnostic Evaluations

Diagnostic testing should include CBC with manual differential, platelet count, biochemistry, urinalysis,

Table 24-5. CLINICAL MANIFESTATIONS IN DOGS AND CATS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Clinical Sign	Dogs (Incidence*)	Dogs (Percentage)	Cats (Incidence*)	Cats (Percentage)
Nonerosive polyarthritis	236/302	78	9/25	36
Fever	186/275	68	11/21	52
Renal disorders	167/302	55	10/25	40
Dermatologic lesions	138/302	46	15/25	60
Lymphadenopathy/ splenomegaly	66/175	38		
Leukopenia	54/302	18		
Hemolytic anemia	45/302	15	6/25	24
Thrombocytopenia	40/302	13	2/25	8
Myositis	16/275	6		
CNS disorders	16/302	5	6/25	24
Neuropathy	7/302	2		

*Number of cases with clinical finding/number of reported cases (from Stone, 2004).

imaging, joint fluid cytology, histopathology of the skin and/or kidney, and serum ANA. Cats should also be tested for FeLV and FIV. Infectious and neoplastic disease must be excluded through imaging, culture of urine, blood and/or joint fluid, serology for tickborne and fungal disease, and therapeutic antibiotic trials. In tick-infested areas, a 3 to 7 day course of doxycycline should be considered prior to concluding the presence of immune-mediated disease.

Treatment

- Avoid sunlight to prevent photosensitization. Dogs with mild lameness may require only intermittent nonsteroidal anti-inflammatory therapy such as carprofen (4.4 mg/kg once daily), etodolac (15 mg/kg once daily), or meloxicam (0.1 mg/kg once daily).
- More severe signs necessitate corticosteroid with or without azathioprine administration. Medication should be administered at full dosages until remission is obtained, and then tapered slowly as described in the Treatment section. The minimum duration of therapy is 6 months.

Prognosis

The prognosis is generally good; however, waxing and waning of signs may occur. Signs may disappear never to reappear, signs may recur, or new manifestations may develop over time. Progressive renal damage may occur due to deposition of circulating immune complexes, and renal function should be carefully monitored. Periodic (every 3 to 4 months) reevaluation of the CBC, biochemical profile, and urinalysis is indicated to detect and monitor occult disease.

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Chapter 25

Diseases of the Spleen

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The spleen can be the site of primary disease, or it can be affected by disease elsewhere as an active or passive participant. The spleen has hematopoietic, reservoir, filtering, and immunologic functions. The spleen may be affected by a variety of neoplastic and non-neoplastic disorders. It has an important role in responding to a number of infectious diseases through phagocytosis, antibody production, and modulation of hemoparasitic infections.

Splenic disorders usually are identified by a change in shape, size, and function of the spleen. Splenomegaly is defined as a localized or diffuse splenic enlargement. Splenomegaly generally can be detected on physical, radiographic, or ultrasonographic examination.

ANATOMY AND HISTOLOGY

- The spleen is located in the left cranial abdomen, attached to the greater curvature of the stomach by the greater omentum. Anatomically, the spleen consists of a capsule, trabeculae, and parenchyma that include the white pulp, marginal zone, and red pulp. The blood vessels of the spleen are the splenic artery, a branch of the celiac artery, and the splenic vein, which drains into the gastrosplenic vein. Blood enters the spleen through approximately 25 splenic branches that enter the capsule through the hilus and then enter the trabeculae. The vessels branch repeatedly, then leave the trabeculae and enter the white and red pulp. Blood from the venous sinuses coalesce into veins of the red pulp and merge to become the trabecular veins. The canine spleen is considered to be sinusoidal, while that in the cat is non-sinusoidal. Blood cells in the canine spleen extravasate by moving between adjacent endothelial cells in order to enter the red pulp sinuses; however, in the feline spleen large gaps are present between adjacent endothelial cells, permitting passage into the sinuses without deformation of cell shape.

Capsule and Trabeculae

- A capsule rich in elastic and smooth muscle fibers surrounds the spleen. Fibromuscular trabeculae form a complicated network within the organ. The muscular capsule and trabeculae in the dog and cat spleen permits a several-fold increase in size in the relaxed versus contracted state. The smooth muscle component allows contraction and distension of the spleen.

White Pulp

- The white pulp consists of diffuse and nodular lymphoid and reticuloendothelial cells. Nodules are usually less than 1 mm in diameter. White pulp lymphocytes and reticuloendothelial cells are associated with the splenic arterial circulation; forming periarteriolar lymphatic sheaths (PALS) rich in T lymphocytes. B lymphocytes are located in nodules along these sheaths and represent areas of B lymphocyte proliferation and antibody production.

Marginal Zone

- The marginal zone separates the white pulp from the red pulp. Arterial vessels terminate either in the marginal zone or in the red pulp. The marginal zone is not well developed in the dog and cat. In other species, the marginal zone is functionally important as a major area of circulatory interchange, cell-to-cell interaction, and cell sorting. The marginal zone is where the distribution of blood flow between slow and fast transit pathways is controlled. The slow pathways permit prolonged exposure of blood cells and particles to phagocytic cells.

Red Pulp

- The red pulp consists of the venous sinuses, pulp cords, and the terminal branches of the arterial system. Together, these elements filter the blood. The periarterial lymphatic sheath is lost as arteries enter the red pulp and is replaced by the periarteriolar macrophage sheath. Particles, cells, and plasma pass through gaps between endothelial cells in the terminal arterial capillaries. The red pulp culls abnormal blood cells and processes particulate antigens for presentation to the white pulp where an immune response is mounted.

PHYSIOLOGY AND FUNCTION

Filtration Function

▼ ***Key Point*** The primary function of the spleen is to filter the peripheral blood.

- The filtering capability of the spleen is significantly enhanced in animals with splenomegaly. In the dog, approximately 2.0 L/kg body weight of blood passes through the spleen each minute. The spleen has a unique vascular structure through which the blood circulates in close contact with the reticuloendothelium, allowing ample biologic filtration of cells and particles. Filtration occurs primarily in the marginal zone of the white pulp and by macrophages. Splenic filtration involves three processes: culling, pitting, and erythroclasis.
- *Culling* refers to the destruction of erythrocytes, or other circulating blood cells, physiologically as they age or in pathologic conditions involving increased red cell destruction. These pathologic changes may be associated with blood cell abnormalities or primary splenic changes. Culling is also the process by which other circulating cells and particulate material, such as bacteria, are removed.
- *Pitting* describes the removal of inclusions from erythrocytes with their return to the circulation. These inclusions may include remnants of nuclear material (Howell-Jolly bodies), denatured hemoglobin (Heinz bodies), and hemoparasites such as *Mycoplasma* and *Babesia* spp. Pitting does not occur in the cat because of larger gaps in the walls of the pulp venule.
- *Erythroclasis* involves the destruction of erythrocytes by fragmentation. In contrast to culling, cellular fragments are returned to the peripheral blood and are removed in subsequent passage. Associated diseases include immune-mediated hemolytic anemia and hemoglobinopathies.

Immunologic Function

▼ ***Key Point*** The white pulp of the spleen is the single largest lymphoid organ in the body.

- The spleen reacts primarily to disseminated blood-borne antigens such as circulating bacteria in septicemia. The white pulp is relatively compartmentalized into B and T cell zones. The periarterial lymphoid sheath is composed primarily of T lymphocytes. The marginal zone contains both B and T lymphocytes. The majority of B lymphocytes are located in the germinal center and mantle zones. Circulating lymphocytes enter the spleen and home to the white pulp. Lymphocytes first enter the marginal zone and then migrate to the PALS and lymphoid follicles. If antigen is present, the lymphocytes undergo activation and proliferation; if no antigen is present, lymphocytes return to the circulation.
- The slow circulation of the spleen enhances contact time and resulting phagocytosis of microorganisms. The spleen plays a key role in the defense against polysaccharide-encapsulated bacteria and other circulating particulate antigens. The liver is more effective than the spleen at removing blood-borne bacteria in the presence of a specific antibacterial antibody; however, in the absence of a specific antibody, the spleen becomes crucial for removal of bacteria. The spleen appears to be the primary organ responsible for the production of an early-appearing antibody in response to intravenous particulate antigens.
- Red blood cells acquire surface immunoglobulins as part of the normal aging process and in immune-mediated hemolytic anemia. Splenic macrophages remove the portion of the erythrocyte membrane coated with immunoglobulin G, resulting in spherocyte formation. Because spherocytes are less deformable, they are culled.

Reservoir Function

- Blood cells of all hematopoietic lineages are stored in the spleen. The dog has a muscular spleen that functions as an expansible organ capable of holding a large volume of blood. Of the red blood cell mass, 90% passes quickly through the spleen; 9%, representing 50% of the total number of red cells in the spleen at one time, take about 8 minutes to transit; and the remaining 1% have a transit time of 1 hour. Normally, the spleen stores from 10% to 20% of the total blood volume.

▼ ***Key Point*** The canine spleen is able to store one-third of the dog's red blood cell mass. This reservoir can be rapidly released, increasing the packed cell volume 10% to 20% in dogs and cats. The spleen also concentrates platelets. Up to one-third of the total body platelets are sequestered in the spleen.

Vigorous exercise results in a transient increase in the circulating platelet count. Margination of granulocytes occurs in the spleen as well.

Hematopoietic Function

- The role of the spleen in hematopoiesis varies considerably with different species. In mammals, the major site of hematopoietic activity is the bone marrow. The spleen is a hematopoietic organ during fetal development, but the normal adult spleen in the dog and cat has no hematopoietic activity. The red pulp retains the ability for extramedullary hematopoiesis (EMH) on demand.
- A wide variety of disorders have been associated with splenic EMH in dogs, including splenic and

extrasplenic hemangiosarcoma, splenic and extrasplenic lymphomas, multiple myeloma, leukemias, immune-mediated hemolytic anemia, eosinophilic gastroenteritis, estrogen-induced bone marrow hypoplasia, pyometra, and ehrlichiosis.
- EMH does not appear to be as common in cats as it is in dogs.
- The hemograms of dogs and cats with EMH may be characterized by the presence of immature red-cell and white-cell precursors.

Miscellaneous Functions

Other functions of the spleen include the following:

- Storage and activation of factor VIII
- Regulation of the formation, liberation, and degradation of angiotensin-converting enzyme
- Modulation of plasma norepinephrine concentrations and/or prostaglandin E2 (PGE2) activity
- Iron storage and recycling of iron to the bone marrow

ETIOLOGY

Splenic disorders can be separated into two categories, localized or asymmetrical splenomegaly and generalized or symmetrical splenomegaly.

Causes of localized splenomegaly (Table 25-1) include the following:

- Primary or metastatic neoplasia
- Nodular hyperplasia
- Hematoma
- Abscess

Generalized splenomegaly (Table 25-2) may result from the following:

- Inflammatory or infectious diseases
- Hyperplastic splenomegaly
- Congestive splenomegaly
- Infiltrative diseases

Localized Splenomegaly

The term *localized splenomegaly* refers to a localized palpable enlargement of the spleen. Most splenic masses are round and irregular and can be found in the left cranial or mid-abdomen. Localized splenomegaly may have a neoplastic or non-neoplastic cause.

Table 25-1. LOCALIZED SPLENOMEGALY

Non-neoplastic	Neoplastic
Nodular hyperplasia	*Primary*
Hematoma	Hemangiosarcoma
Abscess	Hemangioma
	Sarcoma
	Metastatic

Neoplasia

▼ ***Key Point*** Hemangiosarcoma is the most common neoplastic splenic mass occurring in the dog but is rare in the cat.

- Hemangiomas also occur. Hemangiosarcoma occurs predominantly in older, large-breed dogs. German shepherds, golden retrievers, and Labrador retrievers appear to be over-represented. Most other neoplastic splenic masses are sarcomas, including fibrosarcoma, leiomyosarcoma, leiomyoma, osteosarcoma, chondrosarcoma, rhabdomyosarcoma, myxosarcoma, liposarcoma, myelolipoma, fibrous histiocytoma, lipoma, mesenchymoma, and undifferentiated sarcoma. Although lymphoma usually has an infiltrative growth pattern in the spleen, it can have a nodular appearance.
- The most common malignant neoplasms of the spleen in cats, systemic mastocytosis and lymphoma, generally have a symmetrical infiltrative pattern of growth (see below).
- Metastasis to the spleen may occur from different sites; however, metastatic carcinoma to the spleen is rare.

Nodular Hyperplasia

- Splenic nodular hyperplasia can be single or multiple nodules that are benign accumulations of lymphoid cells, hematopoietic cells, and plasma cells. The stimulus for hyperplasia may be known in some instances, such as chronic antigenic stimulation; in other cases the cause is not known.
- Nodular hyperplasia is a common incidental ultrasonographic finding in older dogs and is a common finding in dog and cat spleens at necropsy. Nodular hyperplasia and hematoma accounted for 53% of canine splenectomies in one case series.

Hematoma

- Trauma can result in subcapsular hematoma formation, causing a mass effect in the spleen. In the majority of cases, no underlying cause predisposing to intrasplenic hemorrhage is found. Splenic hematoma has been reported in association with splenic lymphoma.

▼ ***Key Point*** Splenic hematomas cannot be distinguished from hemangiomas or hemangiosarcoma on the basis of size, shape, or other morphologic criteria. Aspiration cytology or biopsy is required to make a presumptive or definitive diagnosis.

- Splenic rupture associated with trauma or tumor rupture (hemangiosarcoma) may require surgical intervention.

Table 25-2. GENERALIZED SPLENOMEGALY

Inflammatory	Hyperplastic	Congestive	Infiltrative
Suppurative	Bacterial endocarditis	Pharmacologic	***Neoplastic***
Penetrating abdominal wounds	Brucellosis	Portal hypertension	Acute and chronic leukemia
Migrating foreign body	Discospondylitis	Splenic torsion	Systemic mastocytosis
Bacterial endocarditis	Immune-mediated disease	Thrombosis	Malignant histiocytosis
Septicemia	Autoimmune hemolytic anemia		Lymphoma
Splenic torsion	Immune-mediated thrombocytopenia		Multiple myeloma
Toxoplasmosis	Systemic lupus erythematosus		Metastatic neoplasia
Mycobacteriosis			
Infectious Canine Hepatitis (Acute)	***Hypersplenism***		***Non-neoplastic***
	Primary (idiopathic)		Extramedullary hematopoiesis
Necrotizing	Secondary		Hypereosinophilic syndrome
Splenic torsion			Amyloidosis
Splenic neoplasia			
Infectious canine hepatitis			
Salmonellosis			
Eosinophilic			
Eosinophilic gastroenteritis			
Hypereosinophilic syndrome			
Lymphoplasmacytic			
Infectious canine hepatitis (chronic)			
Ehrlichiosis (chronic)			
Rocky Mountain spotted fever			
Pyometra			
Brucellosis			
Hemobartonellosis			
Granulomatous			
Histoplasmosis			
Mycobacteriosis			
Leishmaniasis			
Pyogranulomatous			
Blastomycosis			
Sporotrichosis			
Feline infectious peritonitis			

- Splenic rupture also can lead to splenosis, the disseminated development of "daughter" spleens throughout the abdominal cavity.

Abscess

- Splenic abscesses can form from hematogenous spread of microorganisms but are rare in the dog and cat. The most common isolate in the dog is *Staphylococcus*. Splenic abscess has been associated with cholangiohepatitis in cats.

Generalized Splenomegaly

Generalized splenomegaly refers to diffuse enlargement of the spleen. Four major categories of generalized splenomegaly exist: inflammatory and infectious, hyperplastic, congestive, and infiltrative.

Inflammatory and Infectious Disease

- Inflammatory changes within the spleen usually result in diffuse enlargement. A wide range of infectious diseases can result in diffuse splenomegaly. A partial list of disorders that may be associated with generalized splenomegaly is provided in Table 25-2 (see the various chapters in this book on infectious diseases for details concerning these disorders). The various types can be classified based on the primary type of cellular infiltrate (suppurative, necrotizing, eosinophilic, lymphoplasmacytic, granulomatous, or pyogranulomatous splenitis). Different etiologic agents are associated with the different cellular infiltrates.

Hyperplastic Splenomegaly

- The spleen commonly reacts to blood-borne antigens and red blood cell destruction with hyperplasia of the reticuloendothelial and lymphoid cells.
- Hyperplastic splenomegaly is common in dogs with immune-mediated disease including immune-mediated hemolytic anemia or thrombocytopenia.
- It commonly occurs in dogs with subacute bacterial endocarditis and chronic bacteremic disorders such as discospondylitis or brucellosis.
- It has been seen in association with systemic lupus erythematosus.

- The same occurs in certain other hemolytic disorders, including hemophagocytic syndrome, drug-induced hemolysis, pyruvate kinase deficiency anemia, phosphofructokinase deficiency anemia, familial non-spherocytic hemolysis in poodles, Heinz body hemolysis, and *Mycoplasma haemofelis* infection (hemobartonellosis).

Congestive Splenomegaly

- Splenic enlargement resulting from congestion can occur through a number of different mechanisms. Splenic distension occurs as a result of smooth muscle relaxation in the splenic capsule and trabeculae. Phenothiazine tranquilizers and barbiturates increase blood pooling. Pooling of blood in an enlarged spleen may account for up to 30% of the total blood volume. Consider these changes when evaluating red blood cell parameters from anesthetized or tranquilized patients.
- Portal hypertension also can lead to congestive splenomegaly; however, splenic congestion secondary to portal hypertension does not appear to be a common cause of congestive splenomegaly in dogs and cats. Right-sided congestive heart failure, caudal vena cava obstruction (e.g., congenital anomalies, neoplasia, and heartworm disease), and intrahepatic obstruction may cause splenic congestion. Ultrasonography usually reveals markedly distended splenic, portal, and/or hepatic veins.
- Splenic torsion, either isolated or associated with gastric dilatation-volvulus syndrome, commonly results in marked splenomegaly due to congestion. A high percentage of dogs with splenic torsion have hemoglobinuria. The treatment of choice for dogs with splenic torsion is splenectomy (see the description in this chapter).

Infiltrative Splenomegaly

Neoplastic Infiltration

- Infiltration of the spleen with neoplastic cells constitutes one of the most common causes of splenomegaly in small animals. Splenomegaly is common in patients with acute and chronic leukemia. Other neoplastic conditions that result in diffuse splenomegaly include lymphoma, mastocytosis (most commonly in cats), multiple myeloma, and malignant histiocytosis (in dogs). EMH may contribute to the splenomegaly caused by the presence of neoplastic cells.

Non-neoplastic Infiltration

- EMH is common in dogs but by itself rarely results in detectable splenomegaly. EMH can be associated with neoplastic infiltrations and also has been observed in dogs with immune-mediated hemolysis, immune-mediated thrombocytopenia, bone marrow hypoplasia, pyometra, and infectious diseases.
- Hypereosinophilic syndrome of cats can lead to infiltration of the spleen with mature eosinophils. This syndrome is characterized by peripheral blood eosinophilia, bone marrow hyperplasia of eosinophil precursors, and multiple organ infiltration by mature eosinophils.
- Splenic amyloidosis can cause splenomegaly but is rare.

Hypersplenism

Hypersplenism is characterized by the following:

- Cytopenias
- Bone marrow hyperplasia of the affected cell line or a normocellular bone marrow
- Splenomegaly
- Resolution of the cytopenia in response to splenectomy

Hypersplenism results mainly from the filtering and phagocytic functions of the spleen.

- *Primary hypersplenism* occurs when the splenic dysfunction is idiopathic.
- *Secondary hypersplenism* occurs as the result of an underlying disease process that has resulted in splenomegaly.

Hyposplenism

- Hyposplenism, or decreased splenic function, can occur secondary to a wide range of disease processes. A number of hematologic changes are recognized in association with hyposplenism (Table 25-3). These changes are also seen in splenectomized animals.

CLINICAL SIGNS

- Clinical signs of splenic disease typically are nonspecific or related to the underlying disease process.
- Clinical signs may include anorexia, weight loss, weakness, abdominal distension, vomiting, diarrhea, and polyuria or polydipsia.
- Acute collapse and pale mucous membranes are common clinical signs in patients with splenic rupture.

Table 25-3. HEMATOLOGIC ABNORMALITIES IN DOGS AND CATS WITH SPLENOMEGALY

Hypersplenism	Hyposplenism/Asplenia
Regenerative anemia	Target cells
Neutropenia	Acanthocytes
Thrombocytopenia	Howell-Jolly bodies
Bicytopenias	Nucleated red blood cells
Pancytopenia	Reticulocytosis
	Thrombocytosis

DIAGNOSIS

History

- The history and clinical signs for many patients with splenic disease are nonspecific; however, the history can aid the diagnosis of patients with certain types of splenic disease.
- Periodic weakness or collapse, often accompanied by mucous membrane pallor, raises the suspicion of splenic hemangiosarcoma with intermittent hemorrhage, particularly in certain breeds (e.g., golden retrievers and German shepherds).
- Patients presenting with a relatively acute onset of abdominal distension and retching may have splenic torsion in conjunction with gastric dilatation-volvulus. A history of tick exposure in patients with splenomegaly can aid in the diagnosis of ehrlichiosis and Rocky Mountain spotted fever.
- Travel history to endemic disease areas, vaccination history, and reported drug exposures may aid in the diagnosis of underlying infectious diseases or pharmacologic causes of splenic disease.

Physical Examination

- The spleen is located in the left cranial abdominal quadrant. The dorsal extremity of the spleen is relatively fixed near the midline ventral to the left crus of the diaphragm, but the remainder is freely movable and oriented longitudinally along the left flank.
- The normal spleen is palpable in many dogs and cats. Splenomegaly often can be detected with careful abdominal palpation. Position of the spleen and ease of identification can vary depending on a variety of factors including breed conformation, presence of ingesta in the stomach, and body weight. However, not all enlarged spleens are palpable and not every palpable spleen is abnormal. Imaging of the spleen with radiography, ultrasonography, or computed tomography may be required to identify an enlarged spleen.
- Other physical examination findings may be directly or indirectly related to the underlying cause of the splenic disease. These findings may include abdominal distension, peritoneal effusion, pain on abdominal palpation, petechiae, ecchymoses, pale mucous membranes, and fever.
- Peripheral lymphadenopathy can occur in conjunction with underlying neoplastic diseases such as leukemia or lymphoma and infectious diseases such as ehrlichiosis or systemic mycoses.

Hematologic and Serum Biochemical Findings

- The hemogram is often helpful in the diagnosis of splenic disorders. Two patterns of hematologic changes are recognized in dogs and cats with splenomegaly: hypersplenism and hyposplenism (or asplenia). The hematologic abnormalities in patients with splenomegaly are summarized in Table 25-3.
- Hyposplenism is more common and results in hematological changes similar to those in splenectomized patients.
- Spherocytes are common in patients with autoimmune hemolytic anemia.
- Patients with immune-mediated thrombocytopenia may have splenomegaly and thrombocytopenia with no other hematologic abnormalities.
- Common hematologic findings in dogs with hemangiosarcoma include anemia (regenerative or nonregenerative), poikilocytosis, nucleated red blood cells, presence of acanthocytes and schistocytes, presence of Howell-Jolly bodies, thrombocytopenia, and neutrophilia.
- A coagulation profile can aid in the diagnosis of acute or chronic disseminated intravascular coagulation (DIC), which occurs in some patients with splenic disease. DIC is a common complication of hemangiosarcoma, splenic torsion, and autoimmune hemolytic anemia.
- Perform biochemical profile and urinalysis in all patients with splenic disease. Biochemical abnormalities usually are a consequence of the primary underlying disease process rather than of splenic enlargement or other pathology. Hemoglobinemia and resultant hemoglobinuria are common findings in dogs with splenic torsion.

Abdominal Radiography

- In most dogs, the tail of the spleen is visible on the lateral view just caudal to the stomach along the ventral body wall. The head of the spleen usually is seen on ventrodorsal radiographs between the fundus of the stomach, the cranial pole of the left kidney, and the body wall, appearing as a triangular structure. The entire spleen is best seen on the ventrodorsal view along the left lateral body wall.
- In dogs, splenic size is variable. Causes of diffuse splenic enlargement are listed in Table 25-2.
- The most reliable radiographic indicator of splenic enlargement is rounded or blunted margins. Generalized splenic enlargement may result in caudal and dorsal displacement of the small intestine viewed on lateral radiographs.
- In dogs, a splenic mass is the most likely cause of a mid-abdominal mass visible in a lateral abdominal radiograph.
- Splenic size is less variable in cats and is always much smaller than dogs. It usually is seen on the ventrodorsal radiograph along the left lateral body wall.
- The tail of the spleen is visible on lateral radiographs only if the spleen is enlarged.

- Severe splenomegaly develops following torsion. Torsion of the spleen occurs most commonly in large and giant deep-chested dogs. The spleen may have a characteristic C-shaped appearance on the lateral view; however, accompanying peritoneal fluid may obscure this shape. The fundus of the stomach may be displaced caudally and medially due to tension on the gastrosplenic ligament. Torsion may occur as a consequence of gastric volvulus (see Chapter 67).

Abdominal Ultrasound

- Ultrasonographic examination of the spleen is useful for determining size, location, and presence of parenchymal abnormalities when a pathologic condition is suspected (also see Chapter 4).
- Primary indications for ultrasonographic examination include generalized splenomegaly, abdominal or splenic mass, trauma, and hemoperitoneum.

▼ ***Key Point*** The primary value of ultrasonography over radiography is its ability to determine whether focal or non-focal parenchymal disease is present, to differentiate cavitary from solid lesions, and to provide guidance for biopsy procedures.

Generalized Splenomegaly

- The size of the normal spleen is variable and must be assessed subjectively. The normal canine spleen appears hyperechoic and finely textured when compared with the liver bounded by a thin, hyperechoic capsule.
- In most instances, ultrasonography by itself is not helpful in establishing a specific diagnosis in cases of diffuse splenomegaly. Ultrasound-guided aspiration biopsy is usually indicated.
- Passive congestion usually results in splenomegaly with normal or slightly reduced echogenicity.
- Splenic torsion produces a markedly enlarged spleen with diffuse anechoic areas and multiple parallel echogenic lines within the parenchyma. Doppler evaluation of the splenic parenchyma indicates an absence of blood flow. Larger vessels may be thrombotic.
- Diffuse neoplastic disease (e.g., lymphoma, leukemia, malignant histiocytosis, and mastocytosis) may reduce or increase echogenicity, or the parenchyma may appear normal.
- Splenitis is occasionally seen, usually with abnormally hypoechoic and coarsely textured parenchyma. Focal or multifocal hypoechoic areas or nodules may be present concurrently with diffuse changes.

Lymphoma of the spleen may have a wide variety of appearances and may produce diffuse increased or decreased echogenicity, a honeycomb pattern, a moth-eaten appearance, or focal or multifocal hypoechoic nodules or complex mass lesions.

Localized Splenomegaly

- Focal lesions of the spleen are easily detected, but findings must be correlated with history and laboratory findings. Ultrasonography is useful for guided aspiration biopsy of focal lesions to obtain representative cytologic material for analysis.
- Splenic hematomas result from abdominal trauma, clotting disorders, nodular hyperplasia, and neoplasia. The ultrasonographic appearance of a hematoma is extremely variable, depending on its age.
- Focal splenic infarcts occur secondary to embolism or thrombosis. The appearance of infarcts is variable and depends on the time since the infarct occurred. Initially, infarcts appear as poorly marginated hypoechoic or complex lesions, which appear echogenic if there is postinfarctive hemorrhage.
- Abscesses, although uncommon, produce focal or multifocal splenic lesions. Their appearance is variable from poorly marginated hypoechoic lesions to complex lesions with variable cystic and solid components.
- Nodular hyperplasia of the spleen may appear as isoechoic, hypoechoic, hyperechoic, or complex lesions that usually are very vascular.
- Focal or multifocal neoplastic lesions of the spleen commonly result from sarcomas, in the dog most commonly hemangiosarcoma. The specific type of neoplasia cannot be determined from its ultrasonographic appearance alone. Neoplastic lesions are commonly poorly defined, anechoic, hypoechoic, or complex in appearance. Hemoperitoneum is often present with hemangiosarcoma of the spleen. Lymphoma may produce poorly marginated, anechoic to hypoechoic focal or multifocal lesions. Focal lymphomatous masses may distort the splenic contour or cavitate. Mesenteric lymphadenopathy often is seen with splenic lymphosarcoma.

Fine-Needle Aspiration

▼ ***Key Point*** Fine-needle aspiration (FNA) cytology often is the diagnostic technique of choice following abdominal radiography and ultrasound for the evaluation of splenic disease.

FNA is perhaps most useful in the diagnosis of diffuse splenic disease. The radiographic and ultrasonographic appearance of most splenic diseases, with the exception of splenic torsion, is relatively nonspecific. FNA cytology can aid in the selection of patients for exploratory surgery, splenic biopsy, and splenectomy. A cytologic diagnosis of neoplastic (e.g., lymphoma, hemangiosarcoma, and mastocytosis) and non-neoplastic (e.g., EMH and nodular hyperplasia) is often possible. Though this procedure can be done "blindly," it preferably is done using ultrasound guidance.

Contraindications

Aspiration cytology may be contraindicated in patients with large cavitary lesions, which may rupture during aspiration, although this is a rare occurrence. More importantly, aspiration of these lesions is often nondiagnostic, and surgery may be recommended in these cases. In patients with hemangiosarcoma, aspiration can theoretically result in tumor seeding along the needle tract or rupture and seeding of the abdominal cavity. Given the high incidence of spontaneous splenic rupture and seeding in this disease, even without FNA, it probably should not be a practical contraindication to performing the procedure when needed.

Technique

- Position the patient in right lateral or dorsal recumbency.
- Mild sedation may be required in some patients but is usually not necessary.

▼ ***Key Point*** Avoid phenothiazine tranquilizers; they cause splenic enlargement from vascular stasis and may dilute the sample with blood.

- Cleanse the area with alcohol, or do a surgical prep.
- Insert a 25- or 22-gauge, 1- to 1.5-inch needle without a syringe attached using ultrasound guidance to avoid overlying organs and large splenic blood vessels. In obese patients, use a stylet type of needle, removing the stylet once you have entered the parenchyma. This prevents inadvertent sampling of the near-field tissues.
- Avoid penetrating the opposite (far field) capsule to reduce hemorrhage.
- A pincushion sampling technique usually results in less hemodilution of the sample than does an aspiration technique. Without a syringe attached, make multiple penetrations of the needle into the spleen using one hole and without pulling the tip of the needle out of the spleen with each jab.
- Repeat 2 to 3 times, smearing each sample onto a new, clean slide.
- In high-risk cases, reassess the patient sonographically in 2 to 4 hours for evidence of hemorrhage (rare).

Complications

Potential complications include splenic rupture, hemorrhage, damage to other organs, peritonitis, and abdominal seeding of a splenic neoplasm; however, two reports describing the use of this technique reported no complications. Thrombocytopenia is not considered a contraindication for this procedure.

Needle Biopsy

- Considerations are similar to those for aspiration of the spleen.
- Use ultrasound guidance.
- Use 18- (cats), 16-, or 14-gauge biopsy needles.
- Avoid penetrating the opposite splenic capsule to reduce chance of hemorrhage.
- Obtain two to three samples.
- In general, biopsies and aspirates are more commonly performed for diffuse or nodular disease, and surgery is preferred for mass lesions.

Miscellaneous Tests

Bone Marrow Aspiration Cytology

- Bone marrow aspiration cytology or core bone marrow biopsy is indicated in patients with splenomegaly and cytopenias (see Chapter 22 for details on bone marrow biopsy technique).
- Splenectomy may be contraindicated in a patient with splenomegaly due to EMH secondary to bone marrow hypoplasia or aplasia.
- Bone marrow aspiration cytology may support or confirm the underlying disease process.

Lymph Node Aspiration Cytology

- Lymph node needle aspiration cytology or biopsy is indicated in patients with lymphadenopathy.
- Marked peripheral lymphadenopathy usually is associated with lymphoma. Mild or moderate lymphadenopathy can be seen in lymphoma and in a number of different diseases, including infectious and immune-mediated disorders.
- Ultrasound guided biopsy procedures may be needed to aspirate enlarged lymph nodes within the abdomen or other sites.

Serologic Tests and Polymerase Chain Reaction

- Serologic tests for specific infectious and immune diseases can be performed. Rickettsial titers or polymerase chain reaction (PCR) for ehrlichiosis or *Mycoplasma haemofelis* infection (hemobartonellosis), Coombs test for immune-mediated hemolytic anemia, and antinuclear antibody test for systemic lupus erythematosus may be indicated for some patients. Test cats with splenomegaly for feline leukemia virus and feline immunodeficiency virus.

Other Tests

- Thoracic radiographs or computed tomography (CT) may be useful in patients with suspected neoplastic disease and some infectious diseases (e.g., blastomycoses).
- Diagnosis of lymphoma based on FNA cytology of the spleen often must be made with caution, especially in those patients with minimal lymphadenopathy. Demonstration of a monoclonal lymphocyte population using PCR, or assessment of cell immunophenotype using flow cytometry, can be useful for arriving at a diagnosis of lymphoma.

TREATMENT

Splenectomy

Preoperative Considerations

- Splenectomy is indicated for patients with splenic rupture, splenic torsion, or splenic masses and for symptomatic patients.
- Splenectomy in cats with systemic mastocytosis can significantly prolong life expectancy even if mast cells are present in the peripheral circulation.

Splenic Hemangiosarcoma

- Because of the potential for splenic rupture and death in patients with hemangiosarcoma, perform splenectomy. Prior to splenectomy, evaluate a complete blood count, coagulation panel, and thoracic and abdominal radiographs. If available, abdominal ultrasound and echocardiography provide a more thorough assessment of potential metastatic sites. Dogs with hemangiosarcoma typically are not cured by surgery alone and usually have evidence of recurrence within 4 months; however, even dogs with gross evidence of metastatic disease may have favorable responses to splenectomy combined with adjuvant chemotherapy (Table 25-4). Doxorubicin containing protocols, using doxorubicin as a single agent or in combination with cyclophosphamide (AC) or cyclophosphamide and vincristine (VAC), have been shown to be beneficial in dogs with splenic hemangiosarcoma. The relative efficacy of these different protocols appears to be similar; however, they have not been directly prospectively compared.

Table 25-4. TREATMENT PROTOCOLS FOR HEMANGIOSARCOMA

VAC Protocol (21-Day Cycle)
Doxorubicin[*†]: 30 mg/m^2 (or 1 mg/kg if <10 kg), IV, day 1
Vincristine[‡]: 0.75 mg/m^2, IV, days 8, 15
Cyclophosphamide: 200–300 mg/m^2, day 10
Sulfa-trimethoprim: 15 mg/kg, q12h

AC Protocol (21-Day Cycle)
Doxorubicin: 30 mg/m^2 (or 1 mg/kg if <10 kg), IV, day 1
Cyclophosphamide[†]: 200–300 mg/m^2, day 10
Sulfa-trimethoprim: 15 mg/kg, q12h

Doxorubicin (Monotherapy)
Doxorubicin: 30 mg/m^2 (or 1 mg/kg if <10 kg), IV, q21 days

[*]Doxorubicin is potentially cardiotoxic. Perform cardiac evaluation prior to treatment and monitor throughout treatment. The recommended maximum cumulative dose is 180–240 mg/m^2 or 6–8 doses, but it must be applied to each patient individually.
[†]Cyclophosphamide can cause hemorrhagic cystitis. If it occurs, discontinue cyclophosphamide immediately and usually limit therapy to oral antibiotics and corticosteroids. Resolution of signs usually occurs within 8 weeks.
[‡]Evaluate a complete blood count before each doxorubicin or vincristine treatment to check for bone marrow suppression. Monitor patient progress every two cycles (radiographs of thorax, abdominal radiographs or ultrasound, and echocardiography if indicated). Allow completion of two to three cycles of treatment before making a decision about response to therapy.
AC, Adriamycin (doxorubicin)-cyclophosphamide; VAC, vincristine-Adriamycin (doxorubicin)-cyclophosphamide.

Other Splenic Sarcomas

Most other histopathologic types of splenic sarcomas warrant a poor prognosis and are associated with a high rate of metastasis. Adjuvant chemotherapy probably is warranted postoperatively for these patients as well, although limited information is available on the efficacy of therapy.

Other Splenic Disorders

- Splenectomy is contraindicated in patients with immune-mediated hemolytic anemia or thrombocytopenia, except as a last resort after medical therapy has failed, and in patients with bone marrow hypoplasia or aplasia, because the spleen is the major hematopoietic organ in these patients.
- Splenectomy may be a therapeutic option in selected patients with lymphoma and leukemia, notably in patients with massive splenomegaly and/or disease localized to the spleen. In these cases, multimodality therapy combining surgery with systemic chemotherapy should be considered. In humans with non-Hodgkin's lymphoma, the indications for splenectomy are massive splenomegaly, hypersplenism syndrome, and autoimmune complications.

▼ ***Key Point*** Generalized splenomegaly often is not a surgical disease. Attempt to diagnose and treat the underlying disorder before performing a splenectomy.

Technique

Partial Splenectomy

1. Prepare the ventral abdomen for aseptic surgery.
2. Make a ventral midline abdominal incision from the xiphoid to 2 to 4 cm cranial to the pubis or more caudally if necessary.
3. Place a Balfour retractor to expose the abdominal viscera.
4. Examine the spleen and other abdominal organs for evidence of abnormalities.
5. Gently pull the spleen out of the abdominal cavity.
6. Doubly ligate the splenic branches of the splenic artery and vein to the affected area of the spleen with absorbable suture. Divide the vessels among the ligatures. Alternatively, use the ligate-and-divide stapling instrument (LDS).
7. Place two non-crushing clamps (e.g., Doyen) on the spleen between the healthy and the diseased areas.
8. Divide between the clamps and remove the splenic tissue.

9. Oversew the splenic capsule on the remaining spleen (3-0 or 4-0 polydioxanone [PDS], simple continuous suture).
10. Alternatively, use the thoraco-abdominal stapler (TA) (55- or 90-mm cartridge) to staple the splenic parenchyma prior to excision.
11. Check vessels and splenic incision for bleeding. Close the abdomen routinely.

Total Splenectomy

1. to 5. These steps are the same as for partial splenectomy.
6. Doubly ligate all the splenic branches of the splenic artery and vein with absorbable suture. Ligate the vessels close to the hilus of the spleen. Usually, two or three vessels can be included in each ligature. If possible, preserve the left gastroepiploic artery and vein (Fig. 25-1); this may not be possible when removing large splenic tumors.
7. Divide each vessel among the ligatures and remove the spleen.
8. An alternative and more rapid procedure for total splenectomy is to place vascular clamps across the vessels before ligation. Include two or three of the vessels in each clamp. Divide the vessels between each pair of clamps and then place the next pair of clamps (see Fig. 25-1). After all vessels have been clamped and divided, remove the spleen. Ligate all vessels with absorbable sutures.
9. Alternatively, use the LDS to ligate and divide the vessels.
10. When splenic torsion is present, do not untwist the spleen because release of tissue breakdown products and bacteria may result. Ligate the entire vascular pedicle with two or three absorbable ligatures. Consider placing a transfixing ligature in large dogs. Place two clamps across the vascular pedicle, divide between them, and remove the spleen. Remove the remaining clamp and check the pedicle for hemorrhage.
11. Check the vessels for hemorrhage. Close the abdomen in a routine fashion.

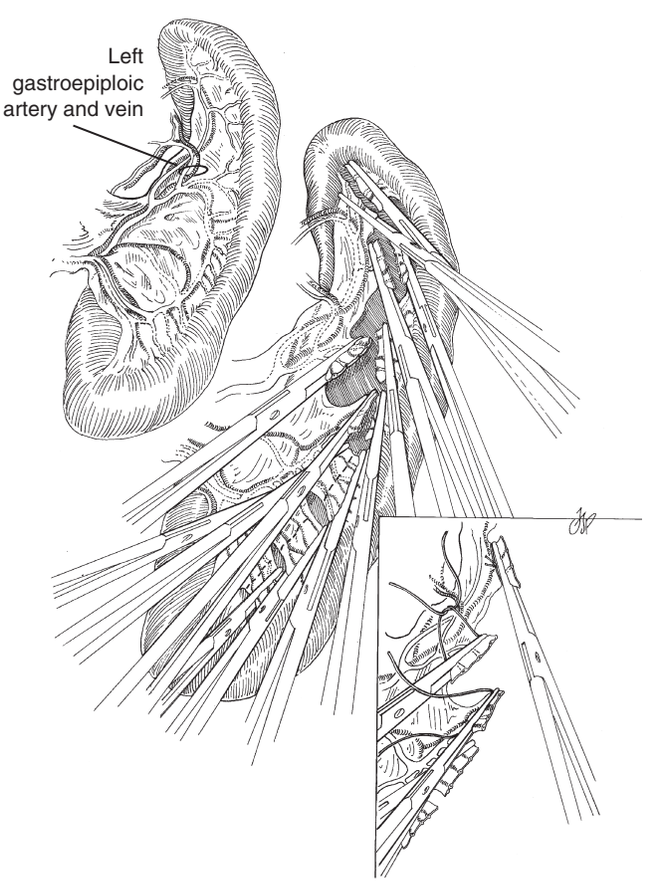

Figure 25-1. General procedure for total splenectomy. See text for details.

Postoperative Care and Complications

- The gross appearance of the spleen cannot be used to differentiate hematoma, hemangioma, and hemangiosarcoma. A histopathologic diagnosis is crucial for determining postoperative treatment and prognosis.
- Postsplenectomy sepsis is a serious complication in humans and can be fatal. Although this is a rare complication in dogs and cats, partial splenectomy or splenic biopsy may be advisable in certain animals. Partial splenectomy is a viable option for those animals with localized masses unless malignancy is suspected.
- Other possible complications of splenectomy include exacerbation of certain diseases such as hemobartonellosis and babesiosis in animals that are latent carriers and cytopenia(s) in patients with EMH secondary to a primary bone marrow disorder.

Treatment of the Underlying Disease Process

- Treat infectious diseases with appropriate antibiotic therapy and supportive care.
- Treat immune-mediated diseases (immune-mediated hemolytic anemia and immune-mediated thrombocytopenia) as follows:
  - Use immunosuppressive doses of corticosteroids and other drugs as necessary (e.g., cyclophosphamide).
  - Use blood component therapy if indicated (as described in Chapters 22 and 23).
- Chemotherapy alone or in conjunction with the necessary supportive care is recommended for patients with acute and chronic leukemia and lymphoma (see Chapter 27) and for dogs with systemic mastocytosis (see Chapter 28) and hemangiosarcoma (Table 25-4).

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Chapter 26

Principles of Oncology

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Cancer management in animals has evolved considerably over the past 3 decades as the result of several significant factors. Improved health care of animals has increased the age distribution of pets and hence their likelihood of developing cancer; clients are more aware of aggressive treatment choices; and there have been significant improvements in treatment success. There remains some controversy and confusion over the best course of treatment for many tumor types, and more studies are needed to provide the necessary data. However, clinicians can use a generic framework for evaluation and treatment management of many tumor types. This chapter provides an outline useful for clinical management of an animal with cancer.

INITIAL CLINICAL PRESENTATION

Signalment

Many neoplasms more commonly affect animals of a certain age, sex, or breed, and such knowledge often aids diagnosis. Table 26-1 is a partial list of specific breeds and characteristics of dogs and cats predisposed to certain types of neoplasia.

History

The onset and duration of a mass, its growth rate, the presence of other masses, signs of paraneoplastic syndromes, and knowledge of prior treatments further help narrow diagnostic and treatment options and define the behavioral characteristics of a neoplasm.

Physical Examination

Examination is used to define the extent of tumor burden and identify concurrent diseases that may limit treatment or affect survival. Tumor characteristics such as *size* (measure with calipers to determine objectively), *location* (e.g., oral melanoma is more malignant than cutaneous melanoma), *invasiveness* (is mass fixed to adjacent tissue), and presence of *ulceration* or *necrosis* of the tumor is important to determine tumor behavior and to plan adequately an appropriate biopsy and treatment regimen. Regional lymph nodes are evaluated for size, consistency, and fixation to adjacent tissues. To complete the clinical evaluation, a list of differential diagnoses is made and a diagnostic and staging plan is determined.

Client Counseling

A diagnosis of cancer can evoke considerable emotional response from owners. For many clients, the diagnosis implies pain, discomfort, and impending death of their pet. Proper counseling on the part of the veterinarian should include the following:

- Listen to the needs of the client and mutually determine a set of realistic goals for treatment.
- Explain treatment procedures, discussing risks, benefits, toxicity, and costs. It is helpful to provide written material for home review of information.
- Provide a realistic and *unbiased* view of all treatment options available and the animal's likely prognosis.
- Beware of the tendency for clinicians untrained in oncology to prematurely recommend euthanasia.
- Consider consultation with or referral to a specialist when appropriate.

DIAGNOSIS

Laboratory Evaluation

Assess general health status to identify concurrent disease or paraneoplastic syndromes that may adversely affect prognosis and limit or alter therapy. After a thorough physical examination, perform screening laboratory evaluations, including a complete blood count, serum biochemistry panel, and urinalysis. Perform other special laboratory tests as indicated to aid diagnosis (e.g., feline leukemia virus, feline immunodeficiency virus, bone marrow aspirate, adrenal or thyroid function tests, etc.).

Diagnostic Imaging

- Obtain survey radiographs to detect metastases (on the thorax, abdomen, or skeleton), to evaluate orthopedic soundness before amputation or limb-sparing

Table 26-1. SOME FACTORS PREDISPOSING DOGS AND CATS TO SPECIFIC NEOPLASMS

Factor	Predilection For
Age	
Histiocytoma	Young dogs
Viral papilloma	Young dogs
Sex	
Malignant melanoma	Males
Perianal adenoma	Males
Anal Sac AdenoCA	Females
Adrenal tumor	Females
Meningiomas	Females (dog), males (cat)
Color	
Squamous cell carcinoma	Nonpigmented regions
Malignant melanoma	Darkly pigmented regions
Breed	
Skin tumors	Basset, boxer, bull mastiff, Scottish terrier, weimaraner
Mast cell tumor	Brachycephalic breeds, Retrievers
Bone tumors	Large/giant breeds
Thyroid tumor	Boxer, beagle, golden retriever
Hemangiosarcoma	Retrievers, German shepherd
Lymphoma	Retrievers, boxers, mastiffs
Histiocytic malignancies	Burnese Mountain Dogs, retrievers, rottweillers

surgery for dogs with osteosarcoma, and to determine bone margins of oral or nasal masses. When taking thoracic radiographs, remember to take both right and left laterals as well as a ventrodorsal/dorsoventral view, to avoid missing metastatic lesions (see Chapter 4).

- Contrast radiography may be helpful for defining the extent of disease in hollow viscera (see Chapter 4).
- Computed tomography and magnetic resonance imaging are useful to delineate deep masses of the body cavities and axial skeleton (see Chapter 4).
- Ultrasound is useful to image abdominal viscera. It can determine accurately the parenchymal nature of a mass and tumor proximity to large vessels, and evaluate for intra-abdominal metastases to lymph nodes or organs. Additionally, it can be used for direction of fine needle aspiration or minimally invasive biopsy procedures (see Chapter 4).

Cytology

Cytology is useful to evaluate fine-needle aspirates of masses and lymph nodes, bone marrow aspirates, and buffy coat and peripheral blood smear preparations. It can provide rapid and inexpensive diagnostic and staging information. Do not over-interpret cytologic preparations. Base treatment decisions on cytologic diagnosis only when a definitive diagnosis can be made by a pathologist, as with lymphoma and mast cell tumors. Although a diagnosis may be accomplished with cytologic preparations, histologic assessment is usually necessary to determine prognosis (i.e., grade of malignancy).

Biopsy

Many techniques are available for tumor biopsy. The method selected should safely and simply procure an adequate tissue sample to provide an accurate diagnosis without making definitive treatment more difficult or invasive.

General Considerations

- In general, larger tissue samples are more likely to provide an accurate diagnosis. Avoid traumatic tissue handling, electrocoagulation, and other tissue damage to provide a histologically useful sample.
- Fix tissue samples for routine histopathologic analysis in 10% buffered formalin (10:1 formalin-to-tissue ratio).
- Obtain samples for culture or other special analyses at the same time to avoid a second biopsy procedure if histologic analysis identifies an inflammatory or other nonneoplastic process.
- Include a complete history and description of the clinical and surgical findings with the biopsy specimen submission.
- If unsure of the most appropriate biopsy technique, consult with or refer the animal to a specialist.

Excisional Biopsy

- Complete removal of a tumor and submission for histologic diagnosis is most useful for cutaneous, mammary, and central nervous system (CNS) tumors and easily resectable masses found during laparotomy or thoracotomy.
- Ideally, an excisable mass is small and freely movable without significant adjacent tissue invasion.
- Excise the mass with a histologically confirmed complete resection margin of normal tissue. Use suture tags to identify areas of possible inadequate resection that require closer histologic scrutiny. Inking of all surgical margins can also aid the pathologist in determination of the completeness of the excision.

Nonexcisional/Incisional Biopsy

- Remove only a portion of a tumor (e.g., cutting needle, endoscopic, punch, or incisional biopsy) when definitive diagnosis or grading would influence treatment decisions.
- Take deep biopsies of superficial ulcerated masses to avoid sampling only overlying necrotic debris on the surface.
- Incisional and needle biopsy tracts are considered contaminated by tumor cells and must be completely within the future field of surgical resection or radiation treatment.
- Ideal histologic samples contain a margin of normal and neoplastic tissue. This allows assessment of tumor invasiveness, and margins are frequently the site of greatest tumor cell activity. Biopsy at the margin is often undesirable, however, because it disrupts the

natural tumor margin and effectively extends it. This necessitates a wider resection or larger radiation field for definitive treatment. Therefore, if biopsies include marginal tissues, collect from areas where there is adequate tissue for wider excision.

▼ ***Key Point*** Improper biopsy technique can significantly alter treatment, increase treatment morbidity, and sometimes adversely affect prognosis.

Evaluation of Pathology Reports

The pathology report should include:

- Histologic diagnosis and, where appropriate, histologic grade (e.g., mast cell tumor, soft tissue sarcoma, osteosarcoma)
- Complete description of cellular characteristics and degree of anaplasia
- Mitotic index
- Identification of lymphatic or vascular invasion
- Evaluation of resection margins

If aspects of the report are questionable or do not match your clinical judgment, always discuss the results with the pathologist.

Tumor Staging

Accurate staging requires understanding the biologic behavior of different tumor types, combined with the results of a thorough diagnostic workup based on this expected behavior. Tumor staging is used to do the following:

- Determine the extent of neoplastic disease
- Provide a framework for rational treatment planning
- Facilitate communication between clinicians
- Allow for uniform comparison and evaluation of treatment results
- Aid in establishing a prognosis

Several staging systems are available. Most are based on assessment of local, regional, and distant disease involvement. Some systems include other factors, such as presence or absence of clinical signs (e.g., lymphomas), tumor histologic grade (e.g., mast cell tumors), or tumor location (e.g., squamous cell carcinoma of mouth, tonsil, pinna, or digit). The TNM staging system (T, tumor size or extent; N, lymph node involvement; M, metastasis) devised by the World Health Organization is the standard system for most tumors in veterinary medicine. Table 26-2 describes this staging scheme and gives an example. Staging systems should be revised as new prognostic information is acquired.

Table 26-2. WORLD HEALTH ORGANIZATION TNM CLASSIFICATION OF TUMORS

T = Tumor Size or Extent

T_1–T_4 represent specific size categories designated for each tumor type and define the extent of local tumor involvement.

N = Lymph Node Involvement

N_1–N_3 (± a, b) describes regional lymph node characteristics for presence or absence of neoplasia, number and location of enlarged lymph nodes, and occurrence of adjacent tissue adhesion.

M = Metastasis

M_0 or M_1 indicates absence or presence of distant metastasis.

Example—TNM Classification of Tumors of the Oral Cavity in Dogs or Cats:

T: Primary Tumor

T_{is} = Preinvasive tumor (in situ)
T_0 = No evidence of tumor
T_1 = Tumor <2 cm diameter
T_2 = Tumor 2–4 cm diameter
T_3 = Tumor 3 cm diameter
subclassification of a (no bone invasion) or b (bone invasion) can be added.

N: Nodes

N_0 = No evidence of lymph node enlargement
N_1 = Movable ipsilateral nodes enlarged
N_2 = Movable contralateral/bilateral nodes enlarged
N_3 = Fixed nodes

M: Metastasis

M_0 = No metastasis
M_1 = Metastasis detected

Example of Stage Grouping for Oral Tumors:

Stage	*T*	*N*	*M*
I	T_1	N_0, N_{1a}, N_{2a}	M_0
II	T_2	N_0, N_{1a}, N_{2a}	M_0
III	T_3	N_0, N_{1a}, N_{2a}	M_0
	Any T	N_{1b}	M_0
IV	Any T	N_{2b}, N_3	M_0
	Any T	Any N	M_1

From Owen LN: Classification of Tumours in Domestic Animals. Geneva: WHO, 1980.

PRINCIPLES OF THERAPY

Rational treatment planning requires an accurate diagnosis, complete staging, and knowledge of expected tumor behavior with regard to local growth and propensity for developing regional and distant metastases. Many treatment options are available for the management of cancer, and each has its advantages and disadvantages. Become familiar with the strengths and weaknesses of each treatment modality and develop a treatment plan that addresses each aspect of expected tumor behavior (i.e., local, regional, and distant disease). Currently, multidisciplinary treatment is employed most commonly to maximize treatment results while minimizing toxicity. Combinations of surgery, chemotherapy, and radiation often can more effectively eradicate cancer, especially multifocal cancer, than any one modality alone. The goal of treatment is to maintain the highest quality of life for the longest period of time.

▼ ***Key Point*** The probability of long-term tumor control is greatest when aggressive therapy is instituted early, before the tumor is disturbed by previous failed therapeutic attempts.

Surgery

Surgery is primarily useful for localized neoplasms. In select cases, en bloc dissection of regional lymph nodes and the primary mass is used for treatment of regional disease, and surgery can be useful for treatment of metastatic disease that is slow growing or causing clinical morbidity.

Applications

Surgery is the most widely applied modality for control of localized cancer. Surgery can also be used for prevention (e.g., ovariohysterectomy before 2.5 years of age for mammary cancer in dogs), diagnosis (see section on Biopsy), staging (see section on Staging), and treatment (cure or palliation). Surgery also is used for treatment of oncologic emergencies (e.g., obstruction or perforation) and for complications related to chemotherapy or radiotherapy (e.g., drug extravasation, radionecrosis).

Principles of Surgery

A special technique is used to prevent surgical spread of cancer cells and to ensure complete tumor resection.

▼ ***Key Point*** Aggressive initial surgical management of neoplasia may be the most important principle for improved cancer control. The best chance for complete resection and cure is with the first surgery.

- Decide resection margins in advance of the surgery based on tumor type, expected behavior, extent of local invasion, and the barrier provided by surrounding tissues (Fig. 26-1). Vascular-poor, collagen-rich tissue (e.g., cartilage and fascia) are most impermeable to tumor invasion. Other tissues (e.g., fat and subcutaneous tissue) provide less of a barrier.
- Resect all neoplastic tissue; if necessary, use skin flaps or grafts to close large defects (see Chapter 57). If uncertain about achieving complete resection or wound closure, consider referral to a specialist.
- Protect healthy tissues from tumor cell contamination by use of barrier drapes and laparotomy sponges. Employ glove, instrument, and drape changes as necessary to prevent contamination of normal tissue with cancer cells. Copious lavage of surface wounds also may reduce the likelihood of residual tumor.
- Minimize tumor manipulation. Handle tumors by placing stay sutures in normal margin tissues.
- Ligate vascular and lymphatic vessels early, and always before severing, to prevent shedding of tumor emboli.

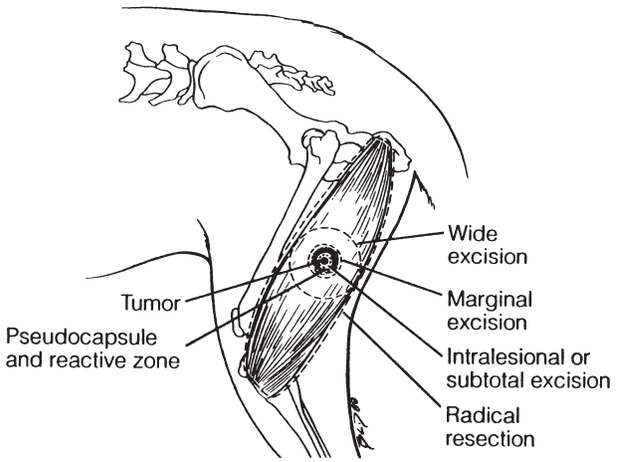

Figure 26-1. Surgical options for removal of a neoplasm. Wide excision or a more radical, compartmental resection is recommended for tumors that are not superficial or are infiltrative. Additional therapy may be indicated from histologic evaluation of tumor specimen. (Reprinted with permission from Gilson SD, Stone EA: Compend Contin Educ Pract Vet 12:1047, 1990.)

- Fulgurate or electrocoagulate any exposed tumor surfaces.
- When en bloc resection is performed, maintain adequate margins and dissect from the most peripheral affected lymph node toward the primary mass.
- When postoperative radiotherapy is used, all surgically exposed tissues plus a margin of normal tissue are irradiated. Position tissue grafts, flaps, and drains to minimize treatment fields. Use of hemoclips or other metallic markers are helpful in radiographically establishing the margins of manipulated tissues for radiation treatment planning.
- Submit all resected specimens for histologic analysis and evaluation of margins.

▼ ***Key Point*** A pseudocapsule made up of compressed cancer cells surrounds most tumors. Although seemingly a convenient plane for dissection, it is not a true capsule and provides no barrier to tumor invasion. A properly excised tumor is encased completely in an envelope of normal tissue.

If histopathology of the excised tumor reveals incomplete excision, promptly plan and perform a re-excision if possible.

Sources of Failure

Treatment failures result from surgery-related morbidity and mortality, local or regional tumor recurrence, and tumor seeding or metastatic disease. Most failures can be minimized by use of proper surgical technique and appropriate patient selection.

Radiotherapy

Radiotherapy is primarily useful for local and regional neoplasia (Table 26-3). In selected cases, it is used for palliation of painful disseminated tumors.

Applications

Radiotherapy is administered as a single modality or is combined with surgery, chemotherapy, or hyperthermia. It can be administered:

- As the initial form of therapy (neoadjuvant radiotherapy)
- Concurrent with other therapies (intraoperative radiation, concurrent chemotherapy)
- As postoperative therapy (adjuvant radiotherapy)

Advantages of Neoadjuvant Radiotherapy (Preoperative)

- Reduced tumor size, requiring less surgery and increasing the effectiveness of adjuvant chemotherapy
- Tumor vasculature is unaltered, decreasing local tumor hypoxia
- Viability of any surgically disseminated tumor cells is decreased
- Peripheral subclinical disease is eliminated

Advantages of Concurrent Therapy (Intraoperative or Combined with Chemotherapy)

- Improved radiation effectiveness by chemotherapy-induced radiosensitization
- Decreased radiation toxicity to normal tissues with intraoperative radiation

Table 26-3. RELATIVE RADIATION SENSITIVITY OF SELECTED CANINE TUMORS

Tumor Type	Site	Response
Squamous carcinoma	Gingiva	Good
	External nose	Poor
	Tonsil	Fair–poor
	Nasal cavity	Fair–poor
Malignant melanoma	Oral	Fair
Acanthomatous epulis	Gingiva	Excellent
Fibrosarcoma	Nasal cavity	Fair–good
Chondrosarcoma	Nasal cavity	Fair–good
Adenocarcinoma	Nasal cavity	Fair–good
Transmissible venereal tumor	Variable (usually penis and vulva)	Excellent
Soft tissue sarcoma	Peripheral	Poor–good
Mast cell tumor	Cutaneous	Fair–excellent
Perianal adenoma	Perianal	Excellent
Meningioma	Brain	Fair–good
Osteosarcoma	Any site	Fair (palliation only)
Solitary lymphoproliferative disease	Any site	Excellent

Advantages of Adjuvant Radiation (Postoperative)

- Improved effectiveness of radiation against smaller tumor burden
- More accurate radiotherapy planning based on information gained from surgery
- No delays in other therapy from radiation-related complications

Principles of Radiotherapy

- Irradiate all potentially affected tissues (such as regional lymph nodes and the tumor itself) and a margin of normal tissue.
- Radiation is more effective against a small tumor burden and well-oxygenated tumor cells.
- Higher energy radiation sources (linear accelerator, cobalt therapy), result in deeper, more uniform radiation penetration and greater sparing of skin and superficial tissues.
- Frequent small doses of radiation (e.g., 3 Gy daily or every other day) are preferable to allow for reoxygenation of tumor cells, repair of normal cells, and decreased late effects of radiation toxicity.
- Damage to normal tissue is minimized by judicious treatment planning and use of multiple treatment portals and shrinking field techniques.
- Administer radiation doses to the maximum dose tolerated by adjacent normal tissues. Radiation-induced tissue changes are permanent; however, re-irradiation of recurrent tumors is possible in some situations.
- Radiation-induced normal tissue effects may be classified as *acute,* occurring during the last portion of therapy or in the first few weeks after irradiation (e.g., mucositis, moist desquamation of skin, hair loss, tissue inflammation), or *late,* occurring many months or years after treatment (e.g., contraction and fibrosis, bone necrosis, cataract formation).
- After treatment, tumor volume may not change and biopsy samples can show the presence of nonviable neoplastic cells. Only gross evidence of active tumor growth indicates tumor recurrence.

Sources of Failure

Treatment failures result from radiation-related toxicity to normal tissues and from tumor- or treatment-related factors. Meticulous technique and the use of advanced radiotherapy planning technology minimize these errors.

Tumor-Related Factors

- Histologic tumor type (some tumor cells are inherently more radioresistant)
- Tumor volume (a larger volume increases the likelihood of radioresistant cells and tumor hypoxia)

Table 26-4. COMMON CHEMOTHERAPEUTIC AGENTS USED IN VETERINARY MEDICINE

	Indication	Recommended Dosages	Toxicity
Alkylating Agents			
Cyclophosphamide (Cytoxan; Mead-Johnson)	Lymphoproliferative disorders, mast cell tumors, hemangiosarcoma, miscellaneous carcinomas	50 mg/m^2 PO q48 hr 50 mg/m^2 PO q24h for 4d weekly 100–300 mg/m^2 IV q3wk	BM, GI, hemorrhagic cystitis
Chlorambucil (Leukeran; Burroughs-Wellcome)	Lymphoproliferative disease, macroglobulinemia	2–4 mg/m^2 q24–48 h	BM
Melphalan (Alkeran; Burroughs-Wellcome)	Multiple myeloma	2–4 mg/m^2 PO q24–48 h	BM
Lomustine/CCNU	Lymphomas, mast cell tumors	60–90 mg/m^2 PO q21–28 d	BM, GI, Liver
Cisplatin (Platinol; Bristol)	Osteosarcoma, transitional cell carcinoma, squamous cell carcinoma	50–70 mg/m^2 IV q3wk (vigorous hydration)	BM, GI, renal; DO NOT USE IN CATS!
Carboplatin (Paraplatin; Bristol)	Similar to cisplatin	250–300 mg/m^2 IV q3wk	BM, GI
Antimetabolites			
Methotrexate (Lederle)	Lymphoproliferative disorders	2.5 mg/m^2 PO q24–48 h 15–20 mg/m^2 IV q3wk	BM, GI, renal
5-Fluorouracil (Roche)	Gastrointestinal and hepatic carcinoma	150–200 mg/m^2 IV q7d	BM, GI, CNS; DO NOT USE IN CATS!
Cytosine Arabinoside (Cytosar-U; Upjohn)	Lymphoproliferative disorders, myeloproliferative disorders	100 mg/m^2 IV or SC for 4 days q3–4wk	BM, GI
Plant Alkaloids			
Vincristine (Oncovin; Eli Lilly)	Lymphoproliferative disorders, sarcomas, carcinomas	0.5–0.7 mg/m^2 IV q7d	GI, vesicant
Vinblastine (Velban; Eli Lilly)	Mast cell tumors	2 mg/m^2 IV q7–14d	GI, BM, vesicant
Antibiotics			
Doxorubicin (Adriamycin; Adria Labs)	Lymphoproliferative disorders, soft tissue sarcoma, carcinomas	20–25 mg/m^2 IV q3wk for dogs ≤l0 kg and cats; 30 mg/m^2 IV q3wk for dogs >10 kg; maximum cumulative dose = 180–240 mg/m^2	BM, GI, cardiac; severe vesicant; urticaria, alopecia
Mitoxantrone (Novantrone; Lederle)	Lymphoproliferative disorders	4–6 mg/m^2 IV q3wk	BM
Hormones			
Prednisone	Lymphoproliferative disorders, mast cell tumors, brain tumors	20–50 mg/m^2 q24–48h	Iatrogenic Cushing's syndrome
Miscellaneous			
l-Asparaginase (Elspar; Merck, Sharp & Dohme)	Lymphoproliferative disorders	10,000 IU/m^2 IM, SC	Anaphylaxis

BM, bone marrow; CNS, central nervous system; GI, gastrointestinal; IM, intramuscularly; IP, intraperitoneally; IV, intravenously; m^2, body surface area in square meters (see Table 26-4); PO, per os; SC, subcutaneously;

Treatment-Related Factors

- Inadequate radiation dose
- Geographic miss (i.e., a portion of the tumor is outside the treatment field)

Chemotherapy

Chemotherapy is most useful for regional and disseminated neoplasms. It is used primarily for palliation; few cures are achieved. Some cancer types are notably chemosensitive. Lymphoid neoplasms and transmissible venereal tumors often are treated effectively; most other nonlymphoid tumors are only moderately sensitive. Chemotherapy is useful, however, for treatment of many tumor types as an adjunct therapy to other treatments or for palliation. Table 26-4 lists the most common neoplastic agents used in veterinary medicine. Indications and major toxicity also are listed. Table 26-5 is a conversion schedule for estimating body surface area for dogs and cats based on body weight. Cytotoxic agents must be used safely to avoid exposure in health care workers. General guidelines for handling cytotoxic agents are given in Table 26-6.

Applications

Most chemotherapeutic agents are administered intravenously or orally. This is convenient and relatively

Table 26-5. CONVERSION FROM BODY WEIGHT (KG) TO BODY SURFACE AREA IN SQUARE METERS (M^2) FOR DOGS*

kg	m^2	kg	m^2
0.5	0.06	29.0	0.94
1.0	0.10	30.0	0.96
2.0	0.15	31.0	0.99
3.0	0.20	32.0	1.01
4.0	0.25	33.0	1.03
5.0	0.29	34.0	1.05
6.0	0.33	35.0	1.07
7.0	0.36	36.0	1.09
8.0	0.40	37.0	1.11
9.0	0.43	38.0	1.13
10.0	0.46	39.0	1.15
11.0	0.49	40.0	1.17
12.0	0.52	41.0	1.19
13.0	0.55	42.0	1.21
14.0	0.58	43.0	1.23
15.0	0.60	44.0	1.25
16.0	0.63	45.0	1.26
17.0	0.66	46.0	1.28
18.0	0.69	47.0	1.30
19.0	0.71	48.0	1.32
20.0	0.74	49.0	1.34
21.0	0.76	50.0	1.36
22.0	0.78	51.0	1.38
23.0	0.81	52.0	1.40
24.0	0.83	53.0	1.41
25.0	0.85	54.0	1.43
26.0	0.88	55.0	1.45
27.0	0.90	56.0	1.47
28.0	0.92	57.0	1.48

*Specific values can be calculated using the following formula:

$$\text{Body surface area } (m^2) = \frac{(k) \times (Wt)^{2/3}}{10^4}$$

where (k) = 10.1 for dogs and 10.0 for cats

Table 26-6. PRACTICAL RECOMMENDATIONS FOR SAFE HANDLING OF CYTOTOXIC ANTINEOPLASTIC AGENTS

1. Designate a specific hospital location for drug handling (reconstitution, preparation, disposal).
2. Use an absorbent, disposable, plastic-backed sheet to cover work surface; change it regularly.
3. Wear latex, non-powdered, non-permeable gloves when handling all cytotoxic agents.
4. Reduce exposed skin surfaces by wearing laboratory coats, gowns, and other protective wear. Wear particulate respiratory filtration masks to prevent inhalation of aerosolized drug particles.
5. Reconstitute all materials carefully and safely, avoiding potential contamination of materials or aerosolization.
6. Clean reconstituted material of any contamination and properly label concentration and date.
7. Dispose of contaminated materials in leak-proof, puncture-resistant containers. Proper disposal by health regulatory officials is necessary.
8. Wash hands thoroughly after removing gloves.

non-invasive. Chemotherapy also is given by intra-arterial or intra-cavitary routes to increase tumor/drug exposure. Drugs can be given before (neoadjuvant) or after surgery (adjuvant); the optimal sequence for most tumors is not yet known.

Advantages of Neoadjuvant Chemotherapy (Preoperative)

- Tumor size is reduced, necessitating less surgery or radiotherapy
- Tumor vasculature is not altered by surgery or radiation, ensuring more uniform delivery of drug
- Drug therapy can be evaluated by monitoring tumor response

Advantages of Adjuvant Chemotherapy (Postoperative)

- Resection of primary mass decreases the tumor burden; chemotherapy is more effective against a smaller tumor burden.
- Recruitment of dormant tumor cells into a more chemosensitive cell cycle phase increases tumor susceptibility to cytotoxic agents.

A preplanned protocol, regardless of sequence, is important for proper management of tumors that are likely to recur after single-modality treatment. Chemotherapy must be used appropriately to maximize treatment results and minimize toxicity.

Principles of Chemotherapy

- Use only drugs with documented activity against the specific tumor type.
- Administer all drugs at maximum tolerated doses and intervals.
- Some protocols are administered in two phases: an initial phase of intensive therapy *(induction),* followed by a period of less frequent drug administration *(maintenance).*
- Combination chemotherapy using agents with different mechanisms of action and no overlap in toxicity results in enhanced cancer cell destruction, reduced induction of drug resistance, and reduced toxicity.
- Continue chemotherapy past the time of complete remission because a microscopic tumor remains after the clinically detectable tumor has resolved.

Sources of Failure

Treatment failures result from excessive chemotherapy-related side effects (e.g., renal, hepatic, or myocardial toxicity or sepsis) or from progressive tumor growth because of intrinsic or acquired drug resistance. Intrinsic resistance results from molecular or biological adaptations or mutations within cancer cells that provide mechanisms for circumventing drug effects. The larger the tumor is, the more likely the existence of resistant

cells. Clinically detectable tumors are likely to have multiple resistant cell lines.

Intrinsic Drug Resistance

Causes of intrinsic resistance include the following:
- Inherent genetic mechanisms of cell protection
- Sanctuary sites (site where cells are protected, such as the CNS)
- Tumor cell dormancy, or insensitivity to specific action of a drug
- Insufficient drug delivery

Acquired Drug Resistance

Acquired resistance arises from selection pressure induced by sublethal drug doses. It occurs when cancer cells survive long enough to do the following:
- Develop alternate metabolic pathways
- Change drug transport mechanisms
- Initiate cellular repair
- Inhibit drug activation

Pleiotropic (Multiple) Drug Resistance

Resistance can develop to a single drug, a group of drugs, or many classes of drugs (pleiotropic resistance). Pleiotropic resistance is associated most commonly with the anthracyclines and vinca alkaloids.

Miscellaneous Therapy

Hyperthermia

Heat is an effective adjunct therapy because it enhances the cytotoxic effect of radiation and many chemotherapy agents. Hyperthermia is induced locally by ultrasound or radio waves or implemented as whole-body hyperthermia induced by a humidified chamber or radiant heat device.

Immunotherapy

Immunotherapy has emerged with renewed potential. Because neoplastic cells may be immunologically different from healthy cells, selective or nonselective induction of the host immune system by various biologic response modifiers (e.g., bacterial agents, interferons, monoclonal antibodies, lymphokines, and tumor vaccines) may enhance elimination of tumor cells. Immunotherapy appears to have the greatest potential as an adjunct to other therapies to eliminate microscopic residual tumor.

Photodynamic Therapy

Many tumor cells selectively accumulate certain systemically administered photoactive chemicals. Tumors then are exposed to light of selected wavelengths (laser light), and the photoactive substances become cytotoxic. Various photoactive drugs and light sources currently are being tested. Early results indicate that photodynamic therapy may be useful for treatment of localized solid tumors and in palliation of tumor-associated signs (esophageal or urethral obstruction, etc.).

Post-Treatment Monitoring

Patient monitoring after therapy is important to assess toxicity, adjust subsequent treatment, and monitor tumor response.

- Reevaluate animals at regular intervals
- Tailor follow-up schedule and appropriate diagnostic tests to each patient and the particular stage and expected behavior of the tumor.
- The goal of follow-up evaluation is to detect tumor recurrence or metastasis at the earliest possible time and to maximize the response to any additional alternate therapies.

ADJUNCT CLINICAL CONSIDERATIONS

Nutritional Management

Many animals with cancer have alterations of metabolism that result in malnutrition. When severe, these alterations result in the clinical syndrome of *cancer cachexia*. Malnutrition impairs the immune system, inhibits wound healing and normal cell repair, and increases treatment morbidity and mortality.

- Factors contributing to malnutrition include the following:
  - Anorexia
  - Decreased nutrient intake
  - Metabolic or digestive abnormalities that cause inefficient or inappropriate use of nutrients
  - Treatment-related factors such as therapy-induced nausea and vomiting
- Proposed mechanisms of cachexia include:
  - Tumor-produced anorexigenic substances
  - Alterations in brain neurotransmitter and anabolic hormone function
- Treatment is directed toward early elimination of the cachexia syndrome (by elimination of neoplasia) and supportive care to minimize its effects during the interim. Nutritional support is provided by enteral or parenteral feeding (see Chapter 3), and should be provided when patients do not eat for more than 5 days or have more than 10% acute loss of body weight. Laboratory parameters indicative of malnutrition include hypoalbuminemia, lymphopenia, and anemia.

Pain Management

Clinical management of pain in cancer patients is an important aspect of care to reduce morbidity and improve the quality of life.

- Pain can be:
  - Acute or chronic
  - Treatment- or tumor-related
  - Visceral, somatic, or neurogenic in origin
- Pain can contribute significantly to development of inappetence, weight loss, reduced mobility, depression, and poor interaction with the owner. Presence of pain is determined by changes, often subtle, in normal behavior patterns (see Chapter 6).
- The severity is determined and a treatment protocol implemented to provide adequate analgesia with minimal sedation and other side effects. Prevention or early treatment of pain is more effective than trying to resolve established significant or chronic pain signs. Therapy is by use of local or regional anesthesia, or with systemic treatment using transdermal delivery of narcotic-based pain medication, or parenterally administered nonsteroidal anti-inflammatory agents, and narcotics (see Chapter 6). Continual reassessment and modification of therapy is necessary.

Euthanasia

When treatment options fail and an animal's disease is progressing, consideration of euthanasia is appropriate. Encourage owners in advance to establish limits for their pet's level of deterioration. When the decision for euthanasia is reached by an owner, it should be supported by the veterinarian. For many owners, euthanasia is the last humane "treatment" they can give to their pet. Review the details of the euthanasia process in advance with owners and options for them to remain present or not. For clients having difficulty coping, provide assistance to help them find bereavement counseling. Condolence cards, telephone calls, or other forms of communication afterward are useful to provide closure. A positive experience with the euthanasia process often leaves clients with a positive feeling about the whole cancer treatment process.

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Chapter 27

Lymphoid Neoplasia

David M. Vail

The lymphoproliferative disorders presented here are characterized by neoplasia involving cells or cell lines of lymphoid origin, including lymphoma, lymphoid leukemia, multiple myeloma, and plasmacytoma. Because of differences in diagnosis, therapy, and prognosis among these conditions, they are discussed here as separate entities.

LYMPHOMA

Lymphoma (lymphosarcoma) is defined as a lymphoid neoplasm primarily affecting lymph nodes or other solid visceral organs such as the liver or spleen. It is the most common of the lymphoproliferative disorders in small animals. Middle-aged to older dogs primarily are affected without sex predilection. Although lymphoma can occur in any purebred or mixed-breed dog, it may be more prevalent in golden retrievers, German shepherds, boxers, poodles, bassets, and Saint Bernards.

No breed predilection exists for cats; however, several reports have observed a 1.5:1 male-to-female ratio. Affected cats that are feline leukemia virus (FeLV) antigenemic tend to be younger (median age 3–5 years) than FeLV-negative cats (median age 7–10 years).

Etiology

Retrovirus

A retroviral etiology for certain forms of lymphoma has been demonstrated in a variety of species, including cats, chickens, and humans. In the cat, evidence exists for direct induction of lymphoma by FeLV and indirect induction by the feline immunodeficiency virus (FIV). Before 1985, most cats with lymphoma (>70%) were FeLV antigenemic. Since then, the general availability of FeLV vaccination and testing has increased and FeLV-positive cats currently make up a minority of lymphoma cases (<25%). This shift is likely due directly to vaccination and to FeLV antigen testing before vaccination, which allowed separation of potentially infective cats from the susceptible population. In either situation, the result is a reduction in the number of FeLV-associated lymphomas. Conclusive evidence of a viral etiology has not been established in the dog.

Genetic

A genetic predisposition for the development of certain forms of lymphoma may exist.

Carcinogenic Agents

Exposure to chemical, physical, and viral carcinogens may play a role in the development of many tumor types. Weak associations with herbicide use and exposure to high tension wires have been reported.

Classification and Clinical Signs

Traditionally, lymphoma is classified based on anatomic site. Clinical signs vary with the sites involved. In cats, the frequency of anatomic forms associated with FeLV antigenemia (i.e., mediastinal and multicentric forms) has declined along with the declining frequency of FeLV-associated lymphomas. Whereas these sites made up the bulk of cases observed in cats before 1985, they are now in the minority. Currently, the alimentary form, which only rarely is associated with FeLV antigenemia, makes up the bulk of lymphomas in cats. Other less common forms occurring in cats include renal, hepatic, and miscellaneous extranodal sites.

World Health Organization (WHO) clinical staging of lymphoma also can be used to classify the extent of the disease (Table 27-1).

Multicentric Lymphoma

This is the most common form in the dog. It usually manifests as increased lymph node size with nonspecific signs such as inappetence, weight loss, polyuria or polydipsia, and lethargy. Hepatic and splenic involvement, manifested as diffuse organ enlargement, also is common in multicentric lymphoma.

Alimentary Lymphoma

This type of lymphoma often is associated with vomiting, diarrhea, and nonspecific signs such as weight loss and lethargy.

Table 27-1. WORLD HEALTH ORGANIZATION CLINICAL STAGING FOR LYMPHOMA*

Stage†	Criteria
I	Involvement limited to single lymph node or lymphoid tissue in a single organ (excluding bone marrow)
II	Involvement of many lymph nodes in regional area (with or without tonsils)
III	Generalized lymph node involvement
IV	Liver and/or spleen involvement (with or without stage III)
V	Manifestations in blood and involvement of bone marrow and/or other organ systems (with or without stages I–IV)

*Reprinted with permission from World Health Organization: Owen LN: *TNM Classification of Tumors in Domestic Animals*. Geneva: WHO, 1980.
†Each stage is subclassified into (a) without systemic signs and (b) with systemic signs.

Mediastinal Lymphoma

This form of lymphoma often causes respiratory signs secondary to pleural effusion, the mass effect of the tumor, or precaval syndrome (i.e., facial and forelimb edema caused by reduced venous and/or lymphatic drainage). Approximately 40% to 50% of mediastinal lymphomas in the dog are associated with hypercalcemia, which can cause polyuria or polydipsia, anorexia, and weakness.

Cutaneous Lymphoma

Cutaneous lymphoma involves single or multiple skin lesions that can vary greatly in appearance. It may mimic other skin disorders such as seborrhea, pemphigus, and pyoderma. The cutaneous lesions can begin as a mild eczematous pruritic plaque and progress to nodular tumors. Approximately half of the reported cases of cutaneous lymphoma are pruritic.

Extranodal Forms

Miscellaneous extranodal forms of lymphoma include lymphoma of the eyes, central nervous system (CNS), bones, heart, kidneys, urinary bladder, and nasal cavity. Their presentations vary with respect to the site of involvement.

Classification by Immunophenotype

Lymphomas also can be classified by immunophenotype, that is, whether they are of B lymphocyte or T lymphocyte origin. Most (70–80%) lymphomas in dogs are composed of B cells. T cell origin lymphoma in dogs is associated more commonly with hypercalcemia and cranial mediastinal involvement. In cats, most FeLV-associated lymphomas are T cell in origin. The breakdown of B versus T cell lymphoma is less clear cut in cats.

Diagnosis

The diagnosis of lymphoma is based on a complete history, physical examination, tissue diagnosis, and clinical staging. Clinical staging should include a complete blood count (CBC), platelet count, bone marrow aspiration or core biopsy, biochemistry profile, and thoracic and abdominal radiographs. Abdominal ultrasound can be added to the workup if indicated based on presentation.

History

The history should include an evaluation of past and present water intake and urination frequency because they may reflect hypercalcemia of malignancy and subsequent renal disease.

Physical Examination

Perform a complete physical examination for all animals with lymphoma.

- Palpate all lymph nodes (including rectal palpation of sublumbar nodes) and abdominal viscera.
- Because bone marrow involvement can result in hematologic abnormalities, closely examine mucous membranes for signs of pallor or petechiae.
- Visceral involvement can lead to organ failure; therefore, look for any physical signs that may be indicative of liver or kidney disease (e.g., icterus and uremic ulcers).
- Ophthalmic abnormalities are present in more than one-third of dogs with lymphoma and include uveitis, hemorrhage, and ocular infiltration. Therefore, optic and fundic examinations should be conducted.

▼ ***Key Point*** Canine lymphoma usually is a disease of middle-aged and older animals; thus, it is essential to perform a complete examination to identify concomitant problems in other systems.

Laboratory Evaluations

Hematologic Abnormalities

- Hematologic abnormalities occur in most dogs and cats with multicentric lymphoma. Common abnormalities, in decreasing frequency, include atypical immature lymphocytes in the circulation, thrombocytopenia, eosinopenia, anemia, and nucleated erythrocytes.
- The anemia is usually that of chronic disease (normocytic, normochromic, and nonregenerative); however, a small percentage of animals have indices compatible with blood loss or hemolysis. FeLV-positive cats are more likely to be anemic than cats that are not infected.
- Bone marrow aspirate or core biopsy may reveal an altered bone marrow myeloid-to-erythroid ratio and bone marrow infiltration with neoplastic lymphocytes.

Biochemical Abnormalities

▼ ***Key Point*** Serum calcium is elevated in 15% to 20% of dogs with lymphoma. The likelihood of hypercalcemia is greatest in dogs with the mediastinal form.

- Paraneoplastic hypercalcemia (i.e., elevated serum calcium) may serve as a marker for response to therapy and, although uncommon, may cause hypercalcemic nephropathy, a potentially irreversible cause of renal failure (see Chapters 32 and 77).
- Elevations in blood urea nitrogen and serum creatinine may result from neoplastic infiltration of the kidneys, hypercalcemic nephrosis, or dehydration.
- Increased serum concentration of liver enzymes or bilirubin may indicate neoplastic infiltration of the liver.
- Abnormally elevated serum globulins may be noted in some B cell lymphomas.

Feline Leukemia Virus Status

Approximately 80% of cats with mediastinal and multicentric lymphoma are FeLV-positive, in contrast to 50% with renal lymphoma, 5% to 10% with alimentary lymphoma, and a minority with cutaneous forms.

Radiography and Ultrasonography

Radiography and ultrasonography (see Chapter 4), although not diagnostic for lymphoma, are often useful for staging or determining the extent of disease.

- Half of all dogs with lymphoma have evidence of enlarged sternal and sublumbar lymph nodes, spleen, and liver.
- Thoracic radiographs are important for identification of thoracic masses that are due to mediastinal lymphoma and are recommended for any dog with hypercalcemia of unknown etiology.
- Abdominal ultrasonography and contrast studies of the upper gastrointestinal (GI) tract are abnormal in most animals with GI lymphoma.

Histopathology and Cytology

Histopathologic and cytologic evaluation of affected tissues is necessary for confirmation of lymphoma.

- Fine-needle aspiration cytology of lymph nodes, visceral organs, and other involved sites can be suggestive of neoplastic disease; however, conclusive histologic diagnosis is often recommended.

▼ ***Key Point*** In the cytologic evaluation of lymph nodes in cats, neoplastic involvement is difficult to distinguish from benign lymphadenopathy syndromes. For this reason, only histopathologic examination is definitive.

- Avoid sampling lymph nodes draining reactive areas of the body (e.g., submandibular lymph nodes in the presence of periodontal disease) because reactive lymphoid hyperplasia can mask (or mimic) the true neoplastic condition.
- In addition to confirming a diagnosis of lymphoma, histologic and cytologic samples can be analyzed by various immunohistochemical and histochemical techniques to determine immunophenotype (B vs. T cell), tumor proliferation rates, and histologic subtype (high-, intermediate-, or low-grade tumors). The availability of such analysis is growing; however, at present only immunophenotype is consistently predictive of prognosis in dogs.

Additional Diagnostic Tests

Additional tests may be necessary to confirm the diagnosis of the extranodal forms of lymphoma.

- Stage the disease by performing a CBC, bone marrow evaluation, and thoracic and abdominal radiography. Staging is important in animals with extranodal lymphoma to ensure that the disease is not a sequela of the more common multicentric forms and to determine whether the disease is localized to a solitary extranodal site.
- Perform exploratory laparotomy and full-thickness biopsy or fine-needle aspiration to diagnose most cases of alimentary lymphoma. Endoscopic biopsies of the mucosa may be too superficial to diagnose GI lymphoma because lymphoma usually originates in the submucosa. In addition, GI lymphoma often is accompanied by lymphocytic/plasmacytic mucosal infiltrations that may be misdiagnosed as a benign condition. However, improved endoscopic sampling techniques may reduce the likelihood of misdiagnosis.
- Cytological evaluation of cerebrospinal fluid (CSF) may be helpful in the diagnosis of CNS lymphoma in the dog, but CSF is rarely abnormal in feline spinal lymphoma because the tumor is usually extradural. Magnetic resonance imaging, computed tomography, and myelography may be helpful.

Differential Diagnosis

The differential diagnosis (DDx) varies with the anatomic form of the disease.

- *DDx for lymphadenopathies* includes infectious diseases (e.g., bacterial, viral, rickettsial, parasitic, and fungal; see Section 2, Infectious Diseases), immune-mediated diseases (e.g., systemic lupus erythematosus; see Chapter 24), and other types of metastatic neoplasia.
- *DDx for alimentary lymphoma* includes lymphocytic/plasmacytic enteritis, other types of intestinal neoplasia, granulomatous and infiltrative bowel disease, and hypereosinophilic syndrome (see Chapter 69).

- *DDx for mediastinal lymphoma* includes ectopic thyroid tumors, heart base tumors, thymoma, and pulmonary lymphomatoid granulomatosis.
- *DDx for cutaneous lymphoma* includes pyoderma, immune-mediated and parasitic skin disorders, and other neoplastic dermatopathies.

Treatment

▼ ***Key Point*** Lymphoma is the most chemoresponsive malignancy encountered in veterinary medicine.

Most dogs and cats with lymphoma have multicentric systemic disease and therefore require systemic chemotherapy to improve quality of life and survival time. Untreated, dogs and cats with malignant lymphoma live an average of only 4 to 6 weeks once a diagnosis has been established. With standard-of-care combination chemotherapy, 75% to 90% of dogs and 60% to 70% of cats go into remission and survive a median of 7 (cats) to 12 (dogs) months with an excellent quality of life. With most combination protocols, approximately 25% of patients survive 2 years or more. Cures are still uncommon. Cost is within the financial reach of many clients, especially with the availability of generic brands of cytotoxic drugs.

Many combination chemotherapy protocols have an "induction" period designed to place a dog or cat into a remission, followed by a less intensive "maintenance" treatment period intended to sustain a remission. Current data suggest that intensive "up front" therapy to induce a sound remission is as effective as less intense protocols with continuously administered maintenance therapy for most cats and dogs (see below).

Complete remission is more difficult to achieve in cats; however, if a remission can be achieved and maintained for approximately 6 months, cats are more likely to experience prolonged survivals compared with dogs. Cats are generally more resistant to the adverse effects of chemotherapy than dogs. The exception to this rule is cats who receive doxorubicin as part of their protocol. Most dogs tolerate doxorubicin every 21 days at a dosage of 30 mg/m^2; however, cats appear to be more sensitive to the drug and therefore are treated at a dosage of 25 mg/m^2 (or 1 mg/kg) given every 21 days. Cats with preexisting azotemia should not receive doxorubicin.

Criteria for Choosing Chemotherapy

When choosing a chemotherapy protocol, several points must be discussed with the companion animal owner.

- *Cost:* Many chemotherapeutic agents are generally affordable. The additional costs of blood work, office visits, and catheters and the potential cost of treating toxicity also must be considered. Combination chemotherapy protocols, although often more effective, are also more expensive.
- *Time:* Time commitments can be more important to some clients than the cost of the therapy. In general, the more elaborate the protocol, the more time invested in the care of the patient.
- *Efficacy:* As a general rule, the more complex the protocol, the longer the duration of remission and of survival time. Conversely, single-agent chemotherapy is generally less effective than combination chemotherapy.
- *Toxicity:* The toxicity of most protocols is designed to be acceptable to the general public; however, the potential risks and benefits of each protocol must be discussed with each owner. Complex protocols increase the potential for toxicity and increase the importance of client education.
- *Experience of the attending clinician:* The successful application of any chemotherapy treatment requires experience and confidence because the effective dosage is very near the toxic dosage.

Induction Chemotherapy Protocols

Several chemotherapy protocols for dogs and cats have been reflecting that cures are still uncommon, and several investigators are continually attempting to improve on previous outcomes. Listing dosage and timing of all available protocols is beyond the scope of this chapter; therefore, I have chosen to elaborate on three protocols of varying cost, time commitment, and effectiveness: the University of Wisconsin-Madison CHOP-based combination protocol, the single-agent doxorubicin protocol, and single-agent prednisone therapy.

Dosages of chemotherapeutic agents are based on body surface area expressed in square meters (m^2). Refer to Chapter 26, Table 26-5, for conversion of body weight to body surface area.

University of Wisconsin-Madison Short Protocol

Most combination protocols are variations on the so-called CHOP-based protocols (C = cyclophosphamide; H = hydroxydaunorubicin [doxorubicin]; O = oncovin^R [vincristine]; P = prednisone). The University of Wisconsin-Madison protocol is one such protocol (Table 27-2). This protocol is complex but gratifying because the majority of dogs and cats achieve remissions and survive for medians of 12 and 7 months, respectively. This is a no-maintenance protocol, and dogs and cats are off all medication after 19 weeks. Notice the absence of L-asparaginase from this protocol, a drug often included in earlier versions. Several studies have shown that the addition of L-asparaginase does not increase the length of remissions and survivals; I reserve the use of this drug for "rescue" situations (see below).

Table 27-2. UNIVERSITY OF WISCONSIN-MADISON LYMPHOMA PROTOCOL

A: Combination Chemotherapy Protocol for Dogs with Lymphoma

Treatment Week	Drug, Dosage, and Route	Treatment Week	Drug, Dosage, and Route*
1	Vincristine, 0.5–0.7 mg/m^2, IV		
	Prednisone, 2.0 mg/kg, PO	11	Vincristine, 0.5–0.7 mg/m^2, IV
2	Cyclophosphamide,† 250 mg/m^2, IV		
	Prednisone, 1.5 mg/kg, PO	12	Cyclophosphamide, 250 mg/m^2, IV
3	Vincristine, 0.5–0.7 mg/m^2, IV		
	Prednisone, 1.0 mg/kg, PO	13	Vincristine, 0.5–0.7 mg/m^2, IV
4	Doxorubicin, 30 mg/m^2, IV		
	Prednisone, 0.5 mg/kg, PO	14	Doxorubicin, 30 mg/m^2, IV
6	Vincristine, 0.5–0.7 mg/m^2, IV	16	Vincristine, 0.5–0.7 mg/m^2, IV
7	Cyclophosphamide, 250 mg/m^2, IV	17	Cyclophosphamide, 250 mg/m^2, IV
8	Vincristine, 0.5–0.7 mg/m^2, IV	18	Vincristine, 0.5–0.7 mg/m^2, IV
9	Doxorubicin, 30 mg/m^2, IV	19‡	Doxorubicin, 30 mg/m^2, IV

B: University of Wisconsin Chemotherapy Protocol for Cats with Lymphoma

Treatment Week	Drug, Dosage, and Route	Treatment Week	Drug, Dosage, and Route
1	Vincristine, 0.5–0.7 mg/m^2, IV		
	Prednisone, 2.0 mg/kg, PO	11	Vincristine, 0.5–0.7 mg/m^2, IV
2	Cyclophosphamide, 200 mg/m^2, IV		
	Prednisone, 2.0 mg/kg, PO	13§	Cyclophosphamide, 200 mg/m^2, IV
3	Vincristine, 0.5–0.7 mg/m^2, IV		
	Prednisone, 1.0 mg/kg, PO	15	Vincristine, 0.5–0.7 mg/m^2, IV
4	Doxorubicin, 25 mg/m^2, IV		
	Prednisone, 1.0 mg/kg, PO¶	17	Doxorubicin, 25 mg/m^2, IV
6	Vincristine, 0.5–0.7 mg/m^2, IV	19	Vincristine, 0.5–0.7 mg/m^2, IV
7‡	Cyclophosphamide, 200 mg/m^2, IV	21§	Cyclophosphamide, 200 mg/m^2, IV
8	Vincristine, 0.5–0.7 mg/m^2, IV	23	Vincristine, 0.5–0.7 mg/m^2, IV
9	Doxorubicin, 25 mg/m^2, IV	25‖	Doxorubicin, 25 mg/m^2, IV

*Refer to Chapter 26, Table 26-5, for conversion of body weight to body surface area.
†Cyclophosphamide is always delivered concurrently with 1 mg/kg of furosemide, IV, to decrease the incidence of sterile hemorrhagic cystitis.
‡If in complete remission at week 19, therapy is discontinued and monthly reevaluations are instituted.
§If renal lymphoma or CNS lymphoma is present, substitute cytosine arabinoside at 600 mg/m^2 divided SC bid over 2 days at these treatments.
¶Prednisone is continued (1 mg/kg, PO) every other day from this point on.
‖If in complete remission at week 25, therapy is discontinued and cat is rechecked monthly for recurrence.

Single-Agent Doxorubicin

Doxorubicin is one of the most effective single-agent treatments for lymphoma in dogs. Of the dogs treated with doxorubicin (30 mg/m^2 IV q21d for five to six total treatments), approximately 70% achieve a complete or partial remission. The duration of remission varies depending on the published report but is approximately 6 to 9 months.

Prednisone Only

When more aggressive or expensive chemotherapy is declined by clients, an inexpensive, although only transiently effective, alternative is prednisone alone. With prednisone therapy, the average dog or cat lives 2 months. One-third of dogs and cats treated with prednisone achieve a complete remission, one-third go into partial remission, and one-third do not respond at all. Similar responses are seen in cats. Dogs and cats that receive high-dose prednisone for a significant period before traditional chemotherapy is initiated may develop resistance to the cytotoxic effects of other chemotherapy agents.

Chemotherapy in the Presence of Cytopenia

Drug therapy for multicentric lymphoma may have to be altered in the presence of thrombocytopenia (<75,000/µl) and neutropenia (<1500/µl). Chemotherapeutic regimens that tend to spare bone marrow and are usually safe in the presence of low white blood cell (WBC) and platelet counts include prednisone, L-asparaginase, and vincristine. If myelosuppression is attributed to chemotherapy, discontinue treatment for 5 to 7 days and repeat the CBC and the platelet count. When the platelet and WBC counts have rebounded, reinstitute therapy at a decreased dose or frequency. However, if the neutropenia, the thrombocytopenia, or both are secondary to myelophthisis (i.e., tumor infiltration into bone marrow) aggressive chemotherapy is required despite the cytopenia to allow normalization of marrow cellular constituents.

Reinduction and Rescue Therapy

Reinduction therapy is defined as therapy instituted when a patient has recrudescence of lymphoma following discontinuation of chemotherapy that had resulted in a successful remission. In those cases, cycle the patient back through the same induction protocol as was used initially. The length of remission following reinduction is generally half that of the initial induction; however, several cases have been known to have equally or more durable second remissions.

Rescue therapy is defined as therapy instituted when either induction or reinduction fails to achieve a remission and other drugs not previously used are initiated. Several rescue protocols have been published and include non-CHOP drugs, including mitoxantrone, L-asparaginase, lomustine (CCNU), and actinomycin D. In general, remissions can be achieved with rescue; however, they are rarely durable and last approximately 1 to 2 months.

Future goals for the treatment of lymphoma in companion animals include increasing the remission time while decreasing cost, toxicity, and time involved to treat the patient. The future role of biologic-based therapies, including signal transduction modification, immunotherapeutics, and staged adjuvant radiotherapy, is under investigation. The question of whether cats benefit from long-term maintenance therapy has yet to be answered.

Small Cell Variant Lymphoma

This less common form of lymphoma is a "low-grade" variant. In represents a moderately common form of GI or hepatic lymphoma in cats and a rare multicentric form in dogs. It tends to be less chemoresponsive than intermediate or high-grade lymphoma; however, it has a more protacted course and patients can survive a long time with their disease. In my practice, small cell lymphoma is initially treated with continuous chlorambucil (20 mg/m^2, by mouth [PO], q14 days) and prednisone therapy.

Extranodal Lymphoma Therapy

Therapy unique to extranodal lymphoma depends on the site of involvement and the extent of disease. Extranodal lymphoma that is determined, after thorough staging, to be a local disease can be treated locally (e.g., excisional surgery or radiotherapy) without the necessity for systemic chemotherapy. Follow diligent reevaluation schedules to identify recurrence or systemic spread of disease. Initiate systemic chemotherapy once systemic involvement has been documented.

Therapy for CNS lymphoma depends on location, the capacity of drugs to cross the blood-brain barrier, and the presence of disease outside the CNS. Surgical intervention can be used for diagnosis or removal of accessible CNS tumors, but usually this is not feasible or practical. More commonly, surgery is combined with adjuvant chemotherapy or radiotherapy. Of the chemotherapeutic agents commonly used in veterinary medicine, only prednisone and cytosine arabinoside consistently cross the blood-brain barrier in therapeutic concentrations. Radiotherapy also has been used successfully for the treatment of CNS lymphoma.

Cutaneous Lymphoma Therapy

Cutaneous lymphoma, if solitary and confined, can be treated with local radiotherapy or surgery; however, the likelihood of ultimate systemic spread is high. Generalized, cutaneous lymphoma tends to be less responsive to chemotherapy than multicentric lymphoma, and clinical signs can wax and wane considerably over time. CCNU (lomustine), cis-retinoic acid therapy, and L-asparaginase have all proven effective in approximately 40% to 60% of dogs with cutaneous lymphoma, although long-term survival is uncommon.

Therapy for Hypercalcemia

Treatment of hypercalcemia secondary to lymphoma is accomplished best by attaining tumor remission. If necessary, diuresis with high sodium crystalloids (0.9% NaCl) delivered at twice the maintenance rate (see Chapter 32) is often sufficient along with initiation of chemotherapy. If hypercalcemia is severe, calcitonin therapy can be initiated. The addition of prednisone also decreases serum calcium levels; initiate only after a histologic or cytologic diagnosis.

Prognosis

Prognostic Indicators for Dogs with Lymphoma

- WHO clinical stage V (see Table 27-1) is associated with shorter survival times, especially when the bone marrow involvement results in significant cytopenias.
- WHO substage b (i.e., presenting ill, with significant clinical signs) is strongly predictive of shorter remission and survival times.
- The presence of a T cell origin lymphoma is strongly predictive of shorter remission and survival times.
- In some reports, female dogs have significantly longer remission and survival times than males.
- Hypercalcemia and mediastinal involvement have been reported to worsen prognosis; however, this has been shown to be due to their T cell association rather than a direct effect.
- Anatomic site of involvement can have prognostic significance. Alimentary, disseminated cutaneous, and leukemic forms have a poorer prognosis than multicentric forms.

Prognostic Indicators for Cats with Lymphoma

- A higher clinical stage is associated with lower remission rates and survival times (approximately 90%

complete remission rate in stage I versus 50% in stage III or higher)
- FeLV status is strongly predictive of remission and survival times. FeLV-antigenemic cats and the anatomic forms of lymphoma associated with them (mediastinal, multicentric) have a poorer prognosis than FeLV-negative cats (most often alimentary form).
- Leukemia, anemia, neutropenia, and sepsis negatively affect response to therapy and survival times.
- Response to therapy is strongly predictive of outcome. Cats that achieve a complete remission early in their treatment often go on to have a prolonged and durable remission. This indicator cannot be assessed before therapy, however, and therefore is not clinically useful at initial diagnosis.

LYMPHOID LEUKEMIA

Leukemia is defined as the proliferation of neoplastic cells in the bone marrow; such cells may or may not be circulating in the peripheral blood. There are two major categories of lymphoid leukemia: acute lymphoblastic leukemia and chronic lymphocytic leukemia. Both forms are relatively rare in dogs; however, they may constitute up to one-third of feline lymphoid neoplasms.

Acute Lymphoblastic Leukemia

Acute lymphoblastic leukemia (ALL) is defined as an abnormal proliferation of morphologically immature lymphoblasts in the bone marrow or peripheral blood. This form of leukemia is rapidly progressive and responds poorly to therapy.

Epidemiology and Clinical Signs

- No sex, breed, or weight predilection exists. Most affected dogs are of late middle age; the mean age in cats with ALL tends to be younger, owing to an association with FeLV.
- Clinical signs can include fever, generalized or abdominal pain, anorexia, splenomegaly, and pale mucous membranes.
- Anemia occurs in nearly half of ALL patients, and one-fourth are thrombocytopenic.
- Most cats with ALL are FeLV-positive.

Diagnosis

- Diagnosis depends on documentation of abnormal lymphocytes in the bone marrow or peripheral blood.
- The presence of 30% or more abnormal cells in the bone marrow is diagnostic.
- Most patients have absolute leukocytosis with circulating abnormal lymphocytes; 10% are classified as having aleukemic leukemia (bone marrow involvement without peripheral blood involvement).
- In some forms, the neoplastic lymphoid cells are very undifferentiated, making special histochemical stains necessary to differentiate them from other forms of leukemia and myeloproliferative conditions.
- ALL may be clinically differentiated from late stages of lymphoma by the following:
  - More acute progression of ALL
  - Less likelihood of lymphadenopathy (<50%)
  - Poor response to therapy
  - Shorter survival times

Treatment and Prognosis

- Most published reports utilize CHOP-based protocols (see earlier discussion in this chapter). Strict attention to treatment of secondary infection and symptomatic care are mandatory.
- A poor prognosis resulting from a meager short-lived response to therapy generally is the rule. Exceptions do exist.

Chronic Lymphocytic Leukemia

Chronic lymphocytic leukemia (CLL) is defined as an abnormal proliferation of morphologically mature lymphocytes in the bone marrow or peripheral blood. It occurs primarily in older dogs and cats.

Clinical Signs

- Presenting complaints for the most part are nonspecific and include lethargy, inappetence, polyuria or polydipsia, bleeding diathesis, intermittent lameness, and episodes of collapse.
- Two-thirds of dogs have lymphadenopathy and splenomegaly; pale mucous membranes and fever are common.

Hematologic Abnormalities

- Most animals are anemic (normocytic, normochromic, and nonregenerative), and approximately half are thrombocytopenic.
- One-third of dogs are hyperproteinemic, and half have monoclonal gammopathies on serum electrophoresis, often with Bence Jones proteins in the urine, indicative of a B cell origin; however, recent evidence suggests the majority of CLL in dogs is of T cell origin.
- All reported cases in cats are FeLV-negative.

Treatment and Prognosis

- Therapy for CLL is recommended only if the patient is symptomatic, if significant cytopenias exist (e.g., anemia, thrombocytopenia, and neutropenia), or if splenomegaly or lymphadenopathy is present.
- Prednisone and chlorambucil are the drugs most commonly used, and nearly 75% of animals respond, with median survivals of nearly 1 year.

- Chlorambucil (Leukeran), 20 mg/m^2 PO given every 1 to 2 weeks or 6 mg/m^2 daily, has provided excellent results.
- The prognosis for CLL is much better than that for ALL. Most dogs respond well to therapy, and quality of life is good.

PLASMA CELL NEOPLASMS

There are three primary clinical forms of plasma cell neoplasms: multiple myeloma (MM), solitary plasmacytoma of bone, and extramedullary plasmacytoma. MM is the most common form; the other two occur rarely. Plasma cell neoplasms are rare in cats.

Multiple Myeloma

Epidemiology and Clinical Signs

- MM occurs primarily in aged dogs and has no sex predilection.
- Clinical signs include nonspecific anorexia, listlessness, and polyuria or polydipsia.
- Most dogs present with lameness secondary to paresis or bone pain.
- Bleeding diathesis (epistaxis or gingival bleeding) secondary to hyperviscosity syndrome or thrombocytopenia develops in approximately 50% of affected dogs.

Hematologic Abnormalities

- Three-fourths of animals with MM have associated monoclonal gammopathy, either the immunoglobulin G or immunoglobulin A subtype. A rare immunoglobulin M-secreting primary macroglobulinemia (Waldenström's disease) also exists.
- Light-chain (Bence Jones) proteins may be detectable in the urine. These proteins cannot be detected by routine urine dipstick analysis and require phoretic technique to be identified.
- Dogs with MM often have nonregenerative, normocytic, or normochromic anemia. Approximately 30% are thrombocytopenic, and 10% have circulating abnormal plasmacytes.
- Approximately 15% to 20% of MM patients are hypercalcemic secondary to bone resorption caused by osteoclast-activating factors or other substances released by the tumor.

Diagnosis

Diagnosis involves identification of the following triad of abnormalities:

- Bone marrow plasmacytosis (>20–30% plasma cells).
- Radiographic evidence of osteolytic bone lesions, often observed in dorsal spinous vertebral processes. Approximately 50% of dogs with MM have radiographic evidence of bone lesions, whereas skeletal lesions are rare in cats with MM.
- Serum or urine myeloma proteins, as revealed by immunoelectrophoresis.

Histological confirmation may be necessary for those cases that do not meet all three criteria.

Differential Diagnosis

- DDx for monoclonal gammopathy includes ehrlichiosis (see Chapter 17) and benign hypergammaglobulinemia syndrome, which has been described in the dog.
- DDx for plasmacytosis includes carcinomas, connective tissue disorders, liver disease, hypersensitivity states, and infections, especially ehrlichiosis (see Chapter 17).

Treatment and Prognosis

- The short-term prognosis for MM in dogs is normally good, and long-term remissions are the rule. In cats, the prognosis is poor, and durable remissions after therapy are the exception.
- Extensive bone lesions, light-chain proteinuria, hypercalcemia, and anemia have been reported to be negative prognostic indicators.
- Combination chemotherapy using melphalan (Alkeran, Burroughs Wellcome) (0.1 mg/kg daily for 10 days, then 0.5 mg/kg daily) and prednisone (0.5 mg/kg q24h for 10 days, then every other day) has resulted in published remission rates of 90% and median survival times of 540 days in dogs.
- Serum protein levels should normalize within 2 to 3 months.
- Fractures accompanying MM can be treated by surgical reduction in combination with chemotherapy or radiotherapy. Healing normally accompanies remission of the MM; however, it may take many months and may not be complete.
- Rescue therapy is not well documented once remission is lost. Doxorubicin, vincristine, and dexamethasone combinations appear to work well in humans and may be beneficial in dogs.

Solitary Plasmacytoma of Bone

Solitary plasmacytoma of bone is rare. It usually is not accompanied by a secretory protein but tends to progress to systemic MM. Localized lesions can be treated with surgery or radiotherapy; however, careful clinical staging and a strict reevaluation schedule should be established because of the propensity for the development of systemic disease. Melphalan and prednisone are initiated once systemic involvement is documented.

Extramedullary Plasmacytoma

Two general categories of extramedullary plasmacytoma (EMP) exist, each with a very different biological behavior.

- Solitary cutaneous and oral EMP is generally a benign condition in dogs that is curable with complete surgical excision or local radiotherapy.
- Conversely, GI EMP in the dog tends to behave in a malignant fashion. It rarely is associated with monoclonal gammopathies. Thorough staging (e.g., bone marrow) is necessary to ensure that the disease is localized initially. If that is the case, local excision can be attempted. The likelihood of eventual systemic spread is high, and once documented, combination chemotherapy is initiated.

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Chapter 28

Soft Tissue Sarcomas and Mast Cell Tumors

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SOFT TISSUE SARCOMAS

Soft tissue sarcomas are tumors that arise from mesodermal tissue. They make up 14% to 17% of all malignancies in the dog and approximately 7% to 9% in the cat. These tumors are non-epithelial and extraskeletal and may arise from fibrous tissue, adipose tissue, muscle, synovial tissue, and from blood and lymph vessels. Schwannomas, nerve sheath tumors, or neurofibrosarcomas arise from primitive ectodermal tissues but are included in the soft tissue sarcoma category because of similarities in location, clinical presentation, and clinical behavior. Soft tissue sarcomas are classified histologically according to the specific tissue of origin. However, some tumors are so undifferentiated that this classification is difficult. These tumors are appropriately named undifferentiated sarcomas.

Etiology

The etiology of most soft tissue sarcomas remains unknown. Several causes and predisposing factors have been suggested. These include genetic predisposition, viral agents, chemical carcinogens, ionizing radiation, foreign body implantation, trauma, parasites, and injections of vaccines or medication.

Genetic Predisposition

This is suspected to play a role in tumor development because certain breeds of dogs have a higher incidence of sarcomas. These breeds include boxers, German shepherds, Great Danes, Saint Bernards, golden retrievers, basset hounds, and flat-coated retrievers.

Viral Agents

Viruses have been implicated as causes of sarcoma development in rodents, poultry, non-human primates, and cats. Feline sarcoma viruses (FeSVs) are replication-defective variants of the feline leukemia virus (FeLV). These retroviruses together induce formation of multicentric fibrosarcomas in young cats (see Chapter 8). In contrast, solitary fibrosarcomas found in older cats usually are not associated with FeSV.

Chemical Carcinogens

Chemical carcinogens and environmental contaminants have been shown to induce sarcomas in rodents and humans. Although this has not been documented in dogs and cats, it likely occurs.

Ionizing Radiation

X-rays, gamma rays, and particulate radiation have been shown to cause sarcoma development. In dogs, sarcomas have been reported to occur at treatment sites after orthovoltage radiotherapy of acanthomatous epulides.

Chronic Tissue Inflammation

- Sarcomas have developed at sites of chronic tissue inflammation. Implants, particularly metallic orthopedic implants, are known to cause sarcoma development at the implant site. It is believed that this is the result of a foreign body reaction in the tissues rather than a direct carcinogenic effect of the implant. Most of these tumors are osteosarcomas, although fibrosarcomas and undifferentiated sarcomas have been reported.
- Both single and chronic traumatic episodes have been associated with intraocular sarcomas in the cat.
- Chronic inflammation caused by the parasite *Spirocerca lupi* has resulted in sarcoma development in the esophagus of infected dogs.
- Recently, certain soft tissue sarcomas in cats have been associated with the administration of vaccinations and medication (lufenuron). The exact incidence is unknown but may be greater than 1 in 10,000 vaccinated cats. The mechanism behind injection-associated sarcoma development is under investigation but may involve chronic inflammation

induced by the injection combined with predisposing host factors.

Biologic Behavior

In general, soft tissue sarcomas are locally invasive and infiltrative along fascial planes, resulting in poorly defined tumor margins. The metastatic rate varies according to tumor grade, with low-grade tumors often slow to metastasize. Metastasis is usually via hematogenous spread to the lungs and liver. Regional lymph node metastasis is uncommon. A brief description of various soft tissue sarcomas follows.

Liposarcoma

Malignant tumor of adipocytes

- Rare in dogs and cats
- Invasive and aggressive
- Location may be a prognostic indicator (appendicular and visceral locations worse)
- Metastasis is uncommon except with the visceral location
- "Infiltrative lipomas," believed by some to be well-differentiated liposarcomas, frequently occur on the extremities

Hemangiopericytoma

Tumor of pericytes, spindle-shaped, contractive cells that surround precapillary arterioles

- Common in dogs (German shepherds at risk)
- Slow growing
- Encapsulated appearance but quite infiltrative, and recurrence after excision is common
- Frequently occurs on extremities
- Metastasis is rare

Fibrosarcoma

Tumor of fibrocytes

- Common in dogs and cats
- Locally invasive and slow growing
- Metastasis is uncommon except in injection-site sarcomas (20% to 30%)

▼ ***Key Point*** Multicentric fibrosarcomas of young cats (less than 5 years) may be caused by FeSV. These cats are always FeLV-positive.

Hemangiosarcoma

Tumor of blood vessel endothelium

- Common in dogs (German shepherds at risk); rare in cats
- Very invasive and rapid growing
- Spleen, heart, and skin are common primary sites
- Metastasis is common

Schwannoma, Neurofibrosarcoma, or Peripheral Nerve Sheath Tumor

Tumor of the nerve sheath or Schwann cell

- Invasive and slow growing
- May occur anywhere but frequently occurs in the brachial or lumbosacral plexuses
- Progressive lameness is possible
- Metastasis is rare with grade 1 and 2 tumors

Myxosarcoma

Fibrosarcoma-like tumor with a mucinous matrix

- Rare in dogs and cats
- Infiltrative; no site predilection
- Metastasis is uncommon

Rhabdomyosarcoma

Tumor of striated muscle

- Uncommon in dogs and cats
- Infiltrative
- Heart, bladder, and appendicular muscles are possible sites
- Metastasis is possible
- Botryoid rhabdomyosarcomas (grape-like appearance) is found in bladders of young, large-breed dogs

Leiomyosarcoma

Tumor of smooth muscle

- Rare in dogs and cats
- Solitary, infiltrative, and slow growing
- Spleen, liver, gastrointestinal, and genitourinary tracts are the most common sites
- Metastasis is possible (common with primary liver site)
- Gastrointestinal (GI) obstructive signs or perforation are possible with gastrointestinal sites

Synovial Cell Sarcoma

Tumor of periarticular mesenchymal tissue, not the synovial membrane

- Uncommon in dogs; few reports in cats
- Large-breed dogs are at risk
- Aggressive tumor
- Bones on both sides of major joints may be involved
- Metastasis is possible (22% at time of diagnosis)

Lymphangiosarcoma

Tumor of lymphatic endothelial vessels

- Rare in dogs and cats
- May be invasive
- Metastasis is rare
- Draining tracts on skin or edema are possible presenting signs

Malignant Fibrous Histiocytoma

Tumor containing a mixture of fibroblast-like cells and histiocyte-like cells

- Uncommon in dogs and cats
- Invasive (may cause bone lysis)
- Usually found in subcutaneous tissue
- Metastasis is uncommon

Feline Injection-Site Sarcomas

Most are fibrosarcomas, but the category also includes rhabdomyosarcomas, leiomyosarcomas, chondrosarcomas, osteosarcomas, malignant fibrous histiocytomas, and undifferentiated sarcomas

- The number of giant cells in the histopathology sample may correlate with the grade (higher number of cells = higher grade)
- Aggressive, highly invasive tumors
- Cervical or interscapular area and hind limbs are the most common sites
- Metastasis is possible (20–30% of cases)

Clinical Signs

Clinical signs depend on the location, size, and degree of invasiveness of the tumor as well as on the presence and degree of metastatic disease.

- Soft tissue sarcomas are more common in older animals (mean age 9 years).
- Because of the widespread distribution of mesodermal tissues in the body, soft tissue sarcomas may occur in almost any anatomic location, including the abdomen.
- Tumors may become quite large before any clinical signs are apparent. They often are noticed first by the owner, either by observation or by handling the animal.
- Certain types of sarcoma may invade bone, causing lameness, or may obstruct lymphatics, causing edema.
- GI leiomyosarcomas may cause signs of GI obstruction (vomiting) or melena.
- Smooth muscle sarcomas of the bladder may cause hematuria, pollakiuria, or dysuria.
- Hemangiosarcomas may cause a variety of clinical signs, including collapse due to tumor rupture and hemorrhage.
- Injection-site sarcomas arise in injections sites.

Diagnosis

The goals of diagnosis are to identify the histologic type and grade of the primary tumor, to delineate the extent of the tumor, and to determine whether metastatic disease is present. Although history, physical examination, laboratory evaluation, and diagnostic imaging provide valuable information, the only way to obtain a definitive diagnosis is through biopsy and histopathologic evaluation of the tumor. Histologic grade is useful in predicting tumor behavior and prognosis for dogs with soft tissue sarcomas.

History

The history helps determine how long the mass has been present and the rate of growth. Also important is information regarding exposure to carcinogens, recent vaccination, and past traumatic incidents. Concurrent systemic disorders may be present if metastatic disease or paraneoplastic syndromes have developed.

Physical Examination

Perform a thorough examination to determine the number of masses and their physical characteristics.

- In general, benign neoplasms are well delineated, slow growing, and freely moveable. They seldom are ulcerated or inflamed.
- Malignant tumors are often rapid-growing, fixed masses with ill-defined borders. However, some low-grade sarcomas are slow growing and appear well demarcated. The appearance of these masses can be misleading and should not preclude biopsy.
- Search for evidence of metastasis. Palpate the regional lymph nodes for size and mobility. Look for hepatomegaly, splenomegaly, and increased respiratory sounds or dyspnea as signs of systemic involvement.

Clinical Pathology

Evaluate a complete blood count (CBC), platelet count, serum biochemical profile, and urinalysis in animals with soft tissue sarcomas. Although results are often unremarkable, in some cases these may suggest the presence of metastatic disease, paraneoplastic syndromes, or other concurrent disease. The values obtained also provide a baseline for future therapy. Abnormalities may include the following:

- Anemia of chronic inflammatory disease
- Leukocytosis
- Thrombocytopenia (may be associated with disseminated intravascular coagulation)
- Hypoglycemia
- Increased serum concentrations of alanine transferase (ALT), alkaline phosphatase (ALP), and gamma-glutamyl transpeptidase (GGT)

Diagnostic Imaging

Radiography

- Radiograph the mass to aid in determining the extent of the sarcoma and assess for underlying bone invasion.
- Radiograph the thorax and abdomen to help identify metastatic disease.
- Dystrophic calcification caused by some anaplastic sarcomas may be seen on radiographs.

Ultrasonography

- Use this technique to help determine the character, consistency, and extent of the primary mass.
- Ultrasound procedures are especially useful in the examination of abdominal masses and to examine the internal organs for intra-abdominal metastasis.

Computed Tomography

- This modality, when available, is particularly useful for determining the precise localization and extent of a mass. It is also an ideal test to detect the presence of lung metastasis.

Biopsy

Biopsy is essential to obtain a definitive diagnosis and grade of the tumor.

- Plan carefully to ensure that a representative sample of the mass is obtained.
- Submit all biopsies for histopathologic evaluation.
- Immunohistochemical stains may be necessary to determine the cell of origin.

Several methods for biopsy are available.

Fine-Needle Aspiration Biopsy

- For fine-needle aspiration (FNA), use a 22- or 25-gauge needle and a 6- or 12-ml syringe.
- Because soft tissue sarcomas do not exfoliate well, FNA is limited in value.
- FNA, however, is useful for the diagnosis of lipomas, lymphoma, and inflammatory masses that may appear similar to soft tissue sarcomas.

Needle Punch Biopsy

- For needle punch biopsy (NPB), use a Franklin-modified Vim-Silverman needle (V. Mueller Co., Chicago) or Tru-Cut biopsy needle (Travenol Laboratories, Deerfield, IL).
- NPB is useful for externally palpable masses. A larger sample of tissue can be obtained than with FNA. NPB usually can be performed using local anesthesia with or without sedation.

Incisional Biopsy

- Incisional biopsies yield an even larger sample than NPB samples.
- Plan the biopsy site so that it can be excised later when definitive resection is done.
- Include some normal tissue in the sample when possible.

Excisional Biopsy

- Excisional biopsies are indicated when knowledge of the histologic type of the tumor does not change the treatment and/or total excision is no more invasive than other types of biopsy.

Clinical Staging

Stage all patients with soft tissue sarcomas. Clinical staging is based on the classification system developed by the World Health Organization (WHO) (Table 28-1). In general, the higher the stage, the more guarded the prognosis. Recommended staging tests include CBC, biochemical profile, urinalysis, thoracic radiographs, abdominal radiographs or ultrasound (preferable), and imaging (radiographs, ultrasound, and computed tomography scan) of the primary mass.

Treatment

The goal of treatment is to remove the primary tumor in its entirety, when possible, and to treat microscopic disease and metastasis. In the case of benign and some

Table 28-1. WORLD HEALTH ORGANIZATION CLINICAL STAGING SYSTEM FOR CANINE SOFT TISSUE SARCOMAS

T = Primary Tumor	N = Regional Lymph Node	M = Distant Metastasis
T_0—No evidence	N_0—No evidence	M_0—No evidence
T_1—Tumor < 2 cm	N_1—Movable ipsilateral	M_1—Metastasis present
T_2—Tumor > 2 and <5 cm; minimal invasion	N_2—Movable contralateral	
	N_3—Fixed	
T_3—Tumor > 5 cm	a—Metastasis absent	
T_4—Invasive	b—Metastasis present	
	Stage	
I	$T_1N_0M_0$, $T_2N_0M_0$	
II	$T_1N_1M_0$, $T_2N_1M_0$	
III	$T_1N_{2,3}M_0$, $T_2N_{2,3}M_0$, $T_3N_{0-3}M_0$, $T_4N_{0-3}M_0$, any N_b	
IV	any M_1	

From Owen LN: Classification of tumours in domestic animals. Geneva, Switzerland: World Health Organization, 1980.

malignant tumors, surgical resection can be curative. In animals with non-resectable malignant tumors, attempt to prolong survival time and provide good quality of life.

Surgery

Surgical excision remains the mainstay of therapy for soft tissue sarcomas (see Chapter 26 for principles of oncologic surgery). However, many of these tumors recur because of inadequate resection. A well-planned, aggressive initial surgery has the greatest likelihood of success.

▼ ***Key Point*** Excise soft tissue sarcomas with 3-cm margins in all planes. Remove one fascial plane deep to the tumor if 3-cm margins are not possible.

- Remove overlying subcutaneous tissues and skin as well as underlying tissues to which the mass is fixed. In some cases, limb amputation is indicated.
- Include all previous biopsy sites in the excision.
- Remove the tumor intact to prevent seeding of normal tissues with malignant cells.
- Have the specimen margins histologically evaluated for completeness of excision and grade.
- Do not remove regional lymph nodes unless they are involved.

Radiation Therapy

Soft tissue sarcomas are variably responsive to radiation therapy depending upon the histologic type and grade of the tumor.

- Radiation therapy is used most frequently to irradiate incompletely excised tumor fields or reduce tumor volume preoperatively. Tumor control rates of 95% at 1 year and 91% at 2 years post-radiation therapy have been reported for patients with incompletely excised, well-differentiated sarcomas.
- High-dose (8 Gy) weekly radiation has been reported to be successful for palliative control of soft tissue sarcomas in dogs.
- Repeat irradiation of previously irradiated tumors is possible. A 38% local control rate after 1-year repeat irradiation has been reported. Unfortunately, if the regrowth of tumors is within 4 to 5 months of the first treatment, the chance of complications from additional radiation is much higher.

Hyperthermia

Hyperthermia involves electromagnetic radiation or ultrasound to heat tissues.

- Hyperthermia is cytotoxic when used alone; however, the best results are seen when it is used as a combined modality with radiation or chemotherapy.
- A 91% response rate has been reported in dogs with hemangiopericytoma treated using orthovoltage irradiation in combination with hyperthermia.
- Unfortunately, hyperthermia requires training and equipment found in few hospitals and thus is of limited accessibility.

Chemotherapy

Chemotherapy has been used with some success to treat patients with soft tissue sarcomas.

- Agents most often used are vincristine, doxorubicin, cyclophosphamide, mitoxantrone, dacarbazine, carboplatin, and lomustine. Response rates range from 15% to 50%. Commonly used protocols are outlined in Table 28-2.
- Chemotherapy is not likely to be efficacious in treating patients with large tumor burdens. Rather, it is best used to treat patients with microscopic disease following incomplete excision, metastatic disease, micrometastatic disease, or patients with grade 3 sarcomas.

MAST CELL TUMORS

Mast cell tumors (MCTs) comprise approximately 7% to 20% of cutaneous neoplasms in the dog and 20% in the cat. MCTs may develop in almost any location but are found most commonly in the skin and subcutaneous tissues of the dog, and in the skin, spleen, liver, and intestines of the cat. Mast cells are a normal component of the immune system and are important in the inflammatory response to tissue trauma as well as in allergic reactions. Cytoplasmic granules found in mast cells contain biologically active substances such as heparin, histamine, platelet-activating factor, prostaglandins, cytokines, and leukotrienes. The quantity and type of granules in MCTs depends on the degree of differentiation. Well-differentiated tumors contain more heparin than undifferentiated tumors, which have a higher histamine content.

Etiology

The cause of MCTs is unknown; however, breed predisposition, chronic inflammation, and viruses may play a role.

Breed Predisposition

Boxers, Boston terriers, English bulldogs, English bull terriers, Sharpeis, and Labrador and golden retrievers are at risk. However, MCTs in boxers are more likely to be well differentiated and may have a more favorable prognosis. Siamese cats younger than 4 years of age have been reported to have a higher incidence of cutaneous histiocytic-like MCTs that may spontaneously regress.

Table 28-2. CHEMOTHERAPEUTIC PROTOCOLS FOR SOFT TISSUE SARCOMAS*

Drug (Trade Name)	Dosage**	Route	Day
Doxorubicin (Adriamycin)	30 mg/m^2 (dogs > 10 kg) 1 mg/kg (cats and dogs < 10 kg)	IV	1
Repeat cycle every 21 days for 4–6 treatments; do not exceed 8 treatments			
Mitoxantrone (Novantrone)	5–6 mg/m^2 (dogs) 5.5–6.5 mg/m^2 (cats)	IV	1
Repeat cycle every 21 days for 4–6 treatments			
Carboplatin (Paraplatin)	260–300 mg/m^2 (dogs) 220–260 mg/m^2 (cats)	IV	1
Repeat cycle every 21 days for 4–6 treatments			
Lomustine (CeeNU)	50–70 mg/m^2 (dogs and cats)	PO	1
Repeat cycle every 21 days for 4–6 treatments			
AC Protocol			
Doxorubicin	As above	IV	1
Cyclophosphamide (Cytoxan)	100–150 mg/m^2	IV	1
	or 50 mg/m^2	PO	3–6
Repeat cycle every 21 days for 4–6 treatments; do not exceed 8 treatments			
VAC Protocol (Dogs Only)			
Vincristine (Oncovin)	0.5–0.7 mg/m^2	IV	8 & 15
Doxorubicin	As above	IV	1
Cyclophophamide	As above	IV	1
	or as above	PO	3–6
Repeat cycle every 21 days for 4–6 treatments; do not exceed 8 treatments. Very myelosuppressive protocol; may need prophylactic antibiotics.			
ADIC Protocol (Dogs Only)			
Doxorubicin	As above	IV	1
Dacarbazine (DTIC)	800–1000 mg/m^2	IV	1
	or 200 mg/m^2	IV	2–5
Repeat cycle every 21 days for 4–6 treatments; do not exceed 8 treatments			

*Caution: The use of chemotherapeutics requires careful handling and knowledge of potential toxicities.
**See Chapter 26 (Table 26-5) for conversion of body weight to body surface area in square meters (m^2).

Chronic Inflammation

Chronic inflammatory sites in the dog have been reported to give rise to MCTs.

Topical carcinogens have been suspected to be involved in MCT development because these tumors are so prevalent in the skin. No definitive proof of this exists.

Viruses

The speculation that viruses may have a role in MCTs stems from experimental studies in which dogs developed MCTs after being given injections of cell-free tumor extracts. However, no specific viruses have been identified as causative agents.

Biologic Behavior

The biologic behavior of MCTs is extremely variable.

▼ ***Key Point*** Because it is often difficult to histologically differentiate benign from malignant tumors, all MCTs should be considered potentially malignant.

Dog

- Approximately 30% to 55% of patients have well-differentiated (grade 1) tumors and are cured with complete surgical excision. The behavior of intermediate-grade tumors is less predictable.
- Undifferentiated tumors (grade 3) are found in 20% to 40% of patients and are aggressive. Most dogs with grade 3 tumors die of their disease within 6 months of surgery.
- Tumor location and rate of growth may help predict behavior. Tumors in preputial, inguinal, perineal, oral, and aural areas may be more aggressive.
- Slow-growing localized MCTs may have a better prognosis. In one study, tumors that were present for 28 weeks or longer before removal had a more favorable prognosis.
- Regional lymph nodes, the spleen, and the liver are the most common sites of metastasis. Bone marrow involvement is uncommon (4.5% of patients in one study). Pulmonary metastasis also is uncommon.

Cat

Controversy exists about the frequency and biologic behavior of MCTs in cats. There are two forms of the disease: cutaneous and visceral.

- Most cutaneous MCTs are well-differentiated and do not display malignant behavior.
- A subset of cutaneous MCTs that appear histologically more diffuse and pleomorphic are behaviorally more aggressive.
- A third type of cutaneous MCT, histiocytic, is seen in young cats and has a benign course, often regressing spontaneously.
- The visceral form (splenic or intestinal) of the disease is aggressive, and widespread metastasis is common.

Clinical Signs

Clinical signs depend on the location, the size and number of the tumors, and the secondary systemic complications caused by the MCT.

- In the dog, most MCTs are observed as solitary masses in the skin of the trunk and perineal area (50%), followed by the extremities (40%) and the head and neck (10%).
- In the cat, 40% to 60% of cutaneous MCTs are solitary masses on the head and neck. At least 20% of cats will have tumors in multiple sites.
- Dermal MCTs are usually well-defined, raised masses that can be hairless, ulcerated, and erythematous. Dermal MCTs may be diffuse, erythematous thickenings in the skin.
- Subcutaneous MCTs may resemble lipomas.
- Mechanical manipulation of MCTs may cause degranulation, resulting in erythema and wheal formation (Darier's sign).
- Visceral MCTs arise in the spleen, small intestine, liver, and visceral lymphatics. Cats with visceral MCTs may present with anorexia, vomiting, or diarrhea.
- Gastroduodenal ulcers have been reported in up to 80% of dogs with MCTs and are thought to be related to histamine release. These animals may have anorexia, vomiting, diarrhea, and melena.
- Heparin and proteolytic enzyme release by MCTs at the time of surgery may prolong coagulation times and delay wound healing.

Diagnosis

History, physical examination, clinical pathology, tumor and bone marrow cytology, radiography, ultrasonography, and histopathology are useful in the diagnosis and staging of MCTs. Stage all patients with MCTs to determine prognosis and therapeutic decisions. Recommended staging tests include CBC, biochemical profile, urinalysis, buffy coat cytology or bone marrow aspiration (controversial), regional lymph node aspirate, abdominal radiographs or ultrasound (preferable), and thoracic radiographs (low yield). A classification system for staging has been developed by the WHO (Table 28-3).

Table 28-3. WORLD HEALTH ORGANIZATION CLINICAL STAGING SYSTEM FOR CANINE MAST CELL TUMORS

Stage	Criteria
I	One dermal tumor without regional lymph node involvement
II	One dermal tumor with regional lymph node involvement
III	Multiple dermal tumors or a large infiltrative tumor with or without regional lymph node involvement
IV	Any tumor with distant metastasis or recurrence with metastasis
Stages are subdivided into the following:	
a	Without systemic signs
b	With systemic signs

History

The history can determine the length of time the mass has been present and the rate of growth.

MCTs present for months without worsening in clinical appearance may be associated with a favorable prognosis.

Physical Examination

Thoroughly examine the animal to detect the location and number of masses. Palpate carefully for hepatomegaly, splenomegaly, and lymph node enlargement as signs of metastasis.

Clinical Pathology

Routine laboratory evaluations may be unremarkable. Examine a CBC for evidence of systemic dissemination. Circulating mast cells, eosinophilia, and basophilia are more common in the dog than in the cat (except with the visceral form). Microcytic-hypochromic anemia may suggest gastrointestinal hemorrhage. The significance of mast cells in buffy coat smears is controversial as patients with non-neoplastic diseases may have increased numbers in smears.

Bone Marrow Aspiration

This is a more sensitive indicator of bone marrow involvement than a buffy coat smear. The presence of greater than 10 mast cells per 1000 nucleated cells is abnormal. However, less than 5% of dogs with cutaneous MCTs will have bone marrow involvement.

Radiography and Ultrasonography

Perform abdominal radiography or ultrasonography (preferable) to detect hepatomegaly, splenomegaly, and intra-abdominal lymph node enlargement. FNA of

enlarged organs (especially the spleen) can be helpful in confirming metastatic MCT. Thoracic radiographs are seldom helpful.

Fine-Needle Aspiration

MCTs exfoliate well and usually can be diagnosed by FNA. Aspirates generally contain numerous discrete round cells with abundant basophilic granules (mast cells). Occasionally, the granules may not stain well with Diff-Quik stains.

Histopathology

Histopathology is important to evaluate completeness of excision and histologic grade. Special stains (toluidine blue, Giemsa) are sometimes needed to identify undifferentiated MCTs. Other stains or immunohistochemical assays that can be performed on histopathology samples and may aid with prognosis are agyrophilic nucleolar staining organizing regions (AGNORs), proliferating cell nuclear antigen (PCNA), and Ki-67 staining. The higher the counts, the poorer the prognosis.

Grading of Tumors

The most reliable predictor of MCT behavior and prognosis in dogs is tumor grade. The most widely used grading system (Patnaik) assigns grades I, II, and III to well, moderately, and poorly differentiated tumors, respectively (based on histologic appearance).

- Low-grade tumors are less likely to recur or metastasize, and dogs with low-grade tumors have increased survival times.
- The Patnaik grading system has not been found useful in determining prognosis in cats.

Treatment of Canine Cutaneous Mast Cell Tumors

Treatment of MCTs may include surgery, radiation therapy, chemotherapy, or some combination of the three. The type of treatment instituted depends primarily on the histologic grade of the tumor and the clinical stage of the patient.

Surgery

Wide surgical excision is the treatment of choice for canine MCTs.

▼ ***Key Point*** Although they appear to be discrete masses, MCTs may extend deep into surrounding tissues, making wide surgical excision imperative (especially for grade 3 tumors)

- Administer an antihistamine (e.g., diphenhydramine; 2 mg/kg IM or IV) just before surgical excision of large tumors to decrease the effects of histamine release from the tumor.
- Excise the mass with 3-cm margins on all sides and one fascial plane deep to the tumor.
- Remove regional lymph nodes if enlarged or if metastasis is detected.
- Have the specimen margins histologically evaluated for completeness of excision and grade. If the tumor extends to the margins, plan a second wider excision (if possible).
- If tumors are excised incompletely or are non-resectable, proceed with radiation therapy and/or chemotherapy.
- Wound complications, such as excessive inflammation, edema, and dehiscence, can occur after MCT excision.

Radiation Therapy

Radiation therapy alone or in combination with other treatment modalities may be used to treat incompletely excised or non-resectable MCTs.

- Patients with grade 1 and 2 tumors respond better than those with grade 3. In one study, tumor-free survival rates of 94% at 1 year and 86% at 5 years post-radiation therapy were reported in dogs with incompletely excised grade 1 and 2 MCT.
- Radiation is most effective against microscopic disease.
- Irradiate involved regional lymph nodes, if necessary.

Chemotherapy

Chemotherapy is indicated for patients with systemic mastocytosis, grade 3 tumors, non-resectable tumors, or incompletely excised tumors when a second surgery or radiation therapy is not possible.

- Glucocorticoids (prednisone and prednisolone) are commonly used but are effective in less than 25% of dogs when used alone.
- Vinblastine, cyclophosphamide, and lomustine are chemotherapy drugs reported to have efficacy against MCTs (Table 28-4 shows dosages). Combination therapy is thought to be superior to single-agent use.

Ancillary Drug Therapy

Patients with grade 3 tumors, systemic mastocytosis, or gastrointestinal hemorrhage should receive ancillary drug therapy.

- Use H_2-antagonists to reduce gastric acid secretion and help decrease the incidence and severity of gastrointestinal ulcers in MCT patients. Administer one of the following H_2-blockers:
  - Cimetidine (Tagamet), 5 to 10 mg/kg PO q8h
  - Ranitidine (Zantac), 1 to 2 mg/kg PO q12h
  - Famotidine (Pepcid), 0.5 to 1 mg/kg PO q24h
- When an active gastrointestinal ulcer is suspected in an animal with MCT, also administer the following:
  - Sucralfate (Carafate), 250 to 1000 mg PO q6–8h

Table 28-4. CHEMOTHERAPEUTIC PROTOCOLS FOR MAST CELL TUMORS

Drug (Trade Name)	Dosage*	Route	Day
CVP			
Cyclophosphamide (Cytoxan)	250–300 mg/m^2 divided	PO	8–11
Vinblastine (Velban)	2 mg/m^2	IV	1
Prednisone	1 mg/kg	PO	q24h
Repeat cycle every 21 days			
VLP (Dogs)			
Vinblastine (Velban)	As above	IV	1
Lomustine (CeeNU)	60–70 mg/m^2	PO	14
Prednisone	2 mg/kg Gradually taper to 0.5 mg/kg	PO	q24h
Repeat cycle every 28 days			
Lomustine (CeeNU)	50–70 mg/m^2	PO	1
Repeat cycle every 21 days			
Prednisone	1 mg/kg	PO	q24h

*See Chapter 26 (Table 26-5) for conversion of body weight to body surface area in square meters (m^2).

- Use an H_1-antagonist (diphenhydramine) as needed to reduce inflammation and pruritis associated with histamine release.

Treatment of Feline Mast Cell Tumors

Cutaneous

- Wide surgical excision is the treatment of choice.
- Chemotherapy and radiation therapy have not been well evaluated but may be helpful in recurrent or metastatic tumors. One study found a 57% response rate to lomustine in cats with MCTs.

Visceral

- Splenectomy may ameliorate clinical signs and prolong survival in cats with splenic MCT even when other organs are involved. Median survival times following splenectomy was 19 months in one study of 43 cats.
- Treat intestinal MCTs by wide surgical excision (5- to 10-cm margins). However, the prognosis for cats with intestinal disease is poor.
- Chemotherapy has not been critically evaluated.

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Chapter 29

Mammary Gland Neoplasia

Kechia M. Davis / Elizabeth A. Stone

The mammary gland tumor (MGT) is the most common tumor in the female dog and the third most common neoplasm in the female cat. MGTs have been reported in the male dog and cat but are rare.

ETIOLOGY AND RISK FACTORS

- The cause of mammary gland neoplasia is unknown.
- Predisposing risk factors proposed but incompletely established include dietary intake of red meat and obesity at 1 year of age.
- A genetic etiology has been suggested in one colony of beagles.
- Although virus-like particles have been identified in feline and canine MGTs, their role as a causative agent has not been established.
- Routine administration of medroxyprogesterone acetate, proligestone, or other progestins for estrus prevention or dermatologic therapies increases the risk of MGTs in dogs and cats.
- About 50% of canine mammary carcinomas have estrogen and progesterone receptors at levels lower than in benign or normal mammary gland tissues. Only benign and well-differentiated adenocarcinomas appear to be hormonally sensitive in female dogs.
- Dogs with benign MGTs have more than a threefold risk of subsequently developing a mammary malignancy of a different cell type.
- Dogs that are spayed before their first estrus have almost no risk of developing MGTs.

CLINICAL SIGNS

- A mass or swelling develops in the ventral thoracic or abdominal region. The mass is typically associated with the mammae but may appear distant to the mammary gland.
- Metastatic lesions in the lungs may cause dyspnea.
- Metastatic lesions in the axial skeleton or proximal long bones may cause pain or lameness.
- Anorexia and weight loss may be noted in cats with inflammatory mammary carcinoma (IMC).
- MGTs can be seen concurrent with uterine neoplasms in cats.

DIAGNOSIS

Establish a definitive diagnosis, determine local invasion, and determine the stage of the MGT.

Signalment

Dogs

- In dogs, the risk of developing MGTs increases markedly after 6 years of age.
- Most MGTs are reported in sporting breeds (pointers, English setters, and spaniels), poodles, Boston terriers, and dachshunds.
- Consider predisposing risk factors (see prior section).

Cats

- Feline carcinomas occur most often in intact female cats 8 to 12 years of age.
- Siamese cats are reported to have twice the risk of developing mammary carcinoma as all other breeds combined.

History

- The owner may have noticed the tumor or it may have been an incidental finding during routine examination.
- The owner may have delayed seeking veterinary assistance. Median time from owner observation of mammary masses in cats to presentation to a veterinarian is 5 months.

Physical Examination

- In dogs, MGTs develop most frequently in the caudal mammary glands.

- Depending on the time of recognition, the tumors may be small and movable, lobular and firm, fixed to the body wall, and ulcerated.
- Dogs with inflammatory carcinoma have diffusely swollen glands with poor demarcation between normal and abnormal tissue, which may be confused with mastitis. In mastitis, the swelling is more localized and occurs after estrus, whelping, or false pregnancy.
- Hindlimb edema, popliteal lymphadenopathy, and ulceration may be noted in cats with IMC up to 4 months after mammary mass excision.
- In young, intact female cats, mammary hypertrophy can be mistaken for MGT. Mammary hypertrophy resulting from either endogenous or exogenous progesterone stimulation can be differentiated readily by case history and, if necessary, histologic examination.
- In cats, infiltrated lymphatics may look like linear beads.
- Superficial cervical, axillary, popliteal, and inguinal lymph nodes may be enlarged.
- Carefully examine dogs for evidence of lameness and bony swelling. If these signs are present, radiograph the affected area and obtain a nuclear bone scan if needed. Mammary carcinoma is one of the most common primary tumors with metastases to the skeleton.
- In advanced disease, cachexia may be noted due partially to altered carbohydrate metabolism.

Diagnostic Imaging

▼ ***Key Point*** In cats, mammary adenocarcinoma has been reported as the most common tumor to metastasize to the lungs.

- The radiographic appearance is frequently diffuse or ill-defined pulmonary infiltrates.
- If caudal mammary glands are involved, use abdominal ultrasonography or abdominal radiographs to evaluate the iliac lymph nodes.
- Magnetic resonance imaging with gadolinium contrast has been shown to detect metastatic lymph nodes in canine mammary tumors.

Cytologic Evaluation

- Cytology is generally not recommended for the diagnosis of MGTs.
- Varying degrees of epithelial atypia and inflammation make definitive diagnosis and tumor grading difficult.
- Cytology may be useful to differentiate inflammatory carcinoma from mastitis in dogs and mammary hypertrophy from mammary carcinoma in cats.
- Fine needle aspiration of enlarged inguinal or axillary lymph nodes is recommended.

Histologic Evaluation

Submit all excised mammary masses for histopathologic evaluation. Although about 50% of MGTs are benign, many dogs can have multiple tumors often of different tumor types, both benign and malignant.

- Tumors are graded by cell type (epithelial, mesenchymal, or mixed) and by degree of differentiation. High-grade tumors are typically poorly differentiated.
- Histopathologic evaluation is the preferred method of definitively diagnosing and grading mammary masses. The histopathologic diagnosis does not alter current treatment recommendations for MGT (except for IMC, as explained in "Contraindications"). Thus, surgical excision is performed for both diagnostic and therapeutic purposes. A wide excision is essential to ensure complete removal of tumor cells.
- Regional lymph nodes should be removed as well and submitted for histopathology. Dogs with lymph node metastasis have been shown to have a significantly shorter disease-free interval and a poorer prognosis than those without lymph node involvement.

Other Diagnostic Tests

- If the animal is to undergo surgery, perform a complete blood count, biochemical profile, and urinalysis. These animals are typically older and may have concurrent disease that may need to be addressed.
- Perform thoracocentesis with cytologic analysis if pleural fluid is evident on thoracic radiographs.

TREATMENT: SURGICAL

The primary surgical goal is to excise all of the neoplastic tissue while maintaining quality of life.

Preoperative Considerations

Indications

Surgical excision is beneficial in dogs because it does the following:

- Provides a histologic diagnosis
- Can modify disease progression
- Can improve quality of life
- Can be curative

Contraindications

Preoperative diagnosis of IMC is a contraindication for surgery. Mean survival of dogs with IMC is 25 days with palliative treatment. Cats have lived up to 45 days after diagnosis of IMC. Delayed diagnosis may partially explain the short survival time. Treatment for IMC

should be palliative using anti-inflammatory drugs and antibiotics. Surgery is not recommended for IMC for the following reasons:

- It is impossible to remove all affected tissue.
- Disseminated intravascular coagulation often is induced by surgery.
- Incisions may dehisce as the disease progresses.
- The following discussion excludes inflammatory carcinoma.

▼ ***Key Point*** Radical mastectomy has not been shown to be more effective than excision of only affected glands for dogs with MGTs.

Resection Margins

Determine resection margins before surgery. Dissect only healthy tissues during surgery. Do not disrupt the tumor itself. The margins should be at least 1 cm from the neoplastic tissue.

Gland Excision in Dogs

Past recommendations have suggested regional mastectomy for all MGTs in dogs. These recommendations were based on the lymphatic drainage in normal dogs. However, MGTs have been shown to disrupt normal drainage and open new channels between other glands. Thus, the number of excised glands should be based on having adequate resection margins of normal tissue around the tumor.

Gland Excision in Cats

In cats, removal of all glands on an affected side decreases local recurrence compared with a lumpectomy. However, this may not prolong survival time.

Other Recommendations

- If the tumor has invaded the subcutaneous tissue beneath the gland, include the ventral fascia of the underlying muscle in the excision.
- If the tumor has invaded the body wall, remove a wide section of the body wall en bloc with the tumor.
- Remove the inguinal lymph node routinely during mastectomy of gland 5.
- Axillary lymph nodes usually are not removed with gland 1 unless there is palpable or cytologic evidence of an abnormality.

Surgical Procedures

The choice of surgical procedures for MGTs include lumpectomy, simple mastectomy, regional mastectomy, complete unilateral mastectomy, and one-stage or two-stage complete bilateral mastectomy. Ovariohysterectomy can be combined with any of these.

Lumpectomy

Removal of the tumor and 1 cm of normal tissue without removal of surrounding glandular tissue *(lumpectomy)* is adequate if the tumor is small (<5 mm), circumscribed, and non-invasive.

Simple Mastectomy

In many instances, removal of the entire mammary gland *(simple mastectomy)* is easier than lumpectomy, and this avoids milk and lymph leakage into the wound.

Regional Mastectomy

When the incision must extend into the adjacent gland or glands to obtain adequate margins, the adjacent gland or glands are also removed *(regional mastectomy)*. Consider the blood supply to individual mammary glands when planning and executing the mastectomy. When two or more glands are neoplastic, choose the most efficient approach. Involvement of two or three adjacent glands necessitates a regional mastectomy.

Complete Unilateral Mastectomy

When multiple glands contain tumors, all the ipsilateral glands and intervening tissues are removed *(complete unilateral mastectomy),* rather than excising each gland separately and leaving tissue between glands.

Removal of Tumors in Contralateral Glands

Tumors in contralateral glands may be excised by bilateral simple, regional, or complete mastectomy. The limiting factor is the amount of skin that will be available after excision for closure. In cats and in relatively flat-chested dogs, such as Yorkshire terriers or Pekingese, bilateral complete mastectomy is possible.

In deep-chested dogs, such as Irish setters or pointers, often it is not possible to excise contralateral cranial glands with adequate margins of healthy tissue and still be able to close the skin. In this type of dog, perform a staged bilateral mastectomy. Operate on one side and then, after 2 to 4 weeks, operate on the other side.

Surgical Technique

1. Prepare the affected mammary glands and surrounding skin for aseptic surgery.
2. After skin and subcutaneous tissues are incised, suture drapes or towels to the normal wound edges to protect skin from tumor implantation.
3. Place stay sutures in the margin tissues.
4. Use blunt and sharp dissection to remove mammary glands and underlying subcutaneous tissue. Avoid handling the tumor with instruments or fingers.
5. Use meticulous hemostasis with point electrocautery and vessel ligation.
6. Lavage the wound with 0.5 to 1 L of warm sterile normal saline to remove exfoliated tumor cells.

7. Replace contaminated gloves and surgical instruments before beginning closure.
8. Meticulously close the subcutaneous tissues to relieve tension across the incision and prevent problems associated with dead space.
9. Close skin routinely.
10. Consider a light bandage on the incision after extensive mastectomy to protect from trauma.

Ovariohysterectomy

Ovariohysterectomy (OHE) at the time of mastectomy remains controversial. One study found that dogs spayed less than 2 years before mastectomy survived significantly longer than those spayed more than 2 years prior to surgery. The investigators theorized that MGTs that develop in the presence of reproductive hormones are less aggressive than those that develop in spayed dogs. Another study failed to demonstrate such a difference. OHE does result in atrophy of the remaining glands, which may make it easier to detect new tumors. However, with aggressive MGTs, death from metastatic disease may occur before new tumors become problematic.

If OHE is planned during the same surgery, perform the OHE before the mastectomy to avoid seeding the abdomen with tumor cells. If MGT extends across the midline, perform the mastectomy first, lavage the area, and use new gloves and instruments for the OHE.

Biopsy Preparation

Because multiple tumor types can be present, submit each mass for histopathologic examination. Mark the edges of the tissue with suture material or India ink to help the pathologist maintain proper orientation.

Pain Control

Use perioperative pain control on patients undergoing tumor excision, considering options such as nonsteroidal anti-inflammatory agents (NSAIDs), narcotic analgesics, and local anesthetics (see Chapter 6). For extensive tumor resections involving the body wall or entire chains of mammary glands, use single, preoperative epidural injections or epidural catheters in addition to other modalities of pain control.

TREATMENT: MEDICAL

Chemotherapy, anti-estrogen therapy, and biologic response modifiers have been used to treat MGTs in conjunction with surgery and to treat metastic or unresectable tumors. In general, efficacy remains to be established, and surgery is the treatment of choice whenever possible.

Chemotherapy

Efficacy of chemotherapeutic agents has not been established for canine MGTs. A recent study cited an increase in survival time in dogs treated with cyclophosphamide and 5-fluorouracil after surgery. Cyclophosphamide and doxorubicin may induce a short-term partial or complete response in cats with metastatic or nonresectable local disease. However, these drugs cause severe anorexia and mild myelosuppression.

Anti-Estrogen Therapy

A response of MGTs to anti-estrogen therapy (e.g., tamoxifen) has not been proven. Estrogenic side effects (e.g., vaginal bleeding, vulval swelling, and attractiveness to male dogs) are common.

Biologic Response Modifiers

Biologic response modifiers such as levamisole and bacilli Calmette-Guerin (BCG) have not been proven to be beneficial for MGT.

PROGNOSIS

Dogs

In dogs, histologic grade and stage appear to be important prognostic factors. Various studies in dogs have concluded the following:

- Poorly differentiated or invasive MGTs have a worse long-term prognosis than other types.
- Ductular carcinomas metastasize more frequently and result in a threefold increase in death rate compared with adenocarcinomas.
- Approximately 26% of dogs with benign tumors develop new mammary masses within 2 years of tumor excision regardless of OHE.
- Cancer mortality rate after excision of mammary carcinomas is reportedly 22%, with most deaths occurring within 1 year of surgery.
- The mortality rate for dogs with invasive or metastatic carcinomas is 80%. Invasive carcinomas also recur more often (44%) than benign and non-invasive carcinomas (12%).

▼ ***Key Point*** Dogs with tumors <3 cm in diameter have a better prognosis than dogs with tumors >3 cm in diameter.

Cats

In cats, histologic grade and tumor size appear to be prognostic but cell type is not.

- Cats with mammary adenocarcinomas and carcinomas >3 cm have a poorer prognosis and shorter 12-month median survival time.

- Survival may be decreased in cats with multiple tumors and tumors >8 cm^3.
- Vascular endothelial growth factor expression is an important prognostic indicator in cats.

PREVENTION

▼ ***Key Point*** The risk of MGT is less than 0.5% in dogs that are spayed before their first estrus and less than 8% in those spayed before their second estrus.

- After 2.5 years, OHE has no protective effect on MGT development. In dogs spayed at any age, risk of MGT is reduced if dogs were thin at 9 to 12 months of age.
- Spayed cats have a 0.6% risk for developing mammary carcinoma compared with intact cats.

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Chapter 30

Tumors of the Skin and Subcutaneous Tissues

Janet L. Peterson

The skin and subcutis are the most common sites of neoplasia in the dog, accounting for approximately 30% to 40% of all tumors. In the cat, only 20% of all tumors originate in the skin and subcutis, making it the second most common site of origin. Most canine skin tumors are benign, whereas most feline skin tumors are malignant. Owners often discover skin tumors while petting or grooming their animals.

▼ ***Key Point*** Skin tumors should not be ignored. Advising owners to "watch" the tumor rather than to seek a diagnosis could be life-threatening to their dog or cat.

The most common skin tumors in the dog and cat are shown in Table 30-1.

Dog breeds at an increased risk for skin tumors include the basset hound, boxer, bull mastiff, Scottish terrier, and Weimaraner; there is no apparent breed predilection in the cat. In general, skin and subcutaneous tumors are more common in older dogs and cats. Common tumors in younger dogs are shown in Table 30-1. The etiology of most canine and feline tumors is unknown; however, some tumors have been associated with defined etiologic agents, such as those listed in Table 30-2.

Physical examination may assist the clinician in formulating a list of potential tumors in the small animal patient. A basic working knowledge of the anatomic location and tissue of origin of various tumors can assist the clinician in making educated decisions. Additionally, fine-needle aspiration helps make a definitive diagnosis without requiring an incisional or excisional biopsy.

TUMOR CLASSIFICATION

Skin tumors can be classified by tissue of origin (Table 30-3), anatomic location (Table 30-4), and stratum of origin (Table 30-5). Miscellaneous tumors affecting the skin are listed in Table 30-6.

DIAGNOSIS

General Principles

- Diagnosis and characterization of a skin mass is important for several reasons. Knowledge of the tumor type before surgical excision allows the clinician (1) to plan an appropriate surgical approach (e.g., in a mast cell tumor that requires 3-cm margins beyond the tumor edges), (2) to consider radiation therapy (e.g., non-resectable mast cell tumors), or (3) to institute medical treatment (e.g., vincristine chemotherapy is usually curative for transmissible venereal tumors).
- To detect the presence of metastatic disease before surgery, evaluate every enlarged regional lymph node cytologically (fine-needle aspiration) or histologically. Additionally, consider lymph node excisional biopsy at surgery for more accurate staging.
- Perform thoracic radiographs (three views) on all animals with suspected (or confirmed) malignant tumors to detect potential pulmonary metastases. Perform abdominal radiography and/or abdominal ultrasonography in those cases in which dissemination to the abdominal organs, cavity, or multicentricity is suspected (e.g., mast cell tumor or hemangiosarcoma). Evaluate skeletal structures on thoracic and abdominal radiographs for metastatic disease.

▼ ***Key Point*** Diagnosis and staging of a skin tumor before surgery are critical to ensure complete excision and to determine appropriate additional treatment.

Fine-Needle Aspiration Cytology

Equipment

- 12-ml syringe
- 22- or 25-gauge needle
- Glass slides
- Diff-Quick or Wright-Giemsa stain

Table 30-1. MOST COMMON SKIN AND SUBCUTANEOUS TUMORS

Young Dogs
Histiocytoma
Transmissible venereal tumors
Viral papillomas

Canine
Lipomas
Mast cell tumors
Histiocytomas
Sebaceous gland adenomas

Feline
Basal cell tumors
Squamous cell carcinomas
Fibrosarcomas
Mast cell tumors

Table 30-2. ETIOLOGIC AGENTS

Etiology	Tumor Associations
Viruses	Canine squamous papilloma
	Warts
	Feline sarcoma virus—associated multiple fibrosarcomas
Solar and ionizing radiation	Squamous cell carcinoma
Hormones	Perianal adenoma
Thermal injuries	Squamous cell carcinoma
	Mast cell tumor
Genetic factors	Various tumors
Immunologic compromise	Feline lymphoma
Age	Many tumors

Table 30-3. CLASSIFICATION OF SKIN TUMORS BY TISSUE OF ORIGIN

Epithelial neoplasia
Papilloma
Sebaceous adenoma/hyperplasia/adenocarcinoma
Perianal adenoma/hyperplasia/adenocarcinoma
Basal cell tumor
Ceruminous gland adenoma/adenocarcinoma
Squamous cell carcinoma
Apocrine gland adenocarcinoma
Intracutaneous cornifying epithelioma (keratoacanthoma)
Dermoid/epidermal inclusion cyst

Mesenchymal neoplasia
Lipoma/infiltrative lipoma/liposarcoma
Fibrosarcoma
Nerve sheath tumor
Hemangiosarcoma
Hemangiopericytoma
Histiocytoma
Mast cell tumor
Extramedullary plasmacytoma

Melanoma

Table 30-4. CLASSIFICATION OF SKIN TUMORS BY ANATOMIC LOCATION

Head and neck
Basal cell tumor
Squamous cell carcinoma
Sebaceous adenoma
Papilloma
Histiocytoma
Mast cell tumor (primarily in cats)
Ceruminous gland adenoma/adenocarcinoma
Hemangiosarcoma

Extremities
Mast cell tumor
Hemangiopericytoma
Squamous cell carcinoma (nail bed)
Malignant melanoma (nail bed)
Nerve sheath tumor
Synovial cell sarcoma
Hemangiosarcoma

Trunk
Mast cell tumor
Lipoma
Sebaceous gland adenoma
Fibrosarcoma
Nerve sheath tumor
Hemangiosarcoma

Perineum/genitals
Mast cell tumor
Perianal adenoma
Transmissible venereal tumor
Perianal adenocarcinoma
Anal sac (apocrine gland) adenocarcinoma

Table 30-5. CLASSIFICATION OF SKIN TUMORS BY STRATUM OF ORIGIN

Dermoepidermal
Basal cell tumor
Squamous cell carcinoma
Sebaceous adenoma/hyperplasia
Mast cell tumor
Perianal adenoma
Malignant melanoma
Ceruminous gland adenocarcinoma
Lymphoma
Transmissible venereal tumor
Hemangioma/hemangiosarcoma
Cysts

Subcutaneous
Mast cell tumor
Hemangiopericytoma
Lipoma
Hemangiosarcoma
Nerve sheath tumor
Fibrosarcoma

Table 30-6. MISCELLANEOUS TUMORS AFFECTING THE SKIN

Intracutaneous cornifying epithelioma (keratoacanthoma)
Trichoepithelioma and pilomatrixoma (tumors of the hair follicles)
Epidermal inclusion cyst (epidermoid, epidermoid cyst)
Dermoid cyst

Technique

- Isolate and hold the mass firmly while inserting the needle into it.
- Apply negative pressure to the syringe to obtain cells.
- Release the negative pressure before withdrawing the needle from the mass.
- Remove the needle from the syringe and fill the syringe with air.
- Replace the needle and expel the contents (within the hub of the needle) onto a glass slide or cover slip.
- Prepare the smear by placing the two slides together and pulling them apart in a parallel motion (“horizontal pull-apart” technique).

- An alternative technique is to insert the needle several times without a syringe into the mass ("pass-through" technique). The contents of the needle are expelled using a syringe and are prepared as aforementioned.

Cytologic Classification of Neoplasia

Cytology can be used to classify masses as neoplastic or non-neoplastic. If the mass is not neoplastic, then the decision must be made as to whether it is inflammatory or non-inflammatory. Masses also can be classified as mixed, as in the case of a neoplastic mass with a necrotic center and associated inflammation. Infectious agents also may be identified cytologically (e.g., bacteria, fungi, or protozoa).

Cytologic examination may allow classification of tumors into one of three categories: epithelial, mesenchymal, or round cell neoplasm (includes epithelial, mesenchymal, and melanocytic tumors).

Epithelial Tumors

Epithelial cells cluster because of desmosomes. Aspiration cytology reveals round to polygonal cells with basophilic cytoplasm (with and without vacuoles) and cell-to-cell association. The latter may be absent in squamous cell carcinomas.

Mesenchymal Tumors

Mesenchymal tumors arise from connective tissue, including fibrous tissue, muscle, fat, and blood vessels. They do not exfoliate well on fine-needle aspiration; however, when they do exfoliate, they appear as individual cells or in small groups of cells, with a spindle to polygonal shape.

Round Cell Tumors

On fine-needle aspiration, round cell tumors tend to exfoliate as single cells with the exception of transmissible venereal tumor cells, which usually clump. The cells have distinct cell membranes like epithelial cells. Some cells may have cytoplasmic granules (i.e., mast cells, melanoma cells, and large granular lymphocytes).

Round cell tumors include lymphoma, melanoma, histiocytoma, transmissible venereal tumor, mast cell tumor, and plasma cell tumor. Additionally, squamous cell carcinomas and basal cell tumors can resemble round cell tumors cytologically.

Incisional Biopsy

Punch Biopsy

The skin punch biopsy using the Baker biopsy punch is a relatively simple technique for obtaining a sample of superficial masses. The advantage of skin punch biopsies is that they can be done quickly, using only local anesthetic. See Chapter 37 for skin biopsy technique.

Needle Biopsy

Tru-cut or spring-loaded needle biopsies can be used to obtain representative samples of larger or subcutaneous masses using only local anesthesia.

Wedge Biopsy

A routine surgical procedure is used to obtain a "wedge" biopsy (see Chapter 26).

Excisional Biopsy

Excisional biopsy implies that all or most of the tumor or mass is removed and submitted for histopathologic examination. This approach is indicated for small, easily excisable masses. Margins of excised tissue should be at least 1 cm in all cases. All excised tumors must be properly fixed. Label each tumor by location if there are multiple tumors, and finally, send all tumors to a qualified veterinary pathologist for examination. Principles of surgical biopsy of tumors are described in Chapter 26.

▼ ***Key Point*** Perform histopathologic examinations on all excised skin masses, no matter how "benign" they appear. Appropriate treatment necessitates a definitive diagnosis.

Staging

Clinical staging is helpful in characterizing the extent of the disease. Obtain thoracic radiographs (left and right lateral and ventrodorsal views) when malignancy is suspected. Perform abdominal radiography or ultrasonography for tumors such as cutaneous hemangiosarcoma and mast cell tumor to evaluate for splenic and hepatic involvement (metastases or primary tumor).

SELECTED TUMORS OF THE SKIN AND SUBCUTANEOUS TISSUE

Epithelial Neoplasia

Papilloma

Origin and Etiology

Papillomas (squamous papillomas, squamous cell papillomatosis, warts, and cutaneous papillomatosis) originate from the squamous epithelium. Papillomas have a DNA viral etiology in puppies (see Chapter 16), but the etiology is unknown in older dogs.

Description

Papillomas may appear as cauliflower or wart-like growths that are usually well encapsulated. They can be sessile or pedunculated and may bleed if traumatized.

They can occur as a single tumor (usually non-viral etiology) or as multiple tumors (usually viral etiology) in the skin, mucous membranes, or mucocutaneous regions.

Epidemiology and Biologic Behavior

Papillomas are common in dogs but rare in cats. The virally induced papillomas found in young dogs often appear as multiple or occasionally single masses on the head, eyelids, feet, or mouth. These tumors are contagious to other dogs and have an incubation period of approximately 30 days. In older dogs, non-viral papillomas tend to appear as solitary dermoepidermal masses. Some papillomas in older dogs can transform into squamous cell carcinomas.

Treatment

Papillomas tend to regress spontaneously in younger dogs (usually within 1–2 months) and therefore do not require treatment. Surgically remove viral papillomas that do not regress and non-viral papillomas that cause a clinical problem.

Sebaceous Gland Tumors

Origin and Etiology

Sebaceous gland adenoma, hyperplasia, and adenocarcinoma originate from the epithelium of the sebaceous glands.

Description

These tumors are common in dogs (especially spaniels) and rare in cats. Hyperplasia usually appears as pink, smooth, lobulated, and wart-like growths that are firm, dermoepidermal, and well-circumscribed masses with an alopecic surface. They may be pigmented and can occur anywhere on the body. These tumors are frequently multiple. They often appear as bleeding and ulcerated masses. Sebaceous gland adenocarcinoma is poorly circumscribed, large, invasive, and frequently ulcerated. These are extremely rare.

Cytology

Cytologic examination of sebaceous gland hyperplasia reveals mature secretory epithelial cells, frequently with a "signet-ring appearance" because of the accumulation of secretions within the cell. Sebaceous adenocarcinoma cells exhibit typical features of epithelial malignancy.

Epidemiology and Biologic Behavior

Sebaceous gland hyperplasia tends to be multiple lesions. Sebaceous gland adenomas can occur as single tumors; however, they frequently occur in multiple sites. They occur in older female dogs, especially poodles and cocker spaniels. When metastases from sebaceous gland adenocarcinomas occur, they generally spread to the regional lymph nodes and subsequently to the lungs.

Treatment

Surgical excision of sebaceous gland hyperplasia lesions may not be necessary unless they occur in an area that is easily traumatized. Perform wide surgical excision on all sebaceous adenocarcinomas. Adjunct treatment with radiotherapy and/or chemotherapy may be indicated (Table 30-7).

Perianal Tumors

Origin and Etiology

Perianal adenomas, hyperplasia, and adenocarcinomas originate from the perianal (hepatoid) glands. These are sebaceous glands that encircle the anus of the dog and also are located in the skin of the tail, prepuce, and thigh and over the dorsum of the back. The growth and maintenance of these cells are dependent on the presence of testosterone.

Description

Perianal adenoma and hyperplasia can occur as solitary or multiple nodules. These are most common in *older* intact male dogs, and their behavior is usually benign. They can be found wherever perianal glands are located (see "Origin and Etiology"), but they are most common in the perineal region. Perianal adenocarcinomas are usually larger, ulcerative, and invasive.

Cytology

Cytologic examination usually reveals large hepatoid cells. It is impossible to differentiate perianal adenoma from hyperplasia. Malignancy can be difficult to assess solely on the basis of cytology.

Epidemiology and Biologic Behavior

Perianal adenocarcinomas metastasize to the local lymphatics, especially the iliac lymph nodes, and to the lungs. These tumors occur primarily in male dogs.

Treatment

Perianal adenoma and hyperplasia usually regress with castration because of their testosterone dependency. Castration therefore is recommended for all dogs in which perianal adenoma or hyperplasia constitutes a problem. Perform aggressive surgical excision on all resectable perianal adenocarcinomas and those perianal adenomas that fail to respond to castration. Other treatment options are radiation therapy or chemotherapy using carboplatin, mitoxantrone, and doxorubicin (see Table 30-7 for dosages).

Table 30-7. CHEMOTHERAPY PROTOCOLS

Soft Tissue Sarcoma

1. *ADIC protocol* (*dogs*)
   Doxorubicin (Adriamycin): 30 mg/m^2 BSA, IV, q3 weeks
   DTIC (Dacarbazine): 1000 mg/m^2 BSA, IV drip for 6–8 hours; repeat q3 weeks
2. *VAC protocol* (*21-day cycle*) (*dogs*)
   Vincristine (Oncovin): 0.75 mg/m^2 BSA, IV, days 8, 15
   Doxorubicin (Adriamycin): 30 mg/m^2 BSA, IV, day 1 (dogs)
   Cyclophosphamide (Cytoxan): 100–200 mg/m^2 BSA, IV, day 1
   Tribrissen: 14 mg/kg, PO, q12h
3. *VAC protocol* (*21-day cycle*) (*cats*)
   Vincristine (Oncovin): 0.5 mg/m^2 BSA, IV days 8, 15
   Doxorubicin (Adriamycin): 20 mg/m^2 BSA, IV, day 1
   Cyclophosphamide (Cytoxan): 100–200 mg/m^2 BSA, IV, day 10
   Tribrissen: 14 mg/kg, PO, q12h

Carcinoma—Dog

1. *CMF protocol*
   5-Fluorouracil (5-FU): 150 mg/m^2 BSA, IV, once a week
   Cyclophosphamide (Cytoxan): 50 mg/m^2 BSA, PO, 4 days a week or qod
   Methotrexate: 2.5 mg/m^2 BSA, PO, 2 or 3 times a week
2. *VAF protocol*
   Vincristine (Oncovin): 0.75 mg/m^2 BSA, IV, days 8, 15
   Doxorubicin (Adriamycin): 30 mg/m^2 BSA, IV, day 1
   5-Fluorouracil (5-FU): 150 mg/m^2 BSA, IV, days 1, 8, 15
3. *VAC protocol*
4. *Cisplatin* (*Platinol*)*:* 50–70 mg/m^2 BSA, IV drip, 3 weeks; prior intensive diuresis is required
5. *FAC protocol*
   5-Fluorouracil (5-FU): 150 mg/m^2 BSA, IV, days 8, 15
   Doxorubicin (Adriamycin): 30 mg/m^2 BSA, IV, day 1
   Cyclophosphamide (Cytoxan): 100–200 mg/m^2 BSA, IV, day 1
   Tribrissen: 14 mg/kg, PO, BID
6. *Carboplatin* (*Paraplatin*)*:* 300 mg/m^2 BSA, IV, q21d
7. *Mitoxantrone* (*Novantrone*)*:* 6 mg/m^2 BSA, IV, q21d

Carcinoma—Feline

1. *Vincristine* (*Oncovin*)*/Cyclophosphamide* (*Cytoxan*)
   Vincristine (Oncovin): 0.5 mg/m^2 BSA, IV, once a week
   Cyclophosphamide (Cytoxan): 50 mg/m^2 BSA, PO, 4 days a week or qod
2. *As above, plus methotrexate:* 2.5 mg/m^2 BSA, PO, 2 or 3 times a week
3. *VAC protocol* (*28-day cycle*)
4. *Mitoxantrone* (*Novantrone*)*/Cytoxan Protocol* (*21-day cycle*)
   Mitoxantrone: 3–5 mg/m^2, IV over 45 minutes, day 1
   Cyclophosphamide (Cytoxan): 200–300 mg/m^2 BSA, PO, day 15
5. *Carboplatin* (*Paraplatin*)*:* 150–250 mg/m^2 BSA, IV, q21d
6. *Mitoxantrone* (*Novantrone*)*:* 6.5 mg/m^2 BSA, IV, q21d

Transmissible Venereal Tumor

Vincristine (Oncovin): 0.5 mg/m^2 BSA, IV, once weekly until and at least 1 week beyond resolution of the tumor

Anal Sac or Apocrine Gland Adenocarcinoma

1. *FAC protocol*
2. *Melphalan* (*Alkeran*)
   Melphalan (Alkeran): 2 mg/m^2 BSA, PO, q24h × 1 week; then qod, i.e., 6–8 mg/m^2 PO q24h × 5 days; repeat q3 weeks
3. *Carboplatin* (*Paraplatin*)*:* 300 mg/m^2 BSA, IV, q21d
4. *Mitoxantrone* (*Novantrone*)*:* 6.0 mg/m^2 BSA, IV, q21d

Extramedullary Plasmacytoma

Melphalan (Alkeran): 2 mg/m^2 BSA, PO, q24h × 1 week; then qod

Basal Cell Tumors

Origin and Etiology

Basal cell tumors (basal cell carcinoma, basal cell epithelioma) originate from the basal cells of the epidermis and adnexa.

Description

Basal cell tumors commonly occur as solitary nodules. They can be sessile or pedunculated, firm, and well demarcated from the underlying tissues. These tumors frequently are pigmented, contain cystic spaces, and occasionally are ulcerated (in cats). Basal cell tumors tend to be found more frequently on the head, neck, and shoulder of the dog. They can be found almost anywhere in the cat, in which they represent the most common skin tumor.

Cytology

Cells may be arranged in cords or palisades. "Palisading" clusters and uniform nuclei generally are seen on cytologic examination. The cells usually appear malignant on cytologic and histopathologic examination.

Epidemiology and Biologic Behavior

Basal cell tumors are common in older dogs and cats. Cocker spaniels and poodles may be at increased risk for these tumors. The tumors usually are benign and may have been present from months to years before diagnosis. However, when these tumors are identified histologically as basal cell carcinoma, this is generally a reliable diagnosis, and their behavior must be considered very aggressive.

Treatment

Wide surgical excision is the treatment of choice for basal cell tumors. Complete excision is curative. Nonresectable or invasive tumors can be treated successfully with radiation therapy and/or chemotherapy (see Table 30-7).

Ceruminous Gland Tumors

Origin and Etiology

Ceruminous gland adenomas and adenocarcinomas originate from the epithelium of the ceruminous glands in the ear canal.

Description

They are usually brown tumors associated with cerumen production, which may resemble chronic otitis. Ceruminous gland adenomas are small, pedunculated masses that frequently are located near the tympanic membrane and extend exteriorly. Adenocarcinomas

are similar to adenomas; however, they are frequently invasive.

Cytology

Cytologic examination reveals mature or immature (ceruminous gland adenocarcinoma) secretory cells with epithelial characteristics.

Epidemiology and Biologic Behavior

This is the most common external ear tumor in older dogs and cats but appears to be more common in cats.

Treatment

Total ear canal ablation may be necessary to completely excise these tumors (see Chapter 60). Surgical removal may be sufficient in animals with ceruminous gland adenomas; however, external beam irradiation is highly recommended for dogs and cats with ceruminous gland adenocarcinomas with incomplete resection after an aggressive ear canal ablation and for recurrent or non-excisable adenomas. Chemotherapy also may be considered for patients with incomplete tumor resection or metastases using protocols that contain cisplatin, carboplatin, mitoxantrone, and doxorubicin (see Table 30-7 for dosages).

Squamous Cell Carcinoma

Origin and Etiology

Squamous cell carcinoma may occur secondary to ultraviolet light exposure in cats and dogs with hypopigmented areas. It originates from stratified squamous epithelium. The cell of origin is the keratinocyte.

Description

These tumors frequently appear as ulcerated, necrotic, non-healing lesions. Common sites in dogs include the ventral abdomen, digits (especially nail bed), limbs, scrotum, lips, and nose. In the cat, they include the ear pinnae, lips, nose, and eyelids. Proliferative tumors may resemble a red, firm plaque or a cauliflower-like lesion. Digital squamous cell carcinoma can be proliferative, ulcerative, locally aggressive, and erosive. It also can appear as a non-healing wound. Multiple nail bed squamous cell carcinomas have been observed in black dogs.

Cytology

These epithelial cells are polygonal and may keratinize as they mature. Typical epithelial cells mixed with keratinizing cells frequently are noted. Aging squamous epithelial cells tend to be more angular or polyhedral, with a pyknotic nucleus and bluer cytoplasm. Abundant neutrophils and other inflammatory cells frequently are observed.

Epidemiology and Biologic Behavior

These tumors occur more frequently in cats, especially in white cats or in those with hypopigmented areas that are more likely to be exposed to sunlight, especially ear tips and nose. Dogs have an increased frequency of these tumors in the ventral abdomen (especially), trunk, scrotum, and lips. They are locally invasive with late metastases to the local lymph nodes and lungs.

Treatment

Perform complete surgical excision for squamous cell carcinomas if they are in an easily accessible location. Perform complete pinna resection for tumors of the ear (see Chapter 60) and digital amputation for squamous cell carcinoma of the digit (see Chapter 114). Consider radiation therapy and photodynamic therapy for dogs and cats with non-resectable or incompletely excised squamous cell carcinomas. Retinoids may be considered for those animals with preneoplastic lesions. Consider chemotherapy for non-resectable or metastatic tumors, using cisplatin, carboplatin, bleomycin, mitoxantrone, and doxorubicin (see Chapter 26, Table 30-7 for dosages).

Anal Sac or Apocrine Gland Adenocarcinoma

Origin and Etiology

Apocrine gland adenocarcinomas are derived from the apocrine glands that secrete into the anal sac.

Description

These tumors can vary from very small masses that can be located only after careful rectal and perirectal palpation to large masses protruding from the rectum. They may cause ulceration of the overlying skin.

Cytology

Cytologic examination reveals large cells with abundant cytoplasm and eccentric round nuclei.

Epidemiology and Biologic Behavior

Apocrine gland adenocarcinomas are most commonly found in older female dogs. A paraneoplastic syndrome of hypercalcemia is frequently associated with these tumors (see Chapter 32). Metastases are common (90% of cases) and most frequently involve to the regional (i.e., iliac) lymph nodes.

Treatment

Surgical excision offers the best option for a cure. Chemotherapy also may be considered, using carboplatin or mitoxantrone (see Table 30-7). Hypercalcemia generally resolves after remission of this tumor.

Intracutaneous Cornifying Epithelioma (Keratoacanthoma)

Origin and Etiology

This tumor is derived from the superficial epithelium between hair follicles.

Description

Intracutaneous cornifying epitheliomas may be located on the skin of the neck, the dorsal thorax, the legs, and occasionally on the ventral abdomen. A toothpaste-like material may be expressed from these masses.

Cytology

Cytologic evaluation may reveal keratin associated with inflammatory cells.

Epidemiology and Biologic Behavior

These are benign tumors that can occur in a solitary form in many breeds of dogs and in a multicentric form in Norwegian elkhound and keeshond dogs.

Treatment

Surgical excision is the treatment of choice, although it may not be required. Consider retinoid therapy for the multicentric form (see "Drug Dosage Guidelines Appendix" for dosages).

Dermoid and Epidermal Inclusion Cyst

Origin and Etiology

Dermoid and epidermal inclusion cysts originate from the dermis and epidermis. Epidermal inclusion cysts are frequently secondary to an occluded hair follicle, whereas dermoid cysts may be developmental defects.

Description

Dermoid cysts contain epidermal appendages, hair, and sebaceous and sweat gland secretions, in addition to the keratin that is in the epidermal inclusion cysts. A semisolid material frequently is contained within these cysts.

Cytology

A clear to brown fluid frequently is obtained for cytologic examination.

Epidemiology and Biologic Behavior

These are benign tumors.

Treatment

Surgical excision is the treatment of choice, although it is not always required.

Mesenchymal Neoplasia

Lipomas and Liposarcomas

Origin and Etiology

Lipomas, infiltrative lipomas, and liposarcomas originate from adipocytes or fat cells.

Description

Lipomas can occur either as single or multiple masses and are located over the thorax, sternum, abdomen, and proximal limbs of dogs. These masses are usually subcutaneous; well circumscribed, although not necessarily well encapsulated; fluctuant; soft; and sometimes multilobulated. Infiltrative lipomas infiltrate the deep tissue and are extremely difficult to excise. Liposarcomas are uncommon and usually solitary tumors that tend to be very infiltrative, firm, and poorly circumscribed.

Cytology

Fatty-appearing material or oil droplets usually are present on the slide before staining. Most cells from aspirates of lipomas are "washed off" by the methanol in the fixative. Occasionally, oily material with a few intact adipocytes or fatty cells remains on the slide or cover slip. Cytology of liposarcoma reveals immature mesenchymal cells with vacuoles and round, indented nuclei. Variation in cell size is common, and occasionally, multinucleation is noted.

▼ ***Key Point*** Evaluate all "lipomas" cytologically because they are indistinguishable from mast cell tumors in physical appearance and clinical presentation.

Epidemiology and Biologic Behavior

Lipomas are benign tumors that appear to be more common in older spayed female dogs. They are the most common mesenchymal tumor in the dog but are extremely rare in the cat. Infiltrative lipomas are also benign; however, because of their highly infiltrative nature, they may require extensive surgical excision, including amputation of the affected limb. Liposarcomas are extremely rare tumors in both dogs and cats but are found most often in dogs older than 10 years of age. They are locally invasive and may metastasize to the lungs and/or liver.

Treatment

It may or may not be necessary to remove lipomas, depending on their size, location, and owner preference. If surgery is considered, remove these lipomas while they are small and before they become too large and difficult to resect. Treat infiltrative lipomas with aggressive surgery and radiation therapy if indicated.

Treat all liposarcomas with complete surgical excision and radiation therapy if incomplete margins are obtained.

Fibrosarcoma

Origin and Etiology

These tumors typically originate in the subcutaneous fibrous connective tissue from fibrocytes or fibroblasts. In cats, fibrosarcomas can occur in association with feline sarcoma virus or feline leukemia virus, as vaccine-associated sarcomas (see also Chapter 28), and as sporadic non-retrovirus-induced tumors. Retrovirus-induced fibrosarcomas occur in young cats, are rare, and do not respond to any form of treatment (see Chapter 6). Fibrosarcomas generally occur on the head, trunk, or limbs. There is a strong association between the administration of inactivated vaccines (e.g., feline leukemia virus, rabies, and certain herpes-calici-panleukopenia [FVRCP] vaccines) and subsequent development of soft tissue sarcomas (primarily fibrosarcomas) at the vaccination site.

Description

Fibrosarcomas can occur as solitary or multiple masses. They are frequently firm, lobulated, and infiltrative into underlying tissues.

Cytology

Cytology reveals typical spindle or mesenchymal cells, although cells from these tumors tend not to exfoliate well.

Epidemiology and Biologic Behavior

Most fibrosarcomas occur as solitary tumors in older dogs and cats (i.e., non-retrovirally induced). In contrast, fibrosarcomas associated with feline sarcoma virus tend to occur in younger cats and are multiple. Vaccine-associated fibrosarcomas have an overall prevalence of between 1 and 3 cases per 10,000 vaccinated cats. Other types of fibrosarcoma are very locally invasive but usually metastasize late in their course (less than 10% of cats and dogs with solitary fibrosarcoma have metastases at presentation).

Treatment

Wide and deep surgical excision is recommended, although this can be difficult because the invasive nature of this tumor causes widespread infiltration of adjacent tissues. Histologic evaluation of margins is very important because complete excision is usually curative. Consider amputation in patients with tumors on the extremities.

Response to chemotherapy is variable. Histologically, poorly differentiated fibrosarcomas and fibrosarcomas with giant cells in cats appear to be more responsive to chemotherapy. Chemotherapy could include doxorubicin or mitoxantrone (see Table 30-7 for dosages). Other treatment options include radiation therapy and hyperthermia.

Nerve Sheath Tumors

Neurofibromas, neurofibrosarcomas, schwannomas, and neurilemomas are discussed in Chapter 129.

Hemangiosarcomas

Origin and Etiology

These tumors (also known as malignant hemangioendotheliomas and angiosarcomas) originate from the vascular endothelium.

Description

Hemangiosarcomas generally are solitary masses found on the limbs, flank, or neck. They can occur in the skin and/or subcutaneous tissue. Those in the subcutaneous tissue also may infiltrate the underlying muscle. Hemangiosarcoma must be differentiated from hemangioma.

Cytology

Cytology reveals spindle-shaped or polygonal cells with large nuclei and a lacy chromatin pattern; one or more nucleoli; and a bluish, usually vacuolated cytoplasm. Hemangiosarcomas also can exfoliate cells in sheets similar to those of epithelial cells.

Epidemiology and Biologic Behavior

Hemangiosarcomas of the skin can be either primary or metastatic. Hemangiosarcomas are much more common in dogs, especially German shepherds and golden retrievers, than in cats. The prognoses for these tumors are variable depending on location. Those patients in which the tumor is confined to the dermis have an excellent prognosis, whereas subcutaneous tumors have a poor prognosis, especially if there is muscular involvement.

Treatment

Perform complete surgical excision when feasible. Chemotherapy probably is not necessary for those tumors involving only the dermis, whereas those involving the subcutaneous tissue with or without muscular involvement usually require chemotherapy using doxorubicin.

Hemangiopericytoma

See Chapter 28.

Histiocytoma

Origin and Etiology

The origin of canine cutaneous histiocytomas is the monocyte-macrophage cells in the skin.

Description

These are dermoepidermal tumors frequently located on the head and neck and less commonly on the extremities. They are round, alopecic, and sometimes pink or erythematous, and they occasionally ulcerate. Because of their gross appearance, they also are referred to as "button tumors."

Cytology

Cytology reveals a round cell tumor with a moderate amount of cytoplasm and, possibly, an eccentrically located nucleus. Histiocytomas also tend to be highly pleomorphic and moderately vacuolated. Lymphocytes are abundant. These tumors can appear inflammatory.

Epidemiology and Biologic Behavior

These tumors generally exhibit benign behavior and are found mostly in young dogs (approximately 1 to 3 years). Histiocytomas usually regress spontaneously within 4 to 8 weeks of diagnosis. This tumor does not occur in cats.

Treatment

Observation alone may be appropriate for most histiocytomas because the majority regress with age. Perform surgical excision if this tumor does not regress in a reasonable period; in older dogs, for cosmetic reasons; and finally, to avoid an erroneous diagnosis and further growth of the tumor.

Mast Cell Tumor

Mastocytoma, mast cell sarcoma, and mastocytosis are discussed in Chapter 28.

Extramedullary Plasmacytoma

See Chapter 27.

Cutaneous Lymphoma

Dermal lymphoma, mycosis fungoides, and histiocytic lymphoma are discussed in Chapter 27.

Transmissible Venereal Tumor

Origin and Etiology

Transmissible venereal tumors frequently are transmitted at coitus or through close contact. The cell of origin is considered to be from the monocyte-macrophage system. See also Chapters 88 and 92.

Description

Transmissible venereal tumors tend to occur on the external genitalia and the face and frequently appear as ulcerated, friable, cauliflower-like masses that can be solitary or multiple.

Cytology

Cytology reveals round to ovoid cells with round nuclei and numerous mitotic figures. The cytoplasm is blue or transparent, contains distinct clear vacuoles, and is surrounded by a distinct cell membrane.

Epidemiology and Biologic Behavior

This tumor is transmitted by mucocutaneous transplantation of tumor cells through coitus, licking, biting, and scratching. It occurs more frequently in areas where dogs are free roaming. No breed or sex predilections have been observed. These tumors have a low metastatic potential.

Treatment

Transmissible venereal tumors can be cured with single-agent vincristine chemotherapy, surgery, and/or radiation therapy (see Table 30-7).

Malignant Fibrous Histiocytoma (Extraskeletal Giant Cell Tumors)

See Chapter 28.

Melanocytic Tumors (Melanomas)

Origin and Etiology

Melanomas originate from melanocytes (melanin-producing cells) or melanoblasts, which are cells of neuroectodermal origin.

Description

These are typically brown to black pigmented nodules (although they may be non-pigmented) that occur more frequently on the face, trunk, feet, mucocutaneous regions, and nail beds.

Cytology

Cytologic examination may reveal cells that vary from round to spindle shaped. They frequently contain brown to black granules.

Epidemiology and Biologic Behavior

Melanomas are considerably more common in dogs than in cats. Tumors originating in the skin tend to be benign, whereas tumors of the mucocutaneous regions (e.g., oral cavity and nail beds) tend to be malignant.

Treatment

Local recurrence and distant metastases are very common. Surgery is the treatment of choice. Results of chemotherapy have been unrewarding; however, DTIC, carboplatin, and cisplatin may be the drugs of choice (see Table 30-7 for dosages). Palliative radiation therapy may be another option in some cases.

SUPPLEMENTAL READING

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Section

4 Endocrine and Metabolic Disorders

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Chapter

31 Diseases of the Thyroid Gland

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HYPOTHYROIDISM IN DOGS

Hypothyroidism is a common, multisystemic disease in dogs. Thyroid hormone deficiency affects virtually all body systems, resulting in a wide array of clinical signs. It occurs predominantly in middle-aged, pure-breed dogs, including the golden retriever, Doberman pinscher, Irish setter, boxer, miniature schnauzer, dachshund, and cocker spaniel. There is no strong sex predilection.

Etiology

Primary Hypothyroidism

Primary hypothyroidism, resulting from gradual destruction of the thyroid gland, is responsible for over 95% of cases.

Lymphocytic Thyroiditis

- Immune-mediated destruction
- Circulating antithyroglobulin antibodies in most cases
- Lymphocytic infiltration in the thyroid gland

Idiopathic Thyroid Gland Atrophy

- Replacement of thyroid parenchyma by adipose tissue without inflammation
- Unknown cause
- Not associated with antithyroglobulin antibodies

Other Causes

- Uncommon causes of primary hypothyroidism include congenital types (e.g., dyshormonogenesis and thyroid dysgenesis), replacement of thyroid gland parenchyma by nonfunctional neoplastic tissue, surgical thyroidectomy, and radioiodine treatment.

Secondary (Pituitary) Hypothyroidism

Secondary (pituitary) hypothyroidism is caused by impaired secretion of thyroid-stimulating hormone (TSH). This etiology accounts for less than 5% of cases.

- Pituitary tumors: Destruction of normal pituitary thyrotrophs by neoplastic invasion.
- Cystic Rathke pouch: This form occurs in German shepherd pituitary dwarfs and is associated with concurrent hormone deficiencies including growth hormone deficiency, hypoadrenocorticism, and hypogonadism (see also Chapter 36).

Tertiary (Hypothalamic) Hypothyroidism

Tertiary (hypothalamic) hypothyroidism resulting from deficient production or release of thyrotropin-releasing hormone (TRH) has not yet been documented in dogs.

▼ ***Key Point*** The majority of hypothyroid dogs have primary disease due to lymphocytic thyroiditis or atrophy.

Clinical Signs

The clinical signs of hypothyroidism are insidious in onset because of the gradual destruction of the thyroid gland. Signs are diverse and range from mild to severe (Table 31-1).

General Appearance and Behavior

- Weight gain (mild to marked obesity)
- Lethargy, dullness, and exercise intolerance
- Cold intolerance and hypothermia (uncommon)

Integument

- The majority of hypothyroid dogs have dermatologic abnormalities.
- Excessive scaling and dry haircoat are often the earliest changes.
- Excessive shedding.
- Alopecia.
  - Often begins on the tail and neck (areas of friction).
  - May progress to bilaterally symmetric truncal alopecia sparing the head and extremities.
- Cutaneous hyperpigmentation.
- Recurrent otitis externa or pyoderma.
- Myxedema: Thickening of the skin, especially facial, secondary to glycosaminoglycan accumulation, leading to a "tragic" facial expression.
- Pruritus is not present except when associated with secondary pyoderma, seborrhea, or *Malassezia* infection.

Table 31-1. CLINICAL SIGNS AND LABORATORY FINDINGS IN DOGS WITH HYPOTHYROIDISM

Common Findings	Uncommon Findings
Dermatologic Abnormalities	Neuropathy
Seborrhea	Vestibular
Alopecia	Facial
Pyoderma	Generalized
Myxedema	Laryngeal paralysis
Obesity	Myopathy
Lethargy	Megaesophagus
Weakness/exercise intolerance	Central nervous system abnormalities
Low-voltage ECG complexes	Dwarfism
Bradycardia	Reproductive abnormalities (anestrus)
Hypercholesterolemia	Insulin-resistant diabetes mellitus
Nonregenerative anemia	Ocular abnormalities
	Myxedema stupor or coma

ECG, electrocardiographic.

Nervous System and Muscle

- Uncommon finding in hypothyroidism.
- Peripheral neuropathy.
  - Generalized neuropathy can cause weakness, ataxia, and abnormal proprioception.
  - Vestibular neuropathy.
  - Facial neuropathy, often concurrent with vestibular signs.
  - Unilateral forelimb lameness with pain in the glenohumeral joint.
- Megaesophagus is very rare and may occur secondary to myopathy, neuropathy, or concurrent myasthenia gravis.
- Nonspecific weakness and exercise intolerance may be caused by myopathy or mild neuropathy.
- Behavioral abnormalities including aggression have been reported with hypothyroidism.

Cardiovascular System

- Bradycardia, weak apex beat, and weak pulses.
- Decreased amplitude of R wave or first-degree atrioventricular block on electrocardiogram.
- Atrial fibrillation may occur rarely in dogs with hypothyroidism.
- Decreased myocardial contractility (mild and subclinical).

Reproductive System

- No clinically significant effects on male reproduction.
- Anestrus, infertility, and abortion are possible in females.
- Inappropriate galactorrhea in intact females.

Eyes

- Ocular manifestations of hypothyroidism are rare and appear to be associated with hyperlipidemia.
- Corneal lipid deposits.
- Chronic uveitis.

Bleeding Disorders

- Bleeding tendencies are not caused by hypothyroidism.
- Thyroid hormone administration does not increase the von Willebrand factor in dogs with congenital von Willebrand disease.

Congenital Hypothyroidism

- Lethargy, mental dullness, weak nursing, and constipation.
- Disproportionate dwarfism, broad skull, macroglossia, delayed dental eruption, hypothermia, distended abdomen, retention of puppy haircoat, dry skin, and gait abnormalities.
- Some abnormalities (e.g., short stature, osteoarthritis, and impaired mental function) may persist despite treatment.

Myxedema Stupor and Coma

- Most severe and rarest form of hypothyroidism
- Stupor or coma, hypothermia without shivering, bradycardia, hypotension, and hypoventilation, in addition to the more common signs of hypothyroidism
- Hypercholesterolemia, hyponatremia, hypoglycemia, and high creatine kinase level

▼ ***Key Point*** Dogs may develop various clinical signs of hypothyroidism. Although one sign may predominate, cutaneous abnormalities, lethargy, and/or weight gain are present in most cases.

Diagnosis

Because of the diverse clinical signs and difficulty in interpreting thyroid function tests, hypothyroidism is often diagnosed inappropriately.

▼ ***Key Point*** Many non-thyroidal factors can influence thyroid function tests, resulting in low serum thyroid hormone concentrations in euthyroid dogs.

Diagnosis is dependent on both compatible clinical signs and abnormal thyroid function tests, not either alone.

Screening Laboratory Tests

- Complete blood count shows normocytic, normochromic anemia in 30% of cases.
- Serum biochemical analysis shows hypercholesterolemia in 75% of cases. Hypertriglyceridemia is also common.

Basal Total Thyroid Hormone Concentration (T_4 and T_3)

- Normal serum thyroxine (T_4) concentration infrequently occurs in the hypothyroid dog.
- Serum T_4 is in the low-normal range in about 10% of hypothyroid dogs.
- Serum triiodothyronine (T_3) concentration is unreliable in the diagnosis of hypothyroidism since it is often within the reference range in hypothyroid dogs.
- Serum T_4 is often below normal in euthyroid dogs for the following reasons:
  - Normal daily fluctuation can result in low serum T_4 on repeated sampling of normal dogs.
  - Breed differences result in low serum T_4 in greyhounds, deerhounds, Alaskan sled dogs, and probably other breeds.
  - Non-thyroidal illness (e.g., hyperadrenocorticism, renal disease, or neoplasia) causes a decrease in total T_4 and T_3.
  - Administration of various drugs, including glucocorticoids, sulfonamides, anticonvulsants, non-steroidal anti-inflammatory drugs, and radiocontrast agents, lowers serum T_4 and T_3.

▼ ***Key Point*** Low total T_4 concentration is almost always present in hypothyroidism. If total T_4 is normal, hypothyroidism is very unlikely.

Free Thyroxine Concentration

- Free T_4 is the portion of T_4 that is not bound to plasma carrier proteins (normally 0.1% of total T_4).
- Free T_4 is not affected by most non-thyroidal illnesses and drugs.
- Equilibrium dialysis is the only reliable method for measurement of free T_4 in dogs with non-thyroidal illness. Free T_4 by equilibrium dialysis is the most accurate single test for diagnosing hypothyroidism (see the Endocrine Diagnostic Laboratory of the Michigan State University website: www.ahdl.msu.edu).
- Hypothyroid dogs rarely have a normal serum, free T_4 concentration.

Serum Endogenous Canine Thyroid-Stimulating Hormone Concentration

- Serum TSH concentration is increased in most cases of primary hypothyroidism due to loss of negative feedback of T_4 and T_3 on the pituitary gland.
- High serum TSH and low serum T_4 or free T_4 are diagnostic of hypothyroidism.
- Serum TSH concentration is normal in 20% to 40% of hypothyroid dogs.
- Serum TSH concentration may occasionally be increased in euthyroid dogs with non-thyroidal illness.

Thyroid-Stimulating Hormone Stimulation Test

- The most reliable method of confirming the diagnosis of hypothyroidism in dogs is by demonstrating a low resting T_4 that fails to increase following TSH administration.
- Test protocol: Collect blood for measurement of serum T_4 before and 4 hours after IV administration of 100 μg human recombinant TSH.
- Human recombinant TSH is very expensive, making this test impractical in most cases. Use should be reserved for cases in which the diagnosis cannot be made by measurement of baseline serum hormones.

Thyrotropin-Releasing Hormone Stimulation Test

- TRH administration results in a small and inconsistent increase in serum T_4 and free T_4 in dogs, making this test inadequate for routine use.

Antithyroglobulin Antibodies

- Autoimmune thyroiditis is associated with serum antibodies directed against thyroglobulin.

- Antithyroglobulin antibodies can be present in euthyroid dogs, and they do not indicate hypothyroidism.
- This assay may be useful to identify dogs affected with autoimmune thyroid disease prior to development of hypothyroidism to help plan breeding, but it is not clear if the antibodies predict hypothyroidism in the future.

Thyroid Hormone Autoantibodies

- Antibodies occasionally form against T_3 and T_4 that interfere with radioimmunoassay of these hormones.
- These antibodies cause a false increase in T_3 or T_4 in most assays, with apparent elevation of the hormone into the normal or hyperthyroid range.
- Dogs with thyroid hormone autoantibodies may or may not have signs of hypothyroidism.
- Measurement of free T_4 by equilibrium dialysis is not affected by T_4 autoantibodies.

▼ ***Key Point*** The most reliable method of confirming a diagnosis of hypothyroidism in a dog with compatible clinical signs is the demonstration of decreased serum total T_4 or free T_4 by equilibrium dialysis combined with elevated serum endogenous TSH.

Treatment

Treat dogs with hypothyroidism with daily administration of thyroid hormone. Response to treatment is usually noted within 1 to 2 weeks with an increase in activity and improvement in attitude. Weight loss and neurologic abnormalities usually begin to resolve within 1 to 4 weeks of initiating treatment, whereas dermatologic changes may require 4 to 6 weeks to improve and months to completely resolve. Failure to respond within 6 to 8 weeks of initiating treatment should prompt reevaluation of the diagnosis and reasons for possible therapeutic failure.

Synthetic L-Thyroxine

Synthetic L-thyroxine (levothyroxine) is the treatment of choice in all cases of hypothyroidism. Synthetic L-triiodothyronine (L-T_3), combinations of synthetic L-T_4 and L-T_3, and desiccated thyroid gland preparations or extracts are not indicated in the treatment of canine hypothyroidism.

- The initial dosage of L-T_4 is 0.022 mg/kg q12h PO. Once-daily treatment at the same dose is usually adequate for resolution of clinical signs and can be used initially or after twice-daily treatment has resulted in a good clinical response.
- Decrease the dosage slightly in dogs over 30 kg.
- Reevaluate after 6 to 8 weeks of treatment by examining for resolution of clinical signs and measuring serum T_4.
- A serum T_4 concentration collected 4 to 6 hours after pill administration should be near the upper limit or slightly above the reference range; T_3 concentration may be low despite normal or high T_4.
- If signs of hyperthyroidism occur, such as polyuria, polydipsia, tachycardia, weight loss, diarrhea, or tachycardia, measure serum T_4 and T_3, stop treatment for 1 to 2 days, and reduce the dosage based on this evaluation.
- Treatment for myxedema stupor and coma consists of IV administration of L-T_4 (0.66 mg/kg), passive warming, judicious fluid therapy, glucocorticoid supplementation, and mechanical ventilation if necessary. The prognosis is guarded.

HYPOTHYROIDISM IN CATS

▼ ***Key Point*** Spontaneous hypothyroidism is extremely uncommon in cats.

Most clinical cases of feline hypothyroidism occur as a rare complication of treatment for hyperthyroidism. Non-iatrogenic feline hypothyroidism has been reported primarily in kittens with dwarfism. Cretinism is the most common cause of endocrine congenital dwarfism in cats (growth hormone deficiency has not been reported in cats). Adult onset spontaneous hypothyroidism has been proven in only one cat.

Etiology

- *Congenital hypothyroidism* is associated with thyroid gland atrophy or defective thyroid hormone biosynthesis. In many kittens, this may go undetected and may result in early death.
- *Primary iatrogenic hypothyroidism* results from surgical removal of thyroid glands or their destruction by radioactive iodine in the treatment of feline hyperthyroidism.

Clinical Signs

Congenital Hypothyroidism

- Disproportionate dwarfism (stunted growth of long bones, enlarged head).
- Lethargy and mental dullness.
- Hypothermia.
- Bradycardia.
- Bilaterally symmetric alopecia does *not* occur.

Primary Iatrogenic Hypothyroidism

- History of treatment for hyperthyroidism.
- Lethargy.
- Seborrhea sicca and dry haircoat.
- Obesity is common.
- Bilaterally symmetric alopecia does *not* occur.

Diagnosis

- Strong index of suspicion based on history and clinical signs.
- Confirmed by finding subnormal resting serum T_4 concentration that fails to increase 4 to 6 hours after IV administration of TSH (see "Hypothyroidism in Dogs").
- Can also be confirmed by finding low serum concentrations of total T_4 and free T_4 (see "Hypothyroidism in Dogs").
- Determination of serum TSH concentration is not generally useful in diagnosis of hypothyroidism in cats, inasmuch as most available TSH assays do not measure feline TSH.

Treatment

- Treatment for congenital cretinism is not very rewarding because growth abnormalities and mental deficiencies may not be reversible.
- Treat iatrogenic hypothyroidism with daily T_4 supplementation using an initial dosage of T_4 of 0.01 to 0.02 mg/kg/day (10–20 µg/kg/day) PO.
- Adjust the dosage based on resolution of clinical signs and on postpill serum T_4 concentrations.

HYPERTHYROIDISM IN CATS

Feline hyperthyroidism, a multisystemic metabolic disorder resulting from excessive circulating concentrations of thyroid hormone, is the most common endocrinopathy of middle-aged and older cats. First described in 1979, hyperthyroidism has emerged as the most common endocrine disorder of this species and a disease frequently diagnosed in small animal practice. There is no breed or sex predilection. The clinical signs of the disease are the result of increased basal metabolic rate and the body's inability to meet excessive metabolic demands.

Etiology

Adenomatous Hyperplasia

Functional adenomatous hyperplasia of one or both lobes of the thyroid gland, causing high circulating concentrations of T_4 and T_3, is the most common cause. Both lobes are enlarged in approximately 70% of cases. The pathogenesis of this adenomatous hyperplasia is unknown.

- In cats, the disease most closely resembles toxic nodular goiter in human patients, which is caused by hyperfunctioning adenomatous thyroid nodules.
- Hyperthyroidism in cats is not analogous to the autoimmune disorder Graves disease, the most common form of hyperthyroidism in human patients.

Thyroid Carcinoma

Thyroid carcinoma occurs in only 1% to 2% of cats with hyperthyroidism.

Clinical Signs

All of the clinical manifestations of hyperthyroidism are due to the effects of excessive thyroid hormone. These effects are generally stimulatory. They cause increased heat production and heightened protein, carbohydrate, and lipid metabolism in virtually all body systems and tissues. Clinical signs can range from mild to severe (Table 31-2).

▼ ***Key Point*** The classic clinical signs of feline hyperthyroidism include weight loss despite an increase in appetite.

General Appearance and Behavior

- Weight loss.
- Restlessness, hyperexcitability, and difficulty in examining.
- Impaired stress tolerance. The hyperthyroid cat is prone to respiratory distress and weakness when stressed. Cardiac arrhythmias or arrest can occur in extreme cases.
- Unkempt haircoat, excessive shedding, and matting of hair, especially in long-haired cats.

Thyroid Gland

- Enlargement of one or both lobes of the thyroid gland is palpable in >90% of cats with hyperthyroidism. To palpate the thyroid gland, extend the cat's neck and tilt the head back slightly. Using the

Table 31-2. FREQUENCY OF HISTORICAL AND CLINICAL SIGNS IN CATS WITH HYPERTHYROIDISM

Clinical Finding	Percentage of Cats
Weight loss	95–98
Hyperactivity/difficult to examine	70–80
Polyphagia	65–75
Tachycardia	55–65
Polyuria/polydipsia	45–55
Cardiac murmur	20–55
Vomiting	33–50
Diarrhea	30–45
Increased fecal volume	10–30
Decreased appetite	20–30
Lethargy	15–25
Polypnea (panting)	15–30
Muscle weakness	15–20
Muscle tremor	15–30
Congestive heart failure	10–15
Dyspnea	10–15

thumb and forefinger, gently palpate the tissues on either side of the trachea, starting at the larynx and moving caudally to the thoracic inlet (see Fig. 1-3 in Chapter 1).
- A small percentage of cats have intrathoracic thyroid nodules that evade palpation.

Nervous System and Muscle

- Hyperactivity
- Weakness and increased fatigability

Gastrointestinal System

- Increased appetite is due to increased energy utilization and high metabolic demands. The increased caloric intake observed in most cats is, however, inadequate to compensate for increased demand.
- Approximately 5% of cats with hyperthyroidism experience periods of decreased appetite. The cause is unclear but usually is associated with concurrent disease (e.g., renal or cardiac disease).
- Vomiting, often secondary to rapid polyphagia, occurs shortly after eating.
- Diarrhea and increased volume and frequency of defecation are due to polyphagia, intestinal hypermotility, and decreased fat absorption.

Renal System

- Polyuria and polydipsia. Thyroid hormones may have a diuretic action. Alternatively, a hypothalamic disturbance associated with hyperthyroidism might cause primary polydipsia, with secondary renal medullary solute washout.

Respiratory System

- Dyspnea, panting, and hyperventilation at rest are attributable to any of the following: respiratory muscle weakness, increased tissue carbon dioxide production and inability to meet tissue oxygen demand, and/or congestive heart failure (CHF) (see subsequent discussion).

Cardiovascular System

- Tachycardia, systolic murmurs, gallop rhythm, and arrhythmias may be attributable to the catecholamine-like effects of thyroid hormone and increased tissue oxygen demand, or they may be associated with other signs of CHF secondary to hyperthyroidism.
- Signs of CHF (e.g., dyspnea, muffled heart sounds, tachycardia, and ascites) may develop, especially in cats with severe or advanced hyperthyroidism. Electrocardiographic and echocardiographic findings are often suggestive of hypertrophic or, much less commonly, dilative cardiomyopathy. Hyperthyroidism results in a high-output cardiac state in which vascular resistance is low and cardiac output is high due to increased tissue metabolism and oxygen requirements. The cardiac compensatory mechanisms are dilation (in response to volume overload) and hypertrophy (in response to dilation). There also appears to be a direct myopathic effect of thyroid hormones on cardiac muscle.

Apathetic Hyperthyroidism

- In about 5% of cats with hyperthyroidism, the predominant clinical signs are depression, lethargy, anorexia, and weakness rather than the hyperexcitability, restlessness, and polyphagia observed in 95% of cases.
- Weight loss and cardiac abnormalities are common findings in these cats.
- In most of these cats, a severe concurrent disease is also present, including CHF, renal failure, or cancer.

Diagnosis

- The diagnosis of hyperthyroidism in cats is made on the basis of clinical signs, palpable goiter (thyroid enlargement), screening laboratory testing, and, except in cases of occult hyperthyroidism (see subsequent discussion), high serum T_4 concentrations. Serum T_3 concentrations are less useful in the diagnosis of hyperthyroidism in cats.
- The differential diagnoses for cats with clinical signs of hyperthyroidism include diabetes mellitus, renal disease, gastrointestinal lymphoma, and chronic inflammatory bowel disease. Cardiac manifestations of hyperthyroidism can be confused with cardiomyopathy. Hyperthyroid cats with high serum liver enzyme levels can be difficult to distinguish from cats with primary liver disease.

Screening Laboratory Tests

Complete Blood Count

- Mature leukocytosis and eosinopenia are common findings.
- A slight elevation in packed cell volume is found in more than half of cats with hyperthyroidism. Macrocytic erythrocytes may cause an elevated mean corpuscular volume.

Serum Biochemical Analysis

- High alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase activity occur singly or in combination in 50% to 75% of cats with hyperthyroidism.

Urinalysis

- Urinalysis is generally unremarkable but useful in differentiating other diseases with similar clinical signs such as diabetes mellitus. Urine specific gravity is variable.

Radiography and Cardiac Ultrasonography

- In approximately 50% of cats, there is evidence of mild to severe cardiac enlargement on thoracic radiography.
- Common echocardiographic abnormalities include left ventricular hypertrophy (approximately 70% of cases), left atrial and ventricular dilation (70% and 45%, respectively), and interventricular septum hypertrophy (4%). Myocardial hypercontractility, as evidenced by an increased shortening fraction and velocity of circumferential fiber shortening, is also common.
- These cardiovascular changes resolve or improve following successful treatment of the hyperthyroidism.

Basal Total Thyroid Hormone Concentration (T_4 and T_3)

The diagnosis of hyperthyroidism is confirmed by demonstrating increased production of the thyroid hormones. In cats, T_4 is the main secretory product of the thyroid gland. T_3 is 3 to 5 times more potent than T_4, but approximately 60% of circulating T_3 is produced by extrathyroidal 5'-deiodination of T_4. Over 99% of circulating T_4 is protein-bound, while approximately 0.1% is free and metabolically active. Overall control of thyroid hormone production is provided by a negative feedback mechanism of circulating T_4 and T_3 on TRH from the hypothalamus and TSH from the anterior pituitary. In hyperthyroid cats, there is autonomous and excessive secretion of thyroid hormones from the abnormally functioning thyroid gland.

▼ ***Key Point*** High resting serum concentrations of total T_4 and, less reliably, T_3 are the biochemical hallmarks of hyperthyroidism in the majority of cats with the disease.

- Over 30% of cats with hyperthyroidism maintain normal serum T_3 concentration despite elevation in T_4. These cats generally have milder disease; serum T_3 concentration in these cats is expected to increase eventually.
- Most hyperthyroid cats exhibit a clearly high circulating total T_4 concentration. However, a proportion of hyperthyroid cats (approximately 10% of all cases and 40% of cases with mild hyperthyroidism) have serum total T_4 concentration within the reference range. Such values are usually within the middle to high end of the reference range. Thus hyperthyroidism cannot always be excluded in cats by demonstration of a single total T_4 concentration within the normal reference range.
- Thyroid hormone concentrations in some cats are subject to a degree of fluctuation. In cats with mild disease, serum T_4 concentrations have been shown to fluctuate in and out of the normal range. The finding of a single normal serum T_4 concentration in a cat with clinical signs of hyperthyroidism does not rule out the diagnosis of this disease, especially if an enlarged thyroid can be palpated.
- Severe concurrent, systemic non-thyroidal illness (e.g., primary hepatic disease, renal disease, or diabetes mellitus) can cause serum thyroid hormone concentrations to decrease. Because non-thyroidal illness is expected to reduce the serum thyroid hormone concentration into the subnormal range in a euthyroid cat, concomitant hyperthyroidism should be suspected in any middle-aged to old cat with high-normal serum T_4 concentration in the face of severe non-thyroidal illness, especially if clinical signs of hyperthyroidism are also present.

▼ ***Key Point*** In most cats with hyperthyroidism, the diagnosis can be confirmed by a high serum total T_4 concentration alone.

Free T_4 Concentration

- Determination of the serum concentration of free T_4 by dialysis (Free T_4 kit, Nichols Institute) is useful in the diagnosis of hyperthyroidism in cats, especially in those cats with clinical signs of the disease and a palpable thyroid nodule in which the basal total T_4 value is normal or only slightly elevated.
- Serum free and total T_4 concentrations are highly correlated in hyperthyroidism. However, serum free T_4 concentrations, as measured by equilibrium dialysis, are more consistently (over 98% of cases) elevated in hyperthyroid cats. More significantly, serum free T_4 concentrations are high in 95% of hyperthyroid cats with total T_4 values in the normal reference range as a result of mild disease and hormone fluctuation or of the suppressive effect of concurrent non-thyroidal illness.
- Euthyroid cats with non-thyroidal disease usually maintain normal free T_4 concentrations; however, a false-positive elevation of free T_4 concentration also occurs in approximately 10% of these sick cats without hyperthyroidism. Based on reported clinical studies, the following recommendations can be made regarding the use of free T_4 as a diagnostic test to identify cats with hyperthyroidism:
  - In all hyperthyroid cats with a high serum total T_4 concentration, free T_4 concentration is concurrently high and its measurement adds no further diagnostic information. Given the expense of free T_4 measurement coupled with the necessity for interpretation with a total T_4 estimation, and the high prevalence of high total T_4 values in hyperthyroid cats, it is more cost effective to initially measure total T_4 concentration alone. If a diagnosis is not confirmed, consideration can be given to measurement of the corresponding free T_4 concentration.

- Always measure free T_4 in conjunction with a total T_4 determination. In cats with occult hyperthyroidism, the total T_4 concentration is expected to be in the middle to high end of the reference range limits (i.e., 2.5–4.0 µg/dl; 25–50 nmol/L).
- Never use free T_4 as the sole screening test for hyperthyroidism because high free T_4 concentrations also occasionally are found in cats with non-thyroidal diseases that do not have hyperthyroidism. The reason for high free T_4 concentrations in these cats with non-thyroidal disease is unclear, but almost all of these cats have serum total T_4 concentrations that are below or at the low end of the reference range.
- Free T_4 by dialysis is a useful diagnostic test for hyperthyroidism and eliminates the need for provocative testing (T_3 suppression test or TRH stimulation test; see the following section) in most cases. However, in order to interpret the test result, the cat *must* have clinical signs (i.e., weight loss despite a good appetite) and physical exam findings (i.e., a palpable thyroid nodule) that are consistent with hyperthyroidism.
- If a high free T_4 concentration is found in a cat without classic clinical signs of hyperthyroidism, and especially if a thyroid nodule cannot be palpated, repeat the tests (total and free T_4 determinations) in 2 to 4 weeks. Alternatively, use one of the provocative tests (T_3 suppression or TRH stimulation; see the following section) to confirm hyperthyroidism.

Provocative Thyroid Tests

In the majority of hyperthyroid cats with reference-range total T_4 concentration, identification of concurrent disease, repeat total T_4 analysis, or simultaneous measurement of free T_4 allows confirmation of the diagnosis. Further diagnostic tests are rarely required. However, dynamic thyroid function tests have been recommended in the past as helpful in confirming a diagnosis of hyperthyroidism. Currently, the T_3 suppression or TRH stimulation tests should only considered in cats with clinical signs suggestive of hyperthyroidism when repeated total T_4 concentration remains within the reference range or free T_4 analysis is unavailable or inconclusive.

Triiodothyronine Suppression Test

Administration of exogenous T_3 causes suppression of pituitary TSH secretion and a subsequent drop in thyroidal T_4 secretion in the normal cat. In cats with autonomously hyperfunctioning thyroid adenomas, TSH secretion has been chronically suppressed and exogenous T_3 administration does not appreciably affect the pituitary-thyroid axis. The protocol for the T_3 suppression test is as follows:

- Collect a blood sample for T_4 and T_3 measurements.
- Administer oral T_3 (liothyronine: Cytomel, SmithKline Beecham) starting the next morning at a dosage of 25 µg/cat q8h for 2 days.
- On the morning of the third day, give the cat a final 25-µg dose of T_3 before returning to the veterinarian for blood sampling.
- Measure serum T_4 and T_3 in the same assay run on both basal and post-exogenous T_3 blood samples.
- In cats with hyperthyroidism, minimal, if any, suppression of serum T_4 occurs. A rise in serum T_3 concentration confirms owner compliance in administering the drug to the cat.

Thyrotropin-Releasing Hormone Stimulation Test

Administration of TRH stimulates pituitary TSH secretion and produces a subsequent rise in thyroidal T_4 secretion in the normal cat. In cats with autonomously hyperfunctioning thyroid adenomas, TSH secretion has been chronically suppressed and exogenous TRH administration does not appreciably affect the pituitary-thyroid axis. The protocol for the TRH stimulation test is as follows:

- Collect a blood sample for serum T_4 measurement.
- Administer TRH at a dosage of 0.1 mg/kg IV.
- Collect another blood sample for serum T_4 measurement 4 hours later.
- Although the effects are transient, TRH administration causes hypersalivation, tachypnea, and vomiting in most cats. However, this test is less time consuming than the T_3 suppression test and does not rely on owner compliance.
- Interpretation:
  - Administration of TRH to normal cats and cats with non-thyroidal disease causes a twofold or greater increase in serum T_4 concentrations at 4 hours.
  - In contrast, serum T_4 concentration in cats with mild hyperthyroidism generally increases little, if at all, after administration of TRH.

Thyroid Radionuclide Uptake and Imaging

- Increased thyroidal uptake of radioiodine after the administration of a small tracer dose of radionuclide is a characteristic finding in cats with hyperthyroidism. However, the relative lack of nuclear medicine facilities available to small animal practitioners limits the usefulness of this diagnostic modality to referral hospitals.
- Thyroid imaging (scanning) can be performed using either radioiodine or pertechnetate and is useful in delineating hyperfunctioning thyroid tissue. This technique is a helpful adjunct in the diagnosis of hyperthyroidism in cats and provides valuable preoperative information. The disadvantages are that nuclear medicine facilities are required and that the cat generally needs to be sedated for the procedure.

Treatment

Treatment of hyperthyroidism in cats is usually rewarding and is aimed at reducing circulating concentrations of thyroid hormone. This is accomplished by blocking production of thyroid hormone from the thyroid gland or by destroying or removing hyperfunctioning adenomatous thyroid tissue. Antithyroid drugs can be used effectively to block thyroid hormone synthesis but are not curative. Adenomatous thyroid tissue can be removed by surgical thyroidectomy or destroyed by radioiodine therapy. On return to euthyroidism, the clinical manifestations of thyrotoxicosis, including cardiac abnormalities, generally resolve completely.

▼ ***Key Point*** Azotemia may occur following treatment of hyperthyroidism by any method due to normalization of renal blood flow.

Medical Management

Medical management is a practical treatment option for many cats. It requires no special facilities and is readily available. There is a rapid return to euthyroidism (usually within 2 weeks), which may be desirable in severely affected cases. Anesthesia is avoided as are the peri-operative and postoperative complications associated with surgical thyroidectomy and the hospitalization necessary after radioactive iodine administration. However, medical management is not curative, is highly dependent on adequate owner and cat compliance, and requires regular biochemical monitoring to ensure the efficacy of treatment. In addition, adverse effects are relatively common. It is therefore often reserved for cats of advanced age, for those with concurrent diseases, and for when owners refuse, or facilities are not available for, either surgery or radioactive iodine.

Antithyroid Drugs

- Methimazole (Tapazole, Lilly) and propylthiouracil (PTU) are the two thiourylene antithyroid drugs available in the United States. Both are supplied in oral tablet form and act by inhibiting synthesis of thyroid hormones.
- Carbimazole, a third thiourylene antithyroid drug available in many European countries and Japan, is not available in the United States. After oral administration to cats, carbimazole has been shown to be immediately converted into methimazole.
- Do not use PTU in cats. This drug produces a high incidence of mild to serious adverse effects, including anorexia, vomiting, lethargy, immune-mediated hemolytic anemia, thrombocytopenia, and development of serum antinuclear antibodies in both normal and hyperthyroid cats.
- Methimazole is better tolerated and safer than PTU in the cat and can be considered the antithyroid drug of choice for hyperthyroidism.
- Initially, administer methimazole at a dose of 2.5 to 10 mg/day PO, depending on the severity of the hyperthyroid state. Ideally, the methimazole dose is divided q8h to q12h. Some cats have been effectively managed by giving methimazole once a day. However, results of one study suggested that once-daily administration of methimazole was not as effective as twice-daily administration in cats with hyperthyroidism.
- While antithyroid dugs are routinely administered orally, compliance can be problematic, particularly in fractious cats or in cats that vomit or develop inappetence on the drug. Recent studies have shown that methimazole when applied transdermally to the inner pinnae of the ear is effective in most hyperthyroid cats and is associated with fewer gastrointestinal side effects. Therefore, the use of transdermal methimazole is a viable alternative in the treatment of hyperthyroidism in cats in which the oral route is not efficacious or feasible.
- Perform complete blood counts, including platelet count, and serum T_4 determinations every 2 weeks during the first 3 months of drug therapy.
- Increase or decrease the daily drug dosage by 2.5 to 5 mg and continue further testing at 2- to 3-week intervals until the lowest daily dose is found that effectively maintains serum T_4 concentrations within the low-normal range.
- Mild clinical side effects associated with methimazole treatment are relatively common (approximately 15% of cats) and include anorexia, vomiting, and lethargy. Self-induced excoriations of the face and neck also may develop in a few cats within the first few weeks of therapy.
- A variety of hematologic abnormalities may develop in cats during treatment with methimazole. Those abnormalities that do not appear to be associated with any adverse clinical effects include eosinophilia, lymphocytosis, and transient leukopenia with normal differential count. More serious hematologic reactions that develop in a few cats treated with methimazole include severe thrombocytopenia, agranulocytosis (panleukopenia), and hemolytic anemia.
- If serious hematologic reactions develop during methimazole therapy, stop the drug and give supportive care. These adverse reactions should resolve within 5 days after the methimazole is withdrawn. Most life-threatening side effects usually develop quickly after beginning the drug again. If they occur, consider alternative therapy with surgery or radioiodine.
- Long-term antithyroid drug treatment has some advantages over surgery and radioiodine, including the absence of certain complications such as postsurgical hypoparathyroidism. Unlike surgery and radioiodine, antithyroid drug therapy requires no advanced skills, training, or special licensing and is a practical treatment option for most practitioners.

▼ ***Key Point*** Daily antithyroid drugs can block T_4 secretion and control hyperthyroidism, but surgery or radioiodine can cure the disorder.

Propranolol and Atenolol

- Propranolol and atenolol are the most frequently used β-adrenoceptor blocking agents in hyperthyroid cats. These drugs have no discernable effect on serum thyroid hormone concentrations but are used to symptomatically control the tachycardia, tachypnea, hypertension, and hyperexcitability associated with hyperthyroidism.
- Propranolol is a non-selective β-adrenoceptor blocker and is contraindicated in cats with pre-existing uncontrolled asthma or congestive cardiac failure. Administer the drug at a dose of 2.5 to 5 mg PO q8h.
- Atenolol is often preferred because it is a selective β_1-adrenoceptor blocking agent. Administer the drug at a dose of 6.25 to 12.5 mg PO q12–24h.

Cholecystographic Agents

Cholecystographic agents are a feasible alternative to methimazole for medical treatment of some cats with hyperthyroidism, particularly those that cannot tolerate methimazole and are not candidates for surgery or radiotherapy.

A number of oral cholecystographic agents have been used to decrease T_4 production, an effect presumably mediated by the drugs' effect to inhibit peripheral T_4 to T_3 conversion. In the United States, both ipodate and iopanoic acid have been discontinued by the manufacturer and are no longer available. Iopanoic acid is still available from some compounding pharmacies, but the drug is still of limited availability. Diatrizoate (brand name, Hypaque) is still available for use in the United States and also has shown promise as a viable replacement.

- The drugs' mechanism of action is inhibition of outer-ring 5′-deiodination of T_4 to the more active T_3, as well as some direct inhibitory effects on thyroid hormone secretion. Therefore, use of these drugs induces a rapid, marked decrease in serum T_3 concentration. Serum T_4 concentration usually does not change.
- The initial dosage of iopanoic acid or diatrizoate is 100 mg PO q24h. Monitor the drug's effects on clinical signs, body weight, heart rate, and serum T_3 concentrations. Increase the dosage of these drugs to 150 to 200 mg/day if serum T_3 remains high or a good clinical response is not observed at the lower dose.
- Adverse clinical signs attributable to iopanoic acid or diatrizoate treatment are uncommon.
- Cats with severe hyperthyroidism are less likely to respond to these drugs than are cats with mild or moderate disease. Cats in which serum T_3 concentration does not normalize are unlikely to have an adequate improvement in clinical signs.

Surgical Thyroidectomy

See under "Thyroidectomy" for a detailed description of this surgery.

- Usually successful.
- Preoperative thyroid nuclear imaging is useful if available.
- The modified extracapsular method is most effective for removal of all diseased tissue.

▼ ***Key Point*** Use methimazole for 2 to 4 weeks preoperatively (if possible) to restore euthyroidism and to reduce the anesthetic and surgical risks, especially in cats with severe hyperthyroidism.

- Monitor for postoperative hypocalcemia secondary to removal or damage of the parathyroid glands (only a risk following bilateral thyroidectomy).
- Postoperative laryngeal paralysis due to recurrent laryngeal nerve damage occurs uncommonly.
- After bilateral thyroidectomy, serum T_4 concentration is often below normal but thyroid hormone supplementation is rarely needed longer than 2 to 3 months. Permanent, surgically induced hypothyroidism in cats is rare. Long-term T_4 replacement is needed only in those cats that develop clinical signs of hypothyroidism (e.g., lethargy, weight gain, and dermatopathy) or azotemia with persistently low serum T_4 concentrations.

Radioactive Iodine Therapy

- Treatment with radioactive iodine (^{131}I) is simple, safe, and effective and is the best treatment for most hyperthyroid cats.
- No medical preparation with antithyroid drugs is needed.
- ^{131}I can be administered IV or orally, but the subcutaneous route is preferred. It is equally effective, not associated with gastrointestinal side effects, safer for personnel, and can be performed under light sedation if necessary, thereby avoiding anesthesia.
- There are few complications of ^{131}I therapy. Persistent hyperthyroidism, more common in severely affected cats with large goiters and extreme elevations in serum total T_4 concentration, can be successfully managed with a repeat injection. Permanent hypothyroidism is rare, as is recurrence after successful treatment, and other side effects are minimal.
- The main disadvantage is the long hospitalization time required (generally 1–2 weeks). Adherence to strict radiation safety regulations is required.
- The long-term prognosis for cats treated with radioiodine is excellent. In the largest study of 534 cats,

the median survival time was 24 months and 89%, 72%, 52%, and 34% of cats were alive at 1, 2, 3, and 4 years after treatment, respectively.

Effect of Treatment on Renal Function

- Hyperthyroidism is known to increase glomerular filtration rate (GFR), decrease circulating creatinine concentration, and mask underlying renal disease. All treatments for hyperthyroidism have been associated with a decrease in GFR capable of unmasking latent renal disease. Therefore renal dysfunction should always be considered a potential adverse reaction of treatment and assessed if clinical signs develop.
- Predicting those cats in which renal failure is likely to develop is difficult. In the absence of methods for accurately measuring GFR in practice, serum urea and creatinine concentrations and urine specific gravity should be carefully evaluated in individual cases. If any parameter is considered abnormal, then renal failure may develop upon treatment of the hyperthyroidism.
- Antithyroid medication offers the optimum treatment when there is evidence of pre-existing renal disease. If there is no discernible deterioration of renal function once euthyroidism has been achieved medically, other more permanent treatment options (surgery, radioactive iodine) may be considered. If renal function deteriorates, the effects of the drug will dissipate within 48 hours of withdrawal.
- The decision whether to continue treatment for hyperthyroidism depends on which of the two diseases is more severe. Maintenance of a mildly hyperthyroid state may be beneficial in some cases. However, preliminary studies suggest that although there may be an initial effect of treatment on GFR, this is not a progressive problem in the long term. However, avoidance of hypothyroidism is important because it may have its own detrimental effect on GFR.

THYROID NEOPLASIA IN DOGS

Unlike thyroid tumors found in the cat, the majority of thyroid neoplasms in dogs do not secrete excessive thyroid hormone. Less than 20% of these tumors are associated with hyperthyroidism. Because these tumors can destroy normal thyroid parenchyma, hypothyroidism sometimes occurs.

▼ ***Key Point*** Most canine thyroid tumors, unlike feline thyroid tumors, are large, invasive carcinomas.

About 90% of thyroid tumors in dogs are malignant. Local invasion into the larynx; trachea; cervical muscles, vessels, and nerves; and esophagus frequently occurs. Distant metastasis, especially to the lungs, occurs in 60% to 80% of cases. The prognosis associated with most of these tumors is poor. However, early detection and surgical removal of small, non-invasive thyroid carcinomas can result in good survival rates (up to 3 years).

Clinical Signs

See Table 31-3.

Non-thyrotoxic Thyroid Tumors

Clinical signs are related to structural damage to the cervical area and metastatic disease.

- A palpable cervical mass (goiter) is often firm, attached to surrounding soft tissues, and irregular in shape.
- Respiratory distress and cough.
- Vomiting.
- Dysphagia.
- Anorexia.
- Weight loss.

Hyperfunctional Thyroid Tumors

See "Hyperthyroidism in Cats" for an explanation of the pathophysiology of similar signs.

- A palpable cervical mass (goiter) is often firm, attached to surrounding soft tissues, and irregular in shape.
- Polydipsia and polyuria are common.
- Weight loss.
- Polyphagia.
- Heat and stress intolerance.
- Nervousness and hyperexcitability.

Table 31-3. INCIDENCE OF CLINICAL SIGNS IN DOGS WITH THYROID TUMOR

Sign	Percentage of Cases
Non-toxic (Euthyroid or Hypothyroid) Thyroid Tumor	
Goiter (enlarged thyroid gland)	100
Respiratory distress/cough	30
Metastases to lung or lymph nodes	35
Vomiting	10
Dysphagia	10
Anorexia	10
Weight loss	5
Hyperfunctional (hyperthyroid) Thyroid Tumor	
Goiter	100
Polydipsia and polyuria	95
Weight loss	80
Weakness and fatigue	75
Polyphagia	70
Heat intolerance	60
Nervousness	50
Hyperdefecation/diarrhea	30
Tremor	20

- Diarrhea and increased volume of feces.
- Tremors.

▼ ***Key Point*** In dogs, most thyroid tumors that result in hyperthyroidism are malignant (carcinoma). Polydipsia and polyuria are very prominent clinical signs.

Diagnosis

Consider thyroid carcinoma in any dog with a ventral cervical mass.

- Thyroid gland biopsy is mandatory for the diagnosis of thyroid carcinoma.
- Screening laboratory tests are indicated.
- Thoracic radiography is an essential part of the diagnostic workup because pulmonary metastasis occurs commonly.
- Serum thyroid hormone concentrations are indicated when clinical signs suggest hyperthyroidism or hypothyroidism.
- Thyroid imaging (thyroid scan) can be useful in determining the size and location of neoplastic thyroid tissue.

Treatment

The prognosis for a dog with thyroid carcinoma depends on the developmental stage, size, and palpable characteristics of the tumor. Small, movable tumors that have not metastasized can often be cured by surgical excision. Dogs with bilateral tumors are more likely to have metastasis than those with unilateral tumors. External beam radiation therapy is effective in controlling many tumors that are not surgically resectable. For dogs with very invasive or metastatic tumors, the prognosis is usually poor and treatment is rarely curative regardless of the modality.

Surgery

See under "Thyroidectomy."

- Thyroidectomy can be a difficult procedure.
- Complete excision of a thyroid carcinoma is uncommon unless the tumor is small and not locally invasive (moveable on palpation).

Chemotherapy

- Doxorubicin 30 mg/m^2 body surface area (for a conversion table, see Chapter 26), IV, every 3 weeks for five treatments.
- A potentially limiting long-term side effect of doxorubicin is congestive cardiomyopathy.
- Combination treatment with doxorubicin and cyclophosphamide has been used with varying degrees of success and with less cardiac toxicity.

External Beam (Cobalt) Irradiation

- Useful therapy for thyroid carcinoma.
- Consider a combination of surgical debulking followed by external irradiation in those cases in which most of the tumor was resected.
- External beam irradiation is effective in controlling unresectable thyroid carcinomas, with median survival times exceeding 2 years.

Radioactive Iodine

- Administration of large doses of ^{131}I (10–100 mCi) can temporarily control hyperfunctional thyroid carcinoma and can lead to palliation of clinical signs of hyperthyroidism. However, this treatment will most likely fail to control metastatic growth.
- Radioiodine does not work well in dogs with nontoxic thyroid tumors that have a low degree of radioiodine uptake.

THYROIDECTOMY

Thyroidectomy in dogs and cats is usually performed to treat neoplasia of the gland. Biopsy is occasionally performed but not as commonly as the complete removal of one or both lobes. A thorough understanding of thyroid anatomy and physiology is necessary before performing surgery.

Anatomy

Thyroid

- The thyroid gland consists of two lobes located just caudal to the larynx.
- The normal gland is a pale tan color and approximately 1 to 1.5 cm in length.
- Blood supply is via the cranial thyroid artery (branch of the common carotid artery) (Fig. 31-1).

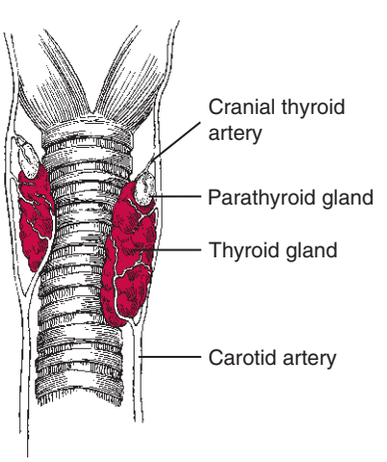

Figure 31-1. Gross appearance of bilateral thyroid tumors in a cat.

- The caudal thyroid artery is usually absent in cats. Venous drainage is via cranial and caudal thyroid veins.
- The thyroid gland has a distinct but thin capsule.

Parathyroid

- Two parathyroid glands are associated with each thyroid lobe: one intracapsular (internal) and one extracapsular (external). The extracapsular parathyroid gland is usually located at the cranial pole of the thyroid.
- The parathyroid gland is usually off-white and can be confused with fat; the gland is usually 2 to 5 mm in length.
- Blood supply to the parathyroid glands is also from the cranial thyroid artery.
- Only one functional parathyroid gland is required for normocalcemia.

Thyroidectomy in the Cat

Preoperative Considerations

- Hyperthyroidism is a multisystemic disease that can be associated with anesthetic and surgical complications.
- In addition to establishing euthyroidism with antithyroid drugs (see earlier in this chapter), correct dehydration preoperatively if necessary.
- Obtain thoracic radiographs to evaluate the heart's size and the presence of any pulmonary problems or mediastinal masses.
- If available, review the thyroid radionuclide scan to determine the extent of the disease (e.g., Is the tumor unilateral or bilateral? Are ectopic tumors present?).
- See Chapter 2 for anesthetic drug dosages and other specifics.
- Premedicate with acepromazine. Avoid anticholinergics such as atropine and glycopyrrolate.
- Induce with propofol IV.
- Maintain anesthesia with isoflurane and oxygen via a cuffed endotracheal tube.
- Closely monitor the electrocardiogram for arrhythmias.
- Have propranolol (Inderal, Wyeth-Ayerst) ready in the event that premature ventricular contractions develop. Dilute to make a solution of 0.1 mg/ml and give 0.01 mg IV slowly (over 3–5 minutes).

Surgical Procedure

Objectives

1. Remove all abnormal thyroid tissue.
2. Maintain meticulous hemostasis.
3. Preserve at least one of the parathyroid glands.
4. Avoid injury to the recurrent laryngeal nerves.

Equipment

- Standard surgical pack
- Bipolar cautery
- Tenotomy scissors
- Gelpi retractors
- Sterile cotton-tipped applicators
- Gelfoam

Technique

1. Place the cat in dorsal recumbency with the front legs tied caudally and the neck slightly hyperextended over a rolled towel.
2. Prepare the ventral cervical region from caudal mandibles to manubrium for aseptic surgery.
3. Incise the skin on the ventral cervical midline from larynx to manubrium.
4. Separate the paired sternohyoideus and sternothyroideus muscles and retract the muscles with self-retaining retractors (Gelpi).
5. Carefully examine both thyroid lobes. Remove the affected lobes. If doubt exists as to involvement of a lobe, remove it because microscopic adenomatous hyperplasia may be present.
6. Attempt to identify the parathyroid glands.
7. Ligate the caudal thyroid vein and grasp the caudal aspect of the capsule.
8. Several techniques can be used to dissect the thyroid lobes (Figs. 31-2 and 31-3), but the modified extracapsular technique is preferred.
   a. This technique offers the best chance of removing all the abnormal thyroid tissue. Use the extracapsular technique if the parathyroid glands are visible and can be easily separated from the thyroid (see Fig. 31-3). If a parathyroid gland is accidentally removed, place it in a small incision in one of the sternohyoideus muscles. Maintain meticulous hemostasis with judicious use of bipolar cautery and small pieces of Gelfoam.
   b. Use the intracapsular technique if the parathyroid glands are not visible (see Fig. 31-2). When implementing the intracapsular technique, be sure to remove all remnants of thyroid tissue that may remain attached to the capsule. The intracapsular technique is easy to perform but is associated with a high rate of postoperative recurrence of hyperthyroidism.
9. Routinely close the sternohyoideus muscle, subcutaneous tissue, and skin (see subsequent discussion of thyroidectomy in dogs).

Postoperative Care and Complications

- Monitor for hypothermia, hemorrhage at the incision site, and hypocalcemia.
- Hypoparathyroidism.
  - Rare with careful surgical technique (5% incidence of hypocalcemic tetany).

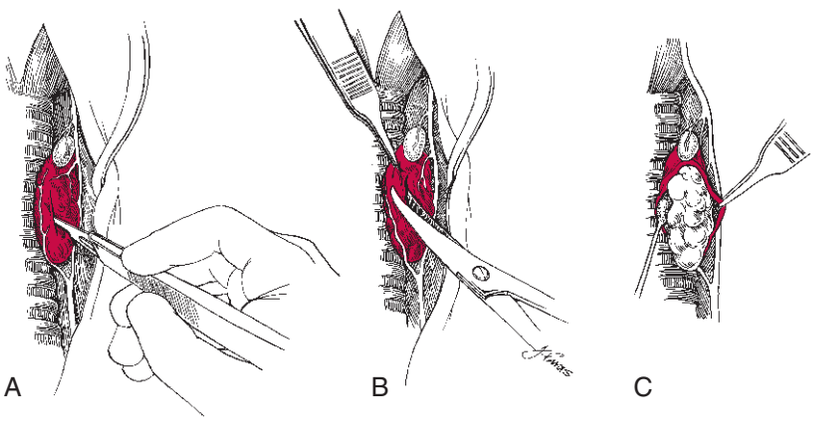

Figure 31-2. Intracapsular dissection for removal of a thyroid tumor in a cat. Make a nick incision *(A)* in a relatively avascular area of the thyroid capsule and extend the incision with scissors *(B)*. Bluntly remove the gland from the capsule using a sterile cotton-tipped applicator *(C)*. Ligate or cauterize blood vessels as necessary.

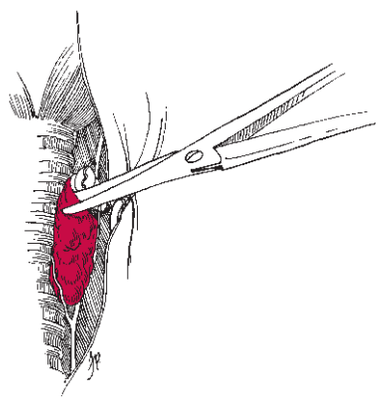

Figure 31-3. Extracapsular dissection for removal of a thyroid lobe in a cat. Incise the thyroid capsule immediately adjacent to the parathyroid gland. Carefully cauterize capsular blood vessels if necessary. Bluntly separate the thyroid gland from the parathyroid gland using a sterile cotton-tipped applicator. After ligating or cauterizing blood vessels as necessary, remove the thyroid gland and its capsule.

  - Check serum calcium concentrations for 48 hours postoperatively or longer if the concentration is dropping.
  - Monitor for tetany if calcium concentration is dropping.
  - Treatment of hypoparathyroidism is described in Chapter 32.
- Thyroid hormone replacement (see "Hypothyroidism in Cats").
- Relapse of hyperthyroidism is rare (10% incidence, 2–3 years postoperatively) but does occur, probably because of the incomplete removal of adenomatous tissue. Treat by administering radioactive iodine or by surgical removal of remaining thyroid tissue. The incidence of hypoparathyroidism tends to be higher than with the first surgery.

Thyroidectomy in the Dog

Preoperative Considerations

- Accurate preoperative diagnosis is important. Carefully palpate the tumor. Small, movable tumors are usually amenable to surgical resection. Surgical resection of encapsulated, movable thyroid tumors was found in one study to result is median survival of 20 months. Fine-needle aspirate or tissue biopsy of the thyroid tumor helps establish the type of tumor. However, recognize that bleeding associated with these procedures can obscure the surgical field and make the procedure more difficult.

▼ ***Key Point*** Biopsy of thyroid tumors in the dog can result in significant hemorrhage. Observe the patient closely after biopsy.

- Cervical radiographs or computed tomography may be helpful to determine tracheal displacement or tumor calcification. Ultrasound examination may be helpful to identify the involved thyroid lobes and evaluate for local tissue invasion. Thoracic radiographs are mandatory to rule out pulmonary metastasis or another cardiopulmonary disorder.

Surgical Procedure

Objectives

1. Completely remove or debulk the thyroid mass.
2. Preserve at least one parathyroid gland.
3. Minimize blood loss.
4. Preserve recurrent laryngeal nerves. Avoid injury to the trachea and esophagus.

Equipment

- Standard general surgical pack and sutures
- Gelpi or Weitlaner retractors
- Army-Navy retractors
- Penrose drains or closed suction drains (e.g., Jackson-Pratt)

Technique

1. Patient preparation and surgical approach are the same as those described for the cat.
2. Dissection

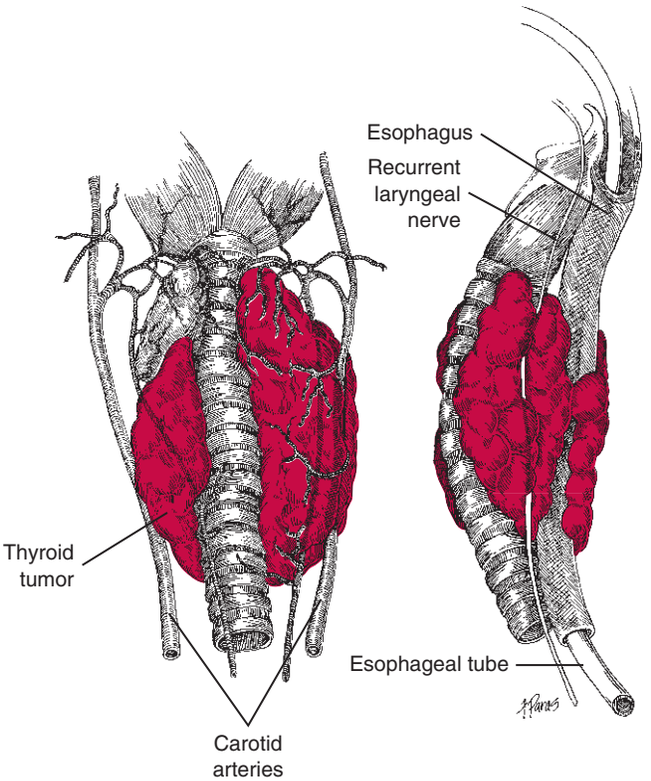

Figure 31-4. Gross appearance of an invasive thyroid carcinoma in a dog.

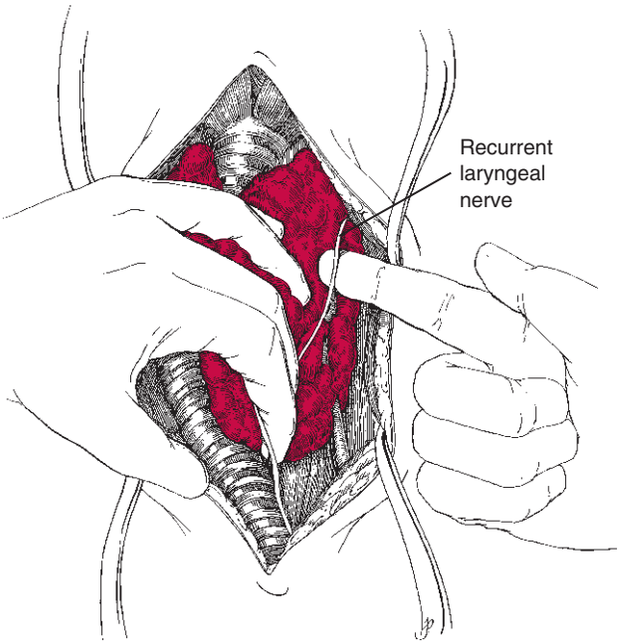

Figure 31-5. Remove canine thyroid tumors with a combination of blunt and sharp dissection. Finger dissection of the tumor and surrounding structures may be necessary for large invasive tumors. Be careful when handling the recurrent laryngeal nerve to avoid the possibility of postoperative laryngeal paralysis.

a. These tumors are very vascular, and dissection is difficult.
b. Avoid injury to the esophagus, carotid artery, jugular vein, vagosympathetic trunk, and recurrent laryngeal nerve (Fig. 31-4).
c. A stomach tube or small endotracheal tube in the esophagus helps identify this structure.
d. Ligate or cauterize the extensive vascular network and carefully dissect out the tumor (Fig. 31-5). Begin dissection at the caudal aspect of the tumor and gradually work cranially.
e. Identify and preserve the parathyroid glands if bilateral thyroidectomy is performed. With large malignant tumors, this may be impossible.
f. If complete removal is impossible, debulk the mass, leaving the portion closest to the larynx intact to preserve the parathyroid glands. Bleeding from the remaining thyroid tissue may be difficult to control.

3. Closure
a. Place Penrose drains or a closed suction drain if significant dead space results from tumor removal. Have the drains exit through separate stab incisions.
b. Close the muscle routinely with simple continuous, absorbable suture; the subcutaneous tissue with simple continuous, absorbable suture; and the skin with simple interrupted, non-absorbable suture.

Postoperative Care and Complications

Short-Term

- Closely monitor for hemorrhage or seroma formation.
- Check serum calcium concentrations at least 2 to 4 days postoperatively if a bilateral thyroidectomy was performed. Monitor the calcium concentrations longer if decreasing. Treat hypoparathyroidism if necessary, according to the guidelines in Chapter 32.
- Check serum T_3 and T_4 levels if bilateral thyroidectomy is performed. Treat hypothyroidism if present (see previous discussion of hypothyroidism).

Long-Term

- Reevaluate the dog frequently (every 3 months) for recurrence of the primary tumor and metastasis.
- Consider postoperative chemotherapy or radiotherapy if the tumor was malignant (see previous discussion on treatment of thyroid tumors and Chapter 26 on chemotherapy).

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Chapter 32

Diseases of the Parathyroid Gland and Calcium Metabolism

Patricia A. Schenck / Dennis J. Chew

NORMAL CALCIUM METABOLISM

Calcium is required for many intracellular and extracellular functions, as well as for skeletal support. Ionized calcium is required for enzymatic reactions, membrane transport and stability, blood coagulation, nerve conduction, neuromuscular transmission, muscle contraction, vascular smooth muscle tone, hormone secretion, bone formation and resorption, control of hepatic glycogen metabolism, and cell growth and division. Normal homeostatic control mechanisms usually maintain serum ionized calcium concentration within a narrow range.

Distribution of Calcium

Calcium in plasma or serum exists in three fractions: ionized (free calcium), complexed, and protein bound.

▼ ***Key Point*** Ionized calcium is the biologically active fraction of serum total calcium.

- ***Ionized calcium:*** This is the biologically active fraction of calcium and accounts for approximately 55% of the total serum calcium concentration in dogs.
- ***Complexed calcium:*** Complexed calcium accounts for approximately 10% of the total serum calcium concentration in dogs but may be elevated in chronic renal failure (CRF). Complexed calcium may be bound to anions such as lactate, phosphate, bicarbonate, sulfate, citrate, and oxalate.
- ***Protein-bound calcium:*** Protein-bound calcium accounts for approximately 35% of the total serum calcium concentration. Albumin is the primary protein bound to calcium. Protein binding is affected by changes in pH, with increased binding as pH increases and decreased binding as pH decreases.

Regulation of Calcium

Regulation of serum calcium concentration is complex and requires the integrated actions of parathyroid hormone (PTH), vitamin D metabolites, and calcitonin. The intestine, kidney, and bone are the major target organs affected by calcium regulatory hormones. The skeleton provides a major supply of calcium and phosphorus when intestinal absorption and renal reabsorption are inadequate to maintain normal serum calcium concentration.

Parathyroid Hormone

PTH is synthesized and secreted by chief cells of the parathyroid gland in response to a decrease in ionized calcium concentration. The most important biologic effects of PTH are as follows:

- Increase the blood calcium concentration
- Increase tubular reabsorption of calcium, resulting in decreased loss of calcium in the urine
- Increase bone resorption and numbers of osteoclasts on bone surfaces
- Accelerate the formation of 1,25-dihydroxyvitamin D_3 (calcitriol) by the kidney

▼ ***Key Point*** The net effects of PTH are to increase serum ionized calcium and to decrease serum phosphorus concentrations.

Calcitonin

Calcitonin is synthesized by C cells in the thyroid gland and is secreted in response to hypercalcemia and to a calcium-rich meal. The effects of calcitonin on normal calcium homeostasis are considered minor. The major target site for calcitonin is bone, where it inhibits resorption of calcium and phosphorus.

Vitamin D Metabolites

The cholecalciferol (vitamin D_3 of animal origin) metabolites 25-hydroxyvitamin D_3 (calcidiol) and 1,25-dihydroxyvitamin D_3 (calcitriol) are the most important vitamin D metabolites. These metabolites may also be derived from ergocalciferol (vitamin D_2 of plant origin), and are equally bioactive. Dogs and cats inefficiently photosynthesize vitamin D in their skin and consequently are dependent on vitamin D in their diet. Hydroxylation of vitamin D occurs in the liver to produce 25-hydroxyvitamin D. This 25-hydroxyvitamin

D is further hydroxylated in the proximal tubule of the kidney to form calcitriol.

Calcitriol

Calcitriol is the only active metabolite of vitamin D. Calcitriol increases serum calcium and phosphorus concentrations and acts on the intestine, kidney, and bone.

- ***Bone:*** Calcitriol stimulates osteoclastic calcium mobilization and resorption of bone.
- ***Intestine:*** Calcitriol increases calcium, phosphorus, and magnesium absorption.
- ***Kidney:*** Calcitriol increases renal tubular resorption of calcium and phosphorus.

▼ ***Key Point*** The net effect of calcitriol is to increase both serum ionized calcium and serum phosphorus concentrations.

DIAGNOSTIC TESTS OF CALCIUM METABOLISM

Measurement of total calcium, ionized calcium, and hormones of calcium metabolism aid in the diagnosis of calcium disorders (see Tables 32-1 and 32-2).

Total Serum Calcium

Total serum calcium is part of most routine serum profile evaluations. However, ionized calcium concentration does not parallel total calcium concentration, and thus ionized calcium concentration must be measured for an accurate assessment of calcium status. Total calcium is usually measured using a colorimetric method and may be spuriously elevated if hyperlipemia or hemolysis is present.

Adjusted Total Calcium Values

Formulas to adjust serum total calcium to albumin or total protein concentration have been published for dogs. Due to a high level of diagnostic discordance between adjusted total calcium and ionized calcium concentrations, the use of these formulas is discouraged.

Ionized Calcium Concentration

- Ion-selective methods are available in some laboratories. Special handling of serum or heparinized plasma is necessary to prevent lowering of ionized calcium due to pH increases. Serum samples appear to be stable for 72 hours at 4°C if handled anaerobically. Some laboratories have developed species-specific pH adjustment formulas to allow measurement of aerobically handled samples.
- A handheld analyzer is also available for cage-side analyses. Heparinized whole blood is used for measurement; for best results, a standard quantity of dry heparin and blood should be utilized for each assay.

Table 32-1. EXPECTED CHANGES IN CALCEMIC HORMONES AND SERUM BIOCHEMISTRY IN HYPERCALCEMIA DISORDERS

Disorder	tCa	iCa	alb	Corr tCa	Pi	PTH	PTHrP	25(OH)-D	1,25(OH)$_2$-D	PTG (US, Surgery)
Primary hyperPTH	↑	↑	N	N	↓N	↑N	N	N	N↑	Single↑
Secondary nutritional hyperPTH	N↓	N↓	N	N↓	N↑	↑	N	↓N	N↓	Multiple↑
Secondary renal hyperPTH	N↓↑	N↓	N	N	↑N	↑	N	N↓	N↓	Multiple↑
Tertiary hyperPTH	↑	↑	N	↑	↑	↑	N	N↓	↓N	Multiple↑
Malignancy associated										
Humoral hypercalcemia	↑	↑	N↓	↑N	↓N	↓N	↑N	N	↓N↑	↓
Local osteolytic	↑	↑	N↓	↑N	N↑	↓N	N↑	N	N	↓
Hypervitaminosis D										
Cholecalciferol	↑	↑	N	↑	↑N	↓	N	↑	N↑	N↓
Calcitriol	↑	↑	N	↑	N↑	↓	N	N	↑	↓N
Calcipotriene	↑	↑	N	↑	↑N	↓	N	N	↓N	↓N
Hypoadrenocorticism	↑	↑	N↓	↑	↑N	↓N	N	N	↓N	N
Hypervitaminosis A	↑	↑	N	↑	N	↓	N	N	N↓	↓N
Idiopathic hypercalcemia (cat)	↑	↑	N	↑	N↑	↓N	N	N	N↓↑	↓N
Dehydration	↑	N↑	↑N	↑N	N↑	N↓	N	N	N	N
Aluminum exposure (renal failure)	↑	↑	N	↑	↑N	↓N	N	N	N↓	N↑↓
Hyperthyroidism (cat)	↑	↑	N	↑	N↑	↑N↓	N	N	N↓	N↑
Raisin/grape toxicity (dog)	↑	—	N	↑	N↑	—	—	—	—	—

1,25(OH)$_2$-D, 1,25-dihydroxyvitamin D$_3$; 25(OH)-D, 25-hydroxyvitamin D$_3$; alb, albumin; Corr tCa, corrected total calcium; iCa, ionized calcium; N, normal; Pi, phosphorus; PTG, parathyroid glands; PTH, parathyroid hormone; PTHrP, parathyroid hormone-related protein; tCa, total calcium; US, ultrasound.

Table 32-2. EXPECTED CHANGES IN CALCEMIC HORMONES AND SERUM BIOCHEMISTRY IN HYPOCALCEMIA DISORDERS

Disorder	tCa	iCa	alb	Corr tCa	Pi	PTH	PTHrP	25(OH)-D	1,25(OH)$_2$-D	PTG (US, Surgery)
Primary hypoparathyroidism	↓	↓	N	↓	↑N	↓N	N	N	N↓	Multiple↓
Pseudohypoparathyroidism	↓	N↓	N	↓	↑N	↑	N	N	N↑	N↑
Sepsis/critical care	↓N	↓	N	↓N	N↑	↑N	N	N	N	N
Ethylene glycol toxicity	↓	↓	N	↓	↑N	↑	N	N	↓N	N
Paraneoplastic	↓	↓	N	↓	↓	↑N	N	N	N	N↑
Phosphate enema	↓	↓	N	↓	↑	↑	N	N	N↓↑	N
Eclampsia	↓	↓	N	↓	↓	Mild↑, N	N	N	N↓	N
Hypoalbuminemia	↓	↓N	↓	N	N	N↑	N	N	N↑	N↑

1,25(OH)$_2$, 1,25-dihydroxyvitamin D$_3$; 25(OH)-D, 25-hydroxyvitamin D$_3$; alb, albumin; Corr tCa, corrected total calcium; iCa, ionized calcium; N, normat; Pi, phosphorus; PTG, parathyroid glands; PTH, parathyroid hormone; PTHrP, parathyroid hormone-related protein; tCa, total calcium; US, ultrasound.

Parathyroid Hormone

The PTH molecule is composed of three portions: amino-terminus, mid-molecule, and carboxy-terminus. The amino-terminus is the biologically active portion of the molecule. An intact PTH assay (a two-site assay) provides accurate determination of PTH concentration. PTH fragments are excreted by the kidneys. In animals with renal failure, concentration of inactive fragments may increase. Only an intact PTH assay should be used in patients with renal disease or failure. Serum or separated plasma samples can be assayed but should be kept refrigerated or frozen prior to assay.

Parathyroid Hormone-Related Protein

The parathyroid hormone-related protein (PTHrP) is a hormone secreted by some malignant neoplasms in animals with hypercalcemia. This hormone can bind to PTH receptors in the kidneys and bone and result in humoral hypercalcemia of malignancy (HHM). Separated plasma samples can be assayed but should be kept refrigerated or frozen prior to assay.

Vitamin D Metabolites

- 25-hydroxyvitamin D$_3$ (calcidiol)
  - Metabolites of vitamin D$_3$ are chemically identical in all species. Calcidiol concentration is a good indicator of vitamin D$_3$ ingestion and can be used to diagnose hypovitaminosis or hypervitaminosis D. Serum or separated plasma can be assayed, but samples should be protected from degradation due to exposure to light.
- 1,25-dihydroxyvitamin D$_3$ (calcitriol)
  - Calcitriol is the most active vitamin D metabolite, and it circulates in low concentrations. Assays have been developed for calcitriol but are not readily available due to cost.

HYPERCALCEMIA

Defining Criteria

- Serum total calcium concentration
  - Dogs: >12.0 mg/dl (3.0 mmol/L)
  - Cats: >11.0 mg/dl (2.75 mmol/L)
- Serum ionized calcium concentration
  - Dogs: >5.8 mg/dl (1.45 mmol/L)
  - Cats: >5.6 mg/dl (1.40 mmol/L)
- Young dogs may have a mild hypercalcemia (usually <13.0 mg/dl total serum calcium concentration) related to skeletal growth.
- Hyperlipemia and/or hemolysis of the sample may result in spurious elevations of calcium.

▼ ***Key Point*** Severe clinical signs are associated with a serum total calcium concentration >18 mg/dl.

Etiology

Hypercalcemia may be parathyroid-dependent (primary hyperparathyroidism) or parathyroid-independent (normal functioning of the parathyroid gland).

- In parathyroid-independent hypercalcemia, elevated ionized calcium concentration causes suppression of PTH production. On analysis, ionized calcium concentration is elevated, and PTH concentration is in the lower part of or below the reference range. PTHrP concentration may be elevated if there is a tumor producing PTHrP. Concentration of 25-hydroxyvitamin D$_3$ may be elevated in cases of vitamin D toxicity.
- Parathyroid-dependent hypercalcemia (primary hyperparathyroidism) is characterized by elevated ionized calcium concentration without the appropri-

ate suppression of PTH production due to a PTH-secreting tumor of the parathyroid gland.

See Table 32-3 for a list of hypercalcemia-related conditions.

Clinical Signs

Clinical signs in hypercalcemia depend on the magnitude of the calcium elevation, how quickly the hypercalcemia developed, and the duration of the hypercalcemia. Serum total calcium concentrations of <15 mg/dl (<3.75 mmol/L) may not be associated with systemic signs; however, serum total calcium concentrations of >18 mg/dl (>4.5 mmol/L) are often associated with severe life-threatening signs. Soft tissue mineralization may occur with prolonged hypercalcemia when the product of total calcium (mg/dl) times serum phosphorus (mg/dl) equals 70 or greater.

- Polydipsia and polyuria are the most common signs of hypercalcemia in dogs due to direct stimulation of the thirst center and a decreased ability of the kidneys to concentrate urine.
- Anorexia, vomiting, and constipation can result from decreased excitability of gastrointestinal smooth muscle.
- Generalized weakness may develop from decreased muscle excitability.
- Depression, muscle twitching, and seizures can occur as neurologic manifestations.
- Cardiac arrhythmias can develop from direct effects on the myocardium or secondary to cardiac mineralization.

▼ ***Key Point*** Polydipsia and polyuria are the most common clinical signs of hypercalcemia.

Table 32-3. CONDITIONS ASSOCIATED WITH HYPERCALCEMIA

Nonpathologic Conditions
Hyperlipemia
Non-fasted serum samples
Young growing dogs
Laboratory error or improper handling of sample

Transient Conditions
Hemoconcentration
Hyperproteinemia

Pathologic Conditions
Parathyroid-dependent hypercalcemia
  Primary hyperparathyroidism
Parathyroid-independent hypercalcemia
  Malignancy-associated hypercalcemia
    Lymphoma
    Adenocarcinoma of the apocrine glands of the anal sac
    Multiple myeloma
    Metastatic bone tumors
    Miscellaneous tumors (lymphocytic leukemia, mammary carcinoma, fibrosarcoma, pancreatic adenocarcinoma, testicular interstitial cell tumor, lung carcinoma, squamous cell carcinoma, thyroid adenocarcinoma, osteosarcoma)
Hypoadrenocorticism
Renal failure
Hypervitaminosis D
  Cholecalciferol (rodenticide) toxicity
  Dovonex ingestion
  Iatrogenic due to dietary supplementation
  Houseplants (*Cestrum diurnum, Solanum malacoxylon, Trisetum flavescens*)
  Granulomatous disease (blastomycosis, schistosomiasis)
Grape toxicity
Bone lesions (sepsis, disuse osteoporosis)
Severe hypothermia
Idiopathic hypercalcemia in cats

Diagnosis

Abnormalities depend on the underlying cause, severity, and duration of hypercalcemia (see later under "Conditions Associated with Hypercalcemia").

History and Physical Examination

- A complete history and thorough physical examination are essential for diagnosing the cause of hypercalcemia. Obtain dietary history to assess the possibility of over-supplementation or under-supplementation with vitamin D.

Laboratory Tests

- Perform a complete blood count (CBC) and serum chemistry profile, and consider tests such as serum ionized calcium, PTH, 25-hydroxyvitamin D, and PTHrP concentrations. Collect samples for diagnostic testing prior to treatment.

Radiography and Ultrasound

- Soft tissue mineralization of the kidneys, heart, lungs stomach, and other tissues may be detected.
- Abdominal masses, mediastinal masses, pulmonary lesions suggestive of metastasis, or lymph node enlargement especially in the tracheobronchial region may be visualized.

Electrocardiography

- Prolongation of the PR interval, shortening of the QT interval, and cardiac arrhythmias (ventricular fibrillation) may develop with severe hypercalcemia.

Principles of Treating Hypercalcemia

▼ ***Key Point*** The definitive treatment for hypercalcemia is to remove the underlying cause.

Unfortunately, the etiology may not be apparent, and supportive measures must be taken to decrease the serum calcium concentration (see Table 32-4 for specific drugs and dosage recommendations). Supportive measures may include the following.

Table 32-4. TREATMENT OF HYPERCALCEMIA

Treatment	Dose	Indications	Comments
Volume Expansion			
SQ saline (0.9%)	75–100 ml/kg/day	Mild hypercalcemia	Contraindicated if peripheral edema is present
IV saline (0.9%)	100–125 ml/kg/day	Moderate to severe hypercalcemia	Contraindicated in congestive heart failure and hypertension
Diuretics			
Furosemide	2–4 mg/kg q8–12h IV, SC, PO	Moderate to severe hypercalcemia	Volume expansion is necessary prior to use of this drug
Glucocorticoids			
Prednisone Dexamethasone	1–2.2 mg/kg q12h PO, SC, IV 0.1–0.22 mg/kg q12h IV, SC	Moderate to severe hypercalcemia	Use of these drugs prior to identification of etiology may make definitive diagnosis difficult
Inhibition of Bone Resorption			
Calcitonin	4–6 IU/kg q8–12h SC	Hypervitaminosis D toxicity	Response may be short lived; vomiting may occur
Bisphosphonates			
Etidronate (EHDP)	5–15 mg/kg daily to q12h	Moderate to severe hypercalcemia	Expensive; use in dogs limited
Clodronate	20–25 mg/kg in 4-hr IV infusion		Approved in Europe; availability in U.S. limited
Pamidronate	1.3 to 2.0 mg/kg in 150-ml 0.9% saline in 2-hr IV infusion; can repeat in 1–3 wks		

EHDP, ethane-1-hydroxy-1,1-diphosphonate.

Volume Expansion

Volume expansion with IV 0.9% NaCl solution decreases hemoconcentration and encourages renal calcium loss by improving glomerular filtration rate and sodium excretion, resulting in less calcium resorption.

Loop Diuretics

- Diuretics such as furosemide increase calcium excretion; however, high doses may be needed. Diuretic use in a dehydrated patient is contraindicated because volume contraction and further hemoconcentration may worsen the hypercalcemia.
- Thiazide diuretics, which decrease calcium excretion by the kidneys, are contraindicated.

Sodium Bicarbonate

Sodium bicarbonate given as an IV bolus or as a continuous infusion has been shown to decrease serum total and ionized calcium concentration. Although the magnitude of calcium reduction is mild, alkalosis favors the binding of ionized calcium to protein, resulting in a decrease in ionized calcium. Sodium bicarbonate therapy is more beneficial when combined with other treatments and is reserved for life-threatening situations.

Glucocorticoids

- Glucocorticoids decrease bone resorption of calcium, decrease intestinal calcium absorption, and increase renal calcium excretion. These effects are nonspecific and lead to a mild decrease in the magnitude of hypercalcemia.
- Glucocorticoids often cause a substantial decrease in serum calcium concentration when hypercalcemia is secondary to lymphoma, myeloma, hypervitaminosis D, or hypoadrenocorticism.

▼ ***Key Point*** The use of glucocorticoids prior to determination of the etiology of hypercalcemia may make definitive diagnosis difficult, especially for lymphoma and myeloma.

Calcitonin

Calcitonin can be useful during treatment of cholecalciferol toxicity. For calcitonin to decrease serum calcium, multiple injections per day are required. Long-term side effects include anorexia and vomiting, and diminished effectiveness of calcitonin treatment may occur over time. Use calcitonin only when other treatments have not adequately lowered serum calcium.

Bisphosphonates (Diphosphonates)

These compounds inhibit osteoclastic bone resorption.

- Etidronate (Didronel, Norwich Eaton) has been used with some success as an oral agent for long-term control of hypercalcemia, but it is not well absorbed.
- Intermittent IV injections of pamidronate (Aredia, Novartis) are effective for the control of vitamin D toxicity, hyperparathyroidism, and malignancy-associated hypercalcemia. Clodronate is an alternative.
- Since bisphosphonates have nephrotoxic potential, use these after rehydration. Use IV fluids during and for several hours after treatment with bisphosphonates.

Mithramycin

This drug is a potent inhibitor of osteoclastic bone resorption; however, mithramycin has been associated with many serious side effects, such as thrombocytopenia, hepatic necrosis, renal necrosis, and hypocalcemia, and is no longer recommended.

Peritoneal Dialysis

Using a calcium-free dialysate, this procedure can be considered as a last resort when other methods fail to decrease serum calcium concentration.

CONDITIONS ASSOCIATED WITH HYPERCALCEMIA

For a complete list of conditions associated with hypercalcemia, see Table 32-3.

Hypercalcemia Associated with Malignancy

▼ ***Key Point*** Malignancy-associated hypercalcemia is the most common cause of persistent hypercalcemia in dogs and the third most common cause in cats.

Hypercalcemia primarily results from increased osteoclastic bone resorption and increased renal tubular resorption. Rarely, increased intestinal absorption also may play a role. Factors that may be produced by tumors and result in humoral hypercalcemia of malignancy include PTH, PTHrP, transforming growth factor, calcitriol, prostaglandin E_2, osteoclast-activating factor, and other cytokines (interleukin-1, interleukin-2, and gamma interferon).

- In dogs, lymphoma, adenocarcinoma of the apocrine glands of the anal sac, and multiple myeloma are the most common tumors associated with hypercalcemia.
- In cats, lymphoma, and squamous cell carcinoma each account for one-third of the cases of malignancy-associated hypercalcemia.

▼ ***Key Point*** A normal (or negative) concentration of PTHrP does not rule out the presence of a malignancy.

Lymphoma

- Lymphoma is the most common tumor associated with hypercalcemia in the dog. Of dogs with lymphoma, 10% to 40% have concurrent hypercalcemia, and a large number of these have mediastinal lymphoma. Although lymphadenopathy is usually detected, hypercalcemia may be the first abnormality noted.
- A thorough physical examination, together with thoracic and abdominal radiography, abdominal ultrasonography, multiple lymph node aspirates or biopsies, and multiple bone marrow aspirates or core biopsies, may be necessary to confirm a diagnosis of lymphoma.
- Treatment with corticosteroids decreases serum calcium concentration; however, their lympholytic effect makes subsequent identification of lymphoma very difficult. The return of hypercalcemia may precede clinical evidence of tumor regrowth in animals undergoing chemotherapy. Treatment of lymphoma is discussed in Chapter 27.

▼ ***Key Point*** Lymphoma is the most common tumor associated with hypercalcemia in the dog.

Apocrine Gland Adenocarcinoma of the Anal Sac

- This tumor usually occurs in older female dogs, with hypercalcemia developing in approximately 50% of cases. Humoral mechanisms are typically responsible for hypercalcemia, as PTHrP has been identified from tumor tissue in dogs. The tumor is usually malignant and has metastasized to regional lymph nodes by the time of diagnosis.
- Surgical resection is associated with reduction of serum calcium. Failure to remove all of the tumor or recurrence of the tumor usually results in the return of hypercalcemia. Despite surgical excision, radiation, and various chemotherapy protocols, the tumor usually recurs, and reported survival times range from 2 to 21 months.

Multiple Myeloma

- Multiple myeloma in dogs has been associated with hypercalcemia in 10% to 15% of cases. Humoral factors as well as direct lysis of bone may account for the increased serum calcium.
- Long-term survival has been reported following treatment of multiple myeloma with chemotherapy, but associated hypercalcemia, light-chain proteinuria, and extensive bony lesions are associated with a shorter survival time.

Hypoadrenocorticism

- Approximately 30% of dogs with hypoadrenocorticism (Addison's disease) have mild to moderate hypercalcemia (total calcium concentration <15 mg/dl). Ionized calcium concentration may be normal or slightly elevated.
- Multiple factors resulting in hypercalcemia include increased calcium citrate (complexed calcium), hemoconcentration (relative increase), increase in renal resorption of calcium, and increased binding of calcium to serum proteins.
- Hypercalcemia usually resolves quickly with therapy for hypoadrenocorticism.

Hypervitaminosis D

With hypervitaminosis D, ionized calcium concentration is elevated with suppression of PTH production. Elevation of 25-hydroxyvitamin D_3 may be observed depending on the vitamin D metabolites present.

▼ ***Key Point*** In vitamin D toxicosis, hyperphosphatemia often accompanies hypercalcemia.

Rodenticides Containing Cholecalciferol

Cholecalciferol-based rodenticides have gained popularity over anticoagulant rodenticides because, unlike anticoagulant rodenticides, there is no rodenticide resistance, and there is no secondary toxicity to species that ingest poisoned rodents. Although one manufacturer (Bell Labs) reports the median lethal dose (LD_{50}) to be 88 mg/kg of body weight, toxicity in dogs and cats has been seen with much lower doses (<10 mg/kg). The effect may last for weeks.

Clinical Manifestations

- Clinical signs are vague and related to hypercalcemia (see "Clinical Signs" under "Hypercalcemia").
- Hypercalcemia is often severe (serum total calcium of 15–20 mg/dl; ionized calcium concentration of 1.9–2.5 mmol/L) and accompanied by hyperphosphatemia at initial presentation. Concentration of 25-hydroxyvitamin D_3 is typically elevated.
- Azotemia may occur several days after ingestion secondary to renal damage from hypercalcemia.

Goals of Treatment

- Decrease cholecalciferol absorption in the gastrointestinal tract.
- Correct the fluid and electrolyte imbalances.
- Reduce hypercalcemia.
- Treat miscellaneous complications such as seizures and cardiac arrhythmias.

Treatment

- Feed a low-calcium diet (most renal diets) and restrict intake of dairy products.
- Give phosphate binders that do not contain calcium (e.g., aluminum hydroxide, Amphojel, Wyeth-Ayerst; 10–30 mg/kg q8h PO with meals), to decrease the calcium X phosphorus product.
- In severe cases of hypercalcemia, aggressive treatment with IV fluids, furosemide, prednisone, and/or calcitonin may be necessary for several weeks.
- Recent reports show that intermittent IV pamidronate is effective treatment in dogs and is superior to calcitonin as ancillary treatment for long-term effects.
- Because of the prolonged half-life of 25-hydroxyvitamin D_3, monitor serum calcium, phosphorus, and creatinine weekly for 4 to 6 weeks. If aggressive therapy is maintained for several weeks, complete recovery can be achieved, depending upon the extent of the initial renal injury.

Dovonex Ingestion

- Dovonex is a calcipotriene-containing cream used to treat human psoriasis. This cream contains 50 µg of calcipotriene per gram of cream, and the oral LD_{50} in dogs is reportedly 100 to 150 µg/kg of body weight.
- Calcipotriene has a shorter duration of action than cholecalciferol, so the duration of effect is shorter.
- Measured concentration of 25-hydroxyvitamin D_3 is usually normal since calcipotriene is not detected by this assay.

Iatrogenic Vitamin D Intoxication

- Iatrogenic vitamin D intoxication may occur following the administration of vitamin D products and dietary supplements. Use of ergocalciferol (vitamin D_2) may cause hypercalcemia because its slow onset of action and prolonged duration of action make it difficult to dose correctly.
- Treatment is directed at discontinuing the supplement or decreasing the dose of vitamin D.

Houseplant Ingestion

Houseplants such as *Cestrum diurnum* (day-blooming jessamine), *Solanum malacoxylon,* and *Trisetum flavescens* contain a substance similar to calcitriol that may cause hypercalcemia when ingested.

Granulomatous Diseases

Granulomatous disorders such as systemic fungal diseases and tuberculosis are rare causes of hypercalcemia in dogs possibly due to increased vitamin D metabolites. Serum calcium concentrations return to normal with treatment (e.g., antifungal drugs or surgical removal).

Grape Toxicity

The ingestion of a small quantity of grapes or raisins has reportedly caused hypercalcemia in a few dogs. Clinical signs occurring within hours of ingestion include vomiting, diarrhea, abdominal pain, and lethargy; clinical signs in some dogs last for up to 3 weeks. Acute intrinsic renal failure occurs, and both serum calcium and phosphorus are elevated. Aggressive therapy for up to 3 weeks is required for recovery. If oliguria or anuria is present, prognosis is poor.

Renal Failure

- Chronic renal failure is associated with an increase in serum total calcium possibly due to an increase in complexed calcium. Hypercalcemia may be present in acute renal failure during the polyuric phase of recovery. Serum ionized calcium concentration is typically normal or low, and secondary hyperparathyroidism may be present.
- As kidney function decreases, calcitriol production decreases, allowing serum ionized calcium to drop. The fall in ionized calcium concentration stimulates secretion of PTH to help maintain the ionized calcium concentration within the normal range, primarily via bone resorption. Chronic elevation of PTH characterizes secondary hyperparathyroidism and is maintained by inadequate calcitriol and ionized calcium concentrations within the parathyroid gland nucleus to inhibit genomic transcription of the DNA to mRNA for PTH synthesis.
- In rare cases, as end-stage renal failure is reached, the calcium set-point may be altered, allowing the ionized calcium concentration to be elevated. In this circumstance, PTH concentration is greatly elevated and ionized calcium concentration may show a mild to moderate elevation (tertiary hyperparathyroidism).

Idiopathic Hypercalcemia in Cats

Clinical Signs

A syndrome in a wide age range of cats has emerged, where hypercalcemia occurs without obvious explanation.

- Longhaired cats appear to be affected more frequently, but there is no sex predilection.
- Serum total and ionized calcium concentrations are increased for many months, without any clinical signs in approximately half of reported cases.
- If clinical signs are present, mild weight loss and uroliths (specifically calcium oxalate stones) are common.
- Chronic constipation and inflammatory bowel disease have also been associated with idiopathic hypercalcemia.
- Most are non-azotemic at presentation, but azotemia may develop later.

Diagnosis

The cause of idiopathic hypercalcemia is unknown.

- There is no evidence of malignancy based on radiography, abdominal ultrasonography, or bone marrow evaluation.
- Concentrations of ionized magnesium and serum 25-hydroxyvitamin D_3 are within normal limits; PTH and calcitriol concentrations are normal to low.
- It is conceivable that hypercalcemia develops only in a genetically susceptible population of cats.

Treatment

- An increase in dietary fiber may decrease serum ionized calcium concentration in some affected cats.
- Prednisolone therapy results in long-term decreases in serum calcium concentration in some cats. There is concern that this treatment could increase hypercalciuria, which could subsequently enhance genesis of urinary calculi. However, the filtered load of calcium decreases as serum ionized calcium declines, which offsets the enhanced formation of calculi.
- When dietary modification and prednisolone therapy have been unsuccessful in resolving hypercalcemia, consider bisphosphonate treatment.

Primary Hyperparathyroidism

Primary hyperparathyroidism results from excessive secretion of PTH by abnormal parathyroid glands. This disease is reported sporadically in dogs and is rare in cats. Primary hyperparathyroidism is characterized by persistent and long-standing hypercalcemia.

Etiology

- A solitary parathyroid adenoma is the most common cause of primary hyperparathyroidism.
- Parathyroid carcinomas are infrequent.
- Parathyroid hyperplasia of one or all four parathyroid glands is rare.
  - Gross enlargement of the affected parathyroid gland may not be present.
  - The diagnosis is made based on microscopic abnormalities.
  - Hereditary neonatal parathyroid hyperplasia has been reported in two German shepherd puppies.

Signalment

- Middle-aged or older animals are at risk.
  - Dogs from 5 to 13 years, mean age 10 years
  - Cats from 8 to 15 years, mean age 12.9 years
- There is no sex predilection in dogs; however, there may be an increased risk in female cats.
- Any breed of dog may be affected. Breeds with an increased risk of primary hyperparathyroidism include the keeshond, briard, American Eskimo, English setter, Siberian husky, Rhodesian ridgeback,

Norwegian elkhound, Irish setter, wirehaired fox terrier, English springer spaniel, Australian shepherd, dachshund, Lhasa apso, Shih Tzu, and golden retriever. Dogs with a decreased risk of primary hyperparathyroidism include the cocker spaniel, German shepherd, Shetland sheepdog, Labrador retriever, and miniature schnauzer.
- Several reported cats were Siamese.

Clinical Signs

- Anorexia, lethargy, and depression are the most common signs, but many animals are asymptomatic.
- Polydipsia and polyuria are usually present, and calcium oxalate urolithiasis may be noted.
- Constipation, weakness, shivering, twitching, vomiting, and stiff gait.

Diagnosis

Physical Examination

- In dogs, the physical examination is usually normal.
- In cats, 50% may have palpable cervical masses due to associated cystic changes.

Biochemistry Profile

- Hypercalcemia and normal to low serum phosphorus are the most consistent findings.
- Azotemia may be present in some patients with moderate hypercalcemia.
- If renal failure is present, the serum phosphorus may be normal or above normal.

Urinalysis

- Decreased urine specific gravity is a common finding.

Endocrine Testing

- Determination of PTH concentration is helpful in the diagnosis of primary hyperparathyroidism. An inappropriately elevated concentration of PTH with an elevated ionized calcium concentration is characteristic of primary hyperparathyroidism.
- In dogs, a mid-normal range or higher concentration of PTH is inappropriately elevated in association with hypercalcemia.
- In cats, primary hyperparathyroidism is diagnosed when PTH concentration is elevated above the reference range and ionized hypercalcemia is present.
- There appears to be no benefit to measuring PTH from left and right jugular venous samples for localization of the adenoma.

▼ ***Key Point*** Primary hyperparathyroidism is characterized by elevated serum ionized calcium with lack of appropriate suppression of PTH production.

Hematology

- The hemogram is usually unremarkable.

Radiography

- Radiographs are often normal but may reveal generalized osteopenia, increased bone resorption at the subperiosteal surfaces, and cyst-like areas in bone.
- Urinary stones may also be identified.

Ultrasonography

- Ultrasound may identify the enlarged parathyroid gland and determine whether it is internal or external to the thyroid gland. A high-resolution probe (above 10 MHz) is necessary for adequate visualization of the parathyroid glands.

Exploratory Surgery

- Consider exploratory surgery of the cervical region if no other cause of hypercalcemia can be determined.
- Negative findings may be due to ectopic PTH production (e.g., parathyroid adenoma in the cranial mediastinum or the unlikely event of a nonparathyroid tumor producing PTH).
- Always submit all excised parathyroid gland tissue for histopathology to confirm the diagnosis.

Treatment

- Treatment of primary hyperparathyroidism is typically surgical excision of the parathyroid adenoma (see "Parathyroidectomy" in this chapter). Ablation of the parathyroid gland adenoma by ethanol injections or radiothermy can be considered an alternative in selected cases.
- Hypocalcemia may occur postoperatively, especially if the serum total calcium concentration is >14 mg/dl prior to surgery. Treatment with supplemental calcium or vitamin D metabolites may be required. Hypocalcemia without clinical signs usually does not require treatment unless the total serum calcium is <6 mg/dl (<1.5 mmol/L).
- Postoperative hypocalcemia can be minimized if the patient is treated with calcitriol (7.5 ng/kg q12h) for 7 to 10 days prior to parathyroidectomy. Calcitriol acts to prime the gut for increased calcium absorption.
- If the patient is unstable, treatment with bisphosphonates (see Table 32-4) for 1 to 2 months prior to surgery may decrease the serum calcium concentration, increase the chance for renal healing, and increase the recovery of the atrophied parathyroid glands.

HYPOCALCEMIA

Hypocalcemia is defined as a serum total calcium concentration <8.5 to 9.0 mg/dl (2.12–2.25 mmol/L)

or an ionized calcium concentration <5.0 mg/dl (1.25 mmol/L) in dogs or <4.0 mg/dl (1.00 mmol/L) in cats. Normal serum total calcium may be slightly lower in older animals than in middle-aged animals.

Etiology

Causes of hypocalcemia are listed in Table 32-5. Hypoalbuminemia is the most common cause of a low serum total calcium concentration; however, it is of no clinical consequence because only the protein-bound fraction is affected. A mildly decreased serum calcium without signs of hypocalcemia can be seen in various systemic conditions such as renal failure, pancreatitis, and intestinal malabsorption. Conditions associated with symptomatic hypocalcemia are discussed.

Clinical Signs

The severity of clinical signs may not always be commensurate with the degree of hypocalcemia. Concurrent acid-base disorders, other electrolyte imbalances, and ionized calcium concentration play a role in the development of clinical signs that are often episodic.

- Tremors, twitching, tetany, muscle spasms, facial rubbing, and gait changes (stiffness and ataxia) result from increased neuromuscular excitability. Occasionally, generalized seizure activity is seen.
- Behavior changes (restlessness, aggression, panting, hypersensitivity to stimuli, and disorientation) are frequent.
- Bradycardia, hyperthermia, polyuria, polydipsia, and vomiting are sometimes seen.

Table 32-5. CONDITIONS ASSOCIATED WITH HYPOCALCEMIA

Causes of Severe Symptomatic Hypocalcemia
Puerperal tetany/eclampsia
Hypoparathyroidism
Spontaneous (lymphocytic parathyroiditis)
Iatrogenic secondary to bilateral thyroidectomy
Postoperative secondary to removal of parathyroid adenoma/carcinoma
Phosphate enemas (acute hyperphosphatemia causes reciprocal calcium decrease)
Causes of Mild Asymptomatic Hypocalcemia
Hypoalbuminemia (most frequent cause of hypocalcemia)
Primary renal disease
Chronic renal failure
Acute renal failure (e.g., urethral obstruction, ethylene glycol toxicity)
Pancreatitis
Intestinal malabsorption syndromes
Chelating agents that bind calcium (EDTA, citrates, oxalates, phosphates)
Rhabdomyolysis due to soft tissue trauma
Nutritional secondary hyperparathyroidism
Dilutional with infusion of calcium-free fluids
Laboratory error/artifact
Idiopathic (unexplained)

EDTA, ethylenediaminetetraacetic acid.

Diagnostic Evaluation

History and Physical Examination

- A complete history (including dietary history) and a thorough physical examination can aid in the diagnosis of the underlying cause of the hypocalcemia.

Routine Laboratory Tests

- Evaluation of CBC and serum chemistry profile may aid in the diagnosis of hypocalcemia. Both serum total calcium and ionized calcium concentrations may be decreased; however, in patients with renal failure or hypoproteinemia, ionized calcium may not parallel changes in total calcium. Measurement of serum ionized magnesium concentration may reveal a decreased concentration. Changes in serum phosphorus may support a specific diagnosis.

Endocrine Testing

- Measurement of PTH concentration is helpful in diagnosing hypoparathyroidism. Determination of serum 25-hydroxyvitamin D_3 concentration may also be of benefit to exclude other causes.

Electrocardiography

- Hypocalcemia may cause prolongation of QT interval and ventricular premature contractions on an electrocardiogram (ECG).

Principles of Treating Hypocalcemia

The definitive treatment for hypocalcemia is to eliminate the underlying cause. Specific treatment options for hypocalcemia are listed in Table 32-6.

Parenteral Calcium

Parenteral calcium may be necessary in patients with active tetany, hyperthermia, and seizures.

- Calcium gluconate and calcium chloride usually are given by slow IV administration.
- Signs of toxicity from injection of excess calcium too quickly include bradycardia and shortening of the QT interval.
- Calcium can also be diluted in saline and given as a continuous IV drip to maintain normal serum calcium concentrations.
- Calcium gluconate (even if diluted with saline) should *not* be given subcutaneously due to the occurrence of dermal necrosis and severe granulomatous inflammation.

Table 32-6. TREATMENT OF HYPOCALCEMIA

Drug	Preparation	Calcium Content	Dose	Comment	
Parenteral Calcium*					
Calcium gluconate	10% solution	9.3 mg of Ca/ml	a. Slow IV to effect (0.5–1.5 ml/kg IV)	Stop if bradycardia or shortened QT interval occurs	
			b. 5–15 mg/kg/hr IV	Infusion to maintain normal calcium SQ calcium salts are not recommended; they can cause severe skin necrosis/mineralization	
Calcium chloride	10% solution	27.2 mg of Ca/ml	5–15 mg/kg/hr IV	Only given IV as extremely caustic perivascularly	
***Oral Calcium**†*					
Calcium carbonate	Many sizes	40% tablet	25–50 mg/kg/day	Most common calcium supplement	
Calcium lactate	325-, 650-mg tabs	13% tablet	25–50 mg/kg/day		
Calcium chloride	Powder	27.2%	25–50 mg/kg/day	May cause gastric irritation	
Calcium gluconate	Many sizes	10%	25–50 mg/kg/day		
Vitamin D				***Time for Maximal Effect to Occur:***	***Time for Toxicity Effect to Resolve:***
Vitamin D_2 (ergocalciferol)			Initial: 4000–6000 U/kg/day Maintenance: 1000–2000 U/kg once daily to once weekly	5–21 days	1–18 wks
Dihydrotachysterol			Initial: 20–30 ng/kg/day Maintenance: 10–20 ng/kg q24–48h	1–7 days	1–3 wks
$1,25\text{-}(OH)_2D_3$ (calcitriol)			Initial: 20–30 ng/kg/day for 3–4 days Maintenance: 5–15 ng/kg/day	1–4 days	2–14 days

*Do not mix calcium solution with bicarbonate-containing fluids as precipitation may occur.
†Calculate dose based on elemental calcium content.

Oral Calcium

- Oral calcium supplementation may be beneficial. The daily requirements are 1 to 4 g for dogs and 0.5 to 1.0 g for cats.
- Base the dose of calcium on the amount of elemental calcium in the product.

Vitamin D Metabolites

Vitamin D supplementation increases calcium absorption in the small intestine.

- Calcitriol is the vitamin D compound of choice for chronic maintenance treatment of symptomatic hypocalcemia.
- Several forms of vitamin D are available, and the response and duration of action of these drugs depend on the form used (see Table 32-6).
- Iatrogenic hypercalcemia is a common complication of treatment with cholecalciferol, ergocalciferol, and dihydrotachysterol. Treatment with calcitriol is rarely associated with hypercalcemia.

▼ ***Key Point*** Calcitriol is the vitamin D compound of choice for chronic maintenance treatment of symptomatic hypocalcemia.

Magnesium

- If serum magnesium concentration is decreased, supplemental oral magnesium may be beneficial. Magnesium deficiency may reduce the ability of the parathyroid glands to produce PTH, preventing correction of hypocalcemia. Magnesium deficiency also impairs PTH receptor interactions at peripheral tissues.

CONDITIONS ASSOCIATED WITH HYPOCALCEMIA

Puerperal Tetany (Eclampsia)

Puerperal tetany or eclampsia occurs in lactating bitches and queens as a result of calcium loss into milk and/or poor dietary calcium intake. In non-lactating animals, this condition may be associated with high calcium supplementation resulting in suppression of PTH secretion and increasing calcitonin secretion. These changes decrease the osteoclast pool and the availability of bone calcium.

Clinical Signs

- Small-breed bitches with large litters are most often affected; puerperal tetany is rare in large-breed dogs or larger cats.
- Onset of signs is acute, occurring most often 2 to 4 weeks postpartum when milk production is at its peak. Clinical signs may also occur in the immediate postpartum period during the initial milk letdown.
- Tetany, tremors, twitching, and seizures are common.
- Hyperthermia may occur in severe cases.
- Panting and restlessness may be early signs.

Diagnosis

Diagnosis is made based on history, clinical signs, hypocalcemia (total serum calcium concentration usually <7 mg/dl), and response to treatment.

Treatment

- Immediately give an IV infusion of calcium (slow IV administration to effect, then 5–15 mg/kg/hr of elemental calcium; see Table 32-6).
- Supplement oral calcium (25–50 mg/kg/day of elemental calcium) for the remainder of lactation.
- Supplement vitamin D if serum calcium concentration remains low.
- If tetany recurs during the same lactation, wean the litter from the bitch.

Hypoparathyroidism

The marked hypocalcemia seen in hypoparathyroidism results from a deficiency in PTH production. Hypoparathyroidism in dogs and cats may be spontaneous or iatrogenic.

Etiology

Spontaneous Hypoparathyroidism

Spontaneous hypoparathyroidism occurs uncommonly in dogs and cats. Lymphocytic parathyroiditis and atrophy are the most common causes and presumably are autoimmune. Agenesis occurs very rarely.

Iatrogenic Hypoparathyroidism

Iatrogenic hypoparathyroidism may occur after bilateral thyroidectomy or parathyroidectomy for parathyroid adenoma or carcinoma and hyperplasia due to atrophy of the remaining glands. Normal function of the atrophic glands usually returns in 4 to 6 weeks.

Signalment

- In dogs, the mean age is 6 years, although a wide age range (6 weeks to 12 years) has been reported. In cats, young to middle-aged patients are reported.
- In dogs, more females are affected; however, in cats, more males appear to be affected.
- Primary hypoparathyroidism may occur in any breed, but breeds at increased risk include the standard schnauzer, miniature schnauzer, Scottish terrier, dachshund, and West Highland white terrier. Breeds at decreased risk for development of primary hypoparathyroidism include the Labrador retriever, German shepherd, and the Shih Tzu.

Clinical Signs

- Signs are usually episodic and most often include the following:
  - Nervousness, tremors, and twitching
  - Rigid limb extension, stiff gait, and muscle spasms
- Other signs include the following:
  - Ataxia, panting, and episodic weakness
  - Facial rubbing, biting at the feet, and aggression
  - Polydipsia and polyuria
  - Vomiting and diarrhea
  - Weight loss, anorexia, depression, and listlessness

Physical Examination

- Neuromuscular findings include extensor rigidity, muscle fasciculations, and seizures.
- Cardiac findings include tachycardia, paroxysmal tachyarrhythmias, and weak pulses.
- Ocular findings include small punctate to linear cataracts (reported in a few dogs and cats).

Diagnosis

Biochemistry Profile

- Serum total calcium concentration is usually <6.0 mg/dl (<1.5 mmol/L). Ionized calcium concentration is usually <4.0 mg/dl (<1.0 mmol/L) in dogs and <3.6 mg/dl (<0.9 mmol/L) in cats.
- Hyperphosphatemia is usually present.

Electrocardiography

- Electrocardiogram findings include prolongation of QT and ST segments, deep wide T waves, and tachyarrhythmias.

Endocrine Testing

- Concentrations of PTH are low compared with normal values. Relative PTH concentrations may appear to be within the normal reference range but are inappropriately low in the presence of hypocalcemia.

Biopsy

- Parathyroid biopsy confirms lymphocytic parathyroiditis, but biopsy is not usually necessary.

Treatment of Idiopathic Hypoparathyroidism

- The goal is to restore serum calcium concentration to the low end of the normal range. Avoid

further elevation of serum calcium levels to prevent calcium-induced renal damage from the resulting hypercalciuria.
- If hypocalcemic tetany or seizures are present, immediately administer calcium IV.
- For maintenance of normocalcemia, supplement oral calcium and vitamin D compounds (see Table 32-6). If serum magnesium concentration is also low, magnesium supplementation may be required for adequate maintenance of ionized calcium concentration.
- Hypercalcemia is a common complication of vitamin D therapy, and onset may be delayed and duration may be prolonged depending on the type of vitamin D supplementation used. When starting vitamin D therapy, monitor serum calcium concentrations weekly at first then monthly when serum calcium has stabilized at the desired level. If hypercalcemia does occur as a complication of treatment, manage as discussed previously under "Hypercalcemia." Discontinue calcium supplementation and use vitamin D alone at a lower dosage for maintenance or switch to a more manageable vitamin D metabolite such as calcitriol.

Treatment for Iatrogenic Hypoparathyroidism

- Supplement calcium and vitamin D compounds postoperatively (see Table 32-6). If serum calcium concentrations remain normal, discontinue calcium supplementation and then gradually decrease and finally discontinue vitamin D supplementation. Evaluate serum calcium concentrations weekly for 1 month. If hypocalcemia returns, reinstitute vitamin D and calcium supplementation. Occasionally, permanent supplementation is necessary.

PARATHYROIDECTOMY

Parathyroidectomy is the treatment of choice for primary hyperparathyroidism caused by benign functional adenomas of the parathyroid gland in dogs. Functional adenocarcinomas are very rare. Parathyroidectomy is an infrequent procedure because primary hyperparathyroidism is uncommon in dogs and extremely rare in cats.

Familiarity with normal thyroid and parathyroid anatomy is essential before surgery.

Preoperative Considerations

- Always submit all excised parathyroid gland tissue for histopathology to confirm the diagnosis.
- Ectopic parathyroid gland adenomas are uncommon but may be present in the cranial mediastinum or near the base of the heart.
- If the animal is hypercalcemic, attempt preoperatively to decrease serum calcium levels (see Table 32-3) to reduce risks of anesthesia and surgery if possible.
- To reduce the possibility of postoperative hypercalcemia, treat with calcitriol (see Table 32-6) for 1 to 2 weeks prior to parathyroidectomy.

Surgical Procedure

Objectives

- Explore the thyroid and parathyroid region.
- Remove the parathyroid adenoma.
- Maintain meticulous hemostasis.

Equipment

- Standard general surgical pack and suture
- Self-retaining retractors (e.g., Gelpi)
- Magnifying loop (optional)

Technique

1. Place the dog in dorsal recumbency with the forelimbs tied caudally and the neck hyperextended with a rolled towel.
2. Prepare the ventral cervical region from caudal mandible to manubrium for aseptic surgery.
3. Incise the skin on the ventral midline from larynx to manubrium.
4. Separate the paired sternohyoideus and sternothyroideus muscles.
5. Exploration.
   a. Identify all four parathyroid glands if possible. The non-adenomatous glands are often atrophied and difficult to identify.
   b. Parathyroid adenomas are firm, whitish, solid structures 4 to 20 mm in diameter. They are sometimes more hyperemic than the normal parathyroids.
   c. If an enlarged parathyroid gland is cystic, it is probably not a neoplasm but an incidental congenital cyst.
   d. If a readily identifiable mass is not found in the thyroid area, explore the accessible region along the trachea to the base of the neck and cranial mediastinum.
   e. Avoid injury to the carotid sheath structures and recurrent laryngeal nerves.
6. Dissection of the mass.
   a. Perform complete excision of the mass, using appropriate blunt and sharp dissection. Remove the associated thyroid lobe if necessary to achieve complete resection of the tumor (see Chapter 31).
   b. Carefully examine the surgical field for evidence of residual hemorrhage prior to closure.
7. Routinely close the muscle (simple continuous absorbable suture), subcutaneous tissue (simple continuous absorbable suture), and skin (simple interrupted non-absorbable monofilament suture).

Postoperative Care and Complications

- Monitor for hypothermia, hemorrhage at the incision site, and hypocalcemia.
- Postoperative hypocalcemia.
  - Return of serum calcium concentrations to normal or subnormal values indicates successful parathyroidectomy.

▼ ***Key Point*** Most dogs exhibit hypocalcemia within 48 hours of tumor removal. Suspect severe hypocalcemia in those patients with long-standing hypercalcemia and those in which hypercalcemia preoperatively was not severe.

  - Check serum calcium concentrations 1 and 2 days postoperatively. Frequent evaluation of calcium concentration is indicated if a hypocalcemic trend is noted.
  - Monitor for muscle tremors, excitement, and tetany if calcium concentrations are decreasing.
  - Treat hypocalcemia according to guidelines in the "Hypocalcemia" section of this chapter.
  - Hypocalcemia without clinical signs usually does not require treatment unless the total serum calcium is <6 mg/dl.
- Use weekly evaluation of serum calcium concentrations as the basis for modifying therapy with vitamin D compounds and calcium.
  - Gradually decrease dosages to maintain low-normal serum calcium levels until the atrophied parathyroid glands begin to function normally.
- Hypercalcemia may result from replacement therapy and should be avoided if possible.

Prognosis

The prognosis is good if the tumor is found and excised. Preexisting hypercalcemia-mediated renal dysfunction may be irreversible.

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Chapter

33 Diseases of the Adrenal Gland

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HYPOADRENOCORTICISM IN DOGS AND CATS

Hypoadrenocorticism is an endocrinopathy characterized by a deficiency of glucocorticoid and/or mineralocorticoid secretion from the adrenal cortex. Spontaneous hypoadrenocorticism is uncommon in dogs and is rare in cats.

Etiology

Primary Adrenocortical Insufficiency

Primary adrenocortical insufficiency (Addison disease) is the result of atrophy or destruction of all layers of the adrenal cortex, usually resulting in glucocorticoid and mineralocorticoid deficiency. Potential causes include the following:

- Idiopathic (probably immune mediated).
- Iatrogenic, which can result from mitotane therapy of hyperadrenocorticism in dogs. Mineralocorticoid concentrations remain normal in most dogs, and the glucocorticoid deficiency is usually transient (weeks to months). However, permanent iatrogenic Addison disease can occur.
- Granulomatous (fungal) adrenalitis, neoplasia, hemorrhage (very rare).

Secondary Hypoadrenocorticism

Secondary hypoadrenocorticism is due to deficient pituitary adrenocorticotropic hormone (ACTH) secretion resulting in inadequate glucocorticoid production, while mineralocorticoid secretion is preserved. Potential causes include the following:

- Abrupt withdrawal of long-term and/or high-dose glucocorticoid administration
- Megestrol acetate (Ovaban, Schering Plough) therapy in cats
- Lesions of the hypothalamus or pituitary gland (e.g., tumors)
- Idiopathic ACTH deficiency (rare)

Signalment

- *Age:* Most dogs and cats are young to middle-aged, but can range in age from 6 months to over 10 years.
- *Breed:* In dogs, any breed can be affected, but Great Danes, Portuguese water dogs, rottweilers, standard poodles, West Highland white terriers, and Wheaton terriers appear to be at an increased risk of developing naturally occurring primary hypoadrenocorticism. No breed predilection has been reported in cats.
- *Sex:* Female dogs are at an increased risk of developing naturally occurring primary hypoadrenocorticism (71% females in one study). No sex predilection has been reported in cats.

Clinical Signs

No historical or clinical finding or set of clinical signs is pathognomonic for hypoadrenocorticism, and most clinical signs occur frequently in various other more common disorders. The severity and duration of clinical signs vary greatly among patients. A high index of suspicion is needed to recognize some cases of hypoadrenocorticism.

Acute Hypoadrenocorticism

- History consistent with chronic hypoadrenocorticism preceding the acute addisonian crisis
- Weakness and depression progressing to collapse
- Slow capillary refill time, weak pulses progressing to hypovolemic shock
- Bradycardia and hypothermia
- Cardiac arrhythmias (secondary to electrolyte abnormalities, acidosis, azotemia, and poor perfusion)

Chronic Hypoadrenocorticism

- Anorexia, vomiting, and diarrhea.
- Muscle weakness, lethargy, and depression.
- Weight loss, dehydration, shaking, polydipsia, polyuria, melena, abdominal pain, and hair loss may be present.
- Waxing and waning course.

- Previous response of clinical signs to administration of fluids and/or glucocorticoids.
- Exacerbation of clinical signs associated with "stress."

Diagnosis

History and Clinical Signs

A high index of suspicion is necessary because both history and clinical signs are nonspecific and seen with many other more common disorders such as the following:

- Gastrointestinal disorders
- Primary renal failure
- Other causes of acute collapse or episodic weakness (cardiovascular disease, neuromuscular disease, and metabolic disorders)

Hemogram

- Absolute eosinophilia and lymphocytosis are present in some cases.
- High hematocrit and total plasma protein may occur secondary to dehydration.
- Mild anemia is present in some cases.

Serum Biochemical and Electrolyte Abnormalities

▼ ***Key Point*** Hyperkalemia and hyponatremia are seen in the vast majority of animals with primary hypoadrenocorticism, but do not rely on these abnormalities for definitive diagnosis as they can also be seen in other more common diseases.

- *Hyperkalemia* and a Na^+/K^+ ratio of less than 27 is present in 95% of cases of primary hypoadrenocorticism.
  - Occasionally, primary hypoadrenocorticism may be associated with normal serum electrolyte concentrations (atypical primary hypoadrenocorticism). Repeated determinations may be necessary to demonstrate the typical electrolyte abnormalities in some animals with primary hypoadrenocorticism.
  - Iatrogenic hypoadrenocorticism caused by mitotane or ketoconazole therapy is usually associated with normal serum electrolyte concentrations.
  - Secondary hypoadrenocorticism is usually associated with normal serum electrolyte concentrations, but hyponatremia can occur.
- *Azotemia* is common (>80%) in primary hypoadrenocorticism and may also occur in secondary hypoadrenocorticism.
- *Hypercalcemia* is seen in 30% of affected dogs and cats, possibly due to decreased renal calcium excretion.
- *Hypoglycemia* (rare) may occur secondary to decreased gluconeogenesis and glycogenolysis.
- *Metabolic acidosis* is not uncommon, especially in an addisonian crisis.

Urine-Specific Gravity

Urine-specific gravity is below 1.030 in over half of cases despite prerenal azotemia. This decreased urine-concentrating ability is probably due to medullary washout secondary to renal sodium wasting and decreased medullary blood flow.

Electrocardiographic Abnormalities

Electrocardiographic (ECG) changes are primarily attributable to hyperkalemia. Although electrocardiography can be of value in estimating the degree of hyperkalemia, these ECG abnormalities may correlate poorly with serum potassium concentrations because of the effects that other serum electrolyte abnormalities, metabolic acidosis, and impaired tissue perfusion have on the cardiac conduction system.

- Widening and flattening of P waves; increased duration of the PR interval
- Increased T wave amplitude
- Decreased amplitude and prolongation of QRS complexes
- Bradycardia
- Sinoatrial standstill (absence of P waves)
- Ventricular premature contractions, atrial fibrillation, and heart block

Radiographic Findings

- Microcardia, microhepatica, and hypoperfusion of lungs (as manifestations of hypovolemia)
- Megaesophagus (rare)

Adrenocorticotropic Hormone Stimulation Test

Definitive diagnosis of hypoadrenocorticism requires demonstration of inadequate adrenal reserve by use of the ACTH stimulation test. This test measures the relative "thickness" of the adrenal cortex.

Intravenous Procedure

- In dogs and cats, obtain a plasma or serum sample for cortisol determination before and 1 hour after IV injection of 5 µg/kg of the synthetic ACTH, cosyntropin (Cortrosyn, Amstar). Once reconstituted, the solution appears to be stable for at least 4 weeks if refrigerated. Alternatively, the remaining solution can be aliquoted and frozen. This method is recommended. Availability and backorder issues, however, may preclude use of this product.

Intramuscular Procedures

- Alternatively, in dogs, obtain a plasma or serum sample for cortisol analysis before and 2 hours after IM injection of 2.2 U/kg of ACTH gel. Acthar Gel (80 U/ml, Questcor Pharmaceuticals) is available but is very expensive. ACTH gel (usually 40 U/ml) is

available from various compounding pharmacies. The bioavailability and reproducibility of these various formulations have *not* been stringently evaluated. Therefore, it may be prudent to assess the activity of each new vial by performing an ACTH stimulation test on a normal dog.
- In cats, obtain a plasma or serum sample for cortisol determination before and 1 and 2 hours after IM injection of 2.2 U/kg of ACTH gel.

Interpretation

- Dogs and cats with hypoadrenocorticism show a blunted or absent cortisol response to ACTH administration.
- *Primary hypoadrenocorticism:* Basal and post-ACTH cortisol concentrations are usually <1 µg/dl (30 nmol/L).
- *Secondary hypoadrenocorticism:* The serum cortisol response to exogenous ACTH is blunted; however, post-ACTH concentrations of cortisol may be as high as 3.0 µg/dl (85 nmol/L) in some cases.
- False elevations of cortisol concentrations may occur after administration of prednisone, prednisolone, cortisone, or fludrocortisone because these cross-react on the cortisol radioimmunoassay. Discontinue these drugs 24 to 48 hours prior to the test.
- Dexamethasone and desoxycorticosterone pivalate (DOCP) do not interfere with the cortisol assay (see "Treatment"); however, dexamethasone is a potent steroid and suppresses the pituitary-adrenal axis.

Plasma Concentration of ACTH

Plasma concentration of ACTH is high (>500 pg/ml) in dogs and cats with primary hypoadrenocorticism and very low or undetectable with secondary hypoadrenocorticism. This assay is available at several diagnostic laboratories. Contact the appropriate laboratory for collection, shipping, and handling instructions (e.g., see www.ahdl.msu.edu for the Diagnostic Laboratory of Michigan State University).

Treatment

▼ ***Key Point*** Collect proper blood and urine samples and perform necessary diagnostic testing before instituting therapy.

The ACTH stimulation test (preferably using synthetic ACTH administered IV) can be performed simultaneously with initial therapy if dexamethasone is used for glucocorticoid replacement because it does not interfere with the cortisol assay. ACTH stimulation testing using ACTH gel should not be performed on dehydrated, hypovolemic, or hypotensive patients, since impaired absorption of the gel may result in erroneous results. Alternatively, testing can be performed after initial stabilization. If prednisone, prednisolone, or hydrocortisone is being administered, these are discontinued and the glucocorticoid supplementation is changed to dexamethasone for at least 24 hours before the ACTH stimulation test is done.

Acute Hypoadrenocorticism

This is a medical emergency requiring immediate intervention.

- Correct hypotension and hypovolemia.
- Improve vascular integrity.
- Provide an immediate source of rapid-acting glucocorticoid.
- Correct electrolyte imbalance and acidosis.
- Following stabilization of the acute addisonian crisis, institute long-term mineralocorticoid and glucocorticoid replacement therapy as described for treatment of chronic hypoadrenocorticism.

Hypovolemia and Hyponatremia

- Infuse 0.9% NaCl solution at a dosage of 60 to 80 ml/kg/hr IV over the first 1 to 2 hours, then gradually reduce the rate to the maintenance requirement, depending on patient response. Monitor urine output. Administer a colloid if necessary to address the hypovolemia and hypotension (uncommon).
- Administer dexamethasone sodium phosphate, 2 to 4 mg/kg IV, or prednisolone sodium succinate, 15 to 20 mg/kg IV. Repeat in 2 to 6 hours as needed. Glucocorticoid supplementation is gradually tapered to a maintenance dose of prednisone (0.2 mg/kg/day) over the following 3 to 5 days as the patient's condition improves.

Hyperkalemia

- Hyperkalemia associated with hypoadrenocorticism can often be successfully treated with parenteral fluid therapy (0.9% NaCl solution) only.
- For severe hyperkalemia causing life-threatening bradyarrhythmias and sinoatrial standstill, more aggressive therapy is indicated. Administer short-acting insulin (e.g., regular insulin) and dextrose IV (first choice), sodium bicarbonate, or calcium salts.
- A rapid-acting parenteral mineralocorticoid formulation is no longer available. However, begin oral supplementation with fludrocortisone (Florinef, Squibb) immediately if the animal is not vomiting.

Acidosis

- Correct mild to moderate acidosis with parenteral fluid therapy (0.9% NaCl solution).
- Treat severe acidosis (pH < 7.1) with serum bicarbonate. Give 25% of the calculated bicarbonate deficit over the first 6 to 8 hours of therapy if the serum bicarbonate concentration is <12 mEq/L. It is unusual for additional bicarbonate administration to be needed.

- Correction of acidosis also drives extracellular potassium into cells, thereby reducing hyperkalemia.

Other Supportive Care as Needed

- Correct hypothermia.
- Treat symptomatic hypoglycemia with a slow IV bolus of 1.5 ml/kg of 50% dextrose and 2.5% to 5% dextrose added to the IV fluids if needed.

Chronic Hypoadrenocorticism

Animals with chronic disease generally do not require aggressive therapy; however, parenteral fluid therapy and parenteral glucocorticoid supplementation may initially be indicated in some cases. Dogs and cats with primary hypoadrenocorticism require lifelong glucocorticoid and mineralocorticoid replacement therapy and sometimes the addition of salt to the diet. Animals with documented secondary hypoadrenocorticism require glucocorticoid replacement only.

Hypovolemia

- Give 0.9% NaCl solution, 60 to 80 ml/kg/day IV, for initial correction of hypovolemia.
- Decrease fluid volume over 48 to 96 hours based on return of clinical and laboratory parameters to normal.

Mineralocorticoid Supplementation

Use one of the following treatment protocols:

- DOCP (Percorten-V, Novartis)
  - DOCP is a long-acting injectable mineralocorticoid; give it initially at 2.2 mg/kg IM or SQ, every 4 weeks. A dosage interval of 3 to 4 weeks is effective in most cases.
  - Percorten-V is approved by the Food and Drug Administration (FDA) for treatment of primary hypoadrenocorticism in dogs.
  - Monitor serum electrolytes, blood urea nitrogen (BUN), and creatinine every 1 to 2 weeks until stabilized in the normal range to ensure an appropriate dose and duration of action; reevaluate every 3 to 6 months during long-term therapy.
  - Less than 10% of dogs require a dose greater than 2.2 mg/kg. Dose less than 2.2 mg/kg may be sufficient in some cases. If financial constraints are present, gradually reduce to the lowest effective dose while monitoring serum electrolyte concentrations.
  - Side effects are rare.
- Fludrocortisone acetate (Florinef, Squibb)
  - Give an initial dosage of 0.01 to 0.02 mg/kg/day PO.
  - Monitor serum electrolytes, BUN, and creatinine every 1 to 2 weeks until stabilized in the normal range, then reevaluate every 3 to 4 months.
  - Adjust dose by 0.05 to 0.1 mg/day based on serum electrolyte concentrations.
  - Average dose to control the disease is 0.02 to 0.03 mg/kg/day; very few animals can be controlled on less than 0.01 mg/kg/day.
  - Side effects include polyuria, polydipsia, polyphagia, and weight gain.
  - Development of side effects, relative resistance to the drug, or financial considerations may necessitate a change to DOCP.

Glucocorticoid Supplementation

Many patients require glucocorticoid supplementation in addition to mineralocorticoid therapy to prevent signs of glucocorticoid deficiency or to control persistent mild azotemia. Use one of the following:

- Prednisone or prednisolone, 0.2 mg/kg/day PO.
- Cortisone acetate, 1 mg/kg/day PO.
- Give 2- to 10-fold higher glucocorticoid doses for brief periods of stress, surgery, or illness.

Sodium Chloride Therapy

- NaCl, 1 to 5 g daily, may be beneficial in some patients to help normalize serum sodium concentration.
- NaCl supplementation may have a sparing effect on the required fludrocortisone dose needed occasionally in dogs.

HYPERADRENOCORTICISM IN DOGS

Spontaneous hyperadrenocorticism (Cushing's syndrome) is a collection of clinical and biochemical abnormalities caused by chronic overproduction of cortisol by the adrenal cortices.

Etiology

Hyperadrenocorticism can be pituitary dependent, secondary to cortisol-secreting adrenocortical neoplasia, or iatrogenic.

Pituitary-Dependent Hyperadrenocorticism

This is the most common cause of naturally occurring hyperadrenocorticism in dogs, accounting for 85% to 90% of cases. The excessive secretion of ACTH from pituitary corticotroph hyperplasia, microadenoma, macroadenoma, or (very rarely) adenocarcinoma results in bilateral adrenocortical hyperplasia.

Cortisol-Secreting Adrenocortical Tumors

These tumors are responsible for approximately 10% to 15% of dogs with spontaneous Cushing's syndrome. About half of adrenocortical tumors are benign and half are malignant.

Iatrogenic Hyperadrenocorticism

Excessive or prolonged administration of corticosteroids can cause iatrogenic hyperadrenocorticism.

- Clinical signs and physical examination findings are similar to those seen in the natural disease.
- Endogenous ACTH production is suppressed, resulting in atrophy of the adrenal cortices.

Signalment

- *Age:* Spontaneous hyperadrenocorticism is primarily a disease of middle-aged to older dogs but can be seen in dogs ranging from 6 months to 20 years of age.
- *Breed:* All breeds can be affected. Poodles, dachshunds, Boston terriers, and boxers appear to be at greater risk of developing pituitary-dependent hyperadrenocorticism. Adrenal tumors are more common in larger dogs (>20 kg).
- *Sex:* No sex predilection is seen in dogs with pituitary-dependent hyperadrenocorticism. In contrast, two-thirds of dogs with adrenal tumors are female.

Clinical Signs

▼ ***Key Point*** Dogs with hyperadrenocorticism usually develop clinical signs that reflect dysfunction of many organ systems, although in some dogs only one or a few clinical signs may predominate.

General Appearance

- Pendulous, distended, or "pot-bellied" abdomen
- Haircoat changes reflecting hair loss
- Muscle atrophy and weakness

Integument

- Hair loss ranging from a thinning of the coat to bilaterally symmetric alopecia
- Thin hypotonic skin susceptible to bruising
- Hyperpigmentation
- Seborrheic changes
- Secondary pyoderma and *Malassezia* dermatitis

Urinary and Reproductive Systems

- Polyuria and polydipsia are seen in up to 90% of dogs with hyperadrenocorticism. Glucocorticoids decrease the renal tubular reabsorption of water by increasing the glomerular filtration rate and renal blood flow and by inhibiting the action of antidiuretic hormone (ADH) at the tubular level.
- Urinary tract infection can occur secondary to the immunosuppressive effects of cortisol excess. The typical signs of pollakiuria, hematuria, and stranguria may be minimal in some dogs as a result of the anti-inflammatory action of cortisol.
- Glomerulopathy and associated proteinuria may occur.
- Testicular atrophy and female infertility (anestrus) can occur secondary to low concentrations of pituitary follicle-stimulating hormone (FSH) and luteinizing hormone (LH) caused by negative feedback from high circulating cortisol concentrations.

Respiratory System

- Excessive panting is quite common and is attributed to decreased pulmonary compliance, respiratory muscle weakness, pulmonary hypertension, or the direct effects of cortisol on the respiratory center.
- Pulmonary thromboembolic disease, a rare complication of hyperadrenocorticism, can cause moderate to severe respiratory distress and sometimes is fatal.

Endocrine System

- Some dogs with hyperadrenocorticism develop diabetes mellitus and the associated clinical signs of polyuria, polydipsia, weight loss, and polyphagia.
- The hallmark of steroid-induced diabetes is the development of insulin resistance, defined clinically as persistent hyperglycemia despite insulin doses of >2.5 U/kg per injection.
- Cortisol antagonizes the actions of insulin by interfering with its action at the cellular level (receptor and postreceptor effects).
- Hypertension may occur.

Central Nervous System and Neuromuscular System

- Lethargy is the most common central nervous system (CNS) disturbance. Lethargy may be associated with high concentrations of ACTH or the effects of excessive cortisol on cerebral enzymes and on neurotransmitter synthesis.
- CNS signs of circling, seizures, behavior change, and depression to obtundation may be caused by the local compressive effects of a large, expanding pituitary tumor.
- Muscle weakness is quite common and results from muscle wasting secondary to the catabolic effects of glucocorticoid excess.

Gastrointestinal System

- Polyphagia is common.
- Hepatomegaly is often detected.
- Pancreatitis secondary to excess cortisol levels is occasionally seen.

Diagnosis

History

Common owner complaints include polyuria and polydipsia, polyphagia, hair loss, weight gain, lethargy, and weakness. Determine recent corticosteroid administration (including eye, ear, and topical preparations).

Physical Examination

Perform a careful examination to determine the clinical signs listed on the previous page.

▼ ***Key Point*** The most important diagnostic procedures for hyperadrenocorticism are a careful and complete history and physical examination.

Routine Laboratory Testing

- The hemogram may reveal a stress leukogram and mild erythrocytosis.
- Up to 80% of dogs with hyperadrenocorticism have high serum alkaline phosphatase activity, composed primarily of the steroid-induced isoenzyme.
- Elevated serum cholesterol concentration is common.
- Increased serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) concentrations are common.
- Mild hyperglycemia is common. Overt diabetes mellitus (glucose >250 mg/dl) occurs in up to 10% of dogs with untreated hyperadrenocorticism.
- Urinalysis often reveals a low specific gravity (<1.020).
- Proteinuria is occasionally seen. A urine protein-to-creatinine ratio >3.0 is usually due to glomerular disease or urinary tract infection.

Radiography

- Hepatomegaly is common.
- Approximately one-third of adrenal tumors are mineralized and, therefore, detectable on abdominal radiographs.
- Mineralization of bronchial walls is an occasional incidental finding.
- Pulmonary metastasis is rarely detected in some dogs with adrenal carcinoma.

Ultrasonography

Ultrasonography is more sensitive than radiography for imaging the adrenal glands and is a recommended part of the workup of all dogs with hyperadrenocorticism. This is a very user-dependent technique.

- Bilateral adrenomegaly is found in most dogs with pituitary-dependent hyperadrenocorticism. The maximal adrenal diameter (thickness) is considered the best indicator of adrenal size (reference value for healthy dogs <7.4 mm); however, this lacks sensitivity and specificity as a definitive test because of overlap in adrenal size among healthy dogs, dogs with non-adrenal disease, and dogs with pituitary-dependent hyperadrenocorticism.
- An adrenal mass is usually readily identified in dogs with adrenal neoplasia. The contralateral adrenal is atrophied and unlikely to be found. Bilateral adrenal tumors are very rare.
- In dogs with adrenal neoplasia, evaluate the liver for metastasis and the caudal vena cava for tumor thrombus.

Computed Tomography and Magnetic Resonance Imaging

- Pituitary tumors >1 cm in diameter (macroadenomas or macroadenocarcinomas) are relatively easy to define with these imaging techniques.
- Pituitary microadenomas may be identified if they are ideally positioned or approach 1 cm in diameter. magnetic resonance imaging (MRI) is more sensitive than computed tomography (CT) for imaging pituitary microadenomas.
- CT and MRI are the most accurate and reliable methods for imaging the adrenal glands, followed by ultrasonography and then radiography. With CT or MRI, the location of the adrenal tumor and evidence of metastasis can be identified in most dogs.

Pituitary-Adrenal Function Tests

Basal Serum Cortisol Concentration

Basal serum (or plasma) cortisol concentrations cannot be used to diagnose hyperadrenocorticism because of significant overlap among dogs with hyperadrenocorticism, dogs with non-adrenal illness, and normal dogs.

Adrenocorticotropic Hormone Stimulation Test

This is an adrenal function test that measures the relative "thickness" of the adrenal cortex. Therefore, the ACTH stimulation test is the best test to differentiate spontaneous from iatrogenic hyperadrenocorticism.

- *Intravenous procedure*
  - Obtain a serum sample for cortisol determination before and 1 hour after IV injection of 5 µg/kg of the synthetic ACTH, cosyntropin (Cortrosyn, Amstar). Once reconstituted, the solution appears to be stable for at least 4 weeks if refrigerated. Alternatively, the remaining solution can be aliquoted and frozen. This method is recommended. Availability and backorder issues, however, may preclude use of this product.
- *Intramuscular procedure*
  - Obtain a serum sample for cortisol analysis before and 2 hours after IM injection of 2.2 U/kg ACTH gel. Acthar Gel (80 U/ml, Questcor Pharmaceuticals) is available but is very expensive. ACTH gel (usually 40 U/ml) is available from various compounding pharmacies. The bioavailability and reproducibility of these various formulations has not been stringently evaluated. Therefore, it may be prudent to assess the activity of each new vial by performing an ACTH stimulation test on a normal dog.

- *Interpretation*
  - Of the dogs with pituitary-dependent hyperadrenocorticism, 75% to 90% demonstrate an exaggerated cortisol response to exogenous ACTH. A post-ACTH cortisol concentration of more than 20 µg/dl (550 nmol/L) is consistent with hyperadrenocorticism.
  - Approximately 50% of dogs with adrenocortical tumors show an exaggerated cortisol response, whereas the remainder have a normal response. Some dogs with adrenal carcinoma have extremely high post-ACTH cortisol concentrations (>50 µg/dl or >1500 nmol/L).
  - Dogs with iatrogenic hyperadrenocorticism have a "blunted" or no response to ACTH administration.

Low-Dose Dexamethasone Suppression Test

This test is also useful for confirming the diagnosis of hyperadrenocorticism. The overall sensitivity of this test is 90% to 95%. In most dogs, this test does not differentiate pituitary-dependent hyperadrenocorticism from cortisol-secreting adrenal neoplasia.

- *Procedure*
  - Collect plasma or serum samples for cortisol determination before and 4 and 8 hours after IV or IM administration of 0.015 mg/kg dexamethasone (Azium, Schering Plough).
- *Interpretation*
  - In normal dogs, serum cortisol concentrations are suppressed below 1 µg/dl (30 nmol/L) by 4 hours after administration of dexamethasone and remain suppressed at 8 hours. In contrast, cortisol concentrations in most dogs with hyperadrenocorticism remain above 1 µg/dl (30 nmol/L) during the 8-hour test period. Some laboratories use a 1.5 µg/dl cutoff for the diagnosis of hyperadrenocorticism and consider the 1.0- to 1.5-µg/dl range a "gray zone."
  - The use of percentage of suppression to diagnose hyperadrenocorticism can be misleading in some cases. We prefer the use of a cutoff value.
  - Approximately 25% of dogs with pituitary-dependent hyperadrenocorticism show a pattern of "escape" from suppression; serum cortisol concentrations fall below 1 µg/dl (30 nmol/L) by 4 hours after administration of dexamethasone and rise above 1 µg/dl (30 nmol/L) by the eighth hour of the test. This pattern is diagnostic for pituitary-dependent hyperadrenocorticism.
  - About 5% of dogs with hyperadrenocorticism will have a normal test result. The test should be repeated in 3 to 6 months if clinical signs of hyperadrenocorticism persist.

Urine Cortisol-to-Creatinine Ratio

This is a convenient screening test for hyperadrenocorticism. A normal value virtually excludes a diagnosis of hyperadrenocorticism. A positive result must be confirmed with an ACTH stimulation test or a low-dose dexamethasone suppression test.

- *Procedure*
  - Submit a single-morning urine sample to the laboratory for measurement of urine cortisol and urine creatinine concentrations. The sample should be collected at home by the owner rather than in the hospital.
- *Interpretation*
  - When urine cortisol is expressed as nmol/L and creatinine is expressed as mmol/L, a ratio >15 is consistent with hyperadrenocorticism in most laboratories.

▼ ***Key Point*** All pituitary-adrenal function tests used to diagnose hyperadrenocorticism commonly show false-positive results in dogs with non-adrenal disease. Whenever possible, pituitary-adrenal function testing should be postponed until the non-adrenal disease has been resolved.

Endogenous Plasma Adrenocorticotropic Hormone Concentration

This test reliably distinguishes pituitary-dependent hyperadrenocorticism from adrenocortical tumors.

- *Procedure*
  - Collect blood in an ethylenediaminetetraacetic acid (EDTA) tube, centrifuge immediately, and remove the plasma. The addition of aprotinin to EDTA tubes allows routine handling of ACTH samples and shipment using cold packs (instead of dry ice). This assay is available at several diagnostic laboratories. Contact the appropriate laboratory for collection, shipping, and handling instructions (e.g., see www.ahdl.msu.edu for the Diagnostic Laboratory of Michigan State University).
- *Interpretation*
  - Dogs with pituitary-dependent hyperadrenocorticism have a normal to high ACTH concentration (>40 pg/ml).
  - Dogs with adrenal tumors have low or undetectable plasma concentration of ACTH (<20 pg/ml).

High-Dose Dexamethasone Suppression Test

This test is used to differentiate dogs with pituitary-dependent hyperadrenocorticism from those with adrenocortical neoplasia. The test is easily performed in practice.

- *Procedure*
  - Collect a serum or plasma sample for cortisol determination before and 4 and 8 hours after IV or IM injection of 0.1 to 1.0 mg/kg of dexamethasone.
  - In dogs with pituitary-dependent hyperadrenocorticism, the degree of cortisol suppression tends to

be greater after administration of the 1.0 mg/kg dose.

- *Interpretation*
  - Dogs with adrenal tumors do not show feedback suppression of cortisol after administration of a high dose of dexamethasone, with serum cortisol concentrations remaining >1.5 µg/dl (>40 nmol/L) during the testing period. Suppression of serum cortisol concentration to <1.5 µg/dl excludes an adrenal tumor.
  - In dogs with pituitary-dependent hyperadrenocorticism, approximately 80% demonstrate suppression of cortisol (<1.5 µg/dl or <40 nmol/L) after administration of a high dose of dexamethasone.
  - The remaining 20% of dogs with pituitary-dependent hyperadrenocorticism fail to demonstrate adequate cortisol suppression (i.e., all cortisol values remain >1.5 µg/dl or >40 nmol/L). Additional testing is necessary to distinguish these dogs from those with an adrenal tumor. Many dogs with non-suppressible pituitary-dependent hyperadrenocorticism have large pituitary tumors.
  - The use of percentage of suppression to differentiate between pituitary- and adrenal-dependent hyperadrenocorticism can be misleading in some cases. We prefer the use of a cutoff value.

Treatment of Pituitary-Dependent Hyperadrenocorticism

Mitotane Therapy

Mitotane (o,p′-DDD; Lysodren, Bristol-Myers Squibb) is the drug most frequently used in the treatment of hyperadrenocorticism in dogs. Mitotane causes selective necrosis of the zona fasciculata and zone reticularis of the adrenal cortex. The administration protocol for mitotane involves an initial induction phase that uses a daily dosage for induction of remission (loading dosage), followed by a maintenance phase that uses a dosage given once or twice weekly (maintenance dosage).

Induction Phase

- The *initial loading dosage* of mitotane is 30 to 50 mg/kg/day, given once daily or divided q12h PO, for 7 to 10 days. Mitotane absorption is enhanced by food (especially fat) and, therefore, should be given with a meal.
- *Concurrent glucocorticoid supplementation* with oral prednisone or prednisolone (0.15–0.25 mg/kg/day, up to a maximum daily dose of 5 mg/day/dog) can be used to mitigate the adverse effects associated with serum cortisol concentrations falling rapidly into the normal or subnormal range during this initial treatment. The major disadvantage of providing glucocorticoid is that it may not be possible to know if overdosage has occurred, since clinical signs of glucocorticoid deficiency may not develop.
- Common side effects during the induction phase of therapy (the loading period) include lethargy, vomiting, anorexia, weakness, and diarrhea. If adverse effects occur during initial therapy, discontinue mitotane and give glucocorticoids until the dog can be evaluated. Monitor the dog's appetite closely during the induction period, and if decreased appetite develops, discontinue mitotane and evaluate by an ACTH stimulation test.
- Monitor therapy with the ACTH stimulation test. Perform this test at the end of the 10-day induction phase or sooner if adverse effects develop.

▼ ***Key Point*** The goal of therapy is to achieve subclinical hypoadrenocorticism, whereby both basal and post-ACTH cortisol concentrations are within the normal basal (or resting) cortisol range (1 to 5 µg/dl or 30 to 150 nmol/L for most laboratories).

- If basal and post-ACTH concentrations fall below the normal basal range (<1 µg/dl or <30 nmol/L), temporarily suspend mitotane administration and supplement glucocorticoids as needed until circulating cortisol concentrations normalize. Cortisol concentrations generally return to the normal range within 2 to 4 weeks but occasionally take several weeks to months.
- If basal or post-ACTH cortisol concentrations are above the normal resting range, continue daily mitotane treatment and repeat ACTH stimulation tests at 5- to 10-day intervals until serum cortisol concentrations fall within the normal resting range.

Maintenance Phase

- When desired cortisol concentrations are documented by ACTH stimulation testing, continue mitotane at a *maintenance dosage* of 40 to 50 mg/kg weekly in two to three divided doses. Lifelong maintenance therapy is needed to maintain remission of the disease.
- If adverse side effects occur during maintenance therapy, discontinue mitotane and supplement glucocorticoids until the dog can be evaluated by serum electrolyte determinations and an ACTH stimulation test. In most dogs with iatrogenic hypoadrenocorticism (but normal serum electrolytes), maintenance mitotane can be resumed 2 to 6 weeks later, when serum cortisol concentrations have returned into the normal resting range. About 20% to 25% of dogs experience side effects, usually mild, at some point during induction or maintenance mitotane therapy.
- Up to 5% of dogs develop iatrogenic hypoadrenocorticism with associated hyponatremia and hyperkalemia. These dogs generally require lifelong supplementation with mineralocorticoids, that is, fludrocortisone acetate or DOCP (see "Hypoadrenocorticism in Dogs and Cats").

- Nearly 50% of dogs with hyperadrenocorticism have a relapse of disease within the first 12 months of maintenance therapy. These cases require reinduction with daily doses of mitotane for 7 to 10 days, followed by a higher maintenance dosage (weekly dosage usually increased 50%).
- To ensure continued control and prevent serious relapse during mitotane treatment, repeat ACTH stimulation testing after 3 and 6 months of maintenance treatment and every 6 months thereafter. Relapse of hyperadrenocorticism can thereby usually be detected before recurrence of clinical signs is evident.

Trilostane Therapy

Trilostane is a synthetic steroid analogue. It competitively inhibits the 3-beta hydroxysteroid dehydrogenase enzyme; thereby blocking cortisol, aldosterone, and sex hormone production. Trilostane is available in the United Kingdom (Vetoryl, Arnolds Veterinary Products). Until an approved product is available in the United States, the manufacturer recommends contacting the FDA for permission to import a 90-day supply for a given patient.

Trilostane is effective in controlling the clinical signs in most dogs with pituitary-dependent hyperadrenocorticism. Reported efficacy is less than or equal to that of mitotane.

Initial Dose

- Give 2 to 12 mg/kg PO with food (the mean starting dose is approximately 6 mg/kg/day).
- Do not use trilostane in animals with renal failure or primary liver disease, lactating animals, or those intended for breeding.

Follow-up Treatment and Monitoring

- Evaluate response to treatment based on resolution of clinical signs of hyperadrenocorticism and results of ACTH stimulation tests.
- Examine the patient and perform an ACTH stimulation test at 10 days, 1 month, 3 months, and every 3 to 6 months thereafter. Evaluate complete blood counts and serum chemistry profiles on a regular basis.
- Perform ACTH stimulation testing 4 to 6 hours after trilostane is administered.
- Increase or decrease the trilostane dosage to achieve pre-ACTH and post-ACTH cortisol concentrations between 1 and 5 µg/dl. During the first 6 months of therapy, at least 50% of dogs can be expected to require a change of dosage (usually an increase).
- Some dogs may need twice-daily administration of trilostane to adequately control clinical signs.
- If the post-ACTH serum cortisol concentration is below 1 µg/dl, discontinue trilostane for 48 to 72 hours and then start again at a lower dose. Perform an ACTH stimulation test in 7 to 10 days.
- If signs of hypoadrenocorticism occur, discontinue trilostane until the dog can be evaluated and ACTH stimulation testing and a chemistry profile (including electrolytes) can be performed. Administer glucocorticoid if necessary.

Adverse Effects

- Trilostane is usually well tolerated. Mild, self-limited adverse effects including lethargy, vomiting, and diarrhea were reported in 63% of dogs in one study.
- Side effects required withdrawal of trilostane in approximately 3% to 4% of dogs.
- Acute death was reported in two dogs a few days after starting trilostane therapy. Other anecdotal reports of acute death have been noted. The exact relationship of trilostane to these deaths is not completely clear at this time.
- One report describes bilateral adrenal necrosis seen on histopathology in two dogs on trilostane.
- Acute hypoadrenocorticism has been reported in two dogs. One of these cases died despite discontinuation of trilostane and appropriate medical intervention.
- Occasional instances of prolonged (up to several months) adrenocortical suppression can be seen in dogs receiving trilostane. It is not clear how an enzyme inhibitor can cause prolonged adrenocortical suppression or acute hypoadrenocorticism.
- Hyperkalemia and/or hyponatremia can be seen in a significant number of dogs at variable times after starting trilostane. These changes are not typically associated with clinical signs of hypoadrenocorticism or altered aldosterone levels.

Ketoconazole Therapy

Ketoconazole (Nizoral, Janssen) reversibly inhibits adrenal steroidogenesis through enzymatic blockade. The major problems of ketoconazole compared with mitotane include its high cost, the necessity for lifelong twice-daily administration, and reported lack of efficacy in some cases (up to 50% in some reports).

- The initial dosage of ketoconazole is 10 mg/kg q12h PO.
- Assess adrenal reserve with an ACTH stimulation test after 7 to 10 days of therapy. The goal of therapy is to achieve subclinical hypoadrenocorticism, whereby both basal and post-ACTH cortisol concentrations are within the normal basal cortisol range (1–5 µg/dl or 25 to 150 nmol/L for most laboratories).
- The dosage of ketoconazole can be increased (up to 20 mg/kg q12h) if necessary.
- Once adequate control is achieved, lifelong twice-daily therapy is required to maintain remission of the hyperadrenocorticism.

- Adverse effects include anorexia, vomiting, diarrhea, lethargy, and idiosyncratic hepatopathy.

L-Deprenyl Therapy

L-deprenyl (selegiline HCl; Anipryl, Pfizer) is a selective, monoamine oxidase type B inhibitor that decreases pituitary ACTH secretion by increasing dopaminergic tone to the hypothalamic-pituitary axis, with a resultant fall in serum cortisol concentrations. Drawbacks of L-deprenyl therapy include low reported efficacy rates, the need for lifelong daily administration, and the expense of the medication.

- Initiate L-deprenyl therapy at a dosage of 1 mg/kg PO daily. If an inadequate response is seen after 2 months of therapy, increase the dosage to 2 mg/kg/day. Should this dose also prove ineffective, use alternative therapy. If effective, continue daily therapy for the remainder of the dog's life.
- The drug is indicated for the treatment of uncomplicated cases of pituitary-dependent hyperadrenocorticism. L-deprenyl is not recommended for treatment in dogs with concurrent diabetes mellitus, pancreatitis, heart failure, renal disease, or other severe illness, and it is not effective for the treatment of cortisol-secreting adrenocortical neoplasia.
- The manufacturer's multicenter trial reported that 75% to 80% of dogs had a good response to therapy as assessed by resolution of clinical signs and monthly low-dose dexamethasone suppression testing. Independent studies have reported efficacy rates of 20% or less.
- The current label recommendation is to evaluate the efficacy of L-deprenyl therapy based solely on resolution of clinical signs of hyperadrenocorticism. It seems prudent, however, to monitor low-dose dexamethasone suppression tests every 4 to 6 weeks to evaluate for normalization (or improvement) of the pituitary-adrenal axis in dogs receiving the drug. The ACTH stimulation test is not indicated for assessing the response to treatment with L-deprenyl.
- Adverse effects such as anorexia, lethargy, vomiting, and diarrhea are uncommon (<5% of dogs) and usually mild.
- Do not administer L-deprenyl concurrently with other monoamine oxidase inhibitors, opioids, or tricyclic antidepressants (e.g., fluoxetine), as significant adverse drug interactions have been reported in humans.

Radiation Therapy for Pituitary-Dependent Hyperadrenocorticism

Radiation therapy may be useful in dogs with hyperadrenocorticism caused by a pituitary macroadenoma or macrocarcinoma.

- Deliver the total dose of radiation in fractions over a period of 4 to 6 weeks. Complications appear to be minimal in most cases.
- The primary prognostic factor is the severity of neurologic signs. Dogs with a pituitary macroadenoma and severe neurologic signs have a grave prognosis.
- The disadvantages of radiation therapy include its high cost, limited availability, and the need for multiple anesthetic episodes.
- Plasma ACTH and serum cortisol concentrations may take weeks to months to normalize. In the interim, medical management of the hyperadrenocorticism may be necessary.

▼ ***Key Point*** Advances in diagnostic imaging (CT and MRI) have enabled the antemortem diagnosis of pituitary macroadenomas. Treatment of pituitary tumors may be attempted with radiotherapy, especially if a diagnosis of macroadenoma can be made before the onset of profound neurologic signs.

Surgical Management of Pituitary-Dependent Hyperadrenocorticism

Hypophysectomy has recently been described in a large series of dogs and has been shown to be a viable and effective treatment for pituitary-dependent hyperadrenocorticism.

- At this writing, the procedure has limited availability in the United States.
- Preoperative advanced imaging studies (preferably MRI) are needed.
- The experience of the surgeon and the provision of intensive 24-hour postoperative care are of vital importance for the success of this procedure.

Adrenocortical Tumors

Surgical Management

See the section on "Adrenalectomy."

Mitotane Therapy

- Mitotane is an effective and relatively safe treatment alternative for most dogs with adrenal tumors. Mitotane therapy has been successful for over 24 months in some dogs with adrenocortical adenomas and carcinomas. In general, higher dosages of mitotane are required than for treatment of dogs with pituitary-dependent hyperadrenocorticism. Only 15% to 20% of dogs with adrenal tumors respond to the standard treatment protocol used in dogs with pituitary-dependent hyperadrenocorticism.

▼ ***Key Point*** In dogs with adrenal tumors, mitotane is used as a true chemotherapeutic agent with the goal of destroying all functional, neoplastic adrenocortical tissue. Therefore, both the serum

basal and the post-ACTH cortisol concentrations should be low to undetectable (<1 µg/dl or <30 nmol/L). The induction of overt hypoadrenocorticism may improve the long-term prognosis, but mitotane toxicity (from the high doses of mitotane needed) prevents this approach in many dogs.

Indications for Mitotane Therapy of Adrenal Tumors

- Gross metastatic disease evident prior to surgery
- Unresectable or incompletely resectable tumor
- Residual disease after adrenalectomy as detected by ACTH stimulation testing
- Unacceptable anesthetic or surgical risks to the patient
- Refusal of surgery by the client

Procedure

- Initiate mitotane therapy at dosage of 50 to 75 mg/kg/day and repeat ACTH stimulation testing every 10 to 14 days to evaluate adrenal reserve. Administer a glucocorticoid (e.g., prednisone or prednisolone, 0.2 mg/kg/day PO) throughout the period of mitotane administration to help prevent adverse effects secondary to hypoadrenocorticism.
- Continue daily mitotane at this dosage or increase it (based on ACTH stimulation test results) until desired cortisol levels are reached or drug intolerance develops. Dogs with adrenal tumors often require a cumulative mitotane induction dose up to 10 times higher than dogs with pituitary-dependent hyperadrenocorticism (due to a longer period of daily mitotane administration).
- Once serum cortisol concentrations are undetectable to low, start maintenance therapy at 75 to 100 mg/kg weekly in divided doses. Continue daily glucocorticoid supplementation. Perform an ACTH stimulation test in 1 month to ensure continued suppression of serum cortisol concentrations.
- Dogs with adrenal tumors typically require higher maintenance dosages of mitotane than dogs with pituitary-dependent hyperadrenocorticism; about 25% need a maintenance dosage >150 mg/kg weekly. Relapses are not uncommon.
- Although not correlated with tumor response in all dogs, cortisol determinations are a practical and relatively reliable means of monitoring therapy. They should be performed 1 month after any change in mitotane dosage and every 3 to 6 months during long-term therapy. Periodic ultrasonographic evaluation is also useful for evaluating tumor response.

Adverse Effects

- Common side effects include anorexia, weakness, vomiting, diarrhea, and lethargy and are seen in up to 60% of cases. Adverse effects may be due to development of hypoadrenocorticism, but in approximately 50% of dogs the side effects appear to result from direct drug toxicity. If adverse reactions occur, stop the drug and evaluate the dog as soon as possible to exclude glucocorticoid and mineralocorticoid deficiency. If direct drug toxicity is occurring, start mitotane again later at a 25% to 50% lower dosage. Reinstitution of the higher maintenance dosage can be attempted later but usually results in recurrence of adverse effects. Complete glucocorticoid and mineralocorticoid deficiency (Addison disease) has been reported in a few cases.

Patient Monitoring

- Mitotane overdosage and underdosage can complicate therapy; long-term monitoring is therefore necessary. Instruct owners to observe for recurrence of symptoms, especially polyuria and polydipsia. Perform an ACTH stimulation test every 3 to 6 months to assess adrenal reserve and to guide mitotane dosage adjustments.

Trilostane Therapy

Trilostane has been used to treat a small number of dogs with adrenal-dependent hyperadrenocorticism with good response in most cases.

- Being an enzyme inhibitor, trilostane provides control of serum cortisol levels but should not affect the underlying neoplastic process. However, there are a few reports of acute hypoadrenocorticism as well as bilateral adrenal necrosis in dogs with pituitary-dependent hyperadrenocorticism receiving trilostane.
- Trilostane is not cytotoxic. Therefore mitotane may be preferable for treatment of malignant adrenocortical tumors.
- Trilostane may be useful for the preoperative control of serum cortisol concentrations and clinical signs in dogs undergoing adrenalectomy.

Prognosis

The prognosis for hyperadrenocorticism is always guarded because of the many complications associated with the disease. Dogs that succumb to such complications usually do so within the first 3 to 6 months after diagnosis. Dogs that survive this period typically die of other geriatric disorders unrelated to hyperadrenocorticism. The average life span after diagnosis is 2 years. Complications include the following:

- Thromboembolism
- Infection
- Hypertension
- Congestive heart failure
- Recurrence of clinical signs

- Progression of CNS signs (expanding pituitary tumor)
- Glomerulopathy
- Pancreatitis

ATYPICAL HYPERADRENOCORTICISM IN DOGS

These dogs have the typical historical, physical examination and routine laboratory findings associated with hyperadrenocorticism but have normal cortisol values after ACTH stimulation and low-dose dexamethasone suppression testing. The adrenal steroid indicator in serum for this disease is 17-hydroxyprogesterone rather than cortisol. Atypical hyperadrenocorticism can be due to pituitary-dependent disease or adrenal tumor.

Diagnosis

Adrenocorticotropic Hormone Stimulation Test

This is an adrenal function test that measures the relative "thickness" of the adrenal cortex.

Intravenous Procedure

- Obtain a serum sample for 17-hydroxyprogesterone determination before and 1 hour after IV injection of 5 µg/kg of the synthetic ACTH, cosyntropin (Cortrosyn, Amstar). Once reconstituted, the solution appears to be stable for at least 4 weeks if refrigerated. Alternatively, the remaining solution can be aliquoted and frozen. This method is recommended. Availability and backorder issues, however, may preclude use of this product.

Intramuscular Procedure

- Obtain a serum sample for 17-hydroxyprogesterone analysis before and 2 hours after IM injection of 2.2 U/kg ACTH gel. Acthar Gel (80 U/ml, Questcor Pharmaceuticals) is available but is very expensive. ACTH gel (usually 40 U/ml) is available from various compounding pharmacies. The bioavailability and reproducibility of these various formulations has not been stringently evaluated. Therefore, it may be prudent to assess the activity of each new vial by performing an ACTH stimulation test on a normal dog.

17-Hydroxyprogesterone Assay

- This adrenal function assay is available at the University of Tennessee's College of Veterinary Medicine Endocrine Diagnostic Lab at www.vet.utk.edu/diagnostic/endocrinology.

Interpretation

- A post-ACTH 17-hydroxyprogesterone concentration >6.5 nmol/L is consistent with atypical hyperadrenocorticism. Dogs with non-adrenal illness can have elevated 17-hydroxyprogesterone levels after ACTH stimulation.

Imaging Studies

- As in cases of "typical" hyperadrenocorticism, radiography, ultrasound, CT, and/or MRI may be helpful in evaluating dogs with atypical hyperadrenocorticism and in differentiating pituitary-dependent from adrenal-dependent cases.

Treatment

- Dogs with pituitary-dependent atypical hyperadrenocorticism can be treated with mitotane or trilostane (see the corresponding sections above). Hypophysectomy is a viable treatment option if available.
- When using mitotane, pre-ACTH and post-ACTH 17-hydroxyprogesterone levels can be used to monitor therapy. Because of the shorter turnaround time, we typically use pre-ACTH and post-ACTH cortisol levels to monitor mitotane therapy. The treatment protocol and desired cortisol levels during therapy are similar to those for dogs with "typical" hyperadrenocorticism (see the previous sections).
- If trilostane is used, 17-hydroxyprogesterone levels cannot usually be used to monitor therapy. Serum concentrations of 17-hydroxyprogesterone appear to be greatly elevated, likely a result of crossreactivity with the assay by 17-hydroxypregnenolone, which is increased by trilostane inhibition of the 3-beta hydroxysteroid enzyme.
- Atypical hyperadrenocorticism caused by an adrenal tumor can be managed with surgical adrenalectomy, mitotane, or trilostane as in cases of "typical" hyperadrenocorticism (see other sections).

HYPERADRENOCORTICISM IN CATS

Etiology

Hyperadrenocorticism in cats can be due to pituitary-dependent disease, adrenocortical neoplasia, or iatrogenic disease. Hyperadrenocorticism is uncommon in cats.

- *Pituitary-dependent hyperadrenocorticism* is the most common cause of the naturally occurring disorder in cats, accounting for 80% of the cases.
- *Cortisol-secreting adrenocortical neoplasia* is present in approximately 20% of cats with spontaneous hyperadrenocorticism. About one-third of adrenal tumors in cats are malignant.
- *Iatrogenic hyperadrenocorticism* can occur in cats, despite the relative resistance of cats to the effects of glucocorticoids when compared with dogs.

Signalment

- *Age:* Spontaneous hyperadrenocorticism is a disease of middle-aged to older cats (range from 5 to 16 years).
- *Breed:* No breed predilection.
- *Sex:* Sixty percent of reported cases have been female.

Clinical Signs

General Appearance

- Pendulous, distended, or "pot-bellied" abdomen
- Bilaterally symmetric alopecia with dull, dry, haircoat and scaling (seborrhea sicca)
- Thin skin
- Muscle atrophy

Endocrine and Urinary System

- *Polyuria, polydipsia,* and *polyphagia.* In contrast to dogs with hyperadrenocorticism, polyuria and polydipsia in affected cats appear to be secondary to concurrent diabetes mellitus in the vast majority of cases.
- Glucose intolerance and insulin resistance are common.

▼ ***Key Point*** The majority of cats (almost 80%) with hyperadrenocorticism have concurrent diabetes mellitus.

Diagnosis

History

Common reported signs include polyuria and polydipsia, pot-bellied appearance, thin skin, bilateral alopecia, lethargy, and weakness. Determine if exogenous glucocorticoids have recently been given.

Physical Examination

Many of the clinical signs listed above may be noted. Other findings may include hepatomegaly, obesity or weight loss, and fragile tearing skin.

Routine Laboratory Testing

- Hyperglycemia and glycosuria are seen in up to 90% of cats.
- Hypercholesterolemia and elevated serum ALT activity are common.
- Leukocytosis, eosinopenia, and lymphopenia may be noted.

▼ ***Key Point*** In contrast to the disease in dogs, elevated serum alkaline phosphatase is *not* a consistent finding in cats with hyperadrenocorticism.

Pituitary-Adrenal Function Tests

Adrenocorticotropic Hormone Stimulation Test

This is a valuable screening test for hyperadrenocorticism in cats.

- *Procedure*
  - Collect a plasma or serum sample before and 60 minutes after IV administration of 5 µg/kg of the synthetic ACTH, cosyntropin (Cortrosyn, Amstar). Once reconstituted, the solution appears to be stable for at least 4 weeks if refrigerated. Alternatively, the remaining solution can be aliquoted and frozen. This method is recommended. Availability and backorder issues, however, may preclude use of this product.
  - Collect a plasma or serum sample for cortisol analysis before and at 60 and 120 minutes after IM injection of 2.2 U/kg ACTH gel. The maximal rise in cortisol concentration occurs at 2 hours in 60% of normal cats, whereas the remaining cats peak at 1 hour after ACTH injection. Acthar Gel (80 U/ml, Questcor Pharmaceuticals) is available but is very expensive. ACTH gel (usually 40 U/ml) is available from various compounding pharmacies. The bioavailability and reproducibility of these various formulations has not been stringently evaluated. Therefore, it may be prudent to assess the activity of each new vial by performing an ACTH stimulation test on a normal cat.
- *Interpretation*
  - Approximately 66% of cats with naturally occurring hyperadrenocorticism show a high-normal or exaggerated cortisol response to exogenous ACTH.
  - Cats with iatrogenic hyperadrenocorticism show a "blunted" or no response to ACTH.
  - The ACTH stimulation test does not differentiate pituitary-dependent hyperadrenocorticism from a functional adrenal tumor.

Low-Dose Dexamethasone Suppression Test

- Suppression of serum cortisol concentration (<1.5 µg/dl or <40 nmol/L) 8 hours after administration of a low dose of dexamethasone (0.01–0.015 mg/kg IV) excludes a diagnosis of hyperadrenocorticism.
- However, cats with non-adrenal illness (e.g., diabetes mellitus) frequently demonstrate inadequate suppression, as do cats with hyperadrenocorticism. Because of these frequent false-positive results (low specificity), this test is not recommended as the sole diagnostic test for hyperadrenocorticism in cats.

High-Dose Dexamethasone Suppression Test

- *Procedure*
  - Collect plasma or serum samples for cortisol analysis before and at 4 and 8 hours after IV administration of 0.1 mg/kg dexamethasone.

- *Interpretation*
  - This test is useful in distinguishing normal cats or cats with non-adrenal disease from cats with hyperadrenocorticism.
  - In contrast to most dogs with pituitary-dependent hyperadrenocorticism, 75% of cats with pituitary-dependent disease fail to show adequate cortisol suppression after high-dose dexamethasone suppression testing.
  - All cats with adrenal-dependent hyperadrenocorticism fail to show adequate cortisol suppression after high-dose dexamethasone suppression testing.
  - Therefore, this test cannot readily distinguish pituitary-dependent hyperadrenocorticism and adrenal tumor in cats.
  - Due to the potential for false-negative results in cats with pituitary-dependent hyperadrenocorticism, do not exclude the diagnosis on the basis of a single normal result, especially if clinical signs or imaging studies support the diagnosis.

▼ ***Key Point*** The low-dose dexamethasone suppression test has not been well standardized in the cat. The high-dose dexamethasone test (0.1 mg/kg IV) appears to be the preferred method of screening for hyperadrenocorticism in cats at this time.

Urine Cortisol-to-Creatinine Ratio

- This may be a useful screening test for hyperadrenocorticism in cats. A normal result makes a diagnosis of hyperadrenocorticism very unlikely.
- As in dogs, a positive test must be interpreted cautiously due to the low specificity of the test, and the diagnosis should be confirmed with an ACTH stimulation or a dexamethasone suppression test.

Plasma Adrenocorticotropic Hormone Concentration

- Endogenous plasma ACTH concentration can be used to distinguish pituitary-dependent hyperadrenocorticism from adrenocortical tumors in cats. Cats with pituitary-dependent hyperadrenocorticism have a normal to high ACTH concentration (>40 pg/ml).
- Cats with cortisol-secreting adrenal tumors have a low plasma concentration of ACTH (<20 pg/ml).
- The feline ACTH assay is available at the Diagnostic Laboratory of Michigan State University, www.ahdl.msu.edu.

Diagnostic Imaging

- *Radiography* has limited value in determining the etiology of hyperadrenocorticism in cats unless an obvious adrenal mass is apparent.
- *Ultrasonography* can be a sensitive means for evaluating the adrenal glands of cats with hyperadrenocorticism. A bilateral adrenal enlargement is seen in most cats with pituitary-dependent hyperadrenocorticism, and a unilateral adrenal mass is seen in almost all cats with adrenal neoplasia.
- *CT and MRI* scans can be useful and sensitive for determining the cause of hyperadrenocorticism; however, they require anesthesia and have limited availability.

Treatment

Medical Treatment

- *Mitotane* (Lysodren, Bristol-Myers Squibb) has been safely administered to cats with hyperadrenocorticism at dosages comparable to those given dogs. However, it has not been effective in controlling the disorder in most reported cases, and some cats tolerate the drug poorly.
- *Ketoconazole* does not reliably decrease serum cortisol concentrations in cats with hyperadrenocorticism. Two of four cats with pituitary-dependent hyperadrenocorticism given 10 to 20 mg/kg daily showed some improvement, whereas two cats with adrenal neoplasia failed to show significant improvement.
- *Metyrapone,* an enzyme inhibitor that blocks adrenal synthesis of glucocorticoids, has been used with mixed results in treating cats with hyperadrenocorticism at dosages ranging from 200 to 500 mg daily. Some cats showed clinical improvement without significant side effects.
- *Trilostane* is another enzyme inhibitor that blocks adrenal synthesis of glucocorticoids. Preliminary reports indicate that trilostane is efficacious in some cats with hyperadrenocorticism.
- *L-deprenyl,* as used for the treatment of dogs with pituitary-dependent hyperadrenocorticism, is not yet established as an effective treatment for cats with hyperadrenocorticism.

Surgical Treatment

- In cats with adrenal tumors, perform unilateral adrenalectomy as the treatment of choice (see under "Adrenalectomy").
- Bilateral adrenalectomy remains, at this writing, a viable and probably the most successful treatment for pituitary-dependent hyperadrenocorticism in cats. Bilateral adrenalectomy requires an experienced surgical team, intensive postoperative care, and lifelong glucocorticoid and mineralocorticoid replacement therapy. Postoperative complications are common, with approximately one-third of cats dying within 1 month of surgery. The 6-month survival rate after bilateral adrenalectomy is approximately 44%.
- Hypophysectomy has recently been reported in a few cats.

Radiation Therapy

Pituitary irradiation has been partially successful in a few cats with pituitary-dependent hyperadrenocorticism. It is the treatment of choice in cats with large pituitary tumors. Concurrent medical management may be necessary for a few to several months. Drawbacks include the high cost, limited availability, and need for multiple anesthetic episodes.

▼ ***Key Point*** Adrenalectomy appears to be the most successful means of treating hyperadrenocorticism in cats. To date, medical therapy has not been consistently successful.

PHEOCHROMOCYTOMA

Etiology

Pheochromocytoma is a rare catecholamine-producing neuroectodermal tumor derived from chromaffin cells of the adrenal medulla. About half of reported pheochromocytomas in dogs have been malignant. Reported metastatic sites include lungs, liver, bone, kidney, and lymph nodes. Concurrent pheochromocytoma and adrenocortical neoplasia has been reported.

Signalment

- Pheochromocytoma generally occurs in older dogs.
- There is no breed or sex predilection.

Clinical Signs

▼ ***Key Point*** Most pheochromocytomas are not detected antemortem and are incidental findings at necropsy because of vague, episodic clinical signs.

- Clinical signs develop either as a result of the space-occupying nature of the adrenal tumor and its metastasis or as a result of excessive secretion of catecholamines with resultant systemic hypertension and other manifestations.
- Weakness, lethargy, anorexia, vomiting, weight loss, polyuria, polydipsia, restlessness, and excessive panting are the most frequent signs, but these occur in less than 50% of affected dogs.
- Other less common signs may include diarrhea, cough, dyspnea, hind leg edema, abdominal distention, acute blindness, epistaxis, anxiety, shaking, ataxia, seizures, cyanosis, pacing, and adipsia.
- Duration of signs varies from days to years.
- An abdominal mass can be palpated in about 10% of dogs with pheochromocytoma.
- Routine laboratory findings are usually not helpful.
- ECG abnormalities may include sinus tachycardia, arrhythmias, and evidence of cardiac chamber enlargement.

Diagnosis

History, Physical Examination, and Routine Laboratory Testing

- History and clinical findings are typically vague and nonspecific (e.g., lethargy and tachypnea).

Radiography and Other Imaging

- Abdominal radiographs reveal a cranial abdominal mass in the region of the adrenal gland in up to one-third of dogs with pheochromocytoma. Ten percent of tumors show evidence of mineralization.
- Specialized imaging techniques such as ultrasonography, CT, and MRI are more sensitive than radiography and are very useful for detecting and staging pheochromocytomas.
- Echocardiography may demonstrate left ventricular hypertrophy.

Arterial Blood Pressure

Up to 50% of dogs with pheochromocytoma are hypertensive. Catecholamine secretion, and therefore hypertension, tends to be episodic.

Biochemical and Pharmacologic Tests

Measurement of urinary and resting plasma catecholamine concentrations, the clonidine suppression test, and the phentolamine test can be used to demonstrate excessive production of catecholamines (epinephrine and norepinephrine) or their metabolites. Unfortunately, the limited availability, technical difficulty, and expense of these tests severely limit routine use of these in veterinary medicine.

▼ ***Key Point*** The antemortem diagnosis of pheochromocytoma in dogs usually depends on surgical exploration and biopsy.

Treatment

- Adrenalectomy is the treatment of choice for pheochromocytoma (see following discussion under “Adrenalectomy”).
- Medical therapy is indicated preoperatively (to control hypertension and to help prevent cardiac arrhythmias before and during surgery), as well as for long-term treatment of patients with inoperable and incompletely resected tumors.
- Treat severe hypertension with phenoxybenzamine (0.2–1.5 mg/kg q12h PO) or prazosin (0.5–2.0 mg/kg q12h PO).
- Administer beta blockers such as propranolol or atenolol if necessary to control tachycardia or arrhythmias, but do not use these without concurrent alpha blockade.

- Chemotherapy and radiation therapy have been employed in humans with pheochromocytoma, but the efficacy of these modalities has not been established in dogs or cats.

ADRENALECTOMY

Adrenalectomy usually is performed for treatment of adrenal tumors and hyperadrenocorticism in the dog and cat. Unilateral adrenalectomy is done primarily for removal of adrenal neoplasia (adenoma, adenocarcinoma, or pheochromocytoma). Bilateral adrenalectomy is less commonly used for bilateral adrenocortical hyperplasia. The anatomy and surgical and medical management for adrenalectomy is the same in the dog and cat. Adrenalectomy is performed infrequently in cats owing to the low incidence of hyperadrenocorticism and adrenal neoplasia.

Surgical Anatomy of the Adrenal Gland

- The adrenal glands are paired, flattened, bilobed glands located retroperitoneally and craniomedial to the kidneys (Fig. 33-1).
- The right adrenal gland lies near the level of the last thoracic to the first lumbar vertebrae.
- The capsule of the right adrenal gland may be contiguous with the tunica externa of the caudal vena cava.
- The left adrenal gland is slightly caudal to the right and is separated from the caudal vena cava by a layer of fat.

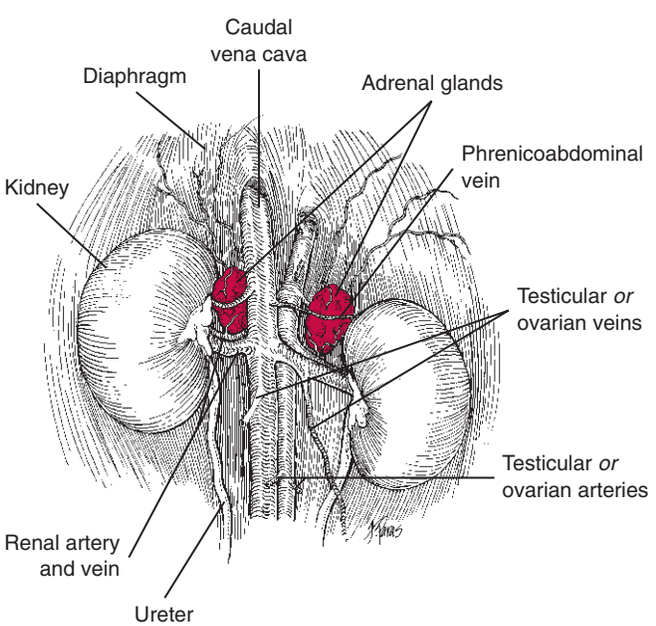

Figure 33-1. Anatomy of the adrenal glands from the ventral midline abdominal approach.

- Adrenal size is breed dependent. In dogs, the average size is 22 mm long, 10 mm wide, and 4 mm thick.
- The adrenal glands are well vascularized by branches of the renal, accessory renal, phrenic, cranial abdominal, phrenicoabdominal, and lumbar arteries.
- Venous drainage is through the left and right adrenal and the phrenicoabdominal veins.
- The phrenicoabdominal artery crosses the dorsal surface of the adrenal glands; the phrenicoabdominal vein courses across the ventral surface. These paired vessels are the largest supplying the adrenal glands.

Preoperative Considerations

- Obtain a minimum database consisting of complete blood count, serum chemistry profile, and thoracic radiographs.
- Abdominal radiographs may help localize a unilateral adrenal mass, especially if the tumor is mineralized.
- Ultrasonography and CT scan are also very helpful in identifying a mass and determining if invasion of the vena cava has occurred.
- Correct any fluid and electrolyte abnormalities.
- Treat arrhythmias and hypertension that may accompany pheochromocytoma (see the next section).
- Surgical removal of large adrenal tumors can be technically challenging, and postoperative intensive care may be necessary. Consider referral to a surgical specialist.

Anesthesia and Perioperative Care

For Hyperadrenocorticism

- Induce and maintain anesthesia following standard procedures.
- Sevoflurane and isoflurane are preferred over halothane, as there is less sensitization of the myocardium to catecholamines.
- Administer a broad-spectrum bactericidal antibiotic by IV bolus 30 minutes before surgery. Administer isotonic fluids an appropriate rate during and after surgery.
- Supplement corticosteroids in the form of dexamethasone (0.1–0.2 mg/kg IV) immediately before the onset of surgery, at the completion of the surgical procedure, and then every 6 to 8 hours during the immediate postoperative period (24–48 hours).

For Pheochromocytoma

- Avoid premedication with atropine because of the potential for severe tachycardia.

▼ ***Key Point*** Dogs with pheochromocytoma produce high circulating concentrations of the catecholamines epinephrine and norepinephrine, which may cause severe hypertension or profound cardiac arrhythmias.

- Induce anesthesia with propofol (3–5 mg/kg) or oxymorphone (0.1–0.3 mg/kg IV) and glycopyrrolate.
- Sevoflurane is the inhalant agent of choice for dogs with pheochromocytoma.
- Administer isoflurane (rather than halothane) if sevoflurane is not available.
- Administer fluids and antibiotics as for hyperadrenocorticism.
- Closely monitor the blood pressure and electrocardiogram.
- To manage ventricular arrhythmias, give either lidocaine (1 mg/kg IV) or propranolol (0.1–0.3 mg/kg IV).
- Treat hypertensive episodes with phentolamine (alpha blocker) (0.02–0.1 mg/kg IV), repeated as needed.
- Manage hypotension with vigorous IV fluid administration.

Surgical Procedure

Objectives

- Handle tissue gently, especially tumor tissue.

▼ ***Key Point*** Surgical handling of a pheochromocytoma may precipitate catecholamine release and hypertension. Profound hypotension may rapidly occur following tumor removal.

- Use meticulous hemostasis to minimize blood loss.
- Avoid trauma to the caudal vena cava.
- Close the linea alba with a non-absorbable suture material.

▼ ***Key Point*** Animals with hyperadrenocorticism are prone to delayed healing and incisional infection because of cortisol inhibition of fibroblast proliferation and collagen synthesis.

Equipment

- Standard general surgical pack and suture
- Balfour retractors
- Malleable retractors
- Bipolar cautery
- Sterile cotton-tipped applicator sticks
- Hemostatic clips
- Gelfoam

Technique

1. Make a ventral midline abdominal incision, extending from the xiphoid to about 2 cm caudal to the umbilicus. This may be combined with a paracostal incision if necessary (Fig. 33-2).
   a. Alternatively, use a retroperitoneal approach (Fig. 33-3). This provides good exposure of the ipsilateral gland but must be performed bilaterally if bilateral adrenalectomy is required.

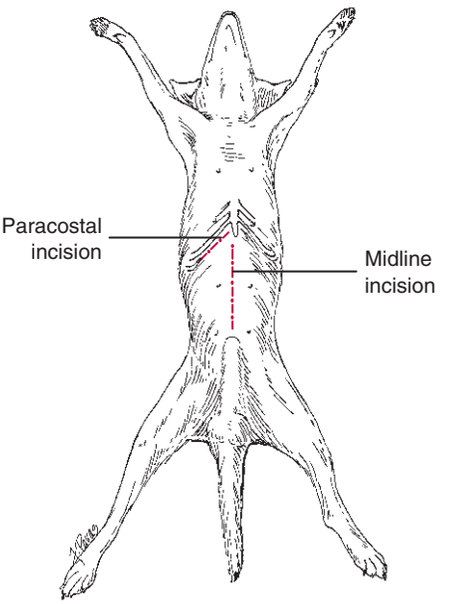

Figure 33-2. Incision for the ventral midline approach may be extended paracostally for better exposure of the adrenal gland.

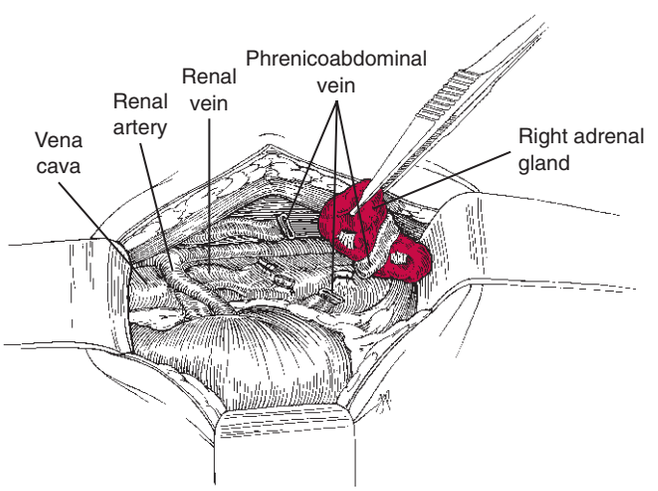

Figure 33-3. Surgical anatomy of the right adrenal gland and its associated vascular structures as viewed from the retroperitoneal approach.

2. Expose the affected gland(s) and isolate with moistened laparotomy sponges.
3. Perform gentle dissection with cotton-tipped applicator sticks, especially when separating the gland from the vena cava.
4. Ligate the phrenicoabdominal artery and vein and any other vascular structures serving the adrenal gland. Hemostatic vascular clips are very helpful for this.

▼ ***Key Point*** Identify and preserve the renal artery and vein, which may lie close to the adrenal glands.

5. Completely resect all abnormal tissue, including the adrenal capsule, and the tumor thrombus in the vena cava if possible.
6. Prior to closure, carefully check the surgical field for hemorrhage. Use Gelfoam to control minor bleeding from the site.
7. Inspect the abdominal viscera, especially the liver, for metastatic disease, and biopsy any suspicious lesions.
8. Perform a routine, three-layer abdominal closure using non-absorbable suture material (e.g., polypropylene) to close the linea alba.

Postoperative Care

Unilateral Adrenalectomy for Adrenocortical Tumor

- Supplement glucocorticoids starting at 24 to 48 hours after surgery with prednisone (0.5 mg/kg q12h PO for 3 days, then taper the dosage over 10–14 days to 0.2 mg/kg q24h PO) until the contralateral adrenal gland is functioning normally.
- Perform an ACTH stimulation test on the first postoperative day and at 2- to 4-week intervals following surgery until the adrenal reserve normalizes.
- The remaining adrenal gland usually functions normally within 2 months following surgery.

Unilateral Adrenalectomy for Pheochromocytoma

Function of the contralateral gland is not suppressed; therefore, there is no need for postoperative glucocorticoid or mineralocorticoid supplementation.

Bilateral Adrenalectomy

- Supplement glucocorticoids (prednisone, 0.2 mg/kg q24h PO).
- Supplement mineralocorticoid (fludrocortisone acetate or DOCP) as described in the preceding section on hypoadrenocorticism.
- Check serum electrolytes periodically to adjust the dosages of mineralocorticoid replacement therapy.

Complications

Complications may include the following:

- Hemorrhage
- Cardiac arrest and/or arrhythmias
- Fluid and electrolyte abnormalities
- Pulmonary artery thrombosis
- Pancreatitis
- Acute renal failure
- Pneumonia
- Adrenal insufficiency

Prognosis

Unilateral Adrenocortical Tumor

- Good if the tumor is benign
- Fair if the tumor is malignant but completely resected
- Extremely poor for invasive adenocarcinoma

Unilateral Pheochromocytoma

- Excellent prognosis for a benign tumor.
- About 50% of pheochromocytomas are malignant and metastatic at the time of surgery, indicating a grave prognosis.

Bilateral Adrenal Hyperplasia

- Fair to good prognosis; however, medical therapy is preferred over surgery for this lesion in dogs.
- Metastatic disease is not a problem; however, regulating the iatrogenic hypoadrenocorticism created by bilateral adrenalectomy may be difficult.

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Chapter 34

Diabetes Mellitus

Deborah S. Greco

ETIOLOGY

Type 1 Diabetes Mellitus

- Insulin-dependent diabetes mellitus (IDDM), also referred to as type 1 diabetes, is a diabetic state in which endogenous insulin secretion is never sufficient to prevent ketone production.
- Insulin secretion may be reduced or absent, and the diabetic state is readily corrected by exogenous insulin.

Type 2 Diabetes Mellitus

- Non–insulin-dependent diabetes mellitus (NIDDM), also referred to as type 2 diabetes, is a diabetic state in which insulin secretion is usually sufficient to prevent ketosis but not enough to prevent hyperglycemia.
- Insulin secretion may be high, low, or normal but is insufficient to overcome insulin resistance in peripheral tissues.
- The metabolic hallmarks of type 2 diabetes are impaired insulin secretion, increased hepatic glucose output, and insulin resistance (Fig. 34-1).
- In cats and in humans with type 2 diabetes, insulin secretion secondary to a glucose load is impaired. The early phase of insulin secretion is delayed or absent, and the second phase of insulin secretion is delayed but exaggerated.
- Amyloid deposition in the pancreatic islets may be the cause of impaired insulin secretion in cats.
- Obesity is a risk factor in type 2 diabetes because it causes insulin resistance.

▼ ***Key Point*** Most dogs suffer from type 1 diabetes, or IDDM. Most cats probably suffer from type 2 diabetes (NIDDM); however, by the time a diagnosis of diabetes is confirmed in many cats with NIDDM, they have become insulin dependent.

Type 3 Diabetes Mellitus

- Type 3, or secondary, diabetes mellitus is the result of another primary disease or drug therapy that produces insulin resistance (e.g., hyperadrenocorticism, hyperthyroidism, acromegaly, or progestational drugs) or destroys pancreatic tissue (pancreatitis). Secondary diabetes is common in both dogs (pancreatitis) and cats (drugs, endocrinopathies, pancreatitis).

PATHOPHYSIOLOGY

Uncomplicated Diabetes Mellitus

- In animals with uncomplicated diabetes mellitus, hyperglycemia results from impaired glucose utilization, increased gluconeogenesis, and increased hepatic glycogenolysis.
- Decreased peripheral utilization of glucose leads to hyperglycemia followed by osmotic diuresis. This causes the classic clinical signs of polyuria with compensatory polydipsia and progressive dehydration.
- Impaired glucose utilization by the hypothalamic satiety center combined with loss of calories in the form of glycosuria results in polyphagia and weight loss, respectively.
- Insulin is anabolic; therefore, insulin deficiency leads to protein catabolism and contributes to weight loss and muscle atrophy.
- As a consequence of protein catabolism, amino acids are used by the liver to promote gluconeogenesis and contribute to hyperglycemia.
- With insulin deficiency, the hormone-sensitive lipase system, which is normally suppressed by insulin, becomes activated. The unrestrained lipolytic activity of hormone-sensitive lipase contributes to weight loss in a previously obese or overweight animal.

Complicated (Ketoacidotic) Diabetes Mellitus

▼ ***Key Point*** Diabetic ketoacidosis (DKA) is the culmination of IDDM that results in unrestrained ketone body formation in the liver, metabolic acidosis, severe dehydration, shock, and possibly death.

- With time, uncomplicated diabetes mellitus may progress to complicated or ketoacidotic diabetes. In these animals, insulin deficiency causes abnormal lipid metabolism in the liver such that non-esterified

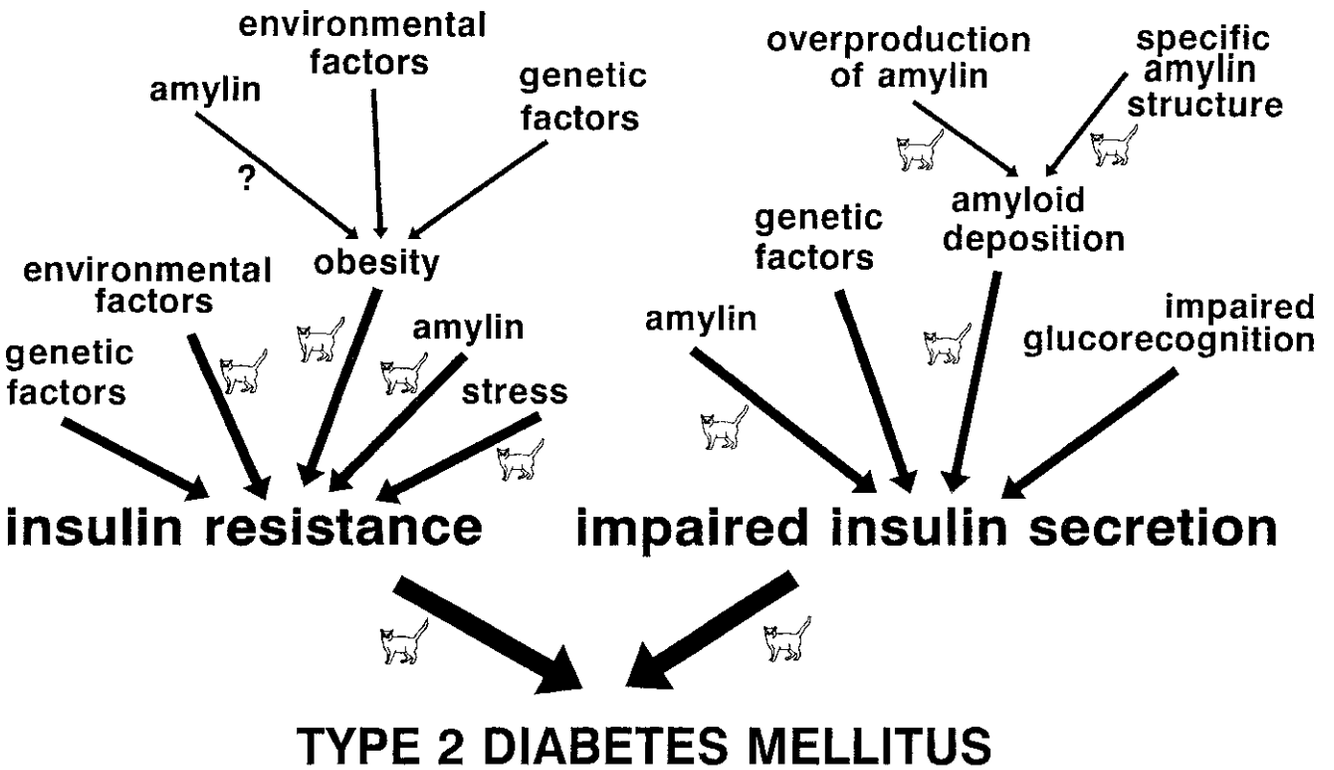

Figure 34-1. Summary of the pathophysiologic factors contributing to hyperglycemia in non–insulin-dependent (type 2) diabetes mellitus. (From Lutz TA, Rand JS: Pathogenesis of feline diabetes mellitus. Vet Clin North Am Small Anim Pract 25:544, 1995; with permission.)

fatty acids are converted to acetyl coenzyme A (acetyl-CoA) rather than being incorporated into triglycerides.

- Acetyl-CoA accumulates in the liver and is converted into acetoacetyl-CoA and then ultimately to acetoacetic acid. Finally, the liver starts to generate ketones including acetoacetic acid, beta-hydroxybutyrate, and acetone.
- As insulin deficiency culminates in DKA, accumulation of ketones and lactic acid in the blood and loss of electrolytes and water in the urine results in profound dehydration, hypovolemia, metabolic acidosis, and shock.
  - Ketonuria and osmotic diuresis caused by glycosuria result in sodium and potassium loss in the urine and exacerbation of hypovolemia and dehydration.
  - Nausea, anorexia, and vomiting, caused by stimulation of the chemoreceptor trigger zone via ketonemia and hyperglycemia, contribute to the dehydration caused by osmotic diuresis.
  - Dehydration and shock lead to prerenal azotemia and a decline in the glomerular filtration rate. This declining rate leads to further accumulation of glucose and ketones in the blood.
- Stress hormones such as cortisol and epinephrine contribute to the hyperglycemia in a vicious cycle.
- Eventually, severe dehydration may result in hyperviscosity, thromboembolism, severe metabolic acidosis, renal failure, and finally death.

CLINICAL SIGNS

Uncomplicated Diabetes Mellitus

- Most diabetic animals have the classic clinical signs of polyuria and polydipsia.
- Weight loss is more common in dogs than in cats.
- Acute onset of blindness caused by bilateral cataract formation is a common presenting complaint of diabetes mellitus in dogs.
- Cats may present with chronic complications of diabetes, such as diabetic neuropathy leading to gait abnormalities, plantigrade stance, difficulty jumping, and inappropriate elimination. Chronic gastrointestinal signs such as vomiting, diarrhea, and anorexia may also result from concurrent pancreatitis or from autonomic neuropathy.

Complicated (Ketoacidotic) Diabetes Mellitus

- Depression, vomiting, anorexia, and weakness are the most common clinical signs of ketoacidosis in dogs and cats.
- Animals with DKA often present in shock.
- Physical examination findings may include depression, tachypnea, dehydration, weakness, vomiting, and occasionally, a strong acetone odor on the breath.
- Cats may present recumbent or comatose, which may be a manifestation of severe ketoacidosis or mixed ketotic hyperosmolar syndrome.
- Approximately one-third of diabetic cats with ketosis exhibit icterus at presentation. Icterus may be a result of associated hemolysis, hepatic lipidosis, or acute pancreatitis.

DIAGNOSIS

Base the diagnosis of diabetes mellitus on typical clinical signs and evidence of fasting hyperglycemia and glycosuria.

Clinicopathologic Findings in Uncomplicated Diabetes Mellitus

- Fasting hyperglycemia
- Hypercholesterolemia
- High serum activity of liver enzymes (alkaline phosphatase, alanine aminotransferase)
- Glycosuria

Clinicopathologic Findings in Diabetic Ketoacidosis

Findings in DKA may include all of the above findings plus the following:

- Azotemia
- Hyponatremia
- Hyperkalemia
- Ketonemia and ketonuria

Diagnostic Pitfalls

- With regard to fasting hyperglycemia, many cats are susceptible to "stress-induced" hyperglycemia in which the serum glucose concentrations may approach 300 to 400 mg/dl.
- Renal glycosuria may be found in animals with renal tubular disease and occasionally with stress-induced hyperglycemia.
- It may be difficult to differentiate early type 2 diabetes in cats from stress-induced hyperglycemia, because cats with early NIDDM are often asymptomatic.

Glycosylated Proteins

Glycosylated proteins, such as glycosylated hemoglobin and fructosamine, may aid in the diagnosis of early type 2 diabetes in cats.

Glycosylated Hemoglobin

- Glycosylated hemoglobin is formed by an irreversible, non-enzymatic binding of glucose to hemoglobin. As plasma glucose concentrations increase, hemoglobin glycosylation increases proportionately.

Fructosamine

- Serum fructosamine is formed by glycosylation of serum protein such as albumin. The concentration of fructosamine in serum is directly related to blood glucose concentration.
- Serum fructosamine measurement may be beneficial in differentiating early or subclinical diabetes mellitus in the cat from stress-induced hyperglycemia.

TREATMENT OF DIABETIC KETOACIDOSIS

Treatment of DKA, as outlined in Table 34-1, includes the following steps in order of importance:

1. Fluid therapy using 0.9% saline initially, followed by 2.5% or 5% dextrose as serum glucose declines
2. Insulin therapy (low-dose IM or IV)
3. Electrolyte supplementation (potassium, phosphorus, magnesium)
4. Treatment of metabolic acidosis

Fluid Therapy

- Use 0.9% NaCl supplemented with potassium as the fluid therapy of choice when insulin therapy is initiated (see Table 34-1).
- Administer fluid therapy using a large central venous catheter, as animals in DKA are severely dehydrated and require rapid fluid administration; central venous pressure may also be monitored via a jugular catheter to avoid overhydration.
- Base the fluid administration rate on the severity of dehydration, maintenance requirements, continuing losses (vomiting and diarrhea), and the presence of concurrent disease (e.g., congestive heart failure; see Chapter 5).

Insulin Therapy

Initiate insulin therapy as soon as possible using either IV insulin or low-dose IM methods. Administer IV insulin via a separate peripheral catheter using the guidelines in Table 34-1.

- The species of origin of regular insulin (beef, pork, or human) does not affect response; however, the type of insulin given is very important. Use only

Table 34-1. STEPWISE TREATMENT OF DIABETIC KETOACIDOSIS

Step One: Fluids

a. Place an IV catheter, preferably central venous.
b. Fluid rate: Estimate dehydration deficit (%) × body weight (kg) × 1000 ml = no. of ml to rehydrate.
Estimate maintenance needs: 2 ml/kg/hr × no. of hr required to rehydrate (in 24 hr).
Estimate losses (vomiting, diarrhea).
Dehydration deficit + maintenance + losses = no. of ml of fluid/24 hr = hourly fluid rate
c. Fluid composition

Blood Glucose (mg/dl)	Fluids	Rate	Route	Monitor	Frequency
>250	0.9% saline	Up to 45 (cat) and 90 (dog) ml/kg/hr to rehydrate	IV	PCV, TS, Na, K, osmolality	q4h
200–250	0.45% saline plus 2.5% dextrose	Up to 90 ml/kg/hr to rehydrate	IV	PCV, TS, Na, K, osmolality	q4h
150–200	0.45% saline plus 2.5% dextrose	Up to 90 ml/kg/hr to rehydrate	IV	CVP, urine output	q2h
100–150	0.45% saline plus 2.5% dextrose	Up to 90 ml/kg/hr to rehydrate	IV	CVP, urine output	q2h
<100	0.45% saline plus 5% dextrose	Up to 90 ml/kg/hr to rehydrate	IV	CVP, urine output	q2h

Step Two: Insulin

Intravenous (regular only), mixed in 250 ml of 0.9% NaCl; discard 50 ml through IV tubing.

Blood Glucose (mg/dl)	Rate	Route	Dose (u/kg)	Monitor	Frequency
Intravenous (Regular Only)					
>250	10 ml/hr	IV	1.1 (cats), 2.2 (dogs)	Blood glucose	q1–2h
200–250	7 ml/hr	IV	1.1 (cats), 2.2 (dogs)	Blood glucose	q1–2h
150–200	5 ml/hr	IV	1.1 (cats), 2.2 (dogs)	Blood glucose	q1h
100–150	5 ml/hr	IV	1.1 (cats), 2.2 (dogs)	Blood glucose	q1h
<100	Stop IV, begin insulin q4h	SC	0.1	Blood glucose	q4h
Intramuscular (Regular Only)					
>250	Initial dose	IM	0.2	Blood glucose	Hourly
	q1h	IM	0.1	Blood glucose	Hourly
<250	q4–6h	IM	0.1	Blood glucose	q4–6h
	q6–8h	SC	0.1–0.4	Blood glucose	q6–8h

Step Three: Electrolytes

Concentration	Amount (mEq/L) Added to 1 L of Fluids	Maximum Rate (ml/kg/hr)
Potassium (mEq/L)		
3.6–5.0	20	26
2.6–3.5	40	12
2.1–2.5	60	9
<2.0	80	7
Phosphorus (mg/dl)		
1–2	0.03 mmol phosphate/kg/hr	Monitor serum phosphorus q6h
<1.0	0.1 mmol phosphate/kg/hr	Monitor serum phosphorus q6h
Magnesium (mg/dl)		
<1.2	0.75–1 mEq/kg/day constant rate infusion; use MgCl or $MgSO_4$	Use 5% dextrose: magnesium is incompatible with calcium-containing and $NaHCO_3$ solutions

Step Four: Acid-Base Balance

pH	Bicarbonate Concentration	Dose of Bicarbonate (ml)	Rate
<7.1	<12 mEq/L	IV = 0.1 × body weight (kg) × (4 − HCO_3 [mEq/L])	Over 2 hr

CVP, central venous pressure; IM, intramuscular; IV, intravenous; PCV, packed cell volume; SC, subcutaneous; TS, total solids.
From Greco DS: Endocrine pancreatic emergencies. Comp Cont Educ Pract 19:23, 1997; with permission.

regular insulin because it has a rapid onset and short duration of action and it can be given IV. Never give Lente, Ultralente, or NPH insulin IV.
- Dilute regular insulin at a dosage of 2.2 U/kg in dogs or 1.1 U/kg in cats in 250 ml of saline.
- Allow approximately 50 ml of fluid and insulin mixture to flow through the IV drip set and discard it, because insulin binds to the plastic tubing.
- With IV insulin administration, blood glucose decreases to below 250 mg/dl by approximately 10 hours in dogs and after about 16 hours in cats.
- Once euglycemia has been achieved, maintain the animal on SC regular insulin (0.1–0.4 U/kg q4–6h SC) until it starts to eat and/or the ketosis has resolved.
- For the transition from hospital to home maintenance insulin therapy, use a low dose (1–2 U) of regular insulin combined with intermediate- or long-acting maintenance insulin at the recommended dosages (see "Treatment of Uncomplicated Diabetes").

Electrolyte Supplementation

Potassium

- Supplement potassium as soon as insulin therapy is initiated (see Table 34-1).
- Although serum potassium may be normal or elevated in ketoacidosis, the animal actually suffers from total body depletion of potassium. Correction of the metabolic acidosis tends to drive potassium intracellularly in exchange for hydrogen ions. Insulin facilitates this exchange, and the net effect is a dramatic decrease in serum potassium, which must be attenuated with appropriate potassium supplementation in fluids.

Magnesium

- Refractory hypokalemia may be complicated by hypomagnesemia. Supplementation of magnesium along with potassium as outlined in Table 34-1 may be indicated in cats or dogs with hypokalemia that are unresponsive to potassium chloride supplementation in fluids.

Phosphorus

- Serum and tissue phosphorus may also be depleted during a ketoacidotic crisis; thus, supplement one-third of the potassium dose as potassium phosphate (see Table 34-1), particularly in small dogs and cats that are most susceptible to hemolysis caused by hypophosphatemia.
- Use caution, as oversupplementation of phosphorus can result in metastatic calcification and hypocalcemia.

▼ ***Key Point*** In cats suffering from ketoacidosis, hemolysis may be caused by hypophosphatemia and/or Heinz body anemia.

Bicarbonate Therapy

- Bicarbonate therapy may be necessary in some patients with blood pH <7.1 or if serum HCO_3 is less than 12 mEq/L.
- Bicarbonate dosages are given in Table 34-1. Use caution, because metabolic alkalosis may be difficult to reverse.

TREATMENT OF UNCOMPLICATED DIABETES

Insulin Therapy

Insulin Source (Species of Origin)

- *Human recombinant insulin* is the most available insulin preparation on the market and is perfectly acceptable as insulin therapy for all dogs and most cats.
- *Porcine insulin* is identical to canine insulin in its amino acid structure, and human insulin is very similar to canine insulin.
- *Beef insulin* is most similar to cat insulin, differing by only one amino acid in the A chain.

Insulin Preparations (Duration of Action)

Insulin preparations may be short-acting (regular insulin), intermediate-acting (Lente, NPH), or long-acting (Ultralente, protamine zinc insulin [PZI]).

NPH and Protamine Zinc Insulin

- NPH insulin and PZI are made by adding protamine in increasing concentrations to retard insulin absorption.
- PZI was discontinued as a human preparation in 1991 but is available as a veterinary preparation (PZI VET, IDEXX Pharmaceuticals).

Semilente, Lente, and Ultralente

- Lente preparations control absorption by regulating the size of the insulin crystals.
- Semilente is composed of small zinc-insulin crystals, and Ultralente is composed of large zinc-insulin crystals that are more slowly absorbed.
- Lente insulin is a mixture of 30% prompt zinc-insulin suspension (Semilente) and 70% extended zinc-insulin (Ultralente).
- Lente insulin, because of the small zinc-insulin crystal component, may be used to attenuate postprandial hyperglycemia.

Synthetic Insulins

- Lispro insulin
- Glargine insulin

Insulin Concentration

- Insulin is commercially available in 40, 100, and 500 units per milliliter concentrations, which are designated U-40, U-100, and U-500, respectively. One unit of insulin is approximately equivalent to 36 µg. PZI is manufactured in U-40 concentration only.
- Regardless of the concentration of insulin used for therapy, it is absolutely essential that owners purchase the appropriate syringe for the concentration of insulin. U-100 insulin syringes are manufactured in low-dose (0.3 ml, 0.5 ml) and 1-ml capacities; U-40 syringes are available only in 1-ml capacity.
- In cats and small dogs (<10 kg), use low-dose (0.3 or 0.5 ml) syringes. These syringes are designed to accurately draw up a small dosage of U-100 insulin without the need for dilution.
- All insulin syringes are packaged with a 27-, 29-, or 31-gauge injection needle.

Insulin Dosage (Table 34-2)

- Intermediate-acting insulin tends to be more bioavailable and, therefore, more potent. For this reason, dose intermediate-acting insulin (NPH, Lente) at the lower end of the range.
- In dogs, if intermediate-acting insulin is administered twice daily, use an initial dosage of 0.4 to 0.5 U/kg q12h SC (see Table 34-2).
- In cats, use an initial insulin dosage range of 0.2 to 0.5 U/kg for intermediate-acting insulin (NPH, Lente). NPH twice daily is preferred in cats over Lente insulin.
- PZI is available as a beef-pork product. Ultralente is available only as human recombinant insulin. Use an initial dosage range of 0.5 to 0.7 U/kg once or twice daily for long-acting insulin such as PZI or Ultralente.

Frequency of Insulin Administration (see Table 34-2)

- To mimic the physiologic release of insulin, ideally insulin should be given with each meal. Feed the animal and inject the insulin at the same time. Table 34-3 lists the fiber and caloric content of various pet foods.
- If the animal does not eat, reduce the insulin dosage (usually by one-half) or skip the insulin entirely and determine the cause of the anorexia.

Adjusting Insulin Dose

- In dogs, make adjustments to insulin dosage in increments of 0.5 to 3 U/dog (depending on the size of the dog).
- In cats, make adjustments to insulin dosage in increments of 0.5 to 1 U/cat.
- Once adequate insulin therapy has been established, reassess diabetic control every 3 to 6 months as described in the following section.

Monitoring Insulin Therapy

Home Monitoring

- Instruct the client to monitor the insulin effect and overall control of hyperglycemia by noting changes in appetite, attitude, body condition, poly-

Table 34-2. INITIAL INSULIN REGIMENS FOR DIABETIC DOGS AND CATS

Insulin Type	Initial Dose	Frequency of Dosing	Feeding Schedule	Insulin Adjustment	Frequency of Adjustment
Dogs					
Lente Humulin-L (Lilly), Novolin-L (Novo Nordisk)	0.5 U/kg	q12h	q12h	0.5–3 U/dog	q5–7d
NPH Humulin-N (Lilly), Novolin-N (Novo Nordisk)	0.5 U/kg	q12h	q12h	0.5–3 U/dog	q5–7d
Ultralente Humulin-U (Lilly)	0.7 U/kg	q24h	$^2/_3$ morning; $^1/_3$ evening	1–4 U/dog	q5–7d
Cats					
NPH NPH (Novo Nordisk)	0.2–0.5 U/kg	q12h	Throughout day	0.5 U/cat	q5–7d
Lente Humulin-L (Lilly), Novolin-L (Novo Nordisk)	0.2–0.5 U/kg	q12h	Throughout day	0.5–1 U/cat	q5–7d
Ultralente Humulin-U (Lilly)	1–3 U/cat	q12–24h	Throughout day	0.5 U/cat	q5–7d
Protamine zinc insulin Protamine analine zinc (Anthony)	1–3 U/cat	q24h	Throughout day	0.5 U/cat	q5–7d

Modified from Greco DS, Broussard JD, Peterson ME: Insulin therapy. Vet Clin North Am Small Anim Pract 25:684, 1995; with permission.

Table 34-3. MACRONUTRIENT CONTENT OF SELECTED AVAILABLE DOG FOODS

Diet	Food Form	% Nutrient (Dry Matter Basis)			
		Protein	Fat	Digestible Carbohydrate	Fiber
Theradiet Reducing*	Canned	27	7	24	29
Prescription Diet r/d†	Canned	26	7	36	21
Prescription Diet w/d†	Canned	16	12	56	13
Science Diet Maintenance Light†	Canned	17	10	61	8
Cycle 3 Light‡	Canned	19	9	53	8
Prescription Diet r/d†	Dry	25	7	39	22
Prescription Diet w/d†	Dry	17	7	54	16
Science Diet Maintenance Light†	Dry	17	7	57	14
Theradiet Reducing*	Dry	26	7	43	14
Purina Dog Chow–Low Calorie Formula§	Dry	16	6	~60	11
Fit N Trim§	Dry	17	9	61	9
Cycle 3 Light‡	Dry	19	9	53	5

*Theradiet, Sanofi Sante Animale, Victoriaville, Quebec.
†Hill's Pet Products, Topeka, KS.
‡Gaines Division, General Foods Corporation, White Plains, NJ.
§Ralston Purina Company, St. Louis, MO.
From Ihle SL: Nutritional therapy for diabetes mellitus. Vet Clin North Am Small Anim Pract 25:593, 1995.

dipsia, polyuria, and urine glucose and ketone concentrations.

- Initially monitor urine glucose and ketones daily (morning). Urine glucose should decrease to trace or 1+ with appropriate therapy. Decrease urine monitoring to once weekly or biweekly in well-regulated diabetic animals.
- Consistently high urine glucose readings coupled with uncontrolled clinical signs, such as polyuria or polydipsia, indicate that the insulin dose may be inadequate.
- Consistently negative readings on urine glucose may indicate that insulin dosages are either adequate or excessive.
- In dogs, collect urine with a long-handled cup holding device (males) or a flat pie tin (females). Collect cat urine by placing a small amount of litter in the pan, by placing plastic wrap over litter, or by using a non-absorbent litter substitute (e.g., aquarium gravel).

Blood Glucose Curves

Evaluate insulin therapy once weekly for the first month and as needed thereafter by serial blood glucose curves (blood glucose, 100–250 mg/dl), assessment of body weight, and resolution of clinical signs.

Procedure for Blood Glucose Curve

1. Collect initial blood sample.
2. Feed usual amount and type of food.
3. Feed and give insulin at the usual time.
4. Watch the owner administer the insulin.
5. Assess the owner's injection technique.
6. Collect serial blood samples at 2-hour intervals for 12 hours.

Ideal Blood Glucose Curve

The ideal blood glucose curve is characterized by three features (Fig. 34-2): the glucose nadir, the timing of the nadir, and the glucose differential.

- The ideal blood glucose curve has a glucose nadir (lowest blood glucose concentration on the curve) between 100 and 120 mg/dl.
- The time of the glucose nadir indicates peak insulin action. The nadir should occur approximately halfway through the dosing interval. For example, if insulin is being given every 12 hours, the nadir should occur 5 to 6 hours after the dose.
- The glucose differential is the difference between the glucose nadir and the blood glucose concentration prior to the next insulin dose.
  - Aim for a glucose differential of <100 mg/dl in dogs without cataracts and <150 mg/dl in dogs with cataracts.
  - Cats generally have a higher glucose differential; however, aim for <200 to 250 mg/dl.
- The duration of insulin action is related to both the time of the glucose nadir and the absolute concentration of the glucose nadir. Insulin duration cannot be determined unless the target glucose nadir concentration (80–120 mg/dl) has been achieved. If the glucose nadir occurs approximately halfway through the dosing interval, the duration of action of insulin should be adequate.

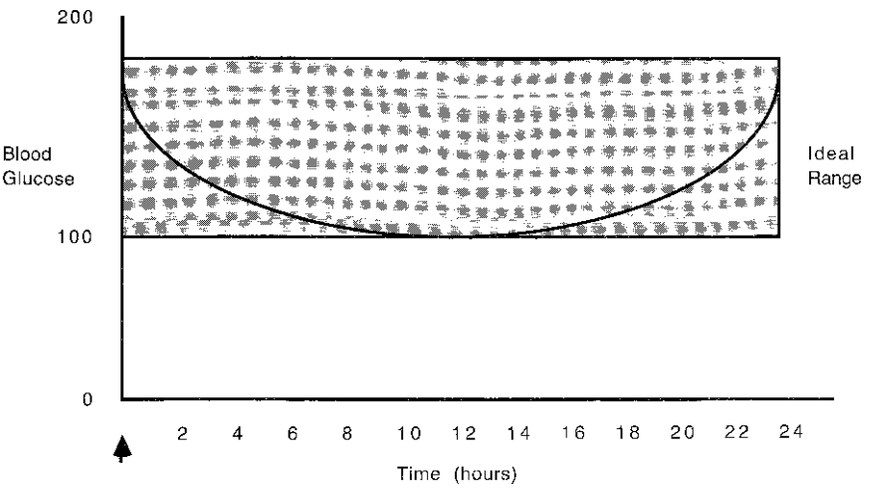

Figure 34-2. Ideal blood glucose curve for an animal on once-daily insulin therapy (*arrow* indicates insulin injection). (From Miller E: Long-term monitoring of the diabetic dog and cat: Clinical signs, serial blood glucose determinations, urine glucose, and glycated blood proteins. Vet Clin North Am Small Anim Pract 25:573, 1995; with permission.)

Problems Identified on the Blood Glucose Curve

It is rare to obtain a perfect glucose curve. Several possible outcomes of blood glucose monitoring are illustrated in Figure 34-3. Generally, blood glucose curve problems can be differentiated by the characteristics of the curve and the insulin dosage (per dosing interval).

- If the patient is receiving >2.2 U/kg of insulin per dose, evaluate for causes of insulin resistance or antagonism, such as hyperthyroidism, hyperadrenocorticism, acromegaly, estrus, drug therapy, and infections. The approach to insulin resistance is outlined in Tables 34-4 for cats and 34-5 for dogs.
- If the animal is receiving <2.2 U/kg of insulin per dose, the blood glucose curve may indicate one of the following (see Fig. 34-3):
  - Insufficient dosage of insulin. Corrective action—Increase the insulin dose.
  - Short duration of action of insulin. Corrective action—Change to a longer-acting insulin or twice-daily insulin regimen.

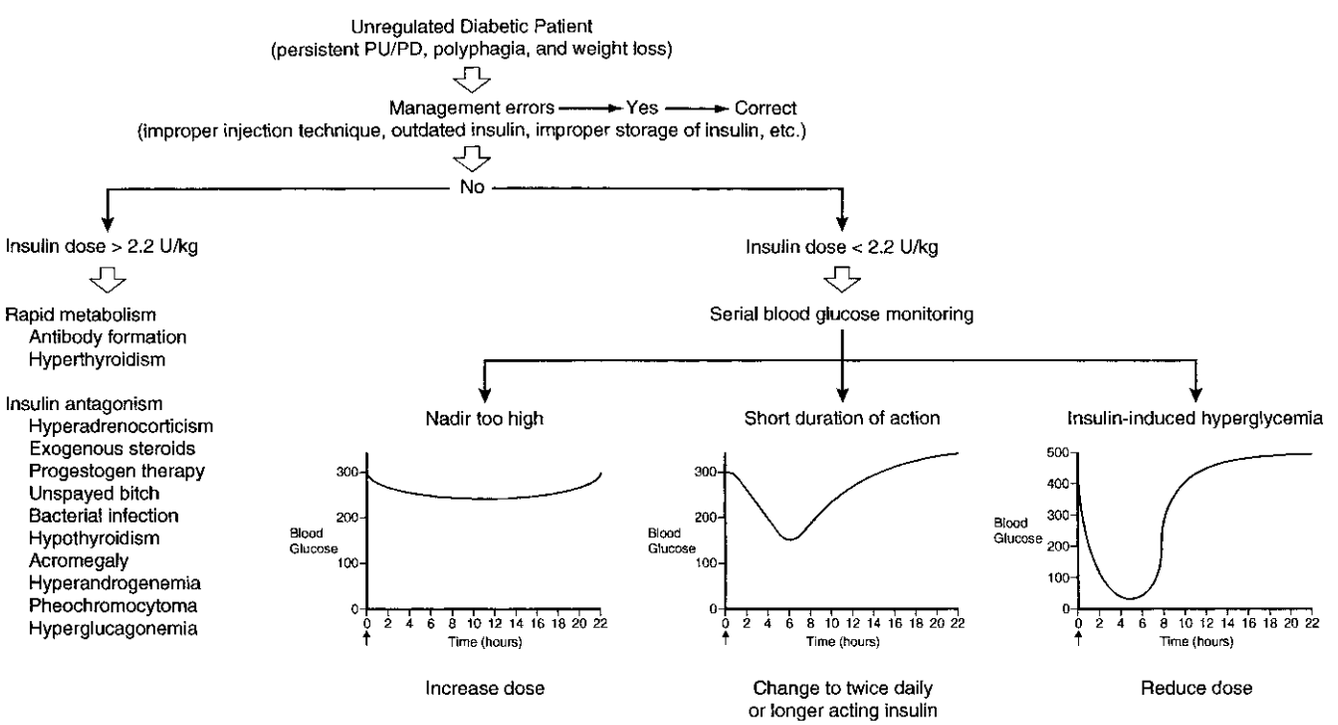

Figure 34-3. Algorithm for the unregulated diabetic dog or cat. (From Miller E: Long-term monitoring of the diabetic dog and cat: Clinical signs, serial blood glucose determinations, urine glucose, and glycated blood proteins. Vet Clin North Am Small Anim Pract 25:582, 1995; with permission.)

Table 34-4. STEPS FOR THE DIAGNOSIS AND TREATMENT OF INSULIN RESISTANCE IN CATS

Steps	Causes of Insulin Resistance	Procedure or Test	Treatment
Step 1	Glucocorticoids or megestrol acetate administration	History	Discontinue use of drugs
Step 2	Obesity	Physical examination, weight	Diet change (low calorie, high fiber)
Step 3	Poor absorption of subcutaneous insulin (long-acting preparation)	Evaluate response to change in insulin type; evaluate serum glucose response to regular insulin administered IV or IM	Change from long-acting insulin to insulin with shorter duration of action; use insulin mixtures (e.g., NPH/regular)
Step 4	Infection, ketoacidosis, or concurrent disease	CBC; serum chemistry profile; urinalysis; urine culture; radiographs; abdominal ultrasound	Appropriate antibiotics; correct ketoacidosis or underlying illness
Step 5	Hyperthyroidism	Serum T_4 concentration	Antithyroid drugs; thyroidectomy; radioiodine
Step 6	Cushing syndrome	Review clinical signs and physical examination; ACTH stimulation and dexamethasone suppression tests; CT scan	Adrenalectomy, pituitary (cobalt) radiation therapy
Step 7	Acromegaly	Review clinical signs and physical examination; CT scan; measure serum insulin-like growth factor concentration	Pituitary (cobalt) radiation therapy
Step 8	Insulin antibodies	Measure serum insulin concentration 24 hr after last insulin injection; insulin antibody titers (not widely available)	Switch to human insulin (or beef insulin, if available)
Step 9	Clinically undefined insulin resistance	All of the above procedures and tests	Raise insulin dose; change to insulin with shorter duration of action; mix NPH/regular insulin

ACTH, adrenocorticotropic hormone; CBC, complete blood count; CT, computed tomography; IM, intramuscularly; IV, intravenously; T_4, thyroxine.
From Peterson ME: Diagnosis and management of insulin resistance in dogs and cats with diabetes mellitus. Vet Clin North Am Small Anim Pract 25:705, 1995.

Table 34-5. STEPS FOR THE DIAGNOSIS AND TREATMENT OF INSULIN RESISTANCE IN DOGS

Steps	Causes of Insulin Resistance	Procedure or Test	Treatment
Step 1	Glucocorticoids or megestrol acetate administration	History	Discontinue use of drugs
Step 2	Diestrus/acromegaly	History (intact female; last estrus); serum progesterone concentration	Ovariohysterectomy
Step 3	Obesity	Physical examination, weight	Diet change (low calorie, high fiber)
Step 4	Poor absorption of subcutaneous insulin (long-acting preparation)	Evaluate response to change in insulin type; evaluate serum glucose response to regular insulin administered IV or IM	Change to insulin with shorter duration of action; use insulin mixtures (NPH/regular)
Step 5	Infection, ketoacidosis, or concurrent disease	CBC; serum chemistry profile; urinalysis; urine culture, radiographs; abdominal ultrasound	Appropriate antibiotics; correct ketoacidosis or underlying illness
Step 6	Cushing syndrome	Review clinical signs and physical examination; ACTH stimulation and dexamethasone suppression tests; CT scan	Mitotane; pituitary (cobalt) radiation therapy; unilateral adrenalectomy for adrenal tumor
Step 7	Hyperlipidemia	Review signalment (Schnauzer); measure serum cholesterol and triglycerides	Low-fat diet; lipid drugs
Step 8	Hypothyroidism	Serum T_4 free T_4, and cTSH concentrations	Thyroid hormone (L-thyroxine) replacement therapy
Step 9	Insulin antibodies	Measure serum insulin concentration 24 hr after last insulin injection; insulin antibody titers (not widely available)	Switch to human or pork insulin
Step 10	Clinically undefined insulin resistance	All of the above procedures and tests	Raise insulin dose; change to insulin with shorter duration of action; mix NPH/regular insulin

ACTH, adrenocorticotropic hormone; CBC, complete blood count; CT, computed tomography; cTSH, canine thyroid-stimulating hormone; IM, intramuscularly; IV, intravenously; T_4, thyroxine; TRH, thyroid-releasing hormone; TSH, thyroid-stimulating hormone.
From Peterson ME: Diagnosis and management of insulin resistance in dogs and cats with diabetes mellitus. Vet Clin North Am Small Anim Pract 25:706, 1995.

  - Insulin-induced hypoglycemic hyperglycemia (Somogyi effect). Corrective action—Reduce insulin dose by 25%.
  - Insulin overlap. Corrective action—Change to a shorter-duration insulin.
  - Prolonged insulin action. Corrective action—Change to an insulin mixture of 30% regular and 70% NPH.
- Causes of hyperglycemia and hypoglycemia in diabetic dogs and cats are listed in Table 34-6.

Fructosamine and Glycosylated Hemoglobin

Monitor long-term insulin therapy by serum fructosamine or glycosylated hemoglobin concentrations. These glycosylated blood proteins are indicative of mean glucose concentrations in serum over an extended period of time.

- Glycosylated blood proteins are particularly useful for monitoring diabetic cats that may be stressed by hospitalization and venipunctures for serial blood glucose curves.
- As plasma glucose concentrations increase, hemoglobin glycosylation increases proportionately. Similarly, serum fructosamine is formed by glycosylation of serum protein such as albumin; thus, serum concentration of fructosamine is also directly related to blood glucose concentration.
- Because of the shorter life span of albumin compared with hemoglobin, fructosamine concentrations reflect more recent (1–3 weeks) changes in serum glucose concentrations.
- In general, fructosamine and glycosylated hemoglobin concentrations that lie within reference range limits indicate good to excellent diabetic control, whereas slightly increased levels indicate fair to good control and very high levels indicate poor glycemic control. Relative changes in serum concentrations may be more helpful than absolute values in some cases.

Table 34-6. CAUSES OF HYPERGLYCEMIA AND HYPOGLYCEMIA IN DIABETIC DOGS AND CATS

Causes of Hyperglycemia in Diabetic Cats and Dogs
Insufficient insulin dosage
Insufficient duration of insulin action
Outdated, inactive insulin
Owner administration problems
Overfeeding
Stress
Insulin resistance caused by Cushing syndrome, infections, drugs, thyroid, disease, pancreatitis, acromegaly
Causes of Hypoglycemia in Diabetic Cats and Dogs
Insulin overdose
Concentrated insulin (old)
Overlap of insulin action
Transient diabetes
Somogyi effect
Anorexia caused by oral disease, ketosis
Maldigestion caused by exocrine pancreatic insufficiency, bacterial overgrowth
Malabsorption caused by inflammatory bowel diseases, lymphangiectasia, lymphoma, and so forth

Hypoglycemia

- Clinical signs of hypoglycemia in diabetic animals are associated with epinephrine excess, which is released to counter the hypoglycemia. Nervousness, anxiety, vocalization, muscle tremors, ataxia, and pupillary dilatation should alert the owner to the possibility of hypoglycemia. Have the owner offer food to the animal then bring it in for reevaluation.
- Late in the course of hypoglycemic shock the animal may become recumbent or comatose, or the animal may have a seizure.
- If access to a vein is not readily available or if the owner is administering therapy, 50% dextrose solution, Karo syrup, or pancake syrup may be applied to the mucous membranes of the mouth using a large syringe. Caution the owner to pour the syrup on the gums from a reasonable distance from the animal's teeth to prevent accidental injury from biting. Have the owner transport the animal to a veterinarian as soon as possible.
- In a veterinary facility, treat hypoglycemia by slow IV bolus of 50% dextrose (0.5 g/kg diluted 1:4) followed by continuous infusion of 5% dextrose until the animal can be fed.
- Many animals that experience insulin overdose suffer cerebral edema and temporary blindness or behavior changes; often these signs are temporary and resolve after several weeks or months.

▼ ***Key Point*** Endogenous glucose stores may have been depleted by the insulin overdose and it may take several days for hyperglycemia to recur. In these cases, discontinue insulin therapy until hyperglycemia recurs.

Diet

The goals of dietary therapy in diabetes mellitus for both cats and dogs are to provide sufficient calories to maintain ideal body weight and correct obesity or emaciation, to minimize postprandial hyperglycemia, and to facilitate ideal absorption of glucose by timing meals to coincide with insulin administration. However, the approach to feeding will vary between dogs and cats. Cats require low-carbohydrate, high-protein foods to promote reversal of glucose toxicity in type 2 diabetes, whereas dogs require low-fat, high-fiber foods to prevent ketosis in type 1 diabetes.

- Maintain caloric intake at 60 to 70 kcal/kg/day for smaller dogs and cats, and 50 to 60 kcal/kg/day for larger dogs.

- Reduce the body weight of obese animals gradually over a period of 2 to 4 months by feeding 60% to 70% of the calculated caloric requirements for ideal body weight.
- Feed underweight animals a high caloric-density food based on caloric intake for optimum body weight. Once ideal body weight is reached, switch the animal to a high-fiber diet. Table 34-3 lists the fiber and caloric content of various pet foods.

▼ ***Key Point*** In dogs, increased dietary fiber improves glycemic control by slowing glucose absorption from the intestinal tract, reducing postprandial hyperglycemia, and controlling obesity.

TREATMENT OF TYPE 2 (NON–INSULIN-DEPENDENT) DIABETES

▼ ***Key Point*** Treatment of type 2 diabetes is aimed at decreasing hepatic glucose output and glucose absorption from the intestine, increasing peripheral insulin sensitivity, and increasing insulin secretion from the pancreas.

Diet

The goals of dietary therapy in diabetes mellitus will vary between dogs and cats. Cats require low-carbohydrate, high-protein foods to promote reversal of glucose toxicity in type 2 diabetes, whereas dogs require low-fat, high-fiber foods to prevent ketosis in type 1 diabetes.

- Maintain caloric intake at 60 to 70 kcal/kg/day for cats.
- Reduce the body weight of obese animals gradually over a period of 2 to 4 months by feeding 60% to 70% of the calculated caloric requirements for ideal body weight.
- Feed underweight animals a high caloric-density food based on caloric intake for optimum body weight.

▼ ***Key Point*** A low-carbohydrate, high-protein diet, which is similar to a cat's natural diet (mice), may ameliorate some of the abnormalities associated with diabetes mellitus in the cat. Comparison of canned high-fiber versus low-carbohydrate diets showed that cats fed low-carbohydrate diets were 2 to 3 times more likely to discontinue insulin injections. Most dry cat food formulations contain excessive carbohydrates; therefore, canned cat foods should be used for initial treatment of diabetic cats. Caution should be used when initially changing from dry to canned foods as insulin requirements may decrease dramatically; a reduction in insulin dosage may be required.

Exercise

- Keep the exercise level constant in a diabetic animal. Instruct the owner to walk the dog daily and avoid intermittent episodes of strenuous exercise, such as racing or hiking.
- Increasing exercise in an obese diabetic animal reduces insulin resistance and improves glycemic control.

Oral Hypoglycemic Drugs

Overview

- Human diabetics can be divided into three therapeutic categories according to beta cell function:
  1. Those who require exogenous insulin to control hyperglycemia
  2. Those who require only dietary therapy because of sufficient pancreatic islet cell function and insulin sensitivity to maintain relatively normal glucose levels
  3. Those who have sufficient pancreatic islet cell function and insulin sensitivity to respond to oral hypoglycemic drugs
- In cats, differentiation among these categories is almost impossible before treatment; therefore, use the *response* to oral hypoglycemic agents as a guide to whether the cat can be managed with oral hypoglycemic agents.
- Oral hypoglycemic agents include the following categories (Table 34-7):
  - Sulfonylureas (e.g., glipizide, glyburide, and glimepiride)
  - Biguanides (e.g., metformin)
  - Thiazolidinediones (e.g., troglitazone)
  - Alpha-glucosidase inhibitors (e.g., acarbose)
  - Transition metals (e.g., chromium and vanadium)
- Most oral hypoglycemic agents work by increasing insulin secretion, decreasing insulin resistance, decreasing glucose absorption, decreasing hepatic glucose production, or a combination of these (Fig. 34-4).

▼ ***Key Point*** Indications for oral hypoglycemic therapy in diabetic cats include normal or increased body weight, lack of ketones, probable type 2 diabetes with no underlying disease (pancreatitis, pancreatic tumor), and the owner's willingness to administer oral medication rather than an injection.

Sulfonylureas (e.g., Glipizide)

- The mechanism of action of the sulfonylureas is to increase insulin secretion and improve insulin resistance; however, these agents also cause an increase in hepatic gluconeogenesis. This leads to delayed hyperinsulinemia, weight gain, and atherosclerosis in humans treated with sulfonylureas.

Table 34-7. ORAL HYPOGLYCEMIC DRUGS USED IN THE TREATMENT OF TYPE 2 DIABETES (NIDDM) IN HUMANS AND CATS

Drug (Trade Name)	Dose	Frequency	Side Effects	Mechanism of Action
Glipizide (Glucotrol, Pfizer)	2.5–5 mg/cat	q8–12h, PO	Hepatotoxicity, hypoglycemia, vomiting	Increases insulin secretion and sensitivity
Glimepiride (Amaryl, Hoechst-Marion Roussel)	1–4 mg (humans); 1 mg/cat	q24h (humans); q24h (cat)	Same as above but lower incidence	Same as above
Metformin (Glucophage, Bristol-Myers Squibb)	500–700 mg (humans); unknown (cat)	q12h (humans); unknown (cat)	Anorexia, vomiting	Inhibits hepatic glucose production
Precose (Acarbose, Bayer)	50 mg (humans); 12.5–25 mg (cat)	q8–12h with meals	Flatulence, soft stool	Alpha-glucosidase inhibitor, impairs glucose absorption from gut
Troglitazone (Rezulin, Parke-Davis)	200–400 mg (humans); unknown (cat)	q24h	Mild decreases in WBC, platelet, and Hb counts	Increases insulin receptor sensitivity
Chromium	200 µg/cat	q24h	Unknown	Increases insulin receptor sensitivity
Vanadium	200–400 µg/cat	q24h in food or water	Anorexia, vomiting	Increases insulin receptor sensitivity

Hb, hemoglobin; WBC, white blood cell count.

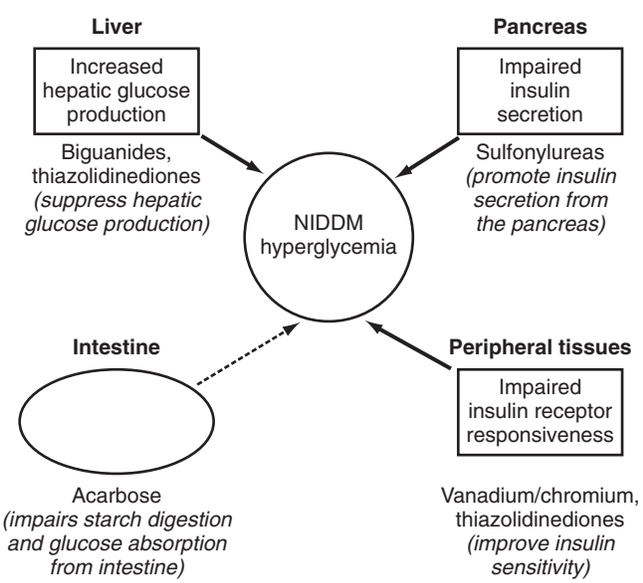

Figure 34-4. Mechanisms of action of oral hypoglycemic agents in the treatment of non–insulin-dependent (type 2) diabetes mellitus.

- Glipizide (Glucotrol, Roerig), a sulfonylurea drug, has been used successfully to treat type 2 diabetes in cats at a dosage of 2.5 to 5 mg q12h PO with food (low-carbohydrate diet). An outline for monitoring and managing cats undergoing glipizide therapy is shown in Figure 34-5.
- Side effects of sulfonylureas include severe hypoglycemia (rare in cats), cholestatic hepatitis, and vomiting. Gastrointestinal side effects, which occur in about 15% of cats treated with glipizide, resolve when the drug is administered with food.

Biguanides (e.g., Metformin)

- Metformin belongs to the biguanide group of oral hypoglycemic agents, which work by *inhibiting* hepatic glucose release and by improving peripheral insulin sensitivity.
- One advantage of the biguanides is that they do not promote insulin release; therefore, there is little potential for the development of hypoglycemia when metformin is used as a sole agent.
- Side effects of the biguanides include lactic acidosis and gastrointestinal signs such as nausea and diarrhea.
- Studies have shown that metformin is not a viable option in the cat.

Alpha-Glucosidase Inhibitors (e.g., Acarbose)

- Acarbose, an alpha-glucosidase inhibitor, impairs glucose absorption from the intestine by decreasing fiber digestion and hence glucose production from food sources.
- Acarbose is used as initial therapy in obese prediabetic patients suffering from insulin resistance or as adjunct therapy with sulfonylureas or insulin to enhance the hypoglycemic effect in patients with overt diabetes mellitus.
- One advantage of acarbose is that it is not absorbed systemically and may be used in conjunction with other oral hypoglycemics.
- Side effects of acarbose include flatulence, loose stool, and overt diarrhea at high dosages.
- Acarbose is not indicated in patients of low or normal body weight because of the negative effects on nutrition.

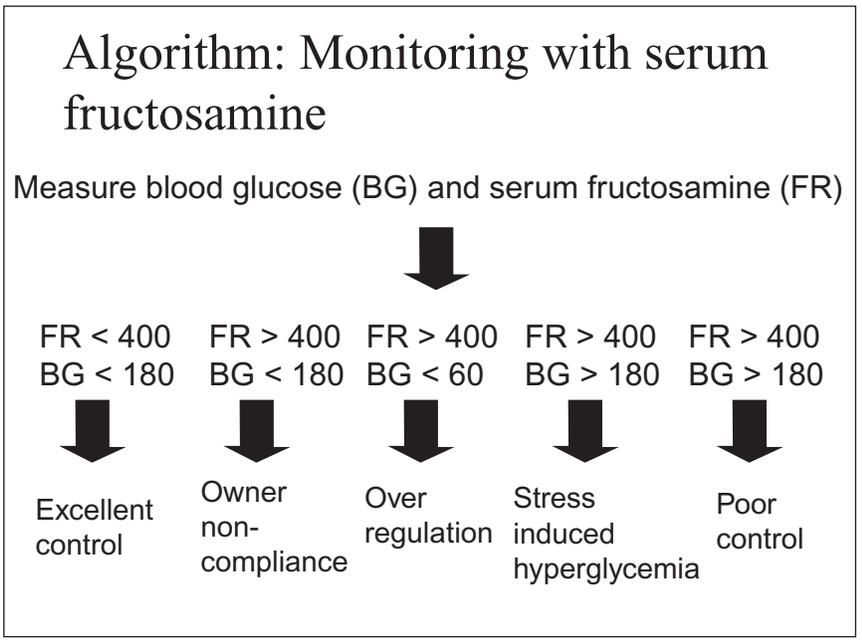

Figure 34-5. Algorithm for monitoring with serum fructosamine.

Thiazolidinediones (e.g., Troglitazone)

- The thiazolidinedione compounds facilitate insulin-dependent glucose disposal and inhibition of hepatic glucose output via attenuation of gluconeogenesis and activation of glycolysis. In addition, the thiazolidinediones have been shown to have beneficial effects on lipid disturbances in type 2 diabetes.
- Thiazolidinedione compounds have been used early in the course of type 2 diabetes to prevent development of overt diabetes.
- Initial studies using troglitazone for the treatment of feline type 2 diabetes are ongoing.

Transition Metals: Vanadium and Chromium

- Vanadium and chromium are transition elements that have been shown to have extensive insulin-like properties. Oral vanadium and chromium cause a marked and sustained improvement in glucose homeostasis in type 2 diabetes by exerting an insulin-like effect on peripheral tissues; furthermore, vanadium prevents the exhaustion of insulin stores in the pancreas. Unlike insulin, vanadium does not lower blood glucose concentrations in normal animals.
- Low doses of oral vanadium decrease blood glucose and serum fructosamine concentrations and alleviate the signs of diabetes (polydipsia, polyuria) in cats with *early* type 2 diabetes mellitus.
- Side effects of oral vanadium include anorexia and vomiting.

Insulin and Oral Hypoglycemics

- Changes from insulin to oral hypoglycemic agents or vice versa may be necessary in some diabetic cats. If a cat is particularly sensitive to insulin or exhibits transient diabetes because of reversal of "glucose toxicity," consider a change to an oral hypoglycemic.
- If a cat is being managed with oral hypoglycemic agents and ketosis develops, switch the cat to insulin therapy.
- Agents that impair glucose absorption from the intestine (acarbose) or increase insulin sensitivity (vanadium, metformin, troglitazone) may be combined with insulin to improve glucose control.
- In the case of "brittle diabetics" in which small incremental changes in the insulin dose may precipitate hypoglycemia, the addition of a drug that enhances the action of insulin may lead to a reduction in the insulin dose required to attain euglycemia.
- In humans, acarbose, chromium, vanadium, and metformin are commonly used in conjunction with insulin or with other oral hypoglycemics (sulfonylureas) that cause insulin release.
- Use caution when combining an oral hypoglycemic agent with insulin, as hypoglycemic reactions may occur.

Monitoring Oral Hypoglycemic Therapy

- It appears that methods of assessing *long-term* glycemic control are better indicators of response to therapy with oral hypoglycemics than are spot glucose determinations or blood glucose curves. Monitor resolution of clinical signs and serum fructosamine concentrations in cats undergoing oral hypoglycemic therapy.
- For clinical signs, body weight should increase or remain stable and polydipsia and polyuria should resolve with effective oral hypoglycemic therapy.

- Normal fructosamine concentrations are consistent with moderate to good long-term control of hyperglycemia. Relative improvement of serum fructosamine may be more important than absolute fructosamine values.

PREVENTION

- In humans, and presumably in cats, obesity management may be helpful in preventing development of type 2 diabetes mellitus.
- In dogs and cats, prevention of secondary forms of diabetes is possible by limiting the use of diabetogenic drugs such as glucocorticoids, progestational compounds, and somatotropin.
- Similarly, prevention and treatment of underlying disease is the mainstay of prevention of secondary diabetes resulting from hyperthyroidism, hyperadrenocorticism, or acromegaly.

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Chapter 35

Pancreatic Beta Cell Neoplasia

Nyssa J. Reine / Jennifer Bonczynski

Tumors of the beta cells of the pancreatic islets are functional tumors that secrete excessive amounts of insulin independent of normal regulatory mechanisms. Hyperinsulinism causes hypoglycemia and corresponding clinical signs. Consider beta cell neoplasia in the differential diagnosis of hypoglycemia in middle-aged and older dogs.

ETIOLOGY

- Insulin-secreting tumors are almost always malignant.
- Metastatic sites include the lymphatics and lymph nodes (duodenal, mesenteric, hepatic, splenic), liver, mesentery, and omentum.
- The hyperinsulinemia caused by beta cell tumors interferes with glucose homeostasis by decreasing the rate of glucose release from the liver and by increasing the uptake of glucose by insulin-sensitive tissues.
- The net effect is hypoglycemia and secretion of the counter-regulatory hormones (most notably glucagons, epinephrine, cortisol and growth hormone).
- The brain is dependent on a constant supply of glucose for energy and has very limited storage capacity. Hypoglycemia results in decreased delivery of glucose to the brain (neuroglycopenia).

CLINICAL SIGNS

- The most common clinical signs of insulinoma are weakness, ataxia, collapse, seizures, muscle fasciculations, polyphagia, and weight gain (Table 35-1).
- Dogs have clinical signs for a duration of 1 to 6 months before presentation to the veterinarian.
- Clinical signs tend to be episodic and often develop during fasting, exercise, excitement, and eating.
- The severity of clinical signs depends on the glucose nadir and the rate of development and duration of hypoglycemia. Patients with chronic hypoglycemia seem to tolerate lower blood sugars without neurologic signs.

DIAGNOSIS

▼ ***Key Point*** The diagnosis of an insulin-secreting beta cell tumor requires initial confirmation of hypoglycemia and then documentation of simultaneous, inappropriately high insulin secretion.

Signalment

Signalment is not always useful in differentiating insulinoma from other common causes of hypoglycemia (Table 35-2).

- Insulin-secreting tumors typically occur in the middle-aged or older dog, with an age range of 6 to 14 years.
- There is no apparent sex or breed predilection, although the Labrador retriever, German shepherd, Irish setter, golden retriever, collie, fox terrier, and standard poodle are commonly affected in our hospital.
- Islet cell neoplasia is rare in cats.

Physical Examination

The physical examination of dogs with insulin-secreting tumors is surprisingly unremarkable.

- Weight gain is evident in some dogs and is probably a result of the potent anabolic effects of insulin.
- Peripheral neuropathies have been reported in dogs with insulin-secreting tumors and may be manifested as proprioception deficits, depressed reflexes, and muscle atrophy.

Laboratory Studies

- The only consistent abnormality found on the hemogram, biochemical panel, and urinalysis is hypoglycemia.
- Hypoalbuminemia, hypophosphatemia, hypokalemia, and an increase in alkaline phosphatase and alanine aminotransferase have been reported, but these findings are considered nonspecific and not helpful in achieving a definitive diagnosis.
- A correlation has not been found between liver enzyme elevations and metastasis of the pancreatic tumor to the liver.

Table 35-1. CLINICAL SIGNS ASSOCIATED WITH BETA CELL NEOPLASIA IN THE DOG

Seizures	Muscle fasciculations
Weakness	Bizarre behavior
Collapse	Lethargy
Ataxia	Weight gain
Posterior paresis	Polyphagia

Table 35-2. DIFFERENTIAL DIAGNOSIS FOR HYPOGLYCEMIA

Beta cell neoplasia
Non-pancreatic neoplasia
Hepatocellular carcinoma, hepatoma
Leiomyosarcoma, leiomyoma
Hemangiosarcoma
Hepatopathy
Vascular shunts
Chronic fibrosis, cirrhosis
Hepatic necrosis
Sepsis
Hypoadrenocorticism
Toy-breed puppy
Chronic renal failure
Glycogen storage disorder
Polycythemia
Starvation
Artifact

- A normal physical examination and lack of abnormalities other than hypoglycemia on hemogram, serum biochemical panel, and urinalysis strongly suggest beta cell neoplasia as the cause of the hypoglycemia. It is important to systematically eliminate other causes before pursuing a diagnosis of insulinoma (see Table 35-2).

Blood Glucose Assay

- Up to 98% of dogs with insulinoma reportedly present with hypoglycemia.
- Dogs with insulin-secreting tumors occasionally may have a normal blood glucose concentration on random testing. Such a finding does not eliminate intermittent hypoglycemia as a cause of episodic weakness or seizure activity.
- If hypoglycemia is not present on initial examination, fast the patient to induce hypoglycemia. Measure blood glucose hourly. Closely observe the patient for worsening of signs (i.e., seizures or collapse).
- Typically, point-of-care glucose monitors are adequate for glucose assessment. If such equipment is not available, separate serum from red blood cells immediately to minimize effects of red blood cell metabolism.
- A fast of 8 hours or less is usually successful in demonstrating hypoglycemia in most dogs with insulin-secreting tumors.
- Concurrent assessment of serum fructosamine level may provide supportive evidence of insulinoma. Patients with insulinoma should have a low serum fructosamine in the presence of normoglycemia. This has recently been reported in a dog with insulinoma without measurable hypoglycemia.

Ultrasonography

Abdominal ultrasonography can be used to identify the tumor in the region of the pancreas and to assess for potential metastatic lesions in the liver and surrounding structures; however, negative findings do not rule out an insulin-secreting tumor or the presence of metastasis.

- Pancreatic masses are reportedly identified in 27% to 93% of dogs.
- In one study, only 42% of the metastatic lesions found with ultrasonography were confirmed at surgery.

Insulin Secretion Measurement

Confirmation of an insulin-secreting neoplasm requires documentation of inappropriate insulin secretion during hypoglycemia. Measuring serum insulin concentration when the blood glucose is <60 mg/dl (<40 mg/dl using glucose reagent strips) usually establishes the diagnosis. A 4- to 8-hour fast may be required to obtain this level of hypoglycemia, but when the blood glucose concentration falls below 60 mg/dl, the simultaneous blood insulin concentration is interpreted as follows:

- Blood insulin is above normal (>120 pmol/L): An insulin-secreting neoplasm is likely.
- Blood insulin is in the high-normal range (60–120 pmol/L): An insulin-secreting tumor is possible.
- Blood insulin is in the low-normal range (30–60 pmol/L): An insulin-secreting tumor has not been confirmed.
  - Blood insulin in the low-normal range with hypoglycemia can be associated with non-islet cell tumors as well as insulin-secreting tumors. This is an indication for further diagnostics, including repeating the blood glucose and insulin determinations.
- Blood insulin is in the below-normal range (<30 pmol/L): Insulinopenia has been documented, and an insulin-secreting tumor has been ruled out.

MEDICAL TREATMENT FOR ACUTE HYPOGLYCEMIC CRISIS

The acute onset of clinical signs of hypoglycemia (see Table 35-1) typically occurs in the dog in the home environment or immediately postoperatively in the dog with an inoperable tumor or metastases. Therapy depends on the severity of clinical signs and the location of the dog or cat (i.e., home or hospital).

- In the hospital, administer 50% dextrose solution (1 ml/kg) slowly IV until clinical signs are controlled.
- If the dog is home, instruct the owner to rub a sugar-containing solution (e.g., Karo syrup) on the buccal mucosa until clinical signs are controlled.
- Dogs and cats with hypoglycemia should respond to the administration of glucose in 30 to 120 seconds.

▼ ***Key Point*** Avoid overstimulation of the tumor when administering dextrose IV. Overzealous administration of dextrose can stimulate the tumor to release excessive amounts of insulin into the circulation and cause severe rebound hypoglycemia. A vicious cycle that is difficult to break may ultimately result in persistent seizures and eventually death.

- The goal of therapy is to control the clinical signs, not correct hypoglycemia, through the judicious administration of dextrose.
- Administer small amounts of dextrose slowly rather than large boluses rapidly to minimize stimulation of the tumor.
- IV dextrose supplementation should be replaced by frequent feedings as soon as possible.
- Constant rate infusion of glucagon has been used to successfully manage acute hyperinsulinemic-hypoglycemic crisis in a dog with insulinoma.

Seizures

Occasionally, seizures will persist despite normalization of blood glucose concentration. This may indicate the presence of cerebral edema or rarely the presence of a permanent cerebral lesion (i.e., necrosis). If intractable seizures due to hypoglycemia develop, take the following actions:

- Discontinue bolus injections of dextrose.
- Begin continuous IV infusion of 2.5% to 5.0% dextrose solution that is $1\frac{1}{2}$ to 2 times the maintenance rate (90–120 ml/kg/day).
- Consider mannitol (0.5 g/kg IV) if signs of cerebral edema are present (i.e., anisocoria).
- Consider the addition of rapid acting glucocorticoids (i.e., dexamethasone sodium phosphate).
- Administer the somatostatin analog SMS 201-995 (octreotide; Sandostatin, Sandoz), 10 to 40 mg q8–12h SC, to decrease insulin secretion by the tumor.
- Anti-convulsants may be needed if seizures persist (i.e., phenobarbital; see Chapter 127).

SURGICAL TREATMENT

Surgical Anatomy

The pancreas consists of the right lobe, left lobe, and the body.

Right Lobe

The right lobe is located in the mesoduodenum adjacent to the descending duodenum. The proximal portion of the right lobe is intimately associated with the duodenum (Fig. 35-1). The proximal half of the

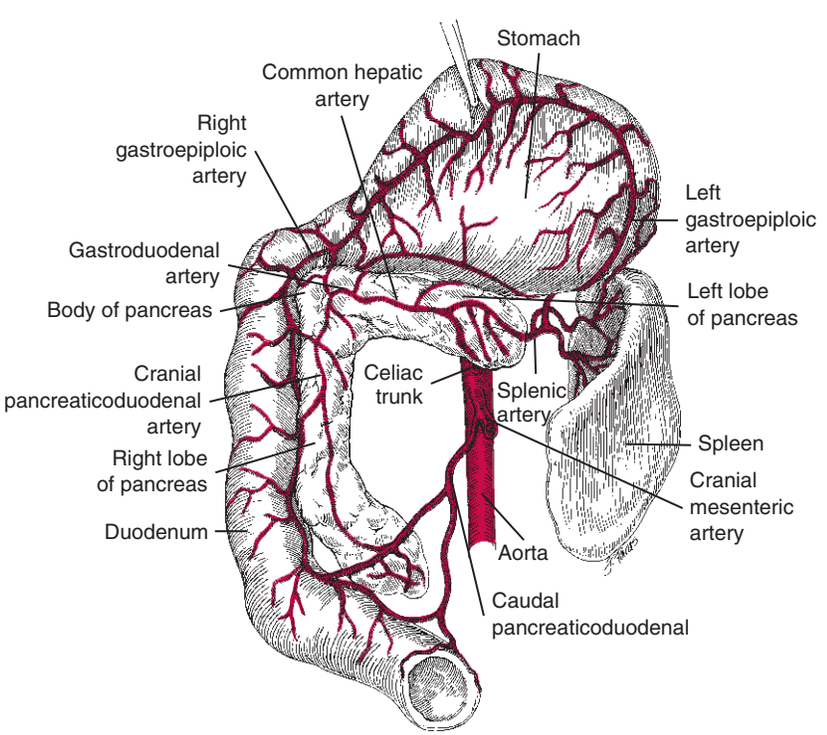

Figure 35-1. Anatomy and blood supply of the right and left lobes of the pancreas.

right limb is supplied by the cranial pancreaticoduodenal artery, which is the terminal branch of the hepatic artery. The distal half of the right limb is supplied by the caudal pancreaticoduodenal artery, which is a branch of the cranial mesenteric artery. Damage to the pancreaticoduodenal vessels may result in avascular necrosis of the duodenum.

Left Lobe

The left lobe is located caudodorsal to the stomach in the deep leaf of the greater omentum. It is exposed by reflecting the greater omentum, spleen, and stomach cranially and retracting the transverse colon caudally. This lobe of the pancreas is mainly supplied by branches of the splenic artery.

Body of the Pancreas

The body of the pancreas is located at the cranial duodenal flexure and is close to the pylorus and common bile duct. Branches of the hepatic artery (gastroduodenal) supply the body of the pancreas. The portal vein crosses the dorsal portion of the body.

Lymphatics

Lymphatics from the pancreas drain into the duodenal, hepatic, splenic, and mesenteric lymph nodes.

Pancreatic Ducts

Excretory ducts of the pancreas exit the pancreatic parenchyma in the area of the body to enter the duodenum. There are usually two, which intercommunicate within the gland. There are several variations in the anatomy of the pancreatic ducts.

- In the dog, the pancreatic duct usually enters the duodenum adjacent to the common bile duct at the major duodenal papilla approximately 5 cm distal to the pylorus. The accessory pancreatic duct, which is the larger pancreatic duct, enters the duodenum at the minor duodenal papilla approximately 8 cm distal to the pylorus (Fig. 35-2).
- In the cat, the pancreatic duct is the main excretory duct; the accessory duct often is absent.

Preoperative Considerations

- The goal of fluid therapy prior to and during surgery is to maintain systemic blood pressure and pancreatic perfusion, thereby minimizing the development of pancreatitis.
- Although correction of hypoglycemia is not usually feasible, maintain blood glucose above 40 mg/dl or so that no clinical signs are apparent.
- To minimize hypoglycemia during the preoperative period, feed the animal frequent small meals and, if necessary, give prednisone, 0.25 to 0.5 mg/kg q12h PO.

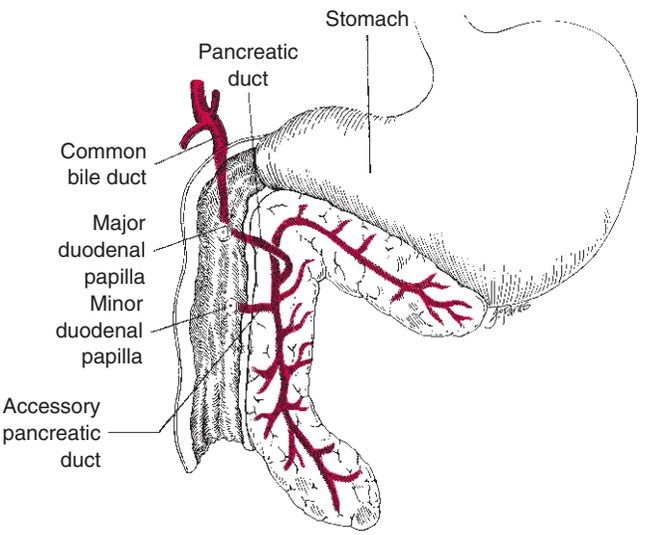

Figure 35-2. Anatomy of the pancreatic ducts in relationship to the duodenum.

▼ ***Key Point*** On the *day of surgery,* administer a balanced electrolyte solution containing 2.5% to 5% dextrose IV that is 1½ to 2 times the daily maintenance requirements. *Intraoperatively,* administer this same solution at a rate of 8 to 16 ml/kg/hr .

Surgical Procedure

Objectives

- Confirm a neoplasm.
- Carefully examine the entire pancreas. Islet cell tumors occur with approximately equal frequency in all areas of the pancreas. Although single lesions are most common, multiple lesions in non-adjacent areas of the pancreas have been reported in about 15% of cases. Diffuse involvement of the pancreas without a discrete mass also has been reported.
- Define the clinical stage of the tumor.

▼ ***Key Point*** A study suggests that abdominal ultrasound findings do not correlate well with surgical findings. Abdominal ultrasound may falsely identify metastatic disease.

- Remove the primary pancreatic tumor and any metastatic lesions (see the following section). Although this may not be a cure, it usually reduces clinical signs and may facilitate medical management.

Equipment

- Standard abdominal surgery instrument pack and suture
- Hemoclips—Various sizes
- Gelfoam
- Malleable retractors

Technique (Using Visual Examination and Palpation)

1. Approach the abdomen via a ventral midline incision from the xiphoid to the pubis.
2. Examine the entire pancreas visually and by careful palpation.
   a. Islet cell tumors are usually firmer than the surrounding tissue.
   b. Islet cell tumors may be small and sandwiched between pancreatic lobules so that they are not readily visible.

Technique (Using Methylene Blue Intravenous Infusion)

The following technique to facilitate tumor identification utilizes IV infusion of methylene blue. It should be considered only if a mass cannot be identified at surgery.

1. Surgically expose the pancreas as described previously.
2. Administer methylene blue as an IV infusion in normal isotonic saline solution to a total dose of 3 mg/kg of body weight. Begin the infusion 30 minutes before the pancreas is exposed.
3. Methylene blue is concentrated by the endocrine pancreas and intensely stains hyperfunctional areas.
   a. Normal pancreatic endocrine tissue is stained a dusky slate blue.
   b. Hyperfunctional tissue is stained more intensely (often a reddish blue).
4. Potential complications include hemolytic anemia and acute renal failure postoperatively.

Technique (Using Intraoperative Ultrasound)

The following technique is commonly used in human patients with 90% diagnostic accuracy. It is not yet widely used in veterinary medicine but offers a safer alternative to methylene blue IV infusion.

1. Use a 7.5- or 10-MHz probe in a sterile sleeve.
2. Apply a thin layer of saline to the tissues to improve contact.
3. Scan for primary tumors in the pancreas and metastasis in the liver.
4. Direct intraoperative ultrasonography decreases the effect of gas in the surrounding gastrointestinal (GI) tract, which allows better identification of the masses.

Technique (Removal of Neoplastic Tissue)

1. Handle the pancreas and masses gently to avoid pancreatitis and potential insulin release.
2. Check the blood glucose frequently during surgery.
3. Remove abnormal pancreatic masses by partial pancreatectomy or by local excision. Make a wide excision if possible.
4. Remove tumors located in the left lobe or the distal portion of the right lobe by partial pancreatectomy (Fig. 35-3).
   a. Isolate the affected pancreas with moistened abdominal sponges.
   b. Divide the mesentery surrounding the affected lobe and ligate and divide the appropriate vessels (see Fig. 35-3*A*).
   c. Incise the mesentery covering both surfaces of the pancreas at the level of transection of the lobe.
   d. Remove the lobe at least 1 to 2 cm proximal to the tumor.

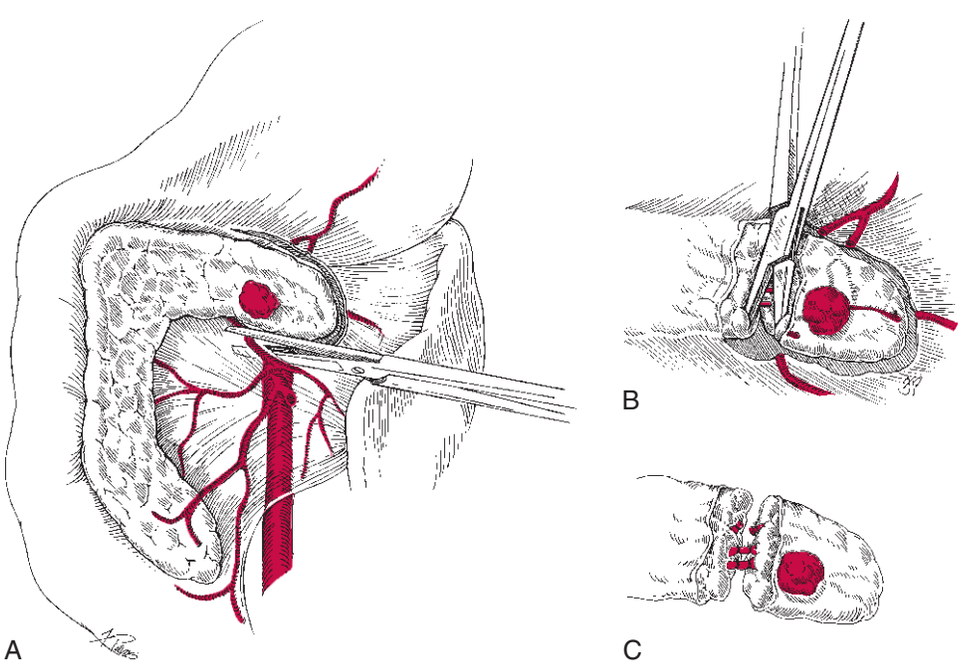

Figure 35-3. Schematic of partial pancreatectomy procedure. See text for details.

e. Bluntly separate the lobules using a mosquito hemostat, dissecting alternately from each side of the gland (see Fig. 35-3*B*).
f. Isolate the main duct, ligate with a monofilament absorbable synthetic suture material, and transect it (see Fig. 35-3*C*).
g. Alternatively, simply ligate the pancreatic tissue in guillotine style to occlude the vessels and ducts (3-0 or 4-0 polydioxanone suture).

5. When the tumor is located in the proximal portion of the right lobe or the body, local excision of the tumor, including at least 1- to 2-cm margins of normal-appearing pancreatic tissue, is the preferred technique because of the vascular and ductal anatomy of the area.
   a. Gently separate the pancreatic lobules by blunt dissection with a mosquito hemostat. Cauterize small vessels and ligate and divide larger vessels.
   b. Preserve the pancreaticoduodenal vessels supplying the duodenum. Avoid damaging the pancreatic ducts and the common bile duct.
6. Explore the entire abdomen for evidence of metastatic disease. The most common sites of metastasis are the liver and regional lymph nodes (duodenal, hepatic, splenic, greater mesenteric).

▼ ***Key Point*** Metastatic disease is common; approximately 30% to 50% of cases have identifiable metastasis to the liver or regional lymph nodes at the time of surgery.

   a. Resect all enlarged lymph nodes and suspicious hepatic lesions if possible and submit them for histopathologic examination.
   b. A recent study (Tobin et al., 1999) showed a poor correlation between gross inspection during surgery and histopathologic examination of biopsy specimens for potential metastatic lesions. Only 57% of the lesions biopsied as metastatic disease were confirmed metastatic beta cell neoplasia by histopathologic examination.
   c. Biopsy lesions that cannot be completely excised.

▼ ***Key Point*** Many dogs with metastases of islet cell neoplasms can be managed medically for longer than a year.

7. Close the abdomen routinely.

Postoperative Care and Complications

Postoperative Care

- Give nothing by mouth for 48 hours.
- Administer a balanced electrolyte solution IV containing 5% dextrose that is 1½ to 2 times the daily maintenance requirements (90–120 ml/kg/day). Maintain adequate blood pressure and perfusion to prevent pancreatitis.
- Monitor blood glucose concentration at least twice daily.
- Discontinue the dextrose infusion if hyperglycemia (>150 mg/dl) develops.
- If vomiting does not occur, offer small amounts of water after 48 hours and then small amounts of a bland, easily digestible diet.
- If the dog tolerates a bland diet well, resume the normal diet in 5 to 7 days.

Complications

- Hyperglycemia may occur following surgery due to inadequate insulin secretion by atrophied non-neoplastic beta cells. This often resolves within a few days.
- If hyperglycemia and glycosuria persist for several days following surgery, initiate insulin therapy (see Chapter 34).
- Diabetes mellitus is usually transient and resolves within a few weeks to several months.
- Periodically, discontinue insulin therapy on a trial basis to determine if endogenous insulin production is resuming.
- If hypoglycemia does not resolve postoperatively or if it recurs following resection of an islet cell tumor, assume metastatic disease to be present and institute medical therapy for chronic hypoglycemia, as described in the following section.
- Other potential postoperative complications include pancreatitis (see Chapter 73 for treatment), duodenal necrosis (from vascular compromise), ventricular arrhythmias, and central nervous system dysfunction secondary to prolonged hypoglycemia.

MEDICAL TREATMENT FOR CHRONIC HYPOGLYCEMIA

Institute palliative medical management for chronic hypoglycemia in preparation for exploratory laparotomy, for patients with persistent postoperative hypoglycemia, when exploratory surgery is refused by the owner or when an inoperable tumor or metastases result in recurrence of clinical signs.

Goals of Chronic Palliative Therapy

- To reduce the frequency and severity of clinical signs. This is typically achieved initially via dietary therapy. If dietary therapy is inadequate, other medical therapies are added.
- To prevent an acute hypoglycemic crisis through dietary management and nonspecific anti-hormonal therapy.

Diet and Exercise Recommendations

- Feed frequent small meals to provide a constant source of calories, which may prevent or reduce the number of hypoglycemic episodes.

- Use a diet that is high in proteins, fats, and complex carbohydrates—similar to those recommended for patients with diabetes mellitus. These are recommended to minimize postprandial hyperglycemia.
- If commercial pet food is used, recommend a combination of canned and dry food, fed three to six small meals daily.
- Avoid simple sugars (including soft moist foods) except as needed to treat signs of hypoglycemia.
- Limit exercise to short walks on a leash.

Anti-Hormonal Therapy

Anti-hormonal therapy minimizes hypoglycemia through the following:

- Increasing absorption of glucose from the intestinal tract
- Increasing hepatic gluconeogenesis and glycogenolysis
- Inhibiting the synthesis, secretion, or peripheral cellular actions of insulin

Glucocorticoid Therapy

Mechanisms

Glucocorticoids antagonize the actions of insulin at the cellular level, stimulate hepatic glycogenolysis, and provide the necessary substrates for hepatic gluconeogenesis.

Goal of Therapy

Initiate glucocorticoids when dietary manipulations are no longer effective in preventing signs of hypoglycemia.

Dosage

- Administer prednisone at an initial dosage of 0.5 mg/kg/day given in divided doses.
- Increase the dosage as needed to control clinical signs of hypoglycemia up to a maximal daily dose of 4 to 6 mg/kg.
- Signs of iatrogenic hypercortisolism ultimately limit the amount of prednisone that can be administered.

Diazoxide Therapy

Mechanism

Diazoxide (Proglycem, Schering-Plough) is a benzothiadiazide diuretic that inhibits insulin secretion, stimulates hepatic gluconeogenesis and glycogenolysis, and inhibits tissue use of glucose. The net effect is hyperglycemia.

Goal of Therapy

The goal of diazoxide therapy is to establish a dosage in which hypoglycemia and its clinical signs are reduced or absent while avoiding hyperglycemia (>180 mg/dl) and its associated clinical signs.

Dosage

- Administer diazoxide at an initial dosage of 10 mg/kg q12h PO.
- Gradually increase the dose as needed to control signs of hypoglycemia, but do not exceed 60 mg/kg/day.

Side Effects

- The most common adverse reactions to diazoxide are anorexia and vomiting. Minimize these by administering diazoxide with a meal or temporarily decreasing the dosage.
- Other potential complications include diarrhea, tachycardia, bone marrow suppression, aplastic anemia, thrombocytopenia, diabetes mellitus, sodium and fluid retention, and cataracts.

Somatostatin Analog (SMS 201-995) Therapy

Mechanism

SMS 201-995 (octreotide; Sandostatin, Sandoz) is an analog of somatostatin that inhibits the secretion of insulin by normal and neoplastic beta cells.

- The responsiveness of insulin-secreting tumors to the suppressive effects of SMS 201-995 is variable, being dependent on membrane receptors for somatostatin on the tumor cells.

Dosage

- The dosage is 10 to 20 µg q8–12h SC. The dose is increased as needed to control hypoglycemia.

Side Effects

- Adverse reactions have not been seen at these dosages. Patients may become refractory to the medication.

CHEMOTHERAPY FOR INSULINOMA

Streptozotocin

Mechanism

Streptozotocin is a nitrosourea alkylating agent that is cytotoxic to pancreatic beta cells. It has been shown to be efficacious in some dogs with insulinoma. It provides a treatment option for patients with unresectable disease or recurrence after surgery.

Goal of Therapy

Decrease insulin secretion by the tumor cells.

Dosage

- The current recommended dose is 500 mg/m^2 (see Chapter 26 for body weight to surface area conversion table). Follow saline diuresis protocol very closely (Table 35-3).

Table 35-3. PROTOCOL FOR STREPTOZOTOCIN ADMINISTRATION FOR INSULINOMA

1. Administer 0.9% NaCl at a constant-rate infusion of 18.3 ml/kg/hr for 3 hours *prior to* administration of chemotherapy.
2. Administer streptozotocin (500 mg/m^2) diluted in the appropriate volume of 0.9% NaCl at a rate of 18.3 ml/kg/hr for 2 hours.
3. Administer 0.9% NaCl at a constant-rate infusion of 18.3 ml/kg/hr for 2 hours after completion of streptozotocin infusion.
4. Administer butorphanol at a dose of 0.4 mg/kg IM after or during streptozotocin infusion.

- Five treatments are given at 3-week intervals unless severe side effects, progression of disease, or hyperglycemia occur.

Side Effects

- Acute renal failure is reported following bolus administration of streptozotocin. The saline administration protocol reduces the risk of nephrotoxicity and enables administration of repeated doses.
- Other potential complications include bone marrow suppression (usually mild), vomiting (can be severe), anorexia, diarrhea, increased alanine aminotransferase, transient hypoglycemia, and type I diabetes mellitus.

PROGNOSIS

- Survival time is influenced by treatment protocols (i.e., surgical versus medical management) and the stage of disease on initial presentation. The stages are as follows:
  Stage 1: Pancreatic nodule only
  Stage 2: Regional lymph node metastasis
  Stage 3: Distant metastasis (usually liver)
- A multi-university study (Caywood et al., 1988) involving a total of 73 dogs with insulin-secreting neoplasia found the following:
  - Younger dogs and dogs with distant metastasis or higher insulin levels resulted in a significantly shorter survival time.
  - Fifty percent of dogs with stage 1 disease at the time of surgery were free of hypoglycemia 14 months after surgery.
  - Less than 20% of dogs with stage 2 or 3 disease were disease-free at 14 months.
  - Eighty percent of dogs with a solitary mass were dead at 24 months from the time of diagnosis.
  - Approximately 50% of dogs with metastasis to the liver (the most common site) were dead by 6 months, and all were dead by 18 months from the time of diagnosis.
- A more recent study (Tobin et al., 1999) documented a significantly longer median survival time in dogs treated with partial pancreatectomy versus those treated with medical therapy alone (381 days versus 74 days, respectively).
  - There was no correlation to survival or significant difference between the two groups in signalment, duration of clinical signs, radiographic findings, abdominal ultrasound findings, severity of hypoglycemia, insulin level, or prevalence of metastasis at the time of diagnosis.
  - The authors attributed the unexpectedly lower survival in non-surgical dogs to an increase in likelihood to euthanize dogs in people who choose not to pursue surgery. Regardless, this paper certainly supports the role of surgery in the treatment of insulinoma.
- Recurrence of tumor and clinical signs is likely. There are reports of successful resolution of clinical signs with surgical re-exploration to decrease tumor burden.

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Chapter 36

Diseases of the Hypothalamus and Pituitary

John F. Randolph / Rhett Nichols / Mark E. Peterson

NORMAL ANATOMY AND PHYSIOLOGY

The *pituitary* gland (hypophysis) consists of the neurohypophysis surrounded by the adenohypophysis.

Neurohypophysis

The neurohypophysis, also called the *pars nervosa* and *infundibulum* (Fig. 36-1), extends ventrally from the hypothalamus.

- It is composed of nerve tracts terminating from nuclei within the hypothalamus.
- Antidiuretic hormone (ADH, vasopressin) and oxytocin, produced by the supraoptic and paraventricular hypothalamic nuclei, travel down the axons to be stored in and secreted from the neurohypophysis.

Adenohypophysis

The adenohypophysis is an embryonic outgrowth of the pharynx connected to the hypothalamus by a vascular network that allows humoral control of adenohypophyseal secretions by the hypothalamus.

- In response to the neurotransmitters, specialized neurosecretory cells within the hypothalamus release factors that control production and secretion of hormones from the adenohypophysis (Table 36-1).
- Hormones produced by target endocrine organs in response to specific adenohypophyseal hormones exert negative feedback (or feedback inhibition) on further elaboration of the hypothalamohypophyseal hormones.
  - Because growth hormone (GH), prolactin, and melanocyte-stimulating hormone do not have target endocrine organs to participate in negative feedback controls, releasing and inhibiting factors from the hypothalamus control production of these hormones (see Table 36-1).
- The adenohypophysis is subdivided into the pars distalis, pars tuberalis, and pars intermedia (see Fig. 36-1).
- The pars intermedia, unlike the pars distalis, does not have an extensive blood supply contiguous with the hypothalamus. The cells of the pars intermedia appear to release their hormones in response to dopaminergic and serotonergic innervation.

Adenohypophyseal Cells

These are classified by staining properties of their secretory granules.

- Immunohistochemical staining identifies the specific hormone content of the cells.
- Hematoxylin and eosin staining identifies adenohypophyseal cells as follows:
  - Acidophils: Somatotrophs and lactotrophs
  - Basophils: Gonadotrophs, corticotrophs, and thyrotrophs
  - Chromophobes (cells that do not stain selectively): Degranulated, undifferentiated, or actively synthesizing cells (some investigators consider chromophobes to include corticotrophs)

Alternative Nomenclature

Alternatively, the pituitary gland is composed of the anterior lobe and posterior lobe, with the two lobes separated by the hypophyseal cleft (the residual lumen of Rathke's pouch) (see Fig. 36-1). The terms *anterior* and *posterior*, although anatomically correct for the human pituitary, are not accurate when used to describe the lobes of the feline or canine pituitary gland.

- Anterior lobe: Pars tuberalis (glandular pituitary stalk) and pars distalis
- Posterior lobe: Pars nervosa and pars intermedia

DISEASES OF PITUITARY HORMONE EXCESS

Growth Hormone-Secreting Pituitary Neoplasia: Acromegaly

Excess production of GH causes overgrowth of bone, connective tissue, and viscera. If GH oversecretion

Table 36-1. ADENOHYPOPHYSEAL HORMONES AND THEIR REGULATORY HYPOTHALAMIC HORMONES

Adenohypophyseal Hormone	Hypothalamic Hormone
Thyroid-stimulating hormone (TSH)	Thyrotropin-releasing hormone (TRH)
Adrenocorticotropic hormone (ACTH)	Corticotropin-releasing hormone (CRH)
Growth hormone (GH, somatotropin)	GH-releasing hormone (GHRH, somatocrinin)
	GH release-inhibiting hormone (somatostatin)
Follicle-stimulating hormone (FSH)	Gonadotropin-releasing hormone (GnRH)
Luteinizing hormone (LH)	Gonadotropin-releasing hormone (GnRH)
Prolactin (lactotropic hormone [LTH])	Prolactin-releasing factor
	Prolactin inhibitor (dopamine)
Melanocyte-stimulating hormone (MSH)	MSH-releasing hormone (MSH-RH)
	MSH release-inhibiting hormone (MSH-RIH)

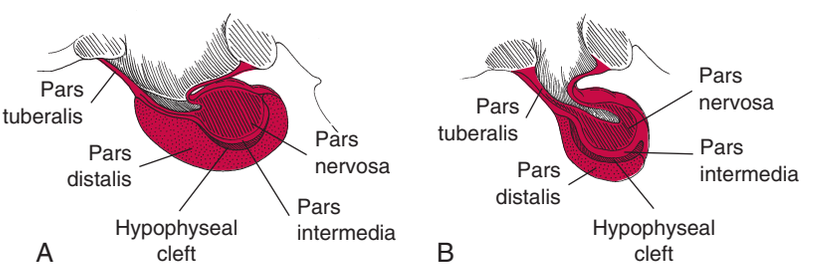

Figure 36-1. Schematic diagram of a mid-sagittal section through the pituitary gland of a normal dog *(A)* and cat *(B)*. (Modified from Dellmann HD: Veterinary Histology: An Outline Text-Atlas. Philadelphia: Lea & Febiger, 1971.)

(hypersomatotropism) occurs after closure of the epiphyses, acromegaly develops. In acromegaly, only the membranous bones (e.g., nose, mandible, and portions of the vertebrae) increase in length, because the long bones cannot grow longitudinally once the epiphyses close.

GH exerts both direct and indirect effects on the body. The indirect actions of GH, mediated by insulin-like growth factor I (IGF-I), are anabolic and include increased protein synthesis and soft tissue and skeletal growth. In contrast, the direct effects of GH are predominantly catabolic (e.g., lipolysis and restricted cellular glucose transport).

Etiology

- *In cats:* The major cause of acromegaly is a GH-secreting tumor of the pituitary gland.
- *In dogs:* Endogenous (diestrus) or exogenous progestogens may cause acromegaly by inducing GH production from the hyperplastic ductular epithelium of the mammary glands.

▼ ***Key Point*** Acromegaly in dogs is caused by progestogens. Feline acromegaly develops from a GH-secreting pituitary tumor.

Clinical Signs

Signalment

- Age: Middle to old age
- Breed: No breed predilection
- Sex: Most acromegalic cats are male, whereas acromegalic dogs are female

General Appearance

▼ ***Key Point*** The clinical features of acromegaly develop so insidiously that they are frequently overlooked.

- Large paws
- Soft tissue swelling of the head and neck with prominent skin folds
- Prognathism due to mandibular enlargement
- Widened interdental spaces
- Macroglossia
- Increase in body size and weight; weight loss in some cases
- Pot-bellied appearance
- Long, thick, or coarse haircoat
- Rapid growth of toenails

Respiratory System

- *In cats:* Dyspnea as a result of pulmonary edema or pleural effusion from GH-induced cardiac failure.
- *In dogs:* Excessive panting, exercise intolerance, and inspiratory stridor develop because oropharyngeal soft tissue proliferation compresses the upper airway.

Cardiovascular System

In cats, cardiac involvement includes the following:

- Systolic murmur
- Cardiomegaly
- Congestive heart failure (43%) characterized by pulmonary edema, pleural effusion, or ascites

Endocrine System

▼ ***Key Point*** Some dogs and most cats with acromegaly have insulin-resistant diabetes mellitus.

- Diabetes mellitus and its accompanying clinical signs of polyuria, polydipsia, and polyphagia develop because GH restricts cellular glucose transport. Insulin resistance results and large dosages of insulin (>2.2 U/kg/day) are frequently needed to control the hyperglycemia.
- In acromegalic cats, the growth-promoting effects of GH lead to enlargement of endocrine glands (thyroid, parathyroid, adrenal), but the function of these glands remains normal.
- In contrast, dogs in which acromegaly is caused by chronic administration of progestogens have subnormal basal cortisol concentrations. The glucocorticoid-like activity of these progestogens probably suppresses adrenocorticotropic hormone (ACTH) secretion and causes secondary hypoadrenocorticism.

Skeletal System

- Spondylosis deformans.
- Hyperostosis of the skull.
- Mandibular enlargement (prognathism).
- Arthropathy: Excess GH causes proliferation of cartilage and soft tissue, resulting in widening of the joint space. Some cats develop degenerative arthropathy with time. Acromegalic dogs seem less likely to develop joint problems.

Nervous System

- Growth of the pituitary tumor in feline acromegaly may impinge on brain tissue, causing circling, seizures, or behavioral changes.

Urinary System

- GH excess causes renal hypertrophy and increased glomerular filtration rate and renal plasma flow.
- Renal failure develops in about 50% of acromegalic cats. The kidneys of these cats have mesangial thickening of the glomeruli that may result from the glomerulosclerosis associated with unregulated diabetes mellitus and GH-mediated glomerular hyperfiltration.

Reproductive System

- Dogs with progesterone-induced acromegaly may develop pyometra, mucometra, and mammary gland nodules.

Diagnosis

Basis for a Presumptive Diagnosis of Feline Acromegaly

- Clinical and laboratory features characteristic of acromegaly
- CT or MRI documentation of a pituitary mass
- Normal results on thyroid and adrenal testing

Basis for a Presumptive Diagnosis of Canine Acromegaly

- Characteristic clinical and laboratory findings
- Exposure to a progestogen source and improvement in clinical signs following removal of that progestogen source
- No evidence of spontaneous hyperadrenocorticism on adrenal testing

▼ ***Key Point*** Suspect acromegaly in female dogs receiving progestogens and in intact female dogs that develop diabetes mellitus or laryngeal stridor due to soft tissue overgrowth. Suspect acromegaly in cats with insulin-resistant diabetes mellitus.

Physical Examination

Look for the clinical signs listed previously. To confirm enlargement of the head and paws, redundant skin folds, and prognathism, compare the animal's appearance with earlier photographs of the animal, if possible.

Routine Laboratory Tests

- Severe hyperglycemia and glycosuria are found in most cats and some dogs with acromegaly. Despite the poorly regulated diabetic state of most acromegalic cats and the enhancement of ketogenesis by GH, ketosis rarely develops.
- Less frequently, increases in cholesterol, alanine aminotransferase (ALT), and serum alkaline phosphatase (ALP) may be caused by the diabetic state. However, in many acromegalic dogs without diabetes, ALP activity is increased.
- Mild to moderate hyperproteinemia occurs in 50% of acromegalic cats, but the serum protein electrophoretic pattern is normal.
- Hyperphosphatemia may develop secondary to increased renal tubular reabsorption of phosphorus promoted by GH.
- There may be a stress leukogram, anemia (in dogs, the cause is uncertain), or mild erythrocytosis (in cats, due to GH-stimulated erythropoiesis).
- Acromegalic cats that develop renal failure have persistent proteinuria (100–300 mg/dl) with dilute urine specific gravity (USG) (1.015–1.025).

Radiography

Examine for the following:

- Visceral enlargement (cardiomegaly, hepatomegaly, renomegaly)
- Soft tissue proliferation (oropharyngeal region, head, limbs)
- Bony changes (spondylosis, hyperostosis of the calvarium, periarticular periosteal reaction)
- Left ventricular and septal hypertrophy in acromegalic cats with cardiomegaly (by echocardiogram)

Other Diagnostic Imaging

Magnetic resonance imaging (MRI) and computed tomography (CT) may be helpful in identifying a possible pituitary tumor (see Chapter 4 for an overview of CT and MRI).

Growth Hormone Determination

Increased circulating GH concentrations confirm a diagnosis of acromegaly. However, GH concentrations may be normal in some acromegalic patients and may be increased in a variety of other diseases.

- Increased GH concentration in the presence of profound hyperglycemia supports a diagnosis of acromegaly because hyperglycemia would normally be expected to suppress GH secretion.
- Alternatively, an integrated 24-hour GH concentration determined by frequent sampling throughout the day may be more indicative of GH hypersecretion than solitary determinations.
- Validated GH radioimmunoassays are not widely available for the dog or cat. Utrecht University in the Netherlands measures canine and feline GH concentrations in plasma. However, until such assays are routinely obtainable, diagnose acromegaly presumptively (see "Diagnosis" on page 400).

Insulin-Like Growth Factor

Determination of IGF-I gives an indirect indication of GH concentration. Increased IGF-I concentrations develop in acromegalic dogs and, seemingly, in acromegalic cats; however, increased IGF-I concentrations may also be found in diabetic cats without evidence of acromegaly. A validated assay is available at the Endocrine Diagnostic Laboratory of Michigan State University (telephone: 517-353-0621, website: www.ahdl.msu.edu).

Treatment of Progesterone-Induced Acromegaly

Treat progesterone-induced acromegaly by ovariohysterectomy or discontinuation of progestogen drugs. The soft tissue overgrowth and respiratory stridor resolve; however, the skeletal changes persist. The insulin requirement for GH-induced diabetes mellitus also declines, but the reversibility of the diabetes depends on the insulin reserve of the pancreatic beta islet cells.

Treatment of Growth Hormone-Secreting Pituitary Tumors

Manage these tumors by surgery, radiation, or drug therapy.

Surgery

- Because surgical excision of the tumor probably necessitates a hypophysectomy, expect deficiencies of pituitary hormones postoperatively.
- Before surgery, precisely localize the pituitary tumor by CT or MRI because neoplastic extension into the hypothalamus precludes surgery.
- Trans-sphenoidal cryotherapy of a pituitary tumor in an acromegalic cat has been performed.

Radiation

The results of *cobalt irradiation* of pituitary tumors (total dose of 4800 cGy divided equally in 12 treatments during 4 weeks) in acromegalic cats have been variable. In one report involving two cats, no effect was seen on tumor size or GH concentration in one cat; in the other cat, the tumor reduced in size with subsequent reduction in GH concentration. These changes developed within 2 months of radiation treatment but lasted only 6 months before relapse. In another report, two of three acromegalic cats treated by irradiation had long-term remission (16 and 28 months).

Pharmacologic Management

This includes dopamine agonists and long-acting somatostatin analogues.

- Dopamine agonists: Bromocriptine lowers GH concentrations in many acromegalic humans, but its effect on GH concentrations in acromegalic cats is unknown. Selegiline (Anipryl, Deprenyl Animal Health) at oral dosages of 0.75 and 1.5 mg/kg/day failed to reduce the insulin requirements or improve the clinical signs in one acromegalic cat.
- Long-acting somatostatin analogues: Analogues such as SMS 201-995 (octreotide) inhibit GH secretion in most humans with acromegaly. However, subcutaneous dosages of octreotide, ranging from 10 to 200 µg/day, did not reduce GH concentrations in four acromegalic cats.

Management of Concurrent Growth Hormone-Induced Conditions

Provide symptomatic treatment of GH-related disorders in the initial management of acromegalic dogs and the long-term care of acromegalic cats.

- Congestive heart failure in some acromegalic cats initially responds to furosemide treatment (see Chapter 147 for more details on treatment of congestive heart failure).

- Inspiratory stridor in acromegalic dogs partially responds to cage rest, cooling, and oxygen therapy.
- The diabetes mellitus of feline acromegaly generally is refractory and requires insulin (neutral protamine Hagedorn [NPH], Lente, protamine zinc insulin, or Ultralente) twice daily. In some cats, combinations of short-acting insulin (regular insulin) with NPH insulin may help control hyperglycemia (see Chapter 34 for more details on management of diabetes mellitus).

Prevention

- No preventive measures currently are known to avoid the development of GH-secreting pituitary tumors in cats.
- Prevent acromegaly in dogs by ovariohysterectomy of non-breeding females and judicious use of progestogen drugs.

ACTH-Secreting Pituitary Hyperplasia or Neoplasia: Cushing Disease

Hyperplasia or neoplasia of the pituitary corticotrophs with resultant oversecretion of ACTH is the major cause of hyperadrenocorticism (Cushing disease) in the dog and cat. Excess ACTH may originate from the corticotrophs in either the pars distalis or the pars intermedia. Clinical signs, diagnostic testing, and treatment of Cushing disease are discussed in Chapter 33.

DISEASES OF PITUITARY HORMONE DEFICIENCY

Hypopituitary Dwarfism: Growth Hormone Deficiency

Etiology

- In German shepherds, hypopituitary dwarfism is associated with cystic distention of the craniopharyngeal duct (Rathke's pouch).
- It is not known whether expansion of the pituitary cyst destroys adjacent adenohypophyseal tissue or whether a primary defect in differentiation and secretory capability of the adenohypophyseal cells creates the cyst.
- Weimaraners develop GH deficiency in association with thymic abnormalities.

Clinical Signs

Signalment

- Age: Young animals are affected. Discrepancies in growth compared with littermates are apparent from 6 to 8 weeks of age.
- Breed: This is an autosomal recessive trait in the German shepherd and Carelian bear dog.
- Sex: There is no sex predilection.

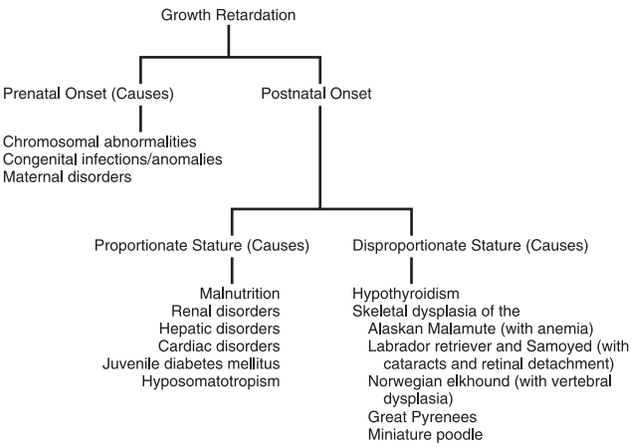

Figure 36-2. Classification of growth retardation by onset of growth problems and stature of dog.

General Appearance

- Growth retardation is characterized by proportionately stunted short stature. Affected German shepherds usually fail to exceed 13.5 kg in body weight or 47.5 cm in shoulder height by 1 year of age.
- The hair is soft and woolly, with retention of secondary (lanugo) hairs and lack of primary (guard) hairs. Progressive, bilaterally symmetrical truncal alopecia develops with age.
- Dental eruption may be delayed.

Concurrent Deficiencies of Other Pituitary Hormones

- Thyroid-stimulating hormone deficiency (secondary hypothyroidism) (see Chapter 31)
- ACTH deficiency (secondary hypoadrenocorticism) (see Chapter 33)
- Follicle-stimulating hormone or luteinizing hormone deficiency (secondary hypogonadism)

Diagnosis

Differentiate hypopituitary dwarfism from other causes of growth retardation (Fig. 36-2).

History

Identify breed predisposition and postnatal onset of growth problems (see Fig. 36-2).

Physical Examination

- The puppy is proportionately stunted.
- The haircoat initially remains as the animal matures, but truncal alopecia eventually develops.
- Additional clinical features characteristic of hypothyroidism, hypoadrenocorticism, or hypogonadism depend on the extent of hypophyseal involvement.

Routine Laboratory Tests

Hematologic, serum biochemical, and urinalysis results usually are normal for immature dogs. Hypophosphatemia may result from lack of GH-mediated renal tubular reabsorption of phosphorus.

Radiographic Abnormalities

- Delayed closure of the epiphyses
- Delayed dental eruption
- Delayed or incomplete calcification of the os penis

Growth Hormone Determination

- Basal GH concentrations do not differentiate normal dogs from dogs with GH deficiency.
- GH stimulation tests classically have been used to evaluate pituitary GH secretory capability.
  - Measure circulating GH concentrations in fasted dogs before and 5, 15, 30, 45, 60, and 90 minutes after intravenous administration of one of the following:
  - 0.1 or 0.3 mg of xylazine/kg (Gemini, Butler)
  - 3 or 10 µg of clonidine/kg (Catapres, Boehringer Ingelheim)
  - 1 µg of human GH-releasing hormone (hGHRH)/kg (Geref, Serono Laboratories)

Interpretation

- In normal dogs, circulating GH concentration increases within 30 minutes of xylazine, clonidine, or GHRH administration and then declines by 60 to 90 minutes.
- In dogs with hypopituitary dwarfism, no substantial increase in GH concentration develops after pharmacologic stimulation.
- In some children with GH neurosecretory dysfunction, GH response to pharmacologic stimulation is normal; nevertheless, spontaneous physiologic pulsatile GH secretion is decreased, as determined by 24-hour blood sample monitoring. A similar disorder may account for the delayed growth reported in a litter of German shepherds.

Insulin-Like Growth Factor I Measurement

Currently, validated GH radioimmunoassays are not routinely available for the dog except at Utrecht University, the Netherlands. However, measurement of serum IGF-I, produced in response to GH, gives an indirect indication of GH concentration. Importantly, IGF-I concentrations positively correlate with body size in various breeds of dogs. This assay is available at the Endocrine Diagnostic Laboratory of Michigan State University (www.ahdl.msu.edu).

- In GH-deficient German shepherds with pituitary dwarfism, IGF-I concentrations are subnormal.
- IGF-I concentrations in related but clinically unaffected dogs that are presumably heterozygous for the dwarf trait are intermediate between the IGF-I concentrations found in normal German shepherds and those obtained in dwarf German shepherds.

Other Endocrine Tests

Investigate for secondary hypothyroidism associated with hypopituitary dwarfism (see Chapter 31) and for secondary hypoadrenocorticism associated with hypopituitary dwarfism (see Chapter 33).

Skin Biopsy

- In canine GH deficiency, nonspecific histologic skin changes (atrophy of hair follicles, epidermis, and sebaceous glands) are similar to those seen in other canine endocrinopathies; however, a decreased number of elastin fibers are present in the dermis.

Treatment

Growth Hormone Replacement Therapy

- Current guidelines recommend bovine or porcine GH preparations subcutaneously at 0.1 IU/kg 3 times weekly for 4 to 6 weeks. Historically, GH replacement for the dog has been difficult to obtain and expensive. With the development of biosynthetic bovine GH (Posilac, Monsanto), an inexpensive source of GH seemed readily available. Unfortunately, this product, designed for use in cattle, cannot be formulated for the dog's smaller dose requirement and is not approved for use in dogs.
- Biosynthetic human GH appears to induce antibody formation in dogs that interferes with its effectiveness, and similar immunogenicity problems may be associated with bovine GH administration to dogs. Porcine GH, similar immunologically to canine GH, is available through Dr. A. F. Parlow, Pituitary Hormones and Antisera Center, Harbor-UCLA Medical Center, Torrance, California.
- No increase in size occurs if dogs are treated after epiphyseal closure.
- Because GH is diabetogenic, monitor blood glucose concentrations during treatment.
- Treatment of canine GH deficiency with progestogens to induce GH production by the ductular epithelium of the mammary glands has been reported.

Thyroid Hormone or Glucocorticoid Replacement Therapy

Initiate therapy if concurrent hypothyroidism or hypoadrenocorticism exists (see Chapters 31 and 33).

Prevention

Because hypopituitary dwarfism is inherited in an autosomal recessive manner in German shepherd and Care-

lian bear dogs, genetic counseling may help eliminate this disease. Identify possible heterozygotes by IGF-I assay, and eliminate these carrier animals from breeding programs.

Central Diabetes Insipidus: Antidiuretic Hormone Deficiency

Diabetes insipidus (DI) is a disorder of water metabolism characterized by polyuria and polydipsia. It is caused by defective secretion or synthesis of ADH (central DI) or the inability of the renal tubule to respond to this hormone (primary nephrogenic DI).

Deficiency of ADH or renal insensitivity to ADH can be partial or complete.

Etiology

Central DI (also called neurogenic DI) is an uncommon condition that results from disorders that disrupt the ADH-producing hypothalamic neurohypophyseal neurons.

- Idiopathic
- Central nervous system (CNS) trauma
- CNS neoplasia
- CNS inflammation
- Congenital anomalies

Clinical Signs

Signalment

- Age is variable, depending on the cause.
  - Idiopathic and trauma-induced DI has no specific age predilection.
  - Animals with suspected congenital DI are <1 year of age.
  - Animals with DI caused by CNS neoplasia are usually middle-aged to older.
- Breed: No predilection
- Sex: No predisposition

Polyuria and Polydipsia

- ADH acts on the distal tubules and collecting ducts of the kidneys to allow increased water reabsorption.
- Lack of ADH or interference with the ability of ADH to bind to its receptors results in water diuresis.
- This primary polyuria results in volume contraction and subsequent compensatory polydipsia.

Diagnosis

The diagnosis of DI requires its differentiation from other more common causes of polyuria and polydipsia, such as renal insufficiency, diabetes mellitus, hypercalcemia, pyometra, feline hyperthyroidism, and canine hyperadrenocorticism.

History

Profound polyuria and polydipsia (>100 ml/kg/day; normal is approximately 40–70 ml/kg/day) are found.

Physical Examination

Findings are usually normal with the following exceptions:

- Weight loss (if the animal is preoccupied with drinking).
- Dehydration (if water is withheld).
- Neurologic signs (e.g., disorientation, seizures, and blindness) may develop in animals with pituitary or hypothalamic neoplasia or trauma.

Routine Laboratory Tests

- Hematologic and serum biochemical results are usually normal or consistent with mild dehydration (mild increases in packed cell volume and serum concentrations of total protein and sodium).

▼ ***Key Point*** Urine dipstick and sediment evaluations are normal, but USG is typically in the range of 1.000 to 1.007.

- Animals with partial deficiencies in ADH may produce more concentrated urine (USG 1.008–1.020).
- Urine culture is negative.

Radiography

Findings usually are normal.

Other Diagnostic Imaging

MRI and CT can aid in identifying a pituitary or hypothalamic lesion.

Water Deprivation Test

This test is designed to determine whether endogenous ADH is released in response to dehydration and whether the kidneys can respond to ADH. Minimal increases in plasma osmolality should stimulate the release of ADH.

▼ ***Key Point*** Water deprivation tests are contraindicated in animals that are already dehydrated (since the stimulus for ADH release already exists) or in the presence of other laboratory abnormalities such as azotemia or hypercalcemia.

Because water deprivation causes dehydration, this test is potentially dangerous and can result in acute renal failure, neurologic complications, and death. For this reason, perform comprehensive diagnostic testing,

Table 36-2. PROCEDURE FOR WATER DEPRIVATION TEST

- Quantitate daily unrestricted water consumption.
- Measure urine specific gravity (USG) and weigh the animal.
- Gradually restrict water intake over 3 to 5 days to 100 ml/kg/day. Monitor body weight and USG daily. Use the criteria below as end points.
- To continue the test, empty the urinary bladder and measure USG (and urine osmolality if possible).
- Withhold all food and water.
- Every 2 hours, reweigh the animal, empty the urinary bladder, and measure USG (and urine osmolality if possible). Use the criteria below as end points.
- *Stop the test when any of the following occur:*
  - The animal loses 5% of its body weight.
  - The animal is clinically dehydrated or ill.
  - USG ≥ 1.030.

including complete blood count, serum biochemical profile with electrolyte determinations, complete urinalysis, urine culture, and imaging of body cavities, to rule out disorders that may decompensate following dehydration (e.g., pyometra, pyelonephritis, renal insufficiency, and hypercalcemia). Tests of renal function (e.g., iohexol or 99m technetium-diethylenetriaminepentaacetic acid clearance), adrenal function (e.g., low-dose dexamethasone test, ACTH stimulation test, or urine cortisol-to-creatinine ratio), and thyroid function (total thyroxine determination in cats) also may be indicated before initiating water deprivation.

Procedure

- See Table 36-2. Initial gradual reduction in water intake in patients with renal medullary washout (which often accompanies polyuric disorders) allows them to reestablish the medullary concentration gradient.

Interpretation

- When deprived of water, normal animals can concentrate the USG to 1.075 in cats and 1.045 in dogs. Nevertheless, a USG of 1.030 is generally considered an adequate response to water deprivation. Failure to concentrate to this degree in the absence of renal disease or other laboratory abnormalities indicates that the animal has central or nephrogenic DI (Fig. 36-3).

Antidiuretic Hormone Response Test

If the animal fails to concentrate urine adequately following water deprivation, perform an ADH response test. The test evaluates the ability of the renal tubule to respond to exogenous ADH and concentrate urine in the face of dehydration.

Procedure

- Immediately following the water deprivation test, administer aqueous vasopressin (Pitressin, Parke-Davis) at 0.5 U/kg (maximum dose is 5 units) IM.
- Withhold all water and food during the test.
- Empty the urinary bladder and measure USG (and osmolality if possible) at 30, 60, 90, and 120 minutes after vasopressin injection.
- The animal may drink after the test is completed.

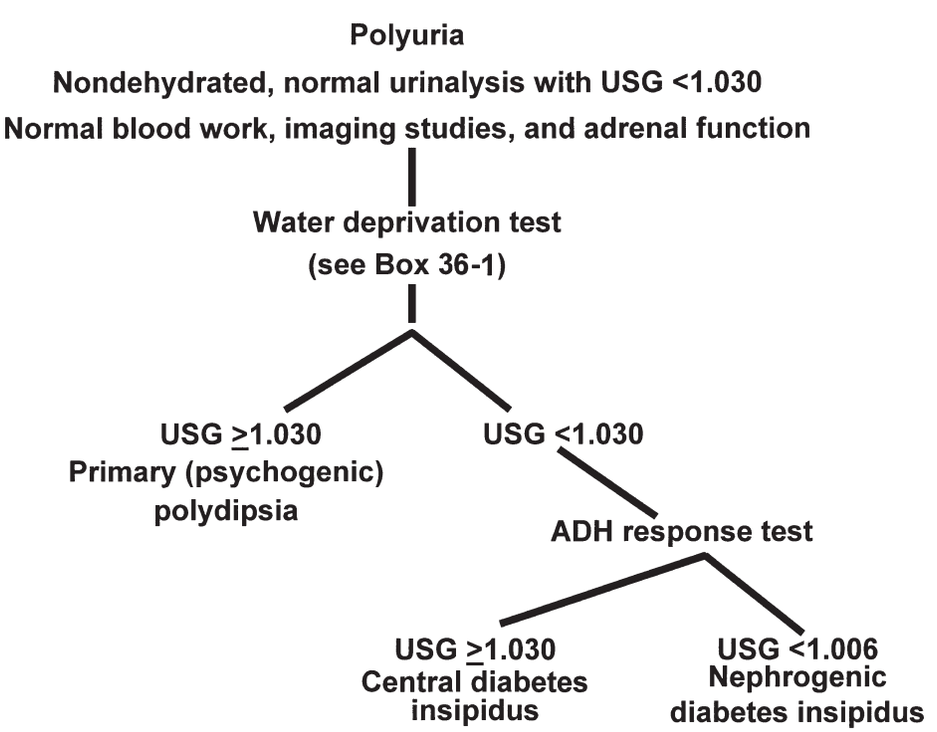

Figure 36-3. Algorithm for evaluation of an animal with polyuria and polydipsia. ADH, antidiuretic hormone; USG, urine specific gravity.

Alternative Procedure

- Immediately following the water deprivation test, administer the synthetic analogue of ADH, desmopressin acetate (DDAVP, Rhone-Poulenc Rorer) at a dose of 10 to 20 µg IV. Although desmopressin is commercially available as a parenteral preparation for IV injection (4 µg/ml), this formulation is more expensive than the intranasal preparation of desmopressin (100 µg/ml). The intranasal DDAVP has been given to animals by injection; but, because this preparation is not sterile, it should be passed through a bacteriostatic filter.
- Offer small amounts of water hourly (2.5–3.0 ml/kg) during the test.
- Measure USG (and osmolality if possible) every 2 hours for 6 to 10 hours after desmopressin injection. The maximum response to IV desmopressin usually occurs in 4 to 8 hours, but in some animals it takes longer than 10 hours to see a maximal response.

Interpretation

Failure to concentrate urine with water deprivation followed by a rise in USG ≥ 1.030 after ADH administration is supportive of central DI; urine that remains hyposthenuric after the ADH response test is suggestive of primary nephrogenic DI (see Fig. 36-3). However, USG values between 1.006 and 1.030 may be difficult to interpret without also evaluating the change in USG and urine osmolality.

Antidiuretic Hormone Determination

Measurement of endogenous ADH levels after water deprivation may aid in differentiating central DI (ADH levels subnormal) from primary nephrogenic DI (ADH levels within or above the normal range). Unfortunately, validated canine and feline ADH assays are not routinely available.

Therapeutic Antidiuretic Hormone Trial

As an alternative to the water deprivation test and the ADH response test following water deprivation, perform a closely monitored therapeutic trial with desmopressin acetate.

▼ ***Key Point*** Prior to performing a therapeutic ADH trial, rule out all common causes of polyuria and polydipsia, thus limiting the differential diagnosis to central DI, primary nephrogenic DI, and primary (psychogenic) polydipsia.

- Procedure: Administer the intranasal preparation of DDAVP in the conjunctival sac (1–4 drops q12h) for 3 to 5 days while monitoring daily water intake.
- Interpretation: A dramatic reduction in water intake (greater than 50%) during the treatment period would strongly suggest a diagnosis of central DI. When polyuria is due to other causes, the decrease is seldom more than 30%. Beware of water intoxication if ADH treatment reduces polyuria yet excessive water intake persists in animals with primary (psychogenic) polydipsia.

Treatment

Antidiuretic Hormone Replacement Therapy

- Desmopressin acetate is the drug of choice for the treatment of central DI in dogs and cats.
- Repositol ADH (vasopressin tannate in oil), once the only long-acting ADH preparation available, is no longer manufactured.
- DDAVP is available as an aqueous solution (100 µg/ml) intended for intranasal use and as oral tablets (0.1 mg and 0.2 mg).
- The intranasal form of DDAVP is also effective when applied topically in the conjunctival sac (1–4 drops q12–24h) or injected subcutaneously (2–5 µg q12–24h after sterilization by passing through a bacteriostatic filter). The oral form of DDAVP (a 0.1-mg DDAVP tablet is equivalent to approximately 1 large drop [5 µg] of intranasal DDAVP) is given initially at 0.1 mg once to twice daily.
- Adjust the daily dose to control polyuria and polydipsia.
- The major disadvantage of this treatment is expense.

Non-hormonal Therapy

- Thiazide diuretics may reduce the polyuria of DI but are never as effective as ADH replacement. Thiazide diuretics reduce total body sodium by an initial natriuresis, resulting in decreased extracellular fluid volume and reduced glomerular filtration rate. These changes cause increased fluid reabsorption in the proximal renal tubule and reduce urine output.
  - Administer chlorothiazide (Diuril; Merck, Sharp, & Dohme) at a dosage of 20 to 40 mg/kg q12h PO.
  - Restrict salt intake to potentiate the drug's effectiveness.
  - Because hypokalemia may develop with thiazide diuretic therapy, monitor serum electrolyte concentrations during treatment.
- Chlorpropamide (Diabinese, Pfizer) is an oral hypoglycemic agent that potentiates the action of ADH on the renal distal tubules and collecting ducts. Because chlorpropamide requires some ADH to be effective, it reduces the polyuria in animals with partial ADH deficiency only.
  - Administer chlorpropamide at a dosage of 10 to 40 mg/kg/day.
  - Monitor blood glucose concentrations during treatment.

Secondary (Pituitary) or Tertiary (Hypothalamic) Hypoadrenocorticism

This is caused by ACTH or corticotropin-releasing hormone deficiency. See Chapter 33.

Secondary (Pituitary) or Tertiary (Hypothalamic) Hypothyroidism

This is caused by thyroid-stimulating hormone or thyrotropin-releasing hormone deficiency. See Chapter 31.

MISCELLANEOUS DISORDERS

Adipsia and Hypodipsia

Adipsia and hypodipsia are defined as absent and reduced thirst, respectively. Normally with water loss, mild increases in plasma osmolality stimulate osmoreceptors in the hypothalamus to increase water consumption and ADH secretion. However, even with maximal ADH secretion, hyperosmolality (specifically hypernatremia) escalates unless the thirst mechanism is intact. With adipsia or hypodipsia, hypernatremia develops with resultant dehydrating effects on the cells of the CNS. It is usually unclear whether the defect in thirst in affected animals is due to an increased osmoreceptor threshold (reset setpoint) or to structural lesions in the thirst center of the hypothalamus.

Etiology

- Idiopathic
- Hypothalamic dysplasia or congenital anomalies
- Hypothalamic degeneration
- Hypothalamic inflammation, neoplasia, or trauma

Clinical Signs

- Signalment
  - Age: Young (usually <1 year) in idiopathic and congenital forms of the disorder
  - Sex: Female predisposition in the miniature schnauzer
  - Breed: Miniature schnauzer
- Depression, stupor, or coma
- Personality change
- Disorientation
- Anorexia
- Weakness or lethargy
- Irritability or seizures

Because hypothalamic conditions associated with adipsia or hypodipsia may cause neurologic signs independent of the sodium concentration, the relative contribution of hypernatremia to the CNS signs can be assessed once a normal sodium concentration is restored.

Diagnosis

History

Adipsia or hypodipsia has occurred despite free access to water, and the clinical signs listed previously are present.

Physical Examination

There is evidence of dehydration and signs of altered mentation.

Routine Laboratory Tests

Hematologic, serum biochemical, and urinalysis results are consistent with dehydration:

- Hypernatremia (profound)
- Hyperosmolality (profound)
- Hyperchloremia
- Azotemia (mild)
- Hyperalbuminemia (mild)
- Hypersthenuria

Radiography

Findings usually are normal.

Other Diagnostic Imaging

MRI and CT may identify a hypothalamic lesion.

Treatment

The brain attempts to adapt to the hyperosmolar state by increasing its cellular osmolality with sodium, potassium, amino acids, and unidentified solutes (idiogenic osmoles). If plasma hyperosmolality is corrected too rapidly, the brain cells continue to be hyperosmolar relative to the plasma, and cerebral edema may develop.

▼ ***Key Point*** Rapid correction of the chronic hyperosmolar state in adipsia or hypodipsia may lead to cerebral edema.

Initial Therapy

- If the animal is dehydrated, reestablish tissue perfusion with isotonic saline or Ringer's solution before using sodium-restricted fluids. The osmolality of these solutions is still less than the patient's serum osmolality, so some reduction in serum sodium concentration and osmolality may occur.
- For initial management of the hydrated animal in order to correct hypernatremia without lowering serum osmolality too rapidly, administer a sodium-restricted isotonic fluid IV (D5W or 0.45% NaCl with 2.5% dextrose) only to correct the animal's water deficit. Preferably, if the animal is cooperative, administer oral fluids to correct the water deficit.

- Calculate the animal's water deficit based on the serum sodium concentration or osmolality and a normal total body weight of water of 60%:

$$\text{Water deficit (liters)} \cong 0.6 \times \text{Body weight (kg)} \times \left(1 - \frac{\text{Normal sodium (mEq/L)}}{\text{Patient sodium (mEq/L)}}\right)$$

- Replace the water deficit to lower serum sodium concentration ≤ 0.5 mEq/L/hr. Generally, this rule translates to replacing the calculated water deficit during a period of 3 days.

- Add maintenance fluid requirement (60 ml/kg/day) with isotonic polyionic solution to the daily infusion.
- Monitor serum electrolytes frequently and adjust fluid type and rate as needed to ensure that serum sodium concentration is not lowered too rapidly.

Maintenance Therapy

For chronic management once the animal is eating, mix maintenance daily water intake (50–60 ml/kg/day) with food.

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Section 5

Skin and Ear Diseases

Andrew Hillier

Chapter 37

Skin Cytology and Biopsy

Sonya V. Bettenay

The use of a variety of cytologic diagnostic tools and skin biopsy may greatly facilitate the treatment and ultimate outcome for the dermatologic patient. Interpretation of the results is as important as the correct collection of the sample.

Skin cytology is a tool that can be used on almost every patient presenting with an inflammatory dermatitis or otitis externa. It often provides therapeutically relevant information, particularly regarding the selection of antimicrobial therapy. Individual preference and the actual clinical presentation will dictate which of the different sampling techniques is selected. The first part of this chapter elaborates on the various cytology techniques, their special indications, and their interpretation. The second part reviews skin biopsies.

There are specific indications for performing a skin biopsy that, along with interpretation tips, will be discussed. The aim is to take steps required to obtain the most diagnostic sample and to give the pathologist the best chance of reaching a diagnosis. Special reference is made to the biopsy techniques used for sampling the inner pinnae and claws.

SKIN CYTOLOGY

Skin cytology techniques range from those that sample the surface to those that sample deep inside a cutaneous nodule. To the practitioner, the importance of in-house skin cytology in the diagnosis and management of many dermatoses has become more apparent over the past decade. The use of in-house skin cytology is no longer restricted to the patient with nodules or draining tracts but has been expanded to most patients with inflammatory skin disease (and some with non-inflammatory dermatitis).

▼ ***Key Point*** Surface cytology is indicated at the initial presentation of many, if not all, dermatology patients.

One of the major reasons for the increased usage of this diagnostic method is the recognition of the prevalence and significance of staphylococcal pyoderma (see Chapter 38) and yeast dermatitis caused by *Malassezia pachydermatis* (see Chapter 41). Furthermore, the widespread availability of "user friendly" diagnostic aids such as in-house rapid cell-staining kits and good quality, price competitive microscopes has facilitated the use of these techniques by general practitioners.

Sampling Techniques

The most common sampling techniques include Scotch tape impression, adhesive glass slide impression, direct glass slide impression, skin-scrape and smear (using a spatula or scalpel blade), cotton bud (Q-tip) "sample and smear," and aspiration. In-house processing typically uses one of the rapid-stain products; these stains

are generally not used by cytologists, who prefer the traditional Wright stain because of a superior appearance of cellular morphology with these stains. Thus air-dry but do not stain samples that will be submitted to a cytologist. Obtain a smear of one cell thickness to clearly observe cellular morphology, irrespective of the stain.

Scotch Tape Impression

This is particularly advantageous for scanning the surface for yeast and/or significant numbers of bacteria (both rods and cocci). It gives poor cellular definition, although inflammatory cells can be identified. Two techniques with different staining have been described, but the collection method is identical. The use of Scotch tape that is not the "invisible" type avoids the problem of numerous small artifactual circles. In my hands, the cheapest brands of clear Scotch tape are often the best.

Technique

- Press a small (4–5 cm) piece of the tape "sticky side down" onto the skin.
- Place the Scotch tape onto a glass slide that has a drop of the "Blue" or third stain in the triple fixative stain packs (e.g., Diff-Quik). Undiluted new methylene blue is too strong a stain to easily see through and will need to be diluted before use.
- The alternative method is to process the Scotch tape as though it were a glass slide, dipping it in all of the "rapid fix" solutions in order.
- Avoid obtaining small, scrunched pieces of tape that appear to have lost some of their contents.
- Using a single piece of tape to screen a variety of sites saves time but lacks site specificity. Nevertheless, it provides a rapid technique of screening for yeast in particular. A negative result rules out *Malassezia* dermatitis quickly.
- If yeast are found, precise knowledge of the yeast-positive sites is important from a therapeutic point of view; each of the sites screened must then be resampled individually.

Adhesive Glass Slide Impression

This technique has been used for suspected *Malassezia* dermatitis cases in particular; it is probably most indicated for use in standardized tests, such as in a scientific study. The slides must be specially ordered and purchased, and they are relatively expensive. The sampling is through direct impression, and the processing is through regular cytologic staining.

Direct Glass Slide Impression

Technique

- Place the glass slide directly onto the skin surface with gentle pressure.
- This technique is most practical for areas that are moist or exudative.
- Take care to obtain a thin enough smear.
- The sample collected may need to be separated onto another slide and thinly smeared. Some anatomic sites are not well suited to this technique, such as the ventral interdigital fold and periocular area. Pressure must often be applied to have the material adhere to the slide; beware of breaking the slide with too much pressure.
- A variation of this technique may yield significantly higher numbers of organisms. The glass slide is not simply pressed downward but also pushed a little along the surface at a 45-degree angle so that the skin is smeared along the glass surface. This technique requires a little more pressure, which is directed at the leading edge of the slide. Take care that this leading edge does not cut the skin.

Surface Skin Scrape

This technique is aimed at collecting cells and organisms (bacteria and yeast) from the skin surface. It is different from the deep skin scrape and the superficial skin scrape, which use mineral oil and are used for the detection of mites (such as *Demodex* and *Sarcoptes,* respectively).

Technique

- Gently scrape a blunt, straight-edged instrument (such as a spatula or #10 scalpel blade) along the surface of the skin and collect cells and debris, even from a dry surface.
- "Scoop" these up using the same motion as buttering bread.
- Transfer the contents on the edge of the instrument to the glass slide; smear the collected material out as you would with a "squash prep" aspirate.
- Heat fix the slide before routine processing.
- This technique is excellent for evaluation of keratinocytes, bacteria, yeast, and other material on the skin surface.
- In human medicine, it is most often used to search for surface fungi such as *Pityrosporum* (yeast forms and hyphae) or dermatophytes (hyphae, rarely endothrix spores) and is first processed with potassium hydroxide (KOH) to remove the keratinocytes and leave the organisms. KOH dissolution of keratinocytes is almost never used in my practice. If it is indicated, then one of the modified formulations that does not require heating is preferred.
- If KOH dissolution *is* planned, then the KOH (modified) solution is dropped on to the slide and the cell debris is mixed through and allowed time to work. This is then smeared thin, air-dried, and stained. In both cases, staining is routine after the sample material dries.

Cotton Bud (Q-Tip) Sample and Smear

Technique

- Because the Q-tip can be inserted into a small opening, this sampling technique is most useful for external ear canals, draining tracts, or interdigital folds.
- Gently roll the collected material onto the glass slide; a thin layer of material is best for cytologic interpretation.
- Rolling with too much pressure or "rubbing" the tip to and fro may disrupt the cells, affecting interpretation (see below).
- Organisms found on the surface of the sample should correlate to those "deepest" in the exudate; consider evaluation of two smears to distinguish organisms on the surface from those that are deeper.
- In cases of otitis externa, in which there is a considerable amount of exudate within the ear canal, a third smear may even be added—taken after most of the exudate has been gently removed. Multiple organisms will often be identified in these situations, and some may be missed if only one "level" of the exudate is sampled. A recent bacterial culture study, using samples taken sequentially from the *same anatomic site* of ears with otitis externa, revealed different organisms on sequential samples.

Tzanck Preparation or Smear

As originally described, this technique is *an aspirate of the contents* of a pustule; however, it is technically difficult unless there is a large pustule and is therefore rarely performed this way. Such large pustules are typically seen on the ventral abdomen and with cases of "puppy impetigo" and pemphigus foliaceus.

Technique

- Gently insert the tip of the needle into the pustule, bevel side upward, and with a lifting motion to use the sharp edge of the bevel to cut through the "roof" or surface of the pustule.
- Transfer the contents of the pustule to a glass slide by gentle impression.
- Rupturing the roof of the pustule changes the possible interpretation and negates the possibility of a "sterile" culture. However, this modified technique is adequate to look for cytologic clues about the etiology of the pustule, which is the major reason to perform this technique.

Assessment for inflammatory cells, bacteria, and the presence or absence of acantholytic keratinocytes may help prioritize the differential diagnosis list. The presence of eosinophils should alert you to the possibility of ectoparasites, in particular scabies or fleas. Neutrophils are most commonly associated with a bacterial infection; when they are intact and the predominant cell type, scan carefully for any evidence of intracellular organisms. Conversely, and importantly, superficial pyodermas are often *not* associated with bacteria on cytologic examination. Acantholytic keratinocytes, which are referred to as "fried eggs" because of their large, rounded shape with a large, round central nucleus, may be used as supportive evidence for a diagnosis of pemphigus foliaceus; however, these rounded keratinocytes may also be seen in superficial pyodermas. Regard acantholytic keratinocytes as suggestive or supportive of a diagnosis of pemphigus foliaceus but not as sufficient evidence to confirm a diagnosis. Never institute immunosuppressive therapy on the basis of those findings alone.

"Aspiration Cytology" Sampling

This type of sampling is used predominantly for nodules. Cytologic evaluation is useful in the initial investigation because it may allow an early differentiation between neoplasia and infection.

Technique

- Firmly fix the nodule with one hand, insert the needle to the center of the nodule, and obtain cells for subsequent cytologic staining.
- The first method uses a needle without an attached syringe. Insert the needle several times at multiple angles without withdrawing it through the skin. Aim the tip of the needle at the center of the nodule. By this movement, the cells will be driven into the body of the needle. This technique is favored by oncologists because they believe there is the least chance of "seeding" tumor cells into the surrounding tissue.
- The alternative technique uses a needle with an attached syringe. Once the needle is inserted into the center of the nodule, apply negative pressure. Release this negative pressure before the needle is removed from the skin to avoid sucking the cells into the body of the syringe.

With either technique, once the needle is removed from the tissue, attach an air-filled syringe and blow the cells out onto the surface of the glass slide. Hold the needle *bevel side down* to collect as many cells as possible. Smear thinly using a blood smear technique or squash prep technique as appropriate, air-dry, and stain. The absence of cellular material using this technique is interpreted by some as indicating a densely cellular mass such as a fibrous cell tumor.

"Touch" Preparation

Use this with a surgical biopsy specimen.

Technique

- Gently touch the undersurface or base of the tissue to the glass slide.

- This technique is also useful for cytologic evaluation of crusts: Gently touch the undersurface of the crust or the exposed surface of the skin once a crust has been removed with the glass slide.
- Air-dry and stain as usual. Submit the tissue from a surgical excision for histopathology. I routinely save four additional air-dried, unstained slides. These may be used by the laboratory for adjunctive tests.
- In rare instances, organisms have been identified on the touch prep but not on histopathology.
- With some atypical neoplasms, cytology may give clues about the cell of origin, which even "special stains" may fail to differentiate on histopathology.
- Immunohistochemical staining may be possible with cytology samples that have been deep-frozen. With some select types of immunohistochemical staining, formalin-fixed tissue cannot be used because of the degeneration of antigens. In those instances, a cytology slide that has been air-dried and deep-frozen can be used immediately, eliminating the expense, discomfort, and delays created by a repeated surgical procedure. Transport these slides to the laboratory so that the formalin fumes that may emit from the tissue specimen do not contact the cells on the slide. Shipping in separate packages may be required.

Processing

As mentioned previously, there are some important principles with regard to the processing of cytology samples.

- Handle the sample gently, whether the material is rolled onto the glass slide or "squashed and pulled" between two slides as in a squash prep. The cells are friable and may rupture if handled roughly. Breakage of the cells not only affects the cytologic evaluation but also may interfere with interpretation. For example, the presence of ruptured neutrophils in a carefully handled sample may be used as an indication of neutrophil toxicity.
- Always make a duplicate slide, which remains unstained and ready for submission to a cytology laboratory should there be a need for more expert interpretation based on the in-house test results. Laboratory cytologists *do not* regard the "instant staining" methods available in general practice as adequate. This may be particularly useful for clinicians with less experience in cytology but who are trying to improve their skills in this area; compare the results reported by the laboratory cytologist with those obtained in-house.
- Process the sample carefully if cellular morphology is important, following the exact instructions for the staining technique. Examples would be impression smears from inflammatory dermatoses or aspirates from nodules. Under- or over-staining may affect the color of the contents of the cell. The Scotch tape impression smear is not suitable for those cases in which cell morphology is important.
- Heat fixing is contraindicated if cellular morphology is of interest. This procedure is most relevant for exudates with a large wax content, such as an otitis externa sample, but even in those cases cellular detail may be important to assess. Air-drying is the preferred technique; in practice, the use of a cold air–low heat hair dryer may help reduce the time required for drying.
- Although clinician preference varies, I typically view these samples using 400× microscopic magnification.

Interpretation

Surface Cytology

Regardless of the collection technique, I use surface cytology to look for organisms and perhaps for inflammatory cells. Microbes identified by the regular cytology stains can be classified by shape, size, and quantity. Perform a culture to determine the species. The subclassification of gram positive or negative is not possible using the regular cytology stains. Therefore, surface cytology screening looks for the presence of yeast, cocci, and rods; hyphae may be seen as ghosts (they do not typically take up the stain) by more experienced cytologists.

You should not be able to see significant numbers of microbes on the surface cytology of normal skin. Surface cytology sampling yields a significant amount of debris, associated with the dirt, environmental mold spores, surface lipids, and free keratin, which all sit on the outer surface of the stratum corneum. Practice on non-lesional skin of normal dogs to become familiar with normal versus abnormal surface cytology.

On the skin, the cocci will be predominantly the *Staphylococcus* species, the yeast predominantly the *Malassezia* species, and the rods generally contaminants.

- Yeast organisms are found in the more humid areas of the skin, such as the ventral neck, perianal, interdigital, and perioral areas. Geographic variation may be possible so that the "normal" number of yeast is higher in warm and humid areas. In one report, the presence of one or two organisms per high power field (HPF) was defined as within normal limits. However, in a temperate climate, this number of yeast is high, and an animal with clinical signs of infection and one or two yeast per HPF (400×) is regarded as having an active infection and will receive topical therapy. Systemic therapy is based not simply on numbers of organisms but also on severity of clinical symptoms and total area of the body affected. Systemic antifungals are expensive, and some have the potential for severe toxicity.
- Cocci may be seen attached to the surface of keratinocytes. This may be interpreted as active colonization, indicating a more pathogenic strain. More

often, cocci are seen scattered throughout the sample, often in small groups either with or between keratinocytes. This is abnormal and typically consistent with a superficial pyoderma. Intracellular cocci are regarded as a sign of increased severity of infection. Prescribe systemic antibiotics in these animals.

▼ ***Key Point*** The absence of cocci on cytology does *not* rule out the possibility of staphylococcal pyoderma.

- The presence of significant numbers of rod-shaped bacteria is not normal on the skin surface and may be interpreted as representing an abnormal surface environment, with overgrowth of a nonpathogen, or colonization. Perform culture if there are abundant rod-shaped organisms, the area of affected skin is large, or a deep pyoderma is clinically determined. Many cases with surface rod overgrowth but mild clinical signs will respond to topical shampoo therapy, often with specific therapy aimed at the underlying disease, such as hypothyroidism or severe chronic allergies. If *systemic* therapy is necessary, never select an antibiotic empirically. Perform culture and susceptibility testing in these cases because rod-shaped bacteria (e.g., *Pseudomonas* spp.) are often resistant to multiple antibiotics.

Ear Cytology

Compared with skin surface cytology (as described previously), interpretations of ear cytology vary significantly with otitis externa because the ear canal provides a unique surface environment. The narrow, long canal is associated with an increased local humidity and temperature compared with the skin surface in general. Variation with season, humidity, degree of hair growth, and anatomy (pendulous versus erect pinna types) is important. Finally, the surface of the canal is not readily visible, so observation of increased exudate or redness by the owners is not possible until it extends to the entrance of the canal and on to the pinna or surrounding skin.

- *Yeast* are a normal inhabitant of the external ear canal. Small numbers are regarded as "normal" because they may be cultured from most normal canine ears. Nevertheless, on surface cytology this number has yet to be clearly quantified. For an external ear canal with significant numbers of yeast on cytology, consider the clinical signs.

▼ ***Key Point*** If there are up to five yeast/HPF and no evidence for clinical otitis, then yeast are regarded as an overgrowth and an ear cleaner is recommended. If there is clinical evidence of inflammation, then as few as two yeast/HPF will be interpreted as supportive of a yeast otitis.

- *Bacteria* form part of the normal otic skin flora. However it is unusual to identify bacteria with surface cytology of the external ear canals; therefore, consider any notable numbers as suspicious of an infection. The presence of small, round organisms that are not well defined or large enough to be staphylococci or streptococci probably represent the *Bacteroides* species, which is a ubiquitous organism whose pathogenicity is controversial. A significant number of these organisms on surface cytology at least represents an aberrant surface population and possibly suggests overgrowth.
- Rod-shaped bacteria on surface cytology of the external ear canal suggests the need for a bacterial culture and susceptibility testing, especially if initial empiric therapy has been attempted and was not successful.
- Record the number of bacteria of each type (cocci and rods), for example, as none, few, many, or abundant or on a semiquantitative scale from 0 to 3 (0 = none, 1 = easily countable, 2 = not easy to count, 3 = impossible to count). This is useful in monitoring response to therapy at recheck visits.

Fine-Needle Aspiration

Interpretation of fine-needle aspiration (FNA) is helpful to differentiate an infectious or cystic process and may or may not identify neoplastic cells (also see Chapters 26 and 30). Performing in-house cell cytology allows the development of a prioritized differential diagnosis list. Evaluate cytologic aspirates with some specific criteria (see below). Send to an experienced cytologist those samples that require more expert interpretation.

Palpate the lesion before obtaining an aspiration sample. Determine if the nodule is within the epidermis, dermis, or subcutaneous tissue. The epidermis contains four major cell groups, which may become neoplastic. These are the squamous (epidermal) cells, melanocytes, a pluripotential follicular cell (which produces basal cell carcinoma), and cells that comprise the hair follicle and adnexae. Most inflammatory nodules are localized in the dermis. The dermis contains nerve cells and vascular and connective tissue. In addition, the dermis is often the host site for neoplastic cells derived from bone marrow. Lymphocytes, mast cells, and macrophages may form cutaneous accumulations of neoplastic cells. The subcutaneous tissue contains predominantly fat.

- From a clinical viewpoint, neoplasms arising in the subcutaneous tissue initially do not affect the hair follicles and adnexae; thus the overlying skin and hair remain normal in appearance.
- More superficially located neoplasms (such as those in the epidermis and superficial dermis) commonly affect adnexal structures, resulting in alopecia.

Palpation can also reveal whether the lesion is mineralized, painful, cystic, or cellular. Fluctuant tumors must be differentiated from an inflammatory lesion

such as an abscess. When they are not warm to the touch or painful, infection is less likely but cannot be ruled out. Cystic epidermal tumors (epidermal cysts and hair follicle tumors) are common in the dog but rare in the cat. The typical keratin-filled cavity is often palpable as a fluid-filled cystic lesion.

Inflammatory Lesions

Inflammation is present in most cases that contain a "mixed cell" population in which no one cell type predominates. Significant numbers of neutrophils are seen with an acute inflammatory process. As the relative numbers of macrophages increase, the process is considered chronic inflammation. A chronic inflammatory process, with few neutrophils and significant numbers of large, foamy macrophages, would be consistent with an inflammatory process in which there had been some tissue destruction but which may even be spontaneously resolving. Alternatively, an increased number of neutrophils, in association with macrophages, indicates the need for cultures to determine whether there is an infectious cause for this active, chronic inflammation. Cultures for bacterial or fungal organisms will not always reveal the infectious etiology of the nodule, however.

▼ ***Key Point*** The most common causes of folliculitis and furunculosis are the "big three" follicular infections, namely, *Demodex* mites, dermatophytes, or Staphylococcal pyoderma.

The latter two may be identified using a tissue culture but may be missed on an aspiration sample. Many of the cutaneous mycoses and unusual infections (e.g., protozoal infections) also require a tissue biopsy for histopathology and possibly culture.

Cutaneous Neoplasms

The most common cutaneous neoplasms (see Chapter 30) in dogs include lipomas, mast cell tumors, and sebaceous gland adenomas. Basal cell tumors are most common in cats. Do not rely on cytology alone as a diagnostic and prognostic indicator of cutaneous neoplasia. Should cytology reveal a uniform population of cells or aberrant cells that may be neoplastic, submit the sample for cytologic evaluation by a clinical pathologist and perform surgical excision for histopathologic evaluation. When cytology is inconclusive, perform either incisional or excisional biopsy (see Chapter 26).

SKIN BIOPSY

Indications (Table 37-1)

Specific indications for skin biopsy include the following:

Table 37-1. SPECIFIC INDICATIONS FOR SKIN BIOPSY

Lesion/Indication	Reason to Biopsy
Nodules	Nodules that have the potential for neoplasia or a deep-seated infection, especially if cytology does not yield a specific diagnosis
Ulcers	Severe, ulcerative, especially mucocutaneous lesions that may be potentially fatal
Expense with treatment	If the major differential diagnosis would require expensive medication or medical follow-up
Open diagnosis	To establish a diagnosis
Further investigations needed	The ability to prioritize differential diagnoses may allow a logical investigative approach, especially when in-house tests, physical exam, and history have failed to narrow the diagnostic list
Severe illness	Allows a fast diagnosis if the disease may have systemic and potentially fatal implications

- *Failure to respond to apparently appropriate presumptive therapy* may indicate that the diagnosis is incorrect or that the correct diagnosis has been made but in this particular case is resistant to the treatment. Use of the skin biopsy *to confirm* the clinical diagnosis is entirely appropriate and may save time, unnecessary "trial drug therapies," and client costs.
- *Before prescribing potentially harmful or expensive therapy, establish a specific diagnosis.* If an unusual or immune-mediated disease is a possible diagnosis, the supportive blood testing and drug costs may be considerable. Immune-suppressing drugs are potentially lethal. Do not prescribe without a specific diagnosis.
- *Biopsy for culture.* Improved antimicrobials have revolutionized the treatment of deep pyodermas and unusual infections in dogs and cats; however, resistance develops rapidly and tissue culture and sensitivity may prevent the choice of an antibiotic to which there is already resistance.
- *Biopsy unusual clinical lesions* or those that occur acutely or are particularly severe.
- *Biopsy to help prioritize a list of differential diagnoses,* especially when the clinical picture supports many possible etiologies. Although skin biopsy may not allow a definitive diagnosis, some differential diagnoses can be ruled out and a prioritization can be made of the others, enabling a therapeutic and diagnostic plan to be formulated.
- *Biopsy potentially neoplastic nodules.* Histopathology is the definitive diagnostic tool when assessing neoplasia.
- *Biopsy severe ulcerative disease,* especially involving mucocutaneous junctions.

Skin Biopsy Sampling Methods

There are two major types of biopsy technique—the punch and the wedge or ellipse. The most common sampling techniques include punch biopsy and incisional and excisional wedge or elliptical biopsies. Two less common and more site-specific techniques include "shave" biopsy and "onychobiopsy without onychectomy" claw biopsy. The biopsy for deep tissue culture has specific modifications to that sampled primarily for histopathologic evaluation.

Punch biopsy refers to the use of the biopsy punch instrument, which for veterinary purposes is used in 4-, 6-, and 8-mm diameters. Punch biopsies are fast and easy to use, and they yield a circular plug of tissue with clean, surgical, non-traumatized edges. *Wedge biopsy* refers to the elliptically shaped surgical biopsy, which takes a deeper section (or wedge) of tissue. Each method is used for specific indications, but in general the choice for smaller samples is one of personal preference.

Principles of Tissue Sampling

Regardless of the technique to be chosen, there are some basic principles when sampling skin for histopathology submission that are contrary to routine surgery. The first of these is that no skin antisepsis is practiced. This is to minimize any changes to the epidermal surface. Surgical cleaning may remove layers of stratum corneum, which contain clues through their thickness, associated pathology, or the presence of organisms. Indeed, even the use of the surgical clip is avoided because it may alter the epidermis. The second principle is that the tissue must be handled gently to avoid crushing. Tissue crush artifact alters the tissue architecture and obscures the cell type.

Punch Biopsy

When selected for non-nodular dermatoses, punch biopsy is useful to sample multiple small areas that may represent various stages of the disease process. Nodules are typically removed with an excision biopsy method. However punch biopsy is indicated when sampling nodules for several reasons:

- A large nodule is present in an area for which complete excision would be difficult, and a smaller sample from the core may provide the diagnosis without the concurrent excisional surgical treatment.
- An animal with a high anesthetic risk, an animal for which extensive surgery or adjunctive oncologic therapy will not be elected by the owners, or when a cytology aspirate from the nodule suggested an inflammatory and possibly an infectious etiology may be further reasons for using a punch biopsy on nodular disease.

In all of these cases, a punch from the center of the lesion may provide a rapid, relatively non-invasive diagnosis.

Punch biopsy is quick, relatively atraumatic, and usually employed with suspected infectious, inflammatory, and endocrine dermatoses. Disposable biopsy punches are readily available in 4-, 6-, and 8-mm diameter sizes. They can be autoclaved and reused at least once without greatly affecting their sharpness. Routinely use 8-mm punches; however, in very small dogs and cats, use 6-mm punches. Reserve 4-mm punches for biopsies of foot pads, nasal planum, or eyelids.

Punch Biopsy for Deep Tissue Culture

If cytology revealed a mixed population of cells or histiocytic cells, and therefore infection etiologies are possible, consider two options for sampling for culture:

- Insert a culture swab into the defect left by the excisional biopsy, taking care not to contaminate this with surface organisms *and remembering that for histopathology purposes the surface has not been aseptically prepared.*
- Alternatively (and preferably), section the tissue sample, once excised and using sterile blades, and place a piece of that tissue into culture transport media. If this was a punch biopsy, then section it longitudinally in half, with one half submitted for histopathology and the other half reserved for tissue culture. Make the longitudinal cut with the blade starting at the deeper tissue area and finishing at the skin surface so that surface organisms are not dragged through the tissue. Remove with a new sterile scalpel blade and make a single cut to remove the upper half of the punched out tissue. Submit this upper part for histopathology as a shave specimen.

Incisional Biopsy

Incisional sampling is used when evaluation of the lesional margin is considered important. Examples include the edge of a depigmented lesion and the edge of an ulcer. Consider incisional samples for areas in which there is a transition from one stage or age of the lesion to another. This may reveal important abnormalities. Choosing to perform an incisional biopsy may decrease the potential for laboratory error during processing (Figure 37-1).

Excisional Biopsy

Excisional sampling is useful to avoid the rupture of a large pustule or vesicle. Also use excision when a lesion involving the deeper tissues, especially the panniculus, must be sampled or when a solitary lesion, which could be cured by excision, is present. For a *solitary nodule,* perform *wide surgical* excision, because this technique provides the entire specimen for histologic examination and allows margins to be examined if the lesion is a tumor. Excise a 2- to 3-cm margin of tissue if a neoplasm

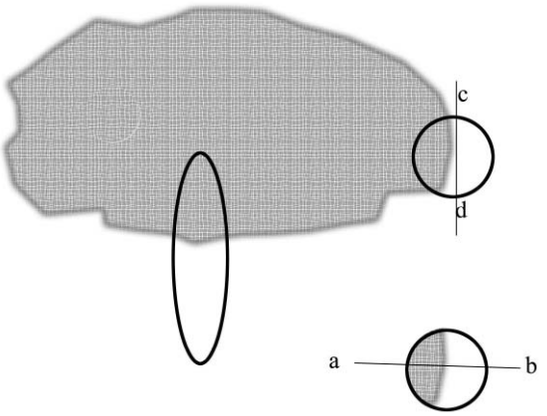

Figure 37-1. The histopathology technician will usually section the elliptical biopsy specimen along the midline of the long axis of the ellipse. Orientation of the ellipse across the junction between abnormal and normal tissues will allow the pathologist to view the skin from affected, through active (depigmenting), to non-affected areas and so gain the best possible appreciation of the stages of the disease and hence the etiology. Obtain a circular punch biopsy and section appropriately using the orientation line. Have the technician section along *line a–b*. Should a circular punch biopsy be taken, without drawing an orientation line, the technician may section the sample, providing only normal tissue to the pathologist (see *line c–d*).

is suspected. Depending on the size of the tumor, it may be necessary to section through the lesion to allow formalin to penetrate into the tissue for proper fixation. Nodules that are relatively small (less than 3 cm) may be left intact. For moderate-sized nodules (between 3 cm and 6 cm), incise the nodule once through the epidermal surface but leave the deep pannicular margin intact. Formalin can then penetrate into the incised surface of the nodule. The deep margin is left intact to prevent the subcutaneous fat and/or muscle from retracting from the incision line, which facilitates examination of the margin. For large masses (greater than 6 cm), make multiple incisions through the mass, leaving the deep pannicular tissue intact if possible.

Shave Biopsy

Use this technique when the clinical lesions are very superficial (i.e., epidermal) and when removal of deeper dermal tissue may result in unwanted scarring. In the canine it is most indicated for the inner pinna, where deeper sampling may affect the underlying cartilage. Remove the surface layers by a shallow scalpel incision that runs almost parallel to the line of the epidermis. Make the cut deep enough that it has some tissue and is not just stratum corneum, but keep it shallow enough to avoid scarring. Because the excision is superficial, there is no need to close with suture.

Onychobiopsy without Onychectomy Claw Biopsy

See Chapter 63.

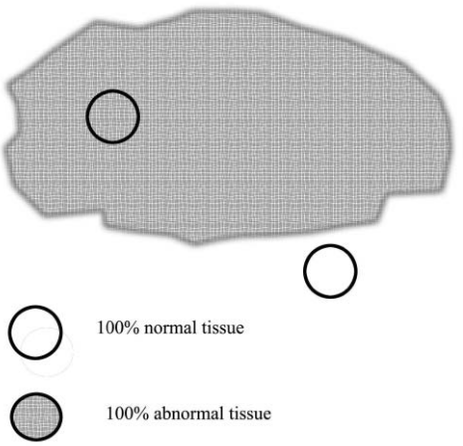

Figure 37-2. When sampling using a biopsy punch, selection of 100% lesional or 100% non-lesional skin will help avoid technical processing errors.

Site Selection

Perform a thorough dermatologic examination to select the biopsy sites. The clinical lesions present, the differential diagnosis list, and the need to provide the pathologist with the complete range of lesions dictates which and how many lesions are sampled. Also follow these guidelines:

- When a variety of different lesions are present (which is most commonly the case), multiple samples may be necessary for a full appreciation of the pathologic changes.
- Always sample pustules intact if present; take at least three if possible.
- Always use an excisional elliptical biopsy technique for *vesicles or large pustules*. These are fragile and may rupture if handled, losing their diagnostic potential.
- Where possible, *do not sample* the non-haired areas of the body in a suspected endocrinopathy. These areas normally contain fewer hair follicles and smaller sebaceous glands, which can make follicular evaluation more difficult. Preferentially, select a normally hairy site such as the shoulder.
- *Include samples of normal and abnormal tissue* when sampling with a punch biopsy (Figure 37-2) to allow comparison.
- *Biopsy depigmenting lesions* in an area of active depigmentation (i.e., a gray color rather than the final stage of depigmentation, which is white).
- *Biopsy alopecia* in the center of the worst area and in junctional and normal areas.
- *Areas of ulceration* require the adjacent intact skin to be included using a wedge biopsy section. If only the ulcerated area is sampled, the pathologist will merely describe a nonspecific ulcer.
- *Include crusts* because they may contain valuable clues about the formation (or malformation) of the skin or the presence of infectious agents.

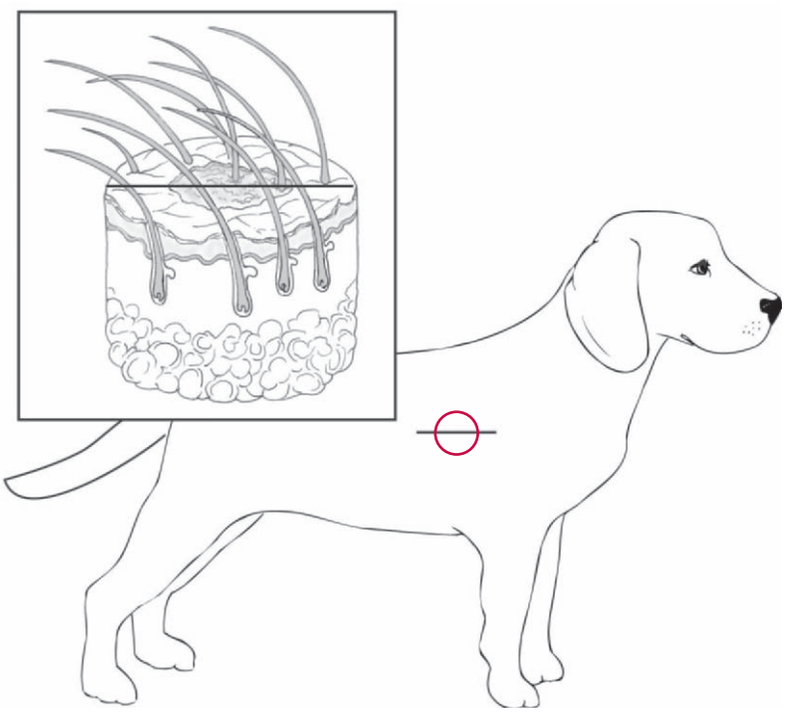

Figure 37-3. Draw a line at the biopsy site, in "permanent" marker pen, in the direction from the nose to the tail. This enables the technician to cut along a plane that runs parallel to the hair shafts, providing the pathologist with hair follicles in longitudinal section. (Borrowed, with permission, from "Practical Veterinary Dermatopathology," Bettenay & Hargis. Teton New Media.)

- *Always include normal skin in biopsies for comparison.* Skin from the ventral chest and abdomen is not regarded as "normal" because the hair follicles are smaller and less numerous and the dermis is generally thinned in this area.

Skin Biopsy Equipment

Regardless of the skin biopsy sampling method, several dedicated skin biopsy instruments can help minimize trauma to the sample, thus enabling the pathologist to obtain the best impression from the tissue. Obtain the tissue sample without placing any external forces on the tissue. These are applied when cutting the tissue and grasping it for handling or processing. I use ophthalmology instruments because they can be used with the 4-, 6-, and 8-mm punches with ease. Select thumb forceps that minimize crushing of the tissue (e.g., Addison thumb forceps). Scissors are often used to separate the tissue sample from the underlying tissue; use blunt, fine-tipped tenotomy of Metzenbaum scissors.

- When sampling tissue for deep tissue culture, use only instruments sterilized by autoclave to avoid having antiseptic residue interfere with the culture.
- For regular biopsy sampling, "cold sterilization" is adequate. Allow the instruments to drain well before use so that the liquid does not run on to and alter the surface of the skin.

Surgical Technique

1. Clip and gently remove the overlying hair. If crusts are present, it may be less traumatic to use scissors than electric clippers. Unless this will be an excision biopsy (i.e., removal of the entire lesion en masse) and therefore require aseptic preparation, a "surgical clip" is not necessary. Leaving a few millimeters of hair may help preserve some of the upper stratum corneum layers.
2. If general anesthesia is employed (as is indicated for nasal, ear pinna, or foot pad biopsies), no further preparation of the skin is necessary. If the biopsy is to be performed under manual restraint or with sedation, subcutaneously inject 0.3 to 1.0 ml of Xylocaine *without* epinephrine. If administered subcutaneously with the needle entry point outside the proposed biopsy area, there should be no disruption to the tissue in the biopsy. Mark the biopsy site with a large circle or four "framing dots" of a permanent marker pen before injection of the local anesthetic.
3. Indicate the orientation of the hair shafts to the laboratory technician with a line drawn in the direction of hair follicle growth (Figure 37-3). Hair shafts are angled caudally; they do not grow vertically from the skin. Section the piece of tissue longitudinally, parallel to the follicle, to enable the pathologist to observe the entire follicular unit in one piece, a distinct advantage for lesions characterized by alopecia and for inflammatory skin lesions. The laboratory

technician will routinely section the elliptical biopsy along the "long axis" of the sample. When the long axis does not correspond to the direction in which the hair follicles grow, the follicles may be cut in "cross section."

4. *For the punch biopsy:*
   a. Hold the punch at right angles to the surface of the skin and gently place it over the selected lesion. Hold the surrounding skin with the other hand.
   b. Apply firm continuous pressure and rotate the punch in *one direction* until a sufficient depth has been reached to free the dermis from its underlying attachment. This is evident when the skin no longer tries to "turn" with the rotation of the punch and by a gentle easing of pressure required for the turning. For thin-skinned areas such as the ventral abdomen, or with cats and small dogs, this may not be noted and some visual note of the depth is warranted.
   c. Remove the punch, lift the section of tissue, grasp *at the base* (which should be the panniculus), and sever the subcutaneous attachments using fine blunt/blunt iris scissors and iris forceps.

▼ ***Key Point*** During skin biopsy, do not grasp the dermis or epidermis with forceps because this leads to crush artifact.

Crushed tissue may be misinterpreted as scarring at best and may render the sample worthless.

5. *For wedge or elliptical biopsy:*
   a. Make an elliptical incision, taking care not to crush or tear the edges.
   b. Attempt to orient the central axis of the ellipse along several different stages of lesion development to allow the pathologist to interpret the development of the pathology.
6. Roll the tissue on gauze to gently blot the blood from its surface.
7. Place large, thin pieces of tissue panniculus side down onto a rigid piece of cardboard or a wooden tongue depressor. This prevents the tissue from curling when placed in the formalin, optimizing the interpretation by the pathologist.
8. Place the tissue and cardboard or tongue depressor into 10% formalin (tissue side down) and allow it to fix for at least 8 hours before sectioning. The volume of formalin required is approximately 10 times the volume of the sample.
9. Section nodules into 1-cm-thick pieces to allow adequate penetration of the formalin into the center of the lesion.
10. A valuable adjunctive test is to perform cytology from the impression of such a freshly excised surface of a nodule. Make multiple slides and submit some air-dried, unstained slides separately to the laboratory for storage.

Processing and Submitting

A differential diagnosis list is *essential* with dermatologic cases. This list is important for the clinician to ensure that he or she has considered the options and obtained from both pet and owner as much information as possible and as necessary before taking the biopsy, and it is important to alert the pathologist to the possible pathologic processes. If the list of clinical differentials fails to correlate with the histopathology, review the sections. If the biopsy submission form clearly states that a deep infectious process is suspected, perform special stains to rule out infectious organisms. If an immune-mediated dermatosis is suspected and convincing supportive evidence is not seen on the first section, order recuts of the biopsy sample. Many dermatoses are diagnosed using a combination of the signalment (age, breed, sex), clinical presentation (distribution, type of primary lesions if present), history (in particular previous response to therapy), and *supportive* histopathology.

Identification of each sample is important. This may be achieved by placing each sample in a separate container or inking the samples. Inking the margins may identify a particular sample (e.g., the one sample of "clinically normal skin") or help the technician with orientation (e.g., inking the haired skin surface of an onychectomy sample). Various commercial dyes are available, or simple India ink can be used. However it is most important that *the ink dries on the surface of the tissue* before it is placed in the formalin.

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Chapter 38

Pyoderma

Edmund J. Rosser Jr.

Pyoderma refers to any pyogenic infection of the skin and is most commonly used in reference to bacterial skin infections. However, fungal organisms (especially yeast) have also been recognized as potentially significant opportunists in the development of surface pyoderma in the dog (see Chapter 41). Pyoderma is a common problem in clinical practice.

- Primary pyoderma refers to a skin infection that does not recur after the appropriate treatment. These infections are most likely the result of a transient and non-recurrent insult to the skin.
- Secondary pyodermas are far more common and are associated with a persistent or recurrent underlying problem that alters the skin's resistance to infection. Until the underlying problem is identified and corrected, the infection usually responds only temporarily to therapy and subsequently recurs.
- Pyodermas are caused by bacterial colonization or invasion of the skin by coagulase-positive staphylococci, usually *Staphylococcus intermedius*. In chronic, recurrent, or deep pyodermas, secondary bacterial invaders may also be present, especially *Pseudomonas* spp., *Proteus* spp., and *Escherichia coli*. When deep pyoderma occurs, anaerobic bacteria such as *Bacteroides* spp., *Peptostreptococcus* spp., *Fusobacterium* spp., *Porphyromonas* spp., and *Clostridium* spp. may be further opportunistic pathogens. Recently, two additional staphylococci have been isolated from cases of recurrent pyodermas, namely *Staphylococcus schleiferi* subsp *schleiferi* and *Staphylococcus schleiferi* subsp *coagulans,* both of which are frequently methicillin-resistant staphylococci.

SURFACE PYODERMAS

Surface pyoderma is a bacterial colonization of the surface of the epidermis only, without invasion into the stratum corneum or hair follicles. Two types of surface pyoderma are recognized: acute moist dermatitis ("hot spot" or pyotraumatic dermatitis) and skin fold pyoderma.

Acute Moist Dermatitis (Hot Spot) (Pyotraumatic Dermatitis)

Etiology

Self-trauma to the skin, due to an underlying pruritic or painful process, can result in a focal surface pyoderma referred to as acute moist dermatitis. Underlying conditions that may be associated with the development of acute moist dermatitis are listed in Table 38-1.

Clinical Signs

- Acute moist dermatitis is usually a single alopecic lesion that is circumscribed, erythematous, thickened, and erosive. An exudative film occurs over the surface, and peripheral hairs are matted onto the lesion. The lesion develops subsequent to the dog's chewing and licking at a focal area of pruritus or pain, and it develops within a matter of hours. The lesion is usually painful.
- Thick-coated, longhaired breeds are most commonly affected.
- Lesions that appear clinically similar to an acute moist dermatitis (pyotraumatic dermatitis), but develop in the absence of a history of self-trauma, are often associated with a deeper bacterial folliculitis and/or furunculosis and are most commonly observed on the side of the face, or cheek region (also referred to as pyotraumatic folliculitis). The breeds more commonly affected by this deeper form of an acute moist dermatitis are golden retrievers, Saint Bernards, Bouviers, and Newfoundlands. In these cases, satellite popular lesions can usually be detected surrounding the area of acute moist dermatitis once the area has been clipped.

Diagnosis

▼ ***Key Point*** Diagnose acute moist dermatitis by the history of self-trauma to the skin, acute onset, rapid development of the lesion (within hours), and the typical appearance of the lesion on physical exam.

Table 38-1. CONDITIONS ASSOCIATED WITH HOT SPOTS

Disease Category	Examples
Allergic skin diseases	Flea allergy dermatitis
	Atopic dermatitis (atopy)
	Cutaneous adverse food reactions (food allergy)
	Allergic contact dermatitis
	Secondary staphylococcal hypersensitivity
Ectoparasites	Canine scabies
	Cheyletiellosis
	Demodicosis
Otitis externa	Allergic otitis externa
	Ceruminous otitis externa
Environmental causes	Irritant contact dermatitis
	Poor grooming
	Burs or plant awns in the skin or haircoat
Musculoskeletal disorders	Hip dysplasia
	Degenerative joint disease
	Arthritis and other arthropathies
Anal sac problems	Impacted anal sacs
	Anal sacculitis

From Rosser EJ, Sams A: Pruritus. In Allen DG (ed): Small Animal Medicine. Philadelphia: JB Lippincott, 1991, p 704.

- History includes questioning the owner about any pruritic skin disease, painful process, or environmental irritant that might indicate the reason for the dog's self-trauma of the area (see Table 38-1). In instances of recurrent acute moist dermatitis, identify the underlying problem to prevent any further recurrences.
- Biopsy lesions that appear clinically similar to an acute moist dermatitis, that develop in the absence of a history of self-trauma, and that respond poorly or are non-responsive to initial treatment. This is to determine if the lesion is associated with a deeper bacterial folliculitis and/or furunculosis, which requires a more aggressive treatment regimen.

Treatment

Whenever an underlying disease process can be identified, institute the specific treatment recommended for that disease as well as the treatment necessary for the hot spot. A main objective of treatment is to clip and clean the lesion to facilitate better aeration and to allow better contact and penetration of topical agents.

Topical Therapy

- First gently clip and thoroughly cleanse the area with an antiseptic shampoo, such as povidone-iodine (Betadine, Purdue Frederick) or chlorhexidine (Hexadene, Allerderm/Virbac; ChlorhexiDerm, DVM Pharmaceuticals). Because the lesion is often very painful, this step may require sedation or general anesthesia.
- Dry the lesion by applying an astringent, such as Burow's solution (Domeboro powder and water; Bayer) or hamamelis extract (DermaCool with Lidocaine, Allerderm/Virbac), and then apply a nystatin-neomycin sulfate-thiostrepton-triamcinolone acetonide cream (Panalog Cream, Fort Dodge; Animax Cream, Pharmaderm; Dermagen Cream, Butler). Repeat these treatments q12h, for 5 to 10 days.

Systemic Therapy

- Corticosteroids are indicated in the treatment of hot spots because the lesion is often painful or pruritic and because the most common underlying causes are allergic skin diseases. Begin treatment with a short-acting, injectable corticosteroid. Since prednisolone and prednisone are no longer available in non-repositol injectable forms, dexamethasone solution—2 mg/ml (Aspen) at 0.05 mg/kg IM (not to exceed 1 mg/dog)—may be given for a rapid anti-inflammatory and anti-pruritic effect. The next day administer oral prednisolone or prednisone at 0.5 mg/kg q12h for 5 to 7 days, then 0.5 mg/kg q24h for the next 5 to 7 days.
- Use systemic antibiotics in cases in which a deep folliculitis and/or furunculosis is suspected or has been confirmed after histopathologic examination of a skin biopsy (see the discussion of treatment under "Deep Pyodermas").

Prevention

- In instances of recurrent acute moist dermatitis, the underlying disease problem must be identified to prevent any further recurrence of the lesions (see Table 38-1).

Skin Fold Pyoderma

Etiology

- Deep skin folds, where the skin rubs against itself and causes irritation and maceration, can result in a surface pyoderma referred to as a skin fold pyoderma (intertrigo). These skin folds create a moist, dark, and warm environment with poor air circulation, which retains skin secretions and desquamated keratinocytes that promotes subsequent bacterial *(S. intermedius)* or yeast *(Malassezia pachydermatis)* overgrowth and inflammation.
- Pyoderma can occur in any skin fold in any breed of dog, but intertrigo is most commonly associated with the skin folds in certain breeds of dogs. Table 38-2 lists the anatomic sites of the more common skin fold pyodermas and their breed predispositions, and it includes lip fold, facial fold, vulvar fold, tail fold, body fold, and leg fold pyodermas.

Table 38-2. SKIN FOLD PYODERMAS

Anatomic Site	Breed Predisposition	Comments
Lip fold	Cocker spaniel Springer spaniel Saint Bernard Irish setter	Lower lip fold, halitosis
Facial fold	Brachycephalic types Shar-Pei	Between nose and eyes Lateral facial region
Body fold	Shar-Pei	Also any breed with pendulous mammary glands, obese patients
Vulvar fold	None	Obese females, juvenile vulva, spayed early in life
Leg fold	Chondrodystrophic types (basset hound, dachshund)	Obese patients
Tail fold	Bulldog Boston terrier Pug	"Corkscrew tails," anal odor

Clinical Signs

- Skin fold pyoderma is characterized by inflammation and mild exudation. This pyoderma is best identified by simply widening the skin fold. The area is often malodorous.
- The animal is usually rubbing, licking, or biting excessively at the area. Evidence may exist of excoriation, alopecia, and erythema around the skin fold region.

Diagnosis

▼ ***Key Point*** Skin fold pyodermas are usually diagnosed by close inspection of the skin fold and demonstration of inflammation, mild exudation, and malodor from within the fold.

- *Direct impression skin cytology:* Press a clean glass microscope slide over the exudative area, and then gently heat fix and stain with Diff-Quik (Dade Behring). Examine microscopically under oil immersion (1000×) to best identify and quantitate the presence of cocci versus rods versus yeast type of opportunistic organisms (see Chapter 37). This will aid in the selection of the most appropriate active ingredient in your topical therapy, especially in chronic, recurrent cases.

Treatment

The objectives of treatment are to cleanse and disinfect the skin fold region using agents that will dry the area and prevent recurrence of pyoderma. Topical therapy is usually adequate to control the problem.

- First gently expose and cleanse the skin fold with a benzoyl peroxide shampoo (OxyDex Shampoo, DVM Pharmaceuticals; Pyoben Shampoo, Allerderm/Virbac; Benzoyl-Plus, EVSCO Pharmaceuticals).
- Dry the area manually and apply a topical mild astringent, such as Burow's solution (Domeboro powder and water; Bayer).
- When only bacteria are found on direct impression skin cytology, follow with a twice-daily application of a benzoyl peroxide-containing gel (OxyDex Gel, DVM Pharmaceuticals; Pyoben Gel, Allerderm/Virbac) into the skin fold region for 10 to 14 days. When only yeast organisms or both bacteria and yeast organisms are found on direct impression skin cytology, follow with a twice-daily application of a miconazole- and chlorhexidine-containing preparation (Malaseb Pledgets, DVM Pharmaceuticals) into the skin fold region for 10 to 14 days.
- In cases involving a more severe inflammatory response, treat for the first 2 to 3 days with twice-daily applications of a nystatin-neomycin sulfate-thiostrepton-triamcinolone acetonide cream (Panalog Cream, Fort Dodge; Animax Cream, Pharmaderm; Dermagen Cream, Butler) into the skin fold region. Once the inflammation has subsided, institute the benzoyl peroxide or miconazole and chlorhexidine preparation.

Prevention

Topical Therapy

Because the skin folds that develop pyoderma are usually deep, owing to a given breed characteristic, this condition tends to be a low-grade, recurrent problem. Once the infection has been treated as recommended, use the benzoyl peroxide or miconazole and chlorhexidine preparation as needed to prevent recurrence. This measure may require application ranging from daily to once or twice weekly.

Corrective Surgery

When a more permanent solution to the problem is desired, or when rapid recurrence of moderate to severe skin fold pyoderma occurs, the only permanent cure is removal of the skin fold using cosmetic surgery techniques (see Chapter 54).

SUPERFICIAL PYODERMAS

- Superficial pyoderma is a bacterial invasion of the epidermis that can manifest itself in one of two ways. First, the bacteria can penetrate the stratum corneum with the subsequent formation of subcorneal pustules and is referred to as impetigo (puppy pyoderma). Second, the bacteria can invade the opening of the hair follicle causing inflammation and is referred to as folliculitis.

- Coagulase-positive staphylococci are the most common pathogens involved in a superficial pyoderma. *S. intermedius* is most frequently isolated.

Impetigo

Etiology

Impetigo is most often observed in young dogs before puberty. The condition may be more likely in the presence of contributing factors such as poor nutrition, dirty environment, and ectoparasite or endoparasite infection. However, well–cared-for individual puppies or litters of puppies may also develop this condition.

Clinical Signs

- Impetigo occurs as pustules in the inguinal and ventral abdominal regions. Occasionally, pustules are noted in the axillary region. When the pustules rupture, a yellow to brownish crust forms.
- The pustules are not oriented around hair follicles (i.e., no hair shafts protrude through the center of the pustule). Minimal erythema is noted, and the patient is usually non-pruritic.
- Impetigo may be an incidental finding during the physical examination of a recently acquired puppy.

Diagnosis

▼ ***Key Point*** Impetigo is usually diagnosed in young dogs before puberty by observing non-follicular pustules in the inguinal and ventral abdominal regions with minimal erythema and absence of pruritus.

- *History:* Ask the owner about the animal's previous and current nutrition and housing environment.
- *Physical examination:* See the related "Clinical Signs" section.
- *Cytologic examination:* Stained contents of an intact pustule most often reveal neutrophils and cocci.
- *Skin scrapings:* Examine routine skin scrapings for ectoparasites such as *Demodex canis, Sarcoptes scabiei,* and *Cheyletiella* spp.
- *Bacterial culture:* This is rarely necessary, but if performed, *S. intermedius* is usually isolated.
- *Skin biopsy:* This is rarely necessary to establish the diagnosis of impetigo. Histopathology indicates subcorneal pustules containing neutrophils and cocci.
- *Fecal flotation:* Evaluate the puppy for intestinal parasites.

Treatment

▼ ***Key Point*** Objectives include identifying contributing factors and correcting these as an adjunct to specific treatment. Improve the nutritional status and the housing environment and treat any endoparasite or ectoparasite infections.

Table 38-3. EMPIRICAL TREATMENT OF PYODERMAS CAUSED BY STAPHYLOCOCCUS INTERMEDIUS

Antibiotic	Recommended Oral Dosage
Erythromycin	11 mg/kg q8h
Cephalexin	22 mg/kg q8h or 33 mg/kg q12h
Cefadroxil	22 mg/kg q8–12h
Trimethoprim/sulfadiazine	30 mg/kg q12h
Ormetroprim/sulfadimethoxine	55 mg/kg on day 1, then 27.5 mg/kg q24h
Amoxicillin/clavulanate	14 mg/kg q12h
Clindamycin	5 mg/kg q12h or 11 mg/kg q24h

Topical Therapy

Once any predisposing factors have been eliminated, topical therapy is usually all that is required for this superficial staphylococcal infection. Bathe the dog with a benzoyl peroxide shampoo (OxyDex Shampoo, DVM Pharmaceuticals; Pyoben Shampoo, Allerderm/Virbac; Benzoyl-Plus, EVSCO Pharmaceuticals) or chlorhexidine shampoo (Hexadene, Allerderm/Virbac; ChlorhexiDerm, DVM Pharmaceuticals) 2 to 3 times weekly for 2 to 3 weeks.

Antibiotics

Systemic antibiotic therapy is rarely necessary in impetigo. However, when topical therapy fails to resolve the pyoderma, add a systemic antibiotic to the topical therapy protocol (Table 38-3).

Superficial Folliculitis

Etiology

- Superficial folliculitis induced by coagulase-positive staphylococci occurs occasionally as a primary problem. These infections are most likely the result of a transient and non-recurrent insult to the skin.
- Secondary superficial folliculitis is far more common and is associated with a persistent or recurrent underlying problem that alters the skin's resistance to infection. Until the underlying problem is identified, the infection usually responds only temporarily to therapy and subsequently recurs (see the discussion under "Recurrent Superficial and Deep Pyodermas").

Clinical Signs

- Superficial folliculitis initially appears similar to impetigo, with papules and pustules in the inguinal and ventral abdominal regions. However, pustules often extend to the axillary region and the ventrolateral thorax.

- The papules and pustules are oriented around the hair follicle (i.e., hair shafts protrude through the center of the pustule). The base of the pustule is often erythematous, and the patient is usually pruritic.
- Other lesions may include papules, crusts, and epidermal collarettes.
- When the truncal skin is affected, the haircoat often takes on a "moth-eaten" appearance.
- Rarely, multifocal areas of alopecia are seen without erythema or other lesions.

Diagnosis

▼ ***Key Point*** Superficial folliculitis is usually diagnosed by observing papules and pustules oriented around hair follicles in the inguinal, ventral abdominal, and axillary regions. The base of the pustule is erythematous and the patient is usually pruritic.

- *History:* Superficial folliculitis is often secondary to an underlying disease problem. Question the owner about the effect of antibiotic therapy alone on the disease problem. This is a very important diagnostic tool in the systematic approach to a patient with a recurrent pyoderma. See also the discussion under "Recurrent Superficial and Deep Pyodermas."
- *Physical examination:* See the related "Clinical Signs" section.
- *Cytologic examination:* The contents of an intact pustule usually reveal neutrophils and cocci.
- *Skin scrapings:* These are routinely examined for the presence of ectoparasites, such as *D. canis, S. scabiei,* and *Cheyletiella* spp.
- *Bacterial culture and susceptibility tests:* Consider these in cases of recurrent superficial folliculitis that have not responded to appropriate empirical antibiotic therapy and are designed to evaluate for resistant bacteria. Cultures usually reveal *S. intermedius.* Use the sensitivity results as a guideline for antibiotic selection.
- *Fungal culture:* Submit a sample of the hairs from follicular pustules for a fungal culture in cases that are non-responsive to appropriate anti-bacterial therapy. In some instances, a folliculitis due to a dermatophyte infection can appear clinically indistinguishable from a folliculitis caused by bacteria.
- *Skin biopsy:* Typical findings include folliculitis or perifolliculitis, with coccoid bacteria within the hair follicle. Folliculitis due to a dermatophyte infection would reveal the presence of spores or hyphae within the hair follicle. Usually, biopsy is not necessary in the diagnosis of superficial pyoderma.

Treatment

▼ ***Key Point*** Be certain that an appropriate antibiotic for staphylococci has been selected (see Table 38-3) and that the duration of therapy has been adequate. The treatment required for folliculitis is generally more vigorous than that required for impetigo. In recurrent cases, define the underlying disease process and initiate a systematic approach to the disease. See the discussion under "Recurrent Superficial and Deep Pyodermas."

Topical Therapy

Use twice-weekly bathing with a benzoyl peroxide shampoo (OxyDex Shampoo, DVM Pharmaceuticals; Pyoben Shampoo, Allerderm/Virbac; Benzoyl-Plus, EVSCO Pharmaceuticals) or a chlorhexidine shampoo (ChlorhexiDerm, DVM Pharmaceuticals; Hexadene, Virbac; SebaHex, EVSCO Pharmaceuticals) for 3 weeks.

Antibiotics

Systemic antibiotic therapy can be initially selected on an empirical basis, choosing an antibiotic effective against coagulase-positive staphylococci (see Table 38-3). Treat for a minimum of 21 consecutive days and for at least 7 days beyond apparent clinical cure.

DEEP PYODERMAS (DEEP FOLLICULITIS AND FURUNCULOSIS)

A deep pyoderma is a bacterial skin infection that extends beyond the epidermis, into the dermis, and occasionally into the subcutaneous tissues. Although there are many possible forms of deep pyoderma, this discussion is limited to the most common form, deep folliculitis and furunculosis.

- The disease begins as a superficial folliculitis then extends deeper into the hair follicle, causing a deep folliculitis.
- This inflammatory process often results in furunculosis, which is the destruction of the hair follicle wall and the release of the bacteria, hair shaft material, and follicular keratins into the surrounding dermis and occasionally the subcutaneous tissues.
- Subsequently, the bacteria can produce septicemia and/or bacteremia, and the released hair shafts and follicular keratins induce a foreign body and pyogranulomatous inflammatory reaction in the dermis.

Etiology

- Coagulase-positive staphylococci are the most common pathogens initially involved in deep pyoderma. *S. intermedius* is the most frequently isolated.
- In contrast to a superficial pyoderma, secondary invasion with other aerobic bacteria often occurs with *Pseudomonas* spp., *Proteus* spp., and *E. coli.* Anaerobic bacteria may also become opportunistic pathogens, especially *Bacteroides* spp., *Peptostreptococcus* spp.,

Fusobacterium spp., *Porphyromonas* spp., and *Clostridium* spp.
- Deep pyoderma is rarely a primary disease process and is invariably related to some other underlying problem.

Clinical Signs

- Deep folliculitis and furunculosis initially begin as superficial folliculitis. See the discussion of clinical signs under "Superficial Pyodermas," and see "Superficial Folliculitis."
- When deep folliculitis and furunculosis develop, the papules and pustules become larger and nodular on palpation. Exudation and crust formation follow. Ulcers and draining tracts may develop. Hemorrhagic bullae may also be noted.
- In addition to the inguinal, ventral abdominal, and axillary regions, the pressure and wear areas of the body can also be affected. The disease may become generalized.
- The lesions are painful and/or pruritic.
- Peripheral lymphadenopathy is a common finding. Signs of systemic illness may be present (anorexia, depression, weight loss). The patient may also be febrile, an indication of bacteremia and/or septicemia.
- A specific form of deep pyoderma can occur in German shepherds (so-called German shepherd dog pyoderma), which is often related to multiple underlying problems in the affected patient.

Diagnosis

▼ ***Key Point*** Deep folliculitis and furunculosis are usually diagnosed by observing papules and pustules that become nodular on palpation, with exudation, crust formation, ulcers, draining tracts, and hemorrhagic bullae.

History and Physical Examination

Deep folliculitis and furunculosis are invariably secondary to an underlying disease process. Question the owner about the effect of antibiotics alone on the disease, as this is a very important diagnostic tool in the systematic approach to a patient with recurrent pyoderma. See the discussion under "Recurrent Superficial and Deep Pyodermas." Physical exam findings were described earlier under "Superficial Pyodermas" and "Superficial Folliculitis."

Laboratory Tests

- *Cytologic examination:* Pustules, exudates, and draining tracts usually reveal neutrophils, macrophages, cocci, and sometimes rods.
- *Skin scrapings:* Evaluate for *D. canis* mites, a common underlying cause of deep pyoderma.
- *Bacterial culture:* Perform both aerobic and anaerobic bacterial culture and susceptibility tests in all cases of deep pyoderma. This form of pyoderma is capable of causing bacteremia and/or septicemia, resulting in a life-threatening situation. Usually, biopsy is not necessary in the diagnosis of superficial pyoderma.
- *Fungal culture:* Do this in cases of deep pyodermas that are refractory to antibiotic therapy. Fungi are another possible cause of a deep folliculitis and furunculosis. Fungal diseases to consider include sporotrichosis, blastomycosis, coccidioidomycosis, aspergillosis, histoplasmosis, and cryptococcosis.
- *Skin biopsy:* This usually reveals deep folliculitis, perifolliculitis, and furunculosis. Bacterial or fungal organisms may or may not be identified on special staining.
- *Blood culture:* Perform these cultures when bacterial sepsis is suspected in patients with a fever and evidence of systemic illness.

Treatment

▼ ***Key Point*** Be certain that an appropriate antibiotic has been selected to eliminate the organism causing the deep pyoderma. Choose the antibiotic based on the results of bacterial culture and sensitivity tests. In general, treatment is more vigorous than that for superficial folliculitis. In recurrent cases, define the underlying disease process and initiate a systematic approach. See the discussion under "Recurrent Superficial and Deep Pyodermas."

Topical Therapy

- Clip the hair around the affected areas. In cases of generalized deep pyoderma in long-coated breeds of dogs, clip the entire body.
- Initially bathe the patient twice daily (preferably in a whirlpool bath) using a povidone-iodine preparation (Betadine Whirlpool Concentrate, Purdue-Frederick) or chlorhexidine solution for the first 1 to 2 weeks of treatment. As the patient responds to treatment and the lesions have dried and begun to heal, change the treatment to once- to twice-weekly bathing with a benzoyl peroxide shampoo (OxyDex Shampoo, DVM Pharmaceuticals; Pyoben Shampoo, Allerderm/Virbac; Benzoyl-Plus, EVSCO Pharmaceuticals) for the next 4 to 8 weeks.

Systemic Antibiotics

- Always base systemic antibiotic selection on the results of a bacterial culture and sensitivity tests in cases of deep pyoderma. Use the appropriate dosage (see Table 38-3). Treat for approximately 6 to 8 consecutive weeks. Severe cases of deep pyoderma may require a longer treatment regimen. Treat for at least

2 weeks beyond the complete clinical remission of the infection.

- In instances when a *Pseudomonas* spp. is the primary isolate, a fluoroquinolone antibiotic is often most appropriate. Base the dosing of fluoroquinolones on the minimal inhibitory concentration (MIC) of the isolated organism, using the flexible labeled dosing schedule provided by the manufacturer, to obtain a serum maximum concentration (C_{max}) that is 8 to 10 times the MIC for that organism. Commonly used fluoroquinolones for these *Pseudomonas* spp. infections include marbofloxacin at a dosage from 2.75 to 5.5 mg/kg PO q24h (Zeniquin, Pfizer), and ciprofloxacin at a dosage from 10 to 22 mg/kg PO q24h (Cipro, Bayer).

RECURRENT SUPERFICIAL AND DEEP PYODERMAS

Antibiotic-responsive but recurrent pyoderma is often a very frustrating problem in clinical practice. This section stresses the need to evaluate the patient with this problem for some of the more common, underlying diseases associated with recurrent pyoderma.

Etiology

Inadequate Treatment

- Inappropriate antibiotic selection or inadequate duration of therapy can be simple reasons for the development of recurrent pyoderma. Antibiotic administration for 10 to 14 days will usually lead to improvement (maybe significant) in the lesions but will usually not lead to total resolution of the infection.
- Long-term glucocorticoid use can predispose the patient to recurrent pyoderma and cause varying degrees of iatrogenic Cushing disease. Most patients with a pyoderma are pruritic; therefore, glucocorticoids are often used as adjuncts to the antibiotic therapy. This treatment may be acceptable the first time; however, discontinue glucocorticoids once it becomes apparent that the pyoderma is a recurrent problem. By treating the pruritic patient that has a pyoderma with antibiotics only, very important information can be learned. This can help guide the clinician to the underlying disease condition. See the related section on "Diagnosis" for guidelines on the use of antibiotics and response to therapy as a diagnostic tool.

▼ ***Key Point*** The following discussion of common underlying diseases resulting in recurrent pyoderma requires that the patient has first been placed on a prolonged systemic antibiotic treatment protocol, as discussed under the related "Diagnosis" section. Therefore, the observations being made are those that are noted after the pyoderma has been symptomatically put into remission.

Allergic Skin Disease

- ***Flea allergy dermatitis:*** Patients with flea allergy dermatitis have pruritus that persists after resolution of the pyoderma and that primarily affects the caudal third of the body. Most patients initially have the problem in warmer weather only. For further discussion, see Chapter 45.
- ***Atopic dermatitis:*** Patients with atopic dermatitis have pruritus that persists after resolution of the pyoderma and that affects various combinations of the following areas of the body: face, ears, axillae, inguinal region, proximal cranial foreleg region, and feet. Most patients initially have the problem in warmer weather only. For further discussion, see Chapter 46.
- ***Cutaneous adverse food reactions (food allergy):*** Patients with food allergy have pruritus that persists after resolution of the pyoderma and that affects various combinations of the following areas of the body: face, ears, axillae, inguinal region, proximal cranial foreleg region, and feet. All patients have a non-seasonal (i.e., year-round) problem from the onset. For further discussion, see Chapter 47.

Parasitic Skin Disease

- ***Demodicosis:*** Patients with demodicosis may or may not be pruritic once the pyoderma has resolved. As previously stated, all patients with pyoderma require that several deep skin scrapings be performed, because demodicosis is a common cause of recurrent pyoderma that can be easily diagnosed. For further discussion, see Chapter 43.
- ***Scabies:*** Patients with sarcoptic mange have pruritus that persists after resolution of the pyoderma and that initially affects the ear, elbow, and hock regions. All patients have a non-seasonal (i.e., year-round) problem from the onset. For further discussion, see Chapter 44.

Keratinization Disorders

Patients with keratinization abnormalities may be pruritic once the pyoderma has resolved. The lesions that persist are suggestive of a keratinization (seborrheic) abnormality. For further discussion, see Chapter 50.

Endocrine Skin Diseases

Patients with hypothyroidism and hyperadrenocorticism (Cushing disease) are non-pruritic once the pyoderma has resolved. Evaluate the patient by history and physical examination for evidence suggestive of these metabolic diseases. For further discussion, see Chapters 31 and 33.

Staphylococcal Hypersensitivity

Patients with staphylococcal hypersensitivity exhibit a temporary resolution of both the pyoderma and the pruritus on antibiotic treatment alone. Staphylococcal hypersensitivity as a primary disease is one of the more controversial topics in veterinary dermatology. In my opinion, staphylococcal hypersensitivity invariably develops as a secondary complication. However, when no underlying cause can be established, the staphylococcal infection alone is the cause of the pruritus (i.e., a primary pruritic pyoderma). This disease is best diagnosed by exclusion of other underlying causes for a recurrent pyoderma. Therefore, systematically rule out all of the underlying diseases discussed up to this point before diagnosing primary staphylococcal hypersensitivity.

Immunodeficiency

Immunodeficiency disorders as the primary cause for a recurrent pyoderma are extremely rare. Disorders to consider are cell-mediated immunity disorders, such as T lymphocyte deficiency, and humoral immunity disorders, such as immunoglobulin A (IgA) deficiency.

Clinical Signs

See discussions of the clinical signs under "Superficial Pyodermas," "Superficial Folliculitis," and "Deep Pyodermas" elsewhere in this chapter.

Diagnosis

- First consider the procedures recommended elsewhere in this chapter for the diagnosis of superficial pyoderma, superficial folliculitis, and deep pyoderma.
- Use antibiotics as a diagnostic tool. Use antibiotics with anti-bacterial shampoo therapy without any antipruritic drugs, especially glucocorticoids. Treat in this manner for 3 weeks and then reexamine. If the patient is still pruritic, note the distribution pattern and question the owner as to whether the condition was initially a predominantly warm-weather seasonal problem or a non-seasonal problem. For common underlying pruritic skin diseases, refer to the section on etiologic and predisposing conditions.
- If the lesions *and* pruritus have both resolved on antibiotics alone, continue the antibiotic treatment for a total of 8 consecutive weeks. In some instances, this treatment results in a permanent resolution of the pyoderma. If the pyoderma recurs after stopping antibiotic therapy, evaluate the animal for underlying endocrine disease, staphylococcal hypersensitivity, and immunodeficiency disorders.
- For the specific testing procedures to diagnose the various underlying disease problems, please refer to the appropriate chapters in this book as recommended under the section on etiologic and predisposing conditions.
- Specific tests for primary immunodeficiency disorders are not readily available and are usually only offered by veterinary university laboratory services. Testing procedures to consider are the mitogen stimulation test for evaluation of lymphocyte function and the measurement of serum IgA levels as an indirect evaluation for a secretory IgA disorder.

Treatment

General Principles

- Specific treatment of identifiable underlying diseases is essential for the resolution of an antibiotic-responsive but recurrent pyoderma.
- Topical therapy is discussed under the treatment sections for "Superficial Pyodermas," "Superficial Folliculitis," and "Deep Pyodermas."
- Systemic therapy is discussed under the treatment sections for "Superficial Pyodermas," "Superficial Folliculitis," and "Deep Pyodermas."

Immunomodulators

- Immunomodulating drug therapy is indicated in cases of primary staphylococcal hypersensitivity and primary immunodeficiency disorders. Many treatment alternatives are available, but my preference is to use a staphylococcal bacterin (Staphage Lysate, Delmont Labs). See Table 38-4 for the recommended Staphage Lysate injection protocol.
- Also administer an appropriate systemic antibiotic for the first 4 to 8 weeks of treatment (until the infection has resolved).

Maintenance Antibiotics

- In instances in which an underlying disease process cannot be identified (so-called idiopathic chronic recurrent pyoderma), consider a maintenance antibiotic treatment protocol.
- Before this recommendation is offered, make the owner aware of the possible risk for resistant bacter-

Table 38-4. STAPHAGE LYSATE INJECTION PROTOCOL*

Week	Volume (ml)
1	0.25
2	0.50
3	0.75
4	1.00

*Follow this protocol with 1–2 ml every 3–21 days as needed to prevent recurrence of the pyoderma. Administer injections subcutaneously.
From Rosser EJ, Sams A: Papular/pustular, vesicular/bullous, and erosive/ulcerative dermatoses. In Allen DG (ed): Small Animal Medicine. Philadelphia: JB Lippincott, 1991, p 719.

ial infections, either in the skin or elsewhere in the body.

- There are several protocols, but my preference is use of the antibiotic on a continuous basis at a suboptimal dose. As an example, if the initial appropriate dose of the antibiotic is 500 mg q8h, give the antibiotic at that dosage until clinical remission of the pyoderma has been reestablished. Then gradually decrease the dosage over several weeks to 500 mg q12h and finally to 250 to 500 mg q24–48h.
- Bactericidal antibiotics with a low potential for development of resistance and minimal side effects have been most effective, such as cephalexin. In cases of a relapse of the pyoderma, perform bacterial culture and sensitivity to examine for possible bacterial resistance to the antibiotic.

METHICILLIN-RESISTANT STAPHYLOCOCCAL SKIN INFECTIONS

Recently, methicillin-resistant staphylococci have been isolated from the skin of dogs with pyoderma. Typically, dogs have had recurrent skin infections and have been treated repeatedly with antibiotics. Response to empirical antibiotic therapy is poor or only partial. Bacterial culture reveals methicillin resistance (equivalent to, and reported as, oxacillin resistance). Antibiotic selection is based on susceptibility results. Be aware that regardless of the apparent in vitro susceptibility of methicillin-resistant strains of staphylococci, they should be regarded as resistant to all B-lactam and cephalosporin antibiotics.

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Chapter 39

Mycobacteriosis

Andrew Hillier / Alan C. Mundell

Mycobacteria are gram-positive organisms that cause sporadic disease in human beings and in animals. All mycobacterial organisms contain a lipid-rich cell wall that inhibits host defense mechanisms and imparts a characteristic staining property in the laboratory. This staining property involves the retention of carbolfuchsin after acid and alcohol decolorization. Thus mycobacteria are classified as acid-fast staining organisms.

Recently, a new conceptual framework for classification of mycobacterial infections of dogs and cats was proposed. This classification takes into account the mammalian host, the infecting bacteria, and the environment. Consideration of mycobacterial infections within this framework provides the clinician with important information for diagnosis, treatment, and prevention. The categories of mycobacterial diseases as they relate to skin disease specifically are as follows:

1. Diseases caused by obligate mycobacterial organisms (e.g., feline leprosy syndromes)
2. Localized disease caused by saprophytic mycobacteria in immunocompetent hosts
   a. Where the infection is self-limiting and the immune response eventually eliminates the organisms (e.g., canine leproid granuloma syndrome)
   b. Where the infection remains localized but requires intervention for cure (e.g., panniculitis syndromes, caused by rapidly growing mycobacteria, and *Mycobacterium avium* complex infections)
3. Disseminated disease caused by mycobacteria in immunodeficient hosts

FELINE LEPROSY SYNDROMES

Feline leprosy is a mycobacterial disease of cats that was first recognized in Australia during the early 1960s. The condition has since been identified in New Zealand, Great Britain, France, the Netherlands, and the west coast of the United States and Canada. The disease is usually confined to cats living in coastal areas.

Feline leprosy refers to mycobacterial disease in which single or multiple skin granulomas are present. The granulomas contain large numbers of organisms that cannot be cultured using standard techniques. Until recently, all cases of feline leprosy were thought to be caused by *M. lepraemurium* and to occur in young cats. Recent studies have identified different syndromes of feline leprosy.

Feline Leprosy Caused by Mycobacterium Lepraemurium

Etiology

- Caused by *M. lepraemurium,* the rat leprosy organism. Although the rat leprosy organism had been suspected for many years, it was only in the 1980s that sophisticated culture techniques and biochemical analysis could identify *M. lepraemurium* as the etiologic agent.
- The mode of transmission is unknown, although cats are thought to become infected following bite injuries from infected rats.
- In experimental infections, the incubation period is 2 to 18 months.

Clinical Signs

- Young adult cats are affected, predominantly males living in either suburban or rural environments.
- Lesions are painless, raised, fleshy, freely movable nodules of a few millimeters up to 4 cm in diameter. They may develop rapidly, and some ulcerate when large.
- Nodules are usually multiple (but may be single), tend to initially concentrate in one body region, and may spread to adjacent areas and regional lymph nodes.
- Nodules may occur anywhere on the body, but the head and limbs are more frequently affected. Additionally, lesions may occur on the lips, oral mucosa, tongue, and nasal mucosa. The condition disseminates rarely to the spleen, bone marrow, liver, kidney, lung, or adjacent muscle. Cats with disseminated

disease usually show signs of systemic illness, which are not seen in cats with localized infection.
- Lesions tend to recur following surgical excision.

Diagnosis

- The diagnosis is achieved primarily through histologic evaluation of biopsy samples in conjunction with compatible history, physical examination, cytology, culture, and laboratory animal inoculation findings.
- The differential diagnoses for feline leprosy include atypical mycobacteriosis, tuberculosis, foreign body dermatitis, deep mycotic infections, mycetomas, dermatophyte pseudomycetomas, chronic bacterial infections, eosinophilic granuloma complex, and neoplastic diseases.

History

- History must be compatible with feline leprosy. The cat will typically be young, allowed to roam, and living in a cool, moist, coastal climate.

Cytology

- Cytology of needle aspirates or lesional impression smears reveals mixed inflammatory cells with macrophages and histiocytes containing variable numbers (often many) of acid-fast bacilli (long slender rods). In Diff-Quik–stained preparations, negative-staining organisms are seen within macrophages. Ziehl-Neelsen stain and a modified Fite's stain are the acid-fast stains most commonly used.

Culture

▼ ***Key Point*** Culture of the feline leprosy mycobacterium is difficult because the organism fails to grow on blood agar and standard mycobacterial media (Löwenstein-Jensen and Stonebrink).

- A 1% Ogawa egg yolk medium can be used to grow the organism when incubated under precise temperature and CO_2 conditions. Most commercial laboratories do not perform Ogawa egg yolk medium cultures.

Biopsy

- Biopsy specimens of lesions are fixed in 10% buffered formalin and evaluated histologically, using both hematoxylin-eosin and acid-fast stains (Ziehl-Neelsen and modified Fite's stains). (See Chapter 37 for skin biopsy technique.)
- Histologically, two forms are seen: tuberculoid and lepromatous forms. The tuberculoid form (most common in the United States and Canada) consists primarily of non-encapsulated epithelioid granulomas that are interspersed with neutrophils and surrounded by a zone of lymphocytes with low numbers of organisms. The lepromatous form is composed of sheets of large foamy macrophages that contain large numbers of acid-fast bacilli. The tuberculoid form is associated with a more competent host immune response.

Polymerase Chain Reaction

- Polymerase chain reaction (PCR) amplification of gene fragments from tissue samples provides a rapid and accurate diagnosis and identification of the causative organisms. Fresh (frozen) tissue or freeze-dried tissue is best, although PCR can also be performed on formalin-fixed, paraffin-embedded samples. (PCR for mycobacterial organisms is performed at the School of Veterinary Medicine, University of California, Davis, CA.)

Laboratory Animal Inoculation

- Laboratory animal inoculation is used primarily in research to propagate and investigate the feline leprosy organism. This procedure is of greatest value for differentiating feline leprosy from tuberculosis. Only tuberculosis-producing mycobacteria routinely kill guinea pigs within 6 to 8 weeks after inoculation.

Treatment

Treatment may not be necessary when lesions are small, unobtrusive, and likely to be self-limiting. However, this strategy is seldom effective and is recommended only for lesions that appear to be resolving spontaneously at the time of diagnosis.

▼ ***Key Point*** Surgical excision is the treatment of choice when lesions are limited in number and wide surgical margins can be obtained. However, disease recurrence is common and may require additional surgical intervention and/or medical management. Even then, adjunct antimicrobial therapy starting a few days prior to surgery is recommended.

Clofazimine is an iminophenazine dye with antimycobacterial properties that is suspended in olive oil and packaged in 50- and 100-mg capsules. Although the pharmacokinetics of clofazimine in the cat are unknown, a dosage of 10 mg/kg once daily PO (25–50 mg every 1–2 days), for 6 to 12 weeks past complete clinical resolution appears to be very effective. Wear latex gloves to prevent staining of hands. Clofazimine is not approved by the U.S. Food and Drug Administration (FDA) for animal use.

- Clofazimine may cause a reversible hepatopathy, and regular biochemical monitoring of cats is mandatory. Vomiting and inappetence are strong indications to

reduce the dose and to perform a biochemical evaluation of the patient. Photosensitivity and pitting corneal edema have also been noted in cats.
- Combination therapy is likely to achieve the best results. Clofazimine may be administered with one or more of the following drugs:
  - Rifampicin (10–15 mg/kg once daily)—Beware of hepatopathy
  - Clarithromycin (62.5 mg per cat once daily)—Less commonly associated with side effects and adverse reactions

Prevention

- This is probably best achieved by confining cats to an exclusively indoor environment. Because of the rare and sporadic nature of the disease, it is unlikely that this measure is necessary.
- Avoidance of immunosuppressive drugs while the disease is active may help prevent exacerbation.

Feline Leprosy Caused by Other Mycobacteria

Etiology

- This condition is caused by a new species, likely a fastidious, slow-growing mycobacterium that is yet to be named.
- Recently, a third form of the disease has been described in the western United States and Canada that is caused by *M. visiblis*.

Clinical Signs

- Older cats (>9 years) living in rural areas are affected.
- Generalized nodular skin lesions are typical (a few may start with localized disease). The lesions are similar in appearance to those caused by *M. lepraemurium*, but they do not ulcerate and disease progression is usually protracted over many months.
- As many as 50% of affected cats are feline immunodeficiency virus (FIV) positive.
- *M. visiblis* causes diffuse (rather than nodular) cutaneous disease with widespread dissemination to multiple internal organs. This syndrome has been termed *feline multisystemic granulomatous mycobacteriosis*.

Diagnosis

- Similar to feline leprosy caused by *M. lepraemurium* as described in the previous section.
- Very large numbers of organisms are usually detected on cytology or histopathology with acid-fast staining.
- PCR provides help with identification of the causative organism.
- Perform bloodwork (complete blood count and serum chemistry profile) and check the FIV status of the patient.

Treatment

- Treat the same as described in the previous section for feline leprosy caused by *M. lepraemurium*, although surgical excision is usually not an option due to the typically generalized nature of the disease.
- Affected cats are usually older and have compromised immune systems (e.g., FIV infection), and response to treatment may not be as good.
- Only one reported case of *M. visiblis* infection has been treated, and response to clofazimine and clindamycin resulted in a cure.

CANINE LEPROID GRANULOMA SYNDROME

Etiology

- Canine leproid granuloma syndrome (CGLS) is caused by a novel, fastidious, slow-growing mycobacteria that has yet to be named.
- This organism appears to be different from any other mycobacteria reported to affect humans or animals; thus the public health risk is believed to be minimal.
- It is believed that organisms are inoculated into tissue by biting flies, midges, or mosquitoes.

Clinical Signs

- Short-coated breeds, especially boxers and boxer crosses, are typically affected.
- Single or multiple well-circumscribed nodules that are firm and painless may be present anywhere on the body. However, the head, and especially the dorsal fold of the ear pinna (locations where dogs are bitten by flies) are most often affected.
- Nodules are 2 mm to 5 cm in diameter. Very large lesions may ulcerate and lead to local disfiguration.
- Regional lymph nodes and internal organs are *not* affected, and dogs are not systemically ill.

Diagnosis

- The distribution of lesions (ear pinna) and at-risk breeds (short-coated dogs, especially boxers) are usually strong clues.
- Cytology (fine-needle aspiration) and histopathology (see Chapter 37 for cytology and biopsy technique) usually reveals variable numbers of acid-fast, medium-length bacilli in macrophages and extracellularly.
- Organisms are fastidious and cannot be cultured.
- PCR may help identify this novel mycobacterial species.

Treatment

- Lesions are self-limiting in most cases, and resolution occurs over 1 to 3 months.
- Surgical excision of single lesions is often curative.

- In the case of chronic, non-resolving, and disfiguring lesions, combination antimicrobial therapy is effective. The following drug combinations have been used with success:
  - Rifampicin (10–15 mg/kg PO once daily) and clarithromycin (15–25 mg/kg total daily dose divided and given 2–3 times daily)
  - Rifampicin (10–15 mg/kg PO once daily) and doxycycline (5–10 mg/kg PO twice daily)

Prevention

- Prevent insects from biting dogs by keeping the dog indoors at the time of day of peak insect activity or use fly and insect repellants.

MYCOBACTERIAL PANNICULITIS

Non-tuberculous, non-lepromatous mycobacteria are classified as atypical or opportunistic. These mycobacteria have been placed by Runyon into four groups, depending on laboratory culture properties. Almost all dog and cat atypical mycobacterial skin infections belong to the rapid-growing group IV. These saprophytic, facultative pathogens are ubiquitous in nature and are typically isolated from water and moist soil. Atypical mycobacteriosis is more prevalent in cats than in dogs, with no apparent age, breed, or sex predilection.

Etiology

- *M. fortuitum, M. chelonei, M. smegmatis, M. thermoresistible,* and *M. xenopi* have produced skin lesions in dogs and cats. In the United States, *M. fortuitum* and *M. chelonae* are responsible for most atypical mycobacterial infections.
- Typically, these organisms have low virulence for mammals and, unless there is a breakdown of defense mechanisms, infections remain localized. The infected patient usually mounts a vigorous immune response that may not be sufficient to resolve the infection but usually prevents hematogenous or lymphatic spread of the infection. Widely disseminated disease is only seen in severely immunocompromised patients.
- The organisms have a preference for fat tissue.
- Skin infection follows contamination of traumatized skin, especially bite wounds and deep scratches. Cats are more commonly infected with rapidly growing mycobacteria than dogs are.

Clinical Signs

- Overweight and obese animals tend to be affected. The infection is most typically seen in cats that are allowed outdoors, where they may get into fights or sustain penetrating wounds and have concurrent exposure to mycobacterial organisms from the environment.

Cats

- The inguinal region (fat pad) is most commonly affected; the axilla, flanks and dorsum are less commonly affected. Lesions may spread to the lateral and ventral abdominal wall. Lesions resemble cat-fight abscesses initially (but without the fetid odor and turbid pus). A nodular to plaque-like lesion is visible, and the skin and subcutis become thickened and firm. Punctate ulcers and fistulas with a watery to purulent discharge appear in the affected area. If surgery is performed, wound breakdown and chronic, non-healing wounds persist. Cats may become systemically ill: depression, fever, inappetence, weight loss, pain, and hypercalcemia of granulomatous disease are occasionally noted.

Dogs

- Typically, mycobacterial panniculitis is suspected in dogs with chronic, non-healing wounds that have failed to respond to empirical treatment. Lesions consist of firm to fluctuant nodules that ulcerate, drain, and spread to affect large areas of the panniculus. A few animals may have fever, pain, and discomfort.

Diagnosis

- Perform bacterial culture and histologic evaluation of lesions. The differential diagnosis for cutaneous atypical mycobacteriosis is extensive and includes feline leprosy (in cats only), tuberculosis, foreign body dermatitis, deep mycotic infections, mycetomas, dermatophyte pseudomycetomas, chronic bacterial infections, generalized demodicosis (in dogs primarily), sterile nodular panniculitis, pansteatitis, eosinophilic granuloma complex, and neoplasia.

▼ ***Key Point*** Atypical mycobacterial organisms are difficult to isolate. In all suspected cases, perform cultures, biopsies for histopathology, and cytologic examination of lesional exudates.

History

- History must be compatible with cutaneous atypical mycobacteriosis. A history of trauma to the involved skin site weeks to months before the onset of lesions is not uncommon.

Cytology

- The cytology of lesional impression smears and smears of biopsy tissue consists of mixed inflammatory cells and, occasionally, acid-fast bacilli. (See

Chapter 37 for cytology and biopsy technique.) Cytologic evaluation frequently fails to confirm acid-fast organisms. Ziehl-Neelsen stain and modified Fite's stain are the acid-fast stains most commonly used. An exhaustive search is sometimes necessary to find organisms. Sometimes, organisms may show "beading" or appear as ghosts if they are poorly stained.

Culture

- Culture consists of growing the organism on standard mycobacterial media (Löwenstein-Jensen and Stonebrink) as well as on blood agar.
- Use sterile swab and biopsy techniques to obtain cultures. Notify the laboratory that atypical mycobacteriosis is suspected so that appropriate cultures are performed. Runyon group IV mycobacteria are called rapid growers because colonies appear within 7 days after media inoculation (often there is significant growth after 2–3 days). In contrast, most other mycobacteria are either difficult to culture or require weeks to months to grow. Species identification of the organisms is very important as this may have a significant impact on antimicrobial drug strategies. The MIC (minimum inhibitory concentration) for selected antibiotics should be determined to aid in the selection of antibiotics—this can be performed with the Etest or broth microdilution.

Biopsy

- Handle biopsy samples of lesions similar to those in feline leprosy except that special techniques, such as snap (instant) freezing the formalin-fixed tissue before staining or rapid Ziehl-Neelsen staining, may be necessary to reveal the organisms. Characteristically, fewer acid-fast bacilli are observed in atypical mycobacteriosis than in feline leprosy. Nodular pyogranulomatous dermatitis along with panniculitis is the common histologic pattern. If organisms are found, they are usually located within extracellular lipid vacuoles that are ringed by neutrophils. Besides the paucity of organisms, atypical mycobacteriosis also differs from feline leprosy by the extracellular location of the organisms.

Laboratory Animal Inoculation

- Laboratory animal inoculation is seldom performed. If cultures fail to identify the mycobacterial organism and the possibility of tuberculosis exists, perform guinea pig inoculation.

Treatment

Most reports of successful disease management are anecdotal or involve low numbers of cases. Because the condition naturally waxes and wanes with occasional prolonged periods of remission, carefully assess the success of all treatment options. Clinical remission may be more easily achieved in the dog than in the cat.

- An approach of no therapy may be taken if the disease involves a reasonably small area and the condition does not bother the animal or owner. This is rarely the case. When owners are unwilling to commit to a prolonged course of therapy, allowing the disease to naturally undergo its cycle may be a viable alternative. In time, the skin lesions may become more extensive; however, the disease rarely becomes systemic.
- Surgical excision is most successful for small, easily excised lesions. Obtain wide surgical margins. Unfortunately, surgical site dehiscence is common. Surgical excision without concurrent antimicrobial therapy is not recommended.

▼ ***Key Point*** Surgically debulking the lesions while treating the animal with a prolonged course of an appropriate antibiotic can be very helpful in providing a cure for mycobacterial panniculitis. Surgical excision may be more effective when managing canine lesions. Recent reports indicate increased success when presurgical antimicrobial therapy is administered for 2 to 3 weeks, followed by surgical debulking and then continued antimicrobial therapy until resolution.

- Medical management has been attempted using a variety of drugs. Table 39-1 provides the dosages of the most effective agents. Most of these drugs are not approved by the FDA for use in dogs or cats. In vitro

Table 39-1. SELECTED DRUGS FOR TREATMENT OF CUTANEOUS ATYPICAL MYCOBACTERIOSIS

Drug	Brand Name	Manufacturer	Dosage
Clofazimine	Lamprene	Ciba-Geigy	10 mg/kg PO q24h
Enrofloxacin	Baytril	Bayer	5–15 mg/kg PO q24h (not to be used in cats)
Marbofloxacin	Zeniquin	Pfizer	5.5 mg/kg q24h
Doxycycline	Vibramycin	Pfizer	5–10 mg/kg PO q12h
Amikacin	Amiglyde-V	Fort Dodge	5–7 mg/kg SC, IM q12h
Kanamycin	Kantrim	Fort Dodge	5–7 mg/kg SC, IM q12h
Gentamicin	Gentocin	Schering-Plough	6 mg/kg SC q24h
Clarithromycin			10–15 mg/kg q12h

sensitivity testing may be helpful when selecting a therapeutic agent. However, the clinical response is frequently less than what the sensitivity test suggests.
  - In general, administer medication for 2 to 6 months past clinical cure. If the medication is effective in achieving clinical remission but the lesions return after discontinuing the medication, prolonged or indefinite therapy may be needed.
  - Closely monitor the animal for adverse side effects. This monitoring typically requires periodic blood and urine laboratory evaluation, especially for drugs with known potential toxicities (e.g., aminoglycosides with nephrotoxicity and ototoxicity). It is beyond the scope of this chapter to discuss drug toxicities and the monitoring procedures. However, this information is available in current human and veterinary pharmacology textbooks. A thorough understanding of all drugs administered increases the safety of the therapeutic protocol.
- *M. fortuitum* and *M. chelonae* (more common in the United States) tend to be more resistant—in fact, the only oral antibiotic that has in vitro susceptibility for *M. chelonae* is clarithromycin.
- Whatever antibiotic is selected (based on in vitro susceptibilities), administer the highest possible dose. It is sometimes, best to start on a lower dose and titrate the dose up, always observing and monitoring for side effects and adverse reactions.

Prevention

- This is best achieved by decreasing the likelihood of traumatic injury to the skin and subcutaneous tissue. If animals are allowed to roam freely, confining them to a house or yard may decrease the likelihood of trauma. However, because of the rare and sporadic nature of the disease, these measures are probably unnecessary.
- Avoidance of immunosuppressive drugs may help prevent exacerbation or recurrence of atypical mycobacteriosis.

SUPPLEMENTAL READING

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Chapter 40

Deep Fungal Infections

Amy M. Grooters

Deep "mycotic" infections are caused by a heterogeneous group of fungal and pseudofungal pathogens. Cutaneous and subcutaneous lesions may result from direct inoculation of an opportunistic fungal pathogen via trauma or may represent dermatologic manifestations of a systemic mycosis. Because the organisms that cause systemic mycoses typically exhibit unique morphologic features in tissue, the diagnosis of diseases such as blastomycosis, histoplasmosis, cryptococcosis, and coccidioidomycosis can often be made by histologic or cytologic identification of the pathogen in biopsy specimens or exudates (see Chapter 20). In contrast, specific identification of the less familiar opportunistic fungal pathogens that typically cause infection via wound contamination is not usually possible without culture. Despite this fact, opportunistic fungal pathogens can often be placed in a general category based on their morphologic features in tissue (such as pigmentation, hyphal diameter, and septation) and the inflammatory response that they induce. These categories include the following:

- Phaeohyphomycosis (pigmented hyphal forms)
- Hyalohyphomycosis (unpigmented hyphal forms)
- Eumycotic mycetoma (fibrosing granuloma with tissue grains containing pigmented or unpigmented fungal elements)
- Pythiosis, lagenidiosis, or zygomycosis (pyogranulomatous and eosinophilic inflammation associated with wide, infrequently septate, unpigmented hyphae)

A list of the pathogens discussed in this chapter and their categorization is found in Table 40-1.

DIAGNOSTIC APPROACH FOR DEEP MYCOSES

Dogs and cats with deep fungal infections are typically presented with dermal or subcutaneous nodules (with or without ulceration) and/or draining tracts. In addition to fungal infection, differential diagnoses for such lesions include bacterial infections (e.g., actinomycosis, nocardiosis, mycobacteriosis, and furunculosis), protozoal infections (e.g., leishmaniasis), neoplastic lesions (e.g., cutaneous lymphoma, cutaneous histiocytosis, and disseminated histiocytic sarcoma), foreign body reaction, and sterile nodular dermatoses (e.g., sterile pyogranuloma syndrome and idiopathic panniculitis). Phaeohyphomycosis and melanoma should be suspected when lesions are visibly pigmented. The presence of granules or grains in exudate is suggestive of actinomycosis, nocardiosis, actinobacillosis, and eumycotic mycetoma.

Cytology

Cytologic examination is often the quickest and least expensive tool for either making a definitive diagnosis or categorizing diseases that cause nodules and draining tracts. Fine-needle aspirates of cutaneous nodules or enlarged lymph nodes, direct smears of exudate, or impression smears of ulcerated lesions often contain infectious organisms in animals with blastomycosis, cryptococcosis, histoplasmosis, or rhinosporidiosis and in cats with sporotrichosis. In other types of deep fungal infections, organisms are variably present in cytologic specimens.

Biopsy

Lesion biopsy for histopathology and culture should be pursued when a definitive diagnosis cannot be established cytologically. When possible, obtain multiple biopsies of representative lesions (including both draining and intact nodules) and include normal tissue at the margin of the biopsy sample.

▼ ***Key Point*** Wedge biopsies are preferred to punch biopsies for the diagnosis of deep fungal infections.

In most cases, tissue biopsies should be submitted for bacterial (aerobic and anaerobic), mycobacterial, and fungal cultures and should be shipped at ambient temperature to arrive at the laboratory within 24 hours of collection. When unusual pathogens are suspected, it is helpful to contact the laboratory prior to collecting and shipping the samples. For additional information on diagnostic skin biopsy techniques, see Chapter 37.

Table 40-1. DEEP CUTANEOUS MYCOSES OF DOGS AND CATS

Disease	Causative Agents	Histologic/Cytologic Characteristics
Pythiosis	*Pythium insidiosum*	Pyogranulomatous and eosinophilic inflammation associated with broad (2–7 µ), infrequently septate hyphae
Lagenidiosis	*Lagenidium* spp.	Pyogranulomatous and eosinophilic inflammation associated with broad (4–25 µ), infrequently septate hyphae
Zygomycosis	*Basidiobolus ranarum, Conidiobolus* spp.	Pyogranulomatous and eosinophilic inflammation associated with broad (5–20 µ), infrequently septate hyphae
Sporotrichosis	*Sporothrix schenckii*	Pyogranulomatous inflammation associated with round, oval, or cigar-shaped yeast forms, 5–9 µ long, within macrophages or extracellular
Rhinosporidiosis	*Rhinosporidium seeberi*	Mixed inflammatory response associated with large (300 µ) sporangia that contain many endospores; released endospores often visible in cytologic samples
Candidiasis	*Candida albicans,* other *Candida* spp.	Suppurative inflammation associated with numerous oval yeasts 2–6 µ), pseudohyphae (chains of oval yeast cells), and true hyphae
Phaeohyphomycosis	*Alternaria, Bipolaris, Cladophialophora* (previously *Cladosporium*), *Curvularia, Exophiala, Fonsecaea, Moniliella, Phialophora, Ramichloridium,* and *Scolecobasidium,* among others	Pyogranulomatous inflammation associated with pigmented, irregularly septate hyphae or yeast-like cells that may be solitary or cluster in small groups or chains
Hyalohyphomycosis	*Acremonium, Fusarium, Geotrichum, Paecilomyces, Pseudallescheria,* and *Scedosporium,* among others	Pyogranulomatous inflammation associated with hyphal elements that have hyaline (transparent, non-pigmented) walls
Mycetoma (black grain)	*Curvularia*	Pyogranulomatous inflammation associated with pigmented tissue grains (which represent aggregates of fungal organisms)
Mycetoma (white grain)	*Pseudallescheria boydii, Acremonium*	Pyogranulomatous inflammation associated with non-pigmented tissue grains (which represent aggregates of fungal organisms)
Blastomycosis	*Blastomyces dermatiditis*	Suppurative to pyogranulomatous inflammation associated with large (8–15 µ), spherical, thick-walled, broad-based budding yeasts
Cryptococcosis	*Cryptococcus neoformans*	Granulomatous inflammation (may be minimal) associated with pleomorphic, narrow-based budding yeasts (3–7 µ) surrounded by a variably thick (1–30 µ) polysaccharide capsule
Histoplasmosis	*Histoplasma capsulatum*	Granulomatous inflammation associated with intracellular, round to oval yeast cells (2–4 µ) characterized by a basophilic center and clear halo
Coccidioidomycosis	*Coccidioides immitis*	Pyogranulomatous inflammation associated with large (20–200 µ), round, thick-walled spherules that at maturity contain many small (2–5 µ) endospores
Aspergillosis	*Aspergillus terreus, A. deflectus, A. flavipes, A. fumigatus*	Suppurative to granulomatous inflammation associated with multiple, non-pigmented, septate hyphae (3–6 µ) with parallel walls and 45-degree angle branching

Other Diagnostics

Additional diagnostic tests that may help further characterize deep fungal infections (and determine involvement of other organ systems) include a complete blood count, chemistry panel, urinalysis, and thoracic radiographs. Although serologic testing may help establish a diagnosis for some mycoses (such as cryptococcosis, blastomycosis, coccidioidomycosis, and pythiosis), in general, a diagnosis of deep fungal infection should not be based on serology results alone.

PYTHIOSIS

Pythiosis, lagenidiosis, and zygomycosis are caused by a taxonomically diverse group of pathogens but share similar clinical and histologic characteristics. Because of these similarities, they have previously been grouped under the now-obsolete term *phycomycosis.*

Etiology

Pythium insidiosum is an aquatic pathogen in the class oomycetes. *Pythium* species and other oomycetes differ from true fungi in producing motile, flagellate zoospores; having cell walls that contain cellulose and beta-glucan but not chitin; and having cell membranes that generally lack ergosterol.

- The infective stage of *P. insidiosum* is thought to be the biflagellate aquatic zoospore, which is released into warm water environments and likely causes infection by encysting in damaged skin or gastrointestinal (GI) mucosa.

- In the United States, pythiosis is most common in the Gulf Coast states but has been recognized in animals living in New Jersey, Virginia, Kentucky, Tennessee, southern Illinois, southern Indiana, Oklahoma, Missouri, and Kansas. Recently, a number of cases of GI pythiosis have been confirmed in dogs living in Arizona and northern California.
- Pythiosis occurs most often in young, large-breed, male dogs (especially outdoor working breeds such as Labrador retrievers). Affected dogs are most frequently presented to the veterinarian between October and March and often have a history of recurrent exposure to lakes or ponds.
- In cats, specific breed and sex predilections have not been observed in the few cases that have been reported to date. However, of 13 cats with cutaneous pythiosis diagnosed through my laboratory since 1999, 8 were less than 10 months old, with an age range of 4 months to 9 years.

Clinical Signs

The two forms of pythiosis are cutaneous and GI, depending on the route of infection. Both forms are rarely found concurrently in the same patient.

Cutaneous Pythiosis

Cutaneous pythiosis causes non-healing wounds and invasive masses that contain ulcerated nodules and draining tracts.

- Infected dogs often have solitary or multiple cutaneous or subcutaneous lesions involving the extremities, tail-head, ventral neck, perineum, or lateral thorax.
- In cats, lesions include subcutaneous masses in the inguinal, tail-head, or periorbital regions, draining nodular lesions or ulcerated lesions on the extremities, and nasopharyngeal lesions associated with retrobulbar masses.

Gastrointestinal Pythiosis

GI pythiosis in dogs is characterized by severe segmental thickening of the stomach, small intestine, colon, rectum, or, rarely, esophagus or pharyngeal region (see Chapter 69). The gastric outflow area, duodenum, and ileocolic junction are the most frequently affected portions of the GI tract, and it is not uncommon to find two or more segmental lesions in the same patient.

- Mesenteric lymphadenomegaly due to reactive hyperplasia is common.
- Involvement of the mesenteric root may form a single large, firm mass in the midabdomen.
- Extension of disease into mesenteric vessels may result in bowel ischemia, infarction, perforation, or acute hemoabdomen.
- Clinical signs associated with GI pythiosis include weight loss, vomiting, diarrhea, and/or hematochezia. Physical examination often reveals thin body condition and a palpable abdominal mass. Signs of systemic illness are usually absent unless intestinal obstruction or infarction occurs.

Diagnosis

Histopathology and Cytology

Pythiosis causes pyogranulomatous and eosinophilic inflammation associated with broad (mean, 4 μ; range, 2–7 μ), infrequently septate hyphae that are not well visualized on H&E-stained sections but are readily detected with a Gomori methenamine silver (GMS) stain. Because these same general features are associated with lagenidiosis and zygomycosis, a histologic diagnosis of pythiosis should be confirmed with culture, serology, polymerase chain reaction (PCR), or immunohistochemical staining of tissue sections with polyclonal antibodies specific for *P. insidiosum*.

- In animals with suspected cutaneous pythiosis, obtain wedge biopsies rather than punch biopsies to adequately reach infected tissues.
- Similarly, because inflammation in GI pythiosis centers on the submucosal and muscular layers rather than the mucosa and lamina propria, surgical biopsies are more likely to detect hyphae than are endoscopic biopsies. Therefore, consider pythiosis when endoscopic biopsies reveal eosinophilic or pyogranulomatous inflammation without identification of an etiologic agent.
- Cytologic examination of exudate associated with cutaneous pythiosis often reveals pyogranulomatous and eosinophilic inflammation but rarely reveals hyphae.

Culture

For best results, ship unrefrigerated tissue samples wrapped in a sterile, saline-moistened gauze sponge overnight at ambient temperature to a laboratory that has experience with the isolation of pathogenic oomycetes. Because *P. insidiosum* isolates rarely produce sexual reproductive structures in the laboratory, identification should be based on specific PCR amplification or ribosomal RNA gene sequencing whenever possible.

Serology

▼ ***Key Point*** Detection of anti–*P. insidiosum* antibodies in canine serum using either enzyme-linked immunosorbent assay (ELISA) or immunoblot techniques has high sensitivity and specificity for the diagnosis of pythiosis.

- Although these techniques have only been evaluated in a small number of cats, they appear to have high diagnostic accuracy for feline pythiosis.
- In addition to providing a means for early, non-invasive diagnosis, the ELISA is also useful for monitoring response to therapy in affected patients. Recheck *P. insidiosum* serology 2 months after surgical resection of infected tissues or every 3 months in animals receiving medical therapy for non-resectable lesions.
- Veterinarians interested in submitting diagnostic samples for serology or culture from animals with suspected pythiosis, lagenidiosis, or zygomycosis should contact Dr. Grooters at 225-578-9600.

Treatment

▼ ***Key Point*** Complete surgical resection of infected tissues provides the best opportunity for cure of pythiosis.

Surgical Resection

- Pursue aggressive surgical resection of pythiosis lesions whenever feasible. If cutaneous lesions are limited to a single distal extremity, recommend amputation.
- In animals with GI pythiosis, resect segmental lesions with a minimum of 3-cm margins if possible. The presence of non-resectable mesenteric lymphadenomegaly (which is more often due to reactive hyperplasia than infection) should not dissuade the surgeon from pursuing complete resection of a segmental bowel lesion. In this situation, biopsy enlarged lymph nodes for prognostic information.

Postoperative Medical Therapy

- Because local postoperative recurrence of pythiosis is common, administer itraconazole (10 mg/kg PO q24hr) and terbinafine (5–10 mg/kg PO q24hr) for at least 2 months after surgery (see Chapter 20 for more information on these drugs).
- To monitor for recurrence, perform ELISA serology prior to and 2 months after surgery. In animals that have had a complete surgical resection and go on to have no recurrence of disease, serum antibody levels drop significantly within 2 months of surgery.

Medical Therapy without Surgery

- Medical therapy is usually unsuccessful in animals with non-resectable pythiosis. However, clinical and serologic cures have been obtained in a small number of *P. insidiosum*–infected dogs treated with a itraconazole and terbinafine and rarely in dogs treated with amphotericin B lipid complex (2–3 mg/kg 3 times weekly to cumulative dose of 24–27 mg/kg) (see Chapter 20 for more information on these drugs).
- A vaccine derived from *P. insidiosum* antigens has been utilized with good success in the treatment of pythiosis causing cutaneous granulomas in horses and vasculitis in humans but has not been documented to have efficacy in small animals and, in my experience, is rarely associated with any clinical improvement in dogs or cats.

LAGENIDIOSIS

Until recently, *P. insidiosum* was considered the only mammalian pathogen in the class oomycetes. However, in 1999, a pathogenic oomycete in the genus *Lagenidium* was identified as a cause of severe multifocal cutaneous lesions and regional lymphadenomegaly in a dog. Since that time, more than 40 dogs with serologic, histologic, and/or culture evidence of *Lagenidium* species infection have been identified.

Etiology

The epidemiologic and clinicopathologic features of lagenidiosis are similar in many respects to those that have previously been associated with cutaneous pythiosis. Affected animals are typically young to middle-aged large-breed dogs living in the southeastern United States. Although most of these dogs have been from Florida or Louisiana, cases in Texas, Tennessee, Virginia, and Indiana have been identified as well. A number of infected dogs have had frequent exposure to lakes or ponds.

Clinical Signs

Dogs with lagenidiosis are usually presented with progressive cutaneous or subcutaneous lesions (often multifocal) involving the extremities, mammary region, perineum, or trunk. Grossly, these lesions appear as firm dermal or subcutaneous nodules or as ulcerated, thickened, edematous areas with regions of necrosis and numerous draining tracts.

Regional lymphadenopathy is often present and may occur in the absence of cutaneous disease. Inguinal and sublumbar lymph node involvement is common in dogs with hind-limb lesions.

▼ ***Key Point*** In contrast to pythiosis, the majority of dogs with lagenidiosis have been found to have lesions in distant sites, including caudal vena cava, aorta, sublumbar and inguinal lymph nodes, lung, pulmonary hilus, and cranial mediastinum.

Dogs with caval lesions or sublumbar and inguinal lymph node involvement may be presented with hind-limb edema. Warn owners that sudden death may result from acute rupture of an occult great-vessel lesion, even in dogs without clinically apparent systemic disease.

Diagnosis

Biopsy and Cytology

Lagenidiosis causes pyogranulomatous and eosinophilic inflammation associated with broad, infrequently septate hyphae that may be visualized on H&E-stained sections but are more easily detected with a GMS stain. *Lagenidium* hyphae vary in size but in general are larger than *P. insidiosum* hyphae, ranging from 4 to 25 µm in diameter, with an average of 12 µm.

Cytologic examination of lymph node aspirates or exudate from draining tracts may reveal pyogranulomatous to eosinophilic inflammation with or without broad, poorly septate hyphal elements.

Serology

Immunoblot serology for the detection of anti-*Lagenidium* antibodies in canine serum can provide a presumptive diagnosis of lagenidiosis but must be interpreted in conjunction with results of serologic testing for *P. insidiosum* infection because of the potential for crossreactivity in serum from dogs with pythiosis. Do not use serology alone to make a diagnosis of lagenidiosis; instead, interpret serology in conjunction with histologic findings.

Culture

The definitive diagnosis of lagenidiosis is best made by culture of infected tissue by a laboratory experienced with the isolation of pathogenic oomycetes. Ship unrefrigerated tissue wrapped in a sterile, saline-moistened gauze sponge to arrive within 24 hours. Because of the current limitations associated with morphologic characterization of this pathogen, identify *Lagenidium* spp. based on ribosomal RNA gene sequencing or specific PCR amplification.

Treatment

In general, the prognosis for dogs with lagenidiosis is grave.

Surgical Resection

Aggressive surgical resection of infected tissues is the treatment of choice for lagenidiosis. In animals with lesions limited to a single distal extremity, recommend amputation. In those with cutaneous or subcutaneous lesions in other areas of the body, pursue aggressive resection with wide margins. Prior to attempting surgical resection of cutaneous lesions, perform radiographic imaging of the chest and abdomen and sonographic imaging of the abdomen to determine the extent of disease. Unfortunately, most *Lagenidium*-infected dogs have non-resectable disease in regional lymph nodes or distant sites by the time the diagnosis is made.

Medical Therapy

Medical therapy for lagenidiosis is typically ineffective. However, a combination of itraconazole with terbinafine (see Chapter 20), along with aggressive surgical resection, was effective in resolving *Lagenidium* spp. infection in two dogs with multifocal cutaneous lesions but no systemic lesions.

ZYGOMYCOSIS

The term *zygomycosis* refers to infections caused by fungi in the class zygomycetes, including the genera *Basidiobolus* and *Conidiobolus* in the order entomophthorales, and the genera *Rhizopus, Absidia, Mucor,* and others in the order mucorales. Infections caused by the mucorales have not been well documented in small animal patients. However, in dogs, *Basidiobolus* spp. and *Conidiobolus* spp. have been reported to cause cutaneous lesions that are grossly and histologically similar to those caused by *P. insidiosum* and *Lagenidium* spp. In addition, *Conidiobolus* spp. can infect the canine respiratory tract.

Etiology and Epidemiology

Basidiobolus ranarum, Conidiobolus coronatus, C. incongruus, and *C. lamprauges* are saprophytes that are widely distributed in nature. Cutaneous infection with *Basidiobolus ranarum* or *Conidiobolus* spp. likely occurs by percutaneous inoculation of spores via minor trauma or insect bites. Infection may also result from inhalation or ingestion of spores.

Clinical Signs

Conidiobolomycosis

Conidiobolomycosis occurs most often as a nasopharyngeal infection with or without involvement of tissues of the face, retropharyngeal region, and retrobulbar space. Infected animals may present with signs of chronic nasal cavity disease, ulcerative dermatitis of the nasal planum, or ulcerative lesions of the hard palate. *Conidiobolus* infection may also cause multifocal nodular draining subcutaneous lesions and regional lymphadenomegaly.

Basidiobolomycosis

Basidiobolomycosis is a rare cause of ulcerative draining skin lesions in dogs and has also been reported in a single case as a cause of tracheobronchitis. Disseminated *Basidiobolus* spp. infection involving the GI tract and other abdominal organs has been described in two dogs.

Diagnosis

The histologic features of zygomycosis (pyogranulomatous to eosinophilic inflammation associated with wide,

poorly septate hyphae) are similar to those associated with pythiosis and lagenidiosis. Hyphal diameter tends to be significantly larger for *Basidiobolus* spp. (mean 9 µ; range, 5–20 µ) and *Conidiobolus* spp. (mean 8 µ; range, 5–13 µ) than for *P. insidiosum*. Because serologic and immunohistochemical techniques are not currently available for the diagnosis of conidiobolomycosis and basidiobolomycosis, definitive diagnosis must be based on isolation of the pathogen from infected tissues.

Treatment

- For focal cutaneous lesions, perform aggressive surgical resection and follow with 2 to 3 months of itraconazole administered orally at a dosage from 5 to 10 mg/kg q24hr (see Chapter 20 for more information on this drug).
- For non-resectable lesions, treat with either itraconazole for 3 to 6 months or amphotericin B lipid complex (see Chapter 20). Monitor closely for signs of recurrence after discontinuation of medical therapy.
- For focal cutaneous lesions that can be completely resected, the long-term prognosis is good.
- For non-resectable lesions and those involving regional lymph nodes, the prognosis is guarded.

SPOROTRICHOSIS

Etiology

Sporotrichosis is caused by the dimorphic fungus *Sporothrix schenckii,* which exists as a yeast in tissue (37°C) but as mold in the environment and in the laboratory from 25°C to 30°C. The organism is a saprophyte typically found in organically rich soils, decaying vegetation, or other organic materials such as sphagnum moss and hay. Infection occurs by direct inoculation of the fungus into tissues, often through puncture wounds associated with thorns or splinters in dogs or through claw wounds in cats.

Although sporadic outbreaks involving significant numbers of animals have been reported, in general, sporotrichosis is uncommon in cats and rare in dogs. It is most often diagnosed in outdoor, roaming male cats and hunting dogs, presumably because of their increased risk for puncture wounds.

Clinical Signs

Sporotrichosis in dogs and cats is manifested as cutaneous, cutaneolymphatic, or disseminated disease. The cutaneous and cutaneolymphatic forms are most common and may be present concurrently. The disseminated form is extremely rare in dogs, but infected cats often have evidence of internal organ or lymphatic infection at necropsy, even when lesions clinically appeared to be limited to cutaneous and subcutaneous tissues. In addition, there is recent evidence that hematogenous dissemination of sporotrichosis may occur in as many as a third of infected cats.

Canine Sporotrichosis

Dogs with the cutaneous form of sporotrichosis are typically presented with multiple firm dermal or subcutaneous nodules on the head or trunk. These nodules may ulcerate, drain a purulent exudate, and become crusted. The cutaneolymphatic form is characterized in dogs by the formation of nodules on a distal limb, followed by proximal ascension of infection through lymphatic vessels with subsequent development of secondary nodules, draining tracts, and regional lymphadenopathy.

Feline Sporotrichosis

Infected cats may initially be presented with abscesses, cellulitis, or draining puncture wounds that resemble routine bacterial fight wound infections but fail to respond to antibiotic therapy. Cutaneous lesions are most often found on the head (especially nose and face), distal limbs, or tail-head region. They generally appear as subcutaneous nodules that ulcerate to form draining tracts and crusted nodules and may progress to form large, coalescing exudative ulcers and crusting lesions. Extensive areas of necrosis may develop, exposing underlying muscle and bone. Regional lymphadenopathy may be present.

▼ ***Key Point*** Because of the high numbers of *Sporothrix* organisms typically present in exudates from cat lesions, people handling infected cats are at risk for acquiring sporotrichosis. Always wear gloves when handling cats with ulcerative cutaneous lesions or draining nodules, and take precautions when handling cytology and culture specimens.

Diagnosis

Suspect sporotrichosis in cats with presumed fight wound abscesses that do not respond to appropriate antibacterial therapy.

Cytology

Cytologic examination of exudates will often demonstrate *S. schenckii* in lesions from infected cats but will demonstrate it only infrequently from infected dogs, in which lesions typically contain low numbers of organisms. The use of a fungal stain such as GMS or PAS (periodic acid-Schiff) may assist in identification of the organisms, which appear as round, oval, or cigar-shaped yeast forms, 5 to 9 µ long, found either within macrophages or extracellularly.

Biopsy

Histologically, sporotrichosis is characterized by nodular to diffuse pyogranulomatous inflammation. When possible, submit biopsy samples from intact nodules. Organisms are usually numerous and easily identified in lesions from cats but are difficult to find in canine lesions, often necessitating the careful examination of multiple GMS or PAS-stained sections for detection of the pathogen.

Culture

For culture of *S. schenckii,* submit exudate obtained from deep in a draining tract for culture on routine fungal media. In addition (especially for dogs), submit a surgically obtained tissue sample to be macerated prior to culture.

Treatment

- The treatment of choice for sporotrichosis in the dog and cat is itraconazole administered orally at a dosage from 5 to 10 mg/kg once daily until 30 days beyond complete resolution of detectable lesions (see Chapter 20 for more information on this drug).
- Oral administration of a supersaturated solution of potassium iodide (40 mg/kg q12hr with food for dogs and 20 mg/kg q12–24hr with food for cats) is often effective but is more likely than itraconazole to cause adverse effects (especially in cats).
- Terbinafine has been shown to be effective for the treatment of cutaneous and lymphocutaneous sporotrichosis in human patients but has not been well evaluated for this use in dogs or cats.

RHINOSPORIDIOSIS

Rhinosporidiosis is caused by *Rhinosporidium seeberi,* a member of a novel group of protists recently designated as the class mesomycetozoea. The disease occurs most commonly in India, southeast Asia, east Africa, and tropical regions of South America. It is rare in the United States, occurring sporadically in large-breed male dogs from southern states. It has not been described in cats.

Infection is likely associated with trauma to a mucosal surface followed by exposure to stagnant water. The infective form of *Rhinosporidium* is a small, round endospore that proliferates in epithelial tissue to form large (300 µ) sporangia, within which develop thousands of endospores that are released when the sporangial wall ruptures.

Clinical Signs

Infected dogs have signs of nasal cavity disease, including sneezing, unilateral nasal discharge, and epistaxis. Single or multiple red to gray polyps are present within the rostral nasal cavity and may be observed protruding from the nares. Sporangia on the surface of the polyps may be visualized as small, white spots.

Diagnosis

The identification of *Rhinosporidium* endospores is often possible during cytologic examination of exudate, nasal swabs, or impression smears of polypoid tissue. Histologic examination of a resected polyp should also provide a straightforward diagnosis through visualization of sporangia and endospores.

Treatment

Surgical resection is the treatment of choice for rhinosporidiosis, but lesions may recur. Despite sporadic reports of response to dapsone or ketoconazole, in general, rhinosporidiosis is poorly responsive to medical therapy.

CANDIDIASIS

Candida spp. are commensal yeasts that normally inhabit the oral cavity, GI tract, upper respiratory system, and genital mucosa of mammals. Cutaneous lesions associated with candidal infection are uncommon in dogs and rare in cats. When present, they represent either local proliferation of the organism or manifestation of disseminated disease.

Potential risk factors for the development of candidiasis include prolonged antibiotic therapy; immunosuppression due to persistent chemotherapy-induced neutropenia, long-term glucocorticoid therapy, hyperadrenocorticism, or diabetes mellitus; and damage to normal cutaneous or mucosal barriers, such as surgical wounds or indwelling vascular or urinary catheters.

Clinical Signs

Localized candidiasis causes non-healing, erythematous, oozing lesions involving mucous membranes, mucocutaneous junctions, and persistently moist regions of skin, such as skin folds, interdigital areas, and nail beds. Lesions on mucous membranes are typically moist ulcers that are surrounded by a hyperemic margin and may be covered by a whitish plaque. Skin lesions may initially appear as pustular lesions that progress to exudative or crusting ulcerated plaques.

Diagnosis

Cytologic and histologic examination of lesions shows suppurative inflammation associated with numerous 2- to 6-µ, oval yeasts, pseudohyphae (chains of oval yeast cells), and true hyphae. *Candida* species can be isolated on routine fungal media, and their identification based on morphologic and metabolic features is fairly straightforward. However, positive culture results are only sig-

nificant in conjunction with histologic demonstration of tissue invasion.

Treatment

Treatment of localized candidiasis consists of removing risk factors (if possible), clipping and drying affected areas of skin, and performing topical antifungal therapy (nystatin, miconazole, or clotrimazole).

PHAEOHYPHOMYCOSIS

Etiology

The term *phaeohyphomycosis* refers to cutaneous, subcutaneous, cerebral, or disseminated infections caused by dematiaceous (pigmented) filamentous fungi that contain melanin in their cell walls. Infection is thought to be the result of traumatic implantation of fungal elements, which leads to chronic granulomatous inflammation.

Fungal genera that have been identified as agents of phaeohyphomycosis in veterinary patients include *Alternaria, Bipolaris, Cladophialophora* (previously *Xylohypha* or *Cladosporium*), *Curvularia, Exophiala, Fonsecaea, Moniliella, Phialophora, Ramichloridium,* and *Scolecobasidium,* among others.

Clinical Signs

▼ ***Key Point*** Cutaneous or nasal lesions in cats are the most common clinical presentations for phaeohyphomycosis in small animals.

Patients are presented with ulcerated cutaneous nodules, upper respiratory signs, and/or a visible nasal mass. Infected tissues may appear grossly pigmented.

Diagnosis

In H&E-stained tissue sections, fungi that cause phaeohyphomycosis appear as dark-walled, irregularly septate hyphae or as yeast-like cells, solitary or in small groups or chains. The presence of melanin in the walls of lightly pigmented hyphae can be confirmed by the examination of unstained sections or the use of a Masson-Fontana stain for melanin.

Treatment

Because response of phaeohyphomycosis to medical therapy is variable, aggressive surgical removal of the lesion is the treatment of choice. Clinical response to either itraconazole or amphotericin B has been reported in cats with cutaneous phaeohyphomycosis, but relapse is common following either surgical or medical therapy.

HYALOHYPHOMYCOSIS

Etiology

The term *hyalohyphomycosis* refers to infections caused by non-pigmented fungi, or those that in tissue form hyphal elements that have hyaline (clear or transparent) walls. By convention, this term is not applied to infections caused by hyaline fungi in the genera *Aspergillus* or *Penicillium* or in the class zygomycetes. Genera that have been described as causing hyalohyphomycosis in veterinary patients include *Acremonium, Fusarium, Geotrichum, Paecilomyces, Pseudallescheria,* and *Scedosporium,* among others. In general, hyalohyphomycosis is less frequently encountered in small animal patients than is phaeohyphomycosis.

Clinical Signs

Infected animals present with lesions ranging from local disease confined to the skin, nasal mucosa, or cornea to disseminated disease in the lungs, bone marrow, lymph nodes, central nervous system, kidneys, liver, spleen, and bones.

Treatment

Surgical removal of the lesion (if feasible) is the treatment of choice for localized hyalohyphomycosis, but warn owners that recurrence or dissemination is likely and recommend postoperative medical therapy with itraconazole or amphotericin B (see Chapter 20).

MYCETOMA

Etiology and Clinical Signs

The term *mycetoma* refers to localized, mass-like, mycotic or actinomycotic infections of the skin, subcutaneous tissue, muscle, or bone that are characterized by the presence of colonies or aggregates of organisms that form "grains" in tissue. Actinomycotic mycetomas are caused by bacteria such as *Actinomyces* spp. and *Nocardia* spp., whereas eumycotic mycetomas are caused by fungi. Lesions result from traumatic implantation of soil organisms into tissue, resulting in chronic pyogranulomatous inflammation and abscessation.

The grains or granules associated with eumycotic mycetomas are characteristically pigmented (black-grain mycetoma, caused by dematiaceous fungi) or hyaline (white-grain mycetoma, caused by non-dematiaceous fungi), depending on the type of fungal pathogen involved.

Black-grain mycetomas are most often caused by *Curvularia* spp., and typically result in the development of chronic non-healing wounds and cutaneous nodules on the extremities. Lesions often develop weeks to months after a traumatic incident in the same area.

Draining sinus tracts are often present, and black grains may be observed in the exudate. Extension of disease through muscle or fascial planes into underlying bone may occur.

White-grain mycetomas, usually caused by *Pseudallescheria boydii* or *Acremonium* spp., are most often manifested as body wall and/or intra-abdominal granulomas that develop subsequent to contamination following surgical wound dehiscence. Affected dogs may be presented with a draining mass on the body wall or may develop clinical signs of peritonitis.

Treatment

The treatment of choice for eumycotic mycetoma is aggressive surgical excision of infected tissues, including amputation if clinically indicated. Response to medical therapy is routinely poor. Dissemination of eumycotic mycetoma beyond local tissues is rare.

DERMATOLOGIC LESIONS IN SYSTEMIC MYCOSES

Refer to Chapter 20 for information regarding the etiology, systemic manifestations, diagnosis, and treatment of systemic mycoses.

Blastomycosis

Because direct inoculation of *Blastomyces* organisms into the skin is rare (and only well documented in situations such as necropsy or laboratory accidents), cutaneous lesions in animals with blastomycosis should be considered signs of disseminated disease, even when obvious pulmonary lesions are absent.

Clinical Signs

Cutaneous lesions are present in 20% to 40% of infected dogs and, although they can be present on any part of the body, are most often found on the face, nasal planum, and nail beds. Skin lesions are often proliferative and ulcerated, draining a serosanguineous or purulent exudate. However, discreet subcutaneous abscesses may also occur.

Cutaneous lesions appear to be common in cats with blastomycosis, and localized cutaneous infection may occur more often in this species.

Diagnosis

The diagnosis of blastomycosis is most often made by identification of the organism on cytologic examination of draining exudates or tissue aspirates or on histologic examination. In more than half of infected dogs, organisms can be identified in cytologic specimens obtained from either cutaneous lesions or enlarged lymph nodes.

Cryptococcosis

Cutaneous lesions are common in cats with cryptococcosis and have been described in nearly half of reported cases. Dermal lesions (which are often multifocal) include small, firm papules or nodules that may enlarge and ulcerate, producing a serous or mucoid exudate. The head (especially around the nares) is a common location for dermal lesions, and a firm, subcutaneous swelling over the bridge of the nose is often present.

In dogs with cryptococcosis, cutaneous lesions are usually characterized by ulcerations involving the nose, oral cavity, palate, tongue, lips, or nail beds or by dermal masses involving the face.

Histoplasmosis

Cutaneous lesions are uncommon in animals with histoplasmosis. Those that have been described include dermal and subcutaneous nodules, ulcerated lesions, and fistulous tracts.

Coccidioidomycosis

In dogs with coccidioidomycosis, cutaneous lesions are often found over sites of infected bone and include ulcerated nodules, draining tracts, and subcutaneous abscesses. Infected cats develop similar lesions, but underlying bone involvement is less common.

Primary cutaneous coccidioidomycosis secondary to direct inoculation is rare but has been described, and is usually associated with regional lymphadenopathy.

Aspergillosis

Dermatologic lesions caused by aspergillosis (including cutaneous nodules, abscesses, and draining tracts) have been associated with disseminated disease in dogs (usually German shepherds). Mucocutaneous lesions (including ulceration and crusting of the external nares) may be associated with nasal aspergillosis in dogs.

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Chapter

41 Malassezia Dermatitis

Daniel O. Morris

Malassezia dermatitis (MD) is a superficial fungal (yeast) infection occurring on and within the stratum corneum of the epidermis of many mammalian species. There are several different species of *Malassezia* yeast recognized, and various animals may serve as the natural hosts for specific species of the yeast. For example, most domestic carnivores harbor *Malassezia pachydermatis* as part of their natural cutaneous microflora, while human beings primarily harbor *Malassezia furfur.* As commensal organisms, *Malassezia* yeast colonize the skin in very low numbers. Overt infection is defined by increased numbers of the yeast on the skin surface in conjunction with inflammation. In dogs with atopic dermatitis (AD), *M. pachydermatis* may be recognized by the immune system as an allergen, in which case a highly inflammatory and pruritic response can be mounted to relatively low numbers of yeast organisms, blurring the line between "colonization" and "infection." The role of *M. pachydermatis* in feline dermatitis is less well defined, although it is a known commensal of feline skin as well.

ETIOLOGY

The genus *Malassezia* is now described to consist of nine species: *M. furfur, M. sympodialis, M. globosa, M. obtusa, M. restricta, M. sloofiae, M. equi, M. japonica,* and *M. pachydermatis. Malassezia* yeasts are characterized by a thick, multilayered cell wall and the production of blastoconidia by budding. With *M. pachydermatis,* the budding process imparts the appearance of unshelled peanuts when examined microscopically.

In dogs and cats, *Malassezia* yeast colonize the skin during the immediate perinatal period. Although *M. pachydermatis* is the species most commonly isolated from normal and inflamed skin of dogs and cats, other species are occasionally identified. *M. globosa,* which has a more spherical shape with tiny budding "heads," is sometimes associated with feline ceruminous otitis, but rarely so in dogs. *M. furfur,* which is a commensal of human skin, has been isolated from normal and inflamed canine skin, although its role in true "infection" is unknown; dogs may serve as mechanical carriers only. Other species isolated from normal canine and feline skin include *M. sympodialis* and *M. obtusa.*

PATHOGENESIS

In dogs, cats, and human beings, *Malassezia* yeast contribute to the pathogenesis of several disease states, including seborrheic dermatitis, AD, endocrine or metabolic diseases, paraneoplastic diseases, and disorders of cornification.

Canine Malassezia Dermatitis

M. pachydermatis colonizes sparsely haired areas and moist areas of the skin and mucosa of normal dogs in higher numbers than in more densely haired and dry areas.

- In a diseased state, alterations of the skin's surface microclimate contribute to increased susceptibility to yeast infection. Primary diseases that cause increased moisture, altered surface lipids, and/or disruption of stratum corneum barrier function encourage secondary overgrowth of the organism.
- Pruritic inflammatory diseases (allergic and parasitic) cause microclimate changes due to scratching (disruption of barrier function), licking (added moisture), and increased production of sebum.
- Endocrinopathies (especially hyperadrenocorticism) directly cause alterations in sebum characteristics and stratum corneum function.
- Metabolic diseases that result in parakeratotic hyperkeratosis (such as zinc-responsive dermatosis, generic dog food dermatosis, and hepatocutaneous syndrome or superficial necrolytic dermatitis) also appear to be risk factors.
- Secondary MD is also associated with primary (idiopathic) seborrhea of dogs, especially in basset hounds, cocker spaniels, dachshunds, and West Highland white terriers. Several other skin disorders can also be associated with MD (Table 41-1).
- A correlation between the onset of MD (or otitis) and the recent use of antibiotics has been documented. However, the opposite has also been noted where MD

Table 41-1. COMMON DIFFERENTIAL DIAGNOSES FOR SKIN DISORDERS THAT MAY BE ASSOCIATED WITH SECONDARY MALASSEZIA DERMATITIS

Reaction Pattern	DDx for Primary Causes	Species
Localized, regional, or generalized pruritus	Allergic diseases (atopy, adverse food reaction, flea bite allergy, contact allergy)	D & C
	Parasitism scabies, cheyletiellosis	D & C
	Demodex gatoi	C
	Infectious diseases (bacterial pyoderma, dermatophytosis)	D & C
Seborrhea oleosa	Most causes of pruritus (as above)	D & C
	Endocrinopathies	D & C
	Iatrogenic hyperglucocorticoidism	D & C
	Idiopathic (primary) seborrhea	D
	Vitamin A–responsive dermatosis	D
Seborrhea sicca	Same as for seborrhea oleosa	
	Sebaceous adenitis	D
Hyperkeratosis or crusting (face, foot pads, pressure points)	Zinc-responsive dermatosis, generic dog food dermatosis, superficial necrolytic dermatitis	D
(facial only)	Idiopathic facial dermatosis of the Persian	C
(regional *or* generalized)	Pemphigus foliaceus	D & C
	Thymoma-associated dermatosis	C
Acquired symmetrical alopecia	Causes of pruritus (as above)	C > D
	Endocrinopathies (including iatrogenic)	D > C
	Paraneoplastic alopecia	C
Facial acne	Bacterial folliculitis, demodicosis, dermatophytosis, adverse food reaction	C
Otitis externa +/− otitis media	Conformational/anatomic (hirsute canals, congenital infantile stenosis, etc.)	D
	Microclimate changes (heat and humidity retention)	D > C
	Allergic diseases	D & C
	Parasitic diseases (ear mites, demodicosis)	D & C
	Endocrinopathies	D > C
	Erosive diseases (drug eruption, pemphigus)	D & C
	Space-occupying masses	D & C
	Immunosuppression (including iatrogenic)	D & C
	Contact irritants	D & C

C, cat; D, dog; DDx, differential diagnosis.

resolved following treatment of concurrent staphylococcal pyoderma with antibiotics alone.

- Similarly, glucocorticoids have also been suggested to be a risk factor for development of MD; but again, some cases will spontaneously resolve with steroid therapy of an underlying inflammatory disease and without specific antifungal therapy.

▼ ***Key Point*** The most common primary disease association with canine MD is AD.

The role of *M. pachydermatis* in AD has been well described clinically and immunologically. The inflamed skin and ear canals of dogs with AD often harbor increased numbers of yeast (compared with the skin of normal dogs), and specific antifungal therapy will ameliorate a large portion of the pruritus experienced by many of these dogs.

- Dogs have been shown to mount an immunoglobulin E (IgE)-mediated (immediate) hypersensitivity response to allergens produced by the yeast in a manner similar to other environmental allergens (such as pollens, dust mites, animal danders, and molds).

▼ ***Key Point*** *Malassezia* overgrowth can provoke an overwhelming pruritic response in atopic dogs, which can occur acutely and be misconstrued as increased exposure to aeroallergens. Resolution of the yeast infection can reduce the pruritic threshold of an atopic dog by 75% to 100% in some cases, depending on concurrent exposure to other allergens. Therefore, undiagnosed MD is one of the most common reasons for perceived failure in the management of atopic dogs.

Canine Malassezia Otitis

- *M. pachydermatis* is commonly associated with otitis externa. As with the skin, there appears to be an increased incidence of *Malassezia* overgrowth in the ear canals of dogs with allergic and seborrheic otitis, endocrinopathies, and iatrogenic immunosuppression.
- It is also commonly seen in general practice occurring in otherwise normal dogs, but after swimming or bathing (i.e., water trapping or "swimmer's ear").
- The ear canals, which express a higher temperature and humidity than the surface skin, are a very favor-

able environment for yeast growth, and the lipid-rich cerumen is also supportive.
- I have noted a higher incidence of primary *Malassezia* otitis and pododermatitis (in otherwise normal dogs) living in a humid coastal climate than in dogs living in more arid and temperate climates.

Canine Malassezia Mucositis

While rare, it has been reported that *M. pachydermatis* can promote oral pathology (stomatitis, pharyngitis, tonsillitis).

Feline Malassezia Dermatitis and Otitis

- While a definitive (immunologic) relationship between *Malassezia* yeast and AD has not been described in cats, it does appear to be associated with pruritic or inflammatory dermatoses such as AD, adverse food reaction, and ectoparasitism.
- Cats with increased numbers of *Malassezia* spp. in the external canals often exhibit a highly pruritic ceruminous otitis.
- In addition to primary pruritic diseases, feline MD appears to occur in conjunction with paraneoplastic skin diseases; in a review of 550 feline skin biopsies, *Malassezia* spp. were most commonly associated with feline paraneoplastic alopecia and thymoma-associated dermatosis or erythema multiforme. All cats with histology consistent with these underlying systemic diseases died within 8 weeks of skin biopsy sampling.

CLINICAL SIGNS

Canine Malassezia Dermatitis

- Although MD is usually intensely pruritic, the only primary lesion produced is *erythema*.
- *Secondary lesions* including excoriations, seborrheic plaques, lichenification, maceration, and intertrigo are common and cannot be reliably distinguished from staphylococcal pyoderma without cytologic examination.
- In rare cases, *M. pachydermatis* can cause a *folliculitis* that mimics staphylococcal folliculitis, dermatophytosis, and demodicosis.
- The *clinical appearance* of the skin in cases of MD is highly variable. It may either be dry and flaky (seborrhea sicca) or tacky and greasy (seborrhea oleosa).
- The *distribution pattern* of canine MD is variable but most commonly affects some combination of the face (especially periocular and perioral skin), feet (interdigital spaces and claw folds), intertriginous areas (axillae, groin or inguinum, facial folds, and vulvar and mammary folds), and perineum.
- Generalized cases of MD may occur in chronic cases of allergic dermatitis.
- *Malassezia* pododermatitis may occur with or without more widespread MD. The feet are the most common single body area affected in allergic dogs. Patients with interdigital *Malassezia* pododermatitis will be presented for the complaint of paw licking or chewing.
- *Paronychia* (inflammation of the claw beds) may also occur as the sole presenting sign of MD and often causes claw biting (also see Chapter 63). Physical examination will usually reveal a reddish-brown staining of the proximal claw or a waxy exudate in the claw fold, with inflammation of the surrounding soft tissue.
- MD can occur in any breed (or mixed breeds) but West Highland white terriers, English setters, Shih Tzus, basset hounds, and American cocker spaniels are at increased risk. This increased risk may in turn reflect the propensity for these breeds to develop allergic dermatitis as a predisposing factor.
- In any dog with a known endocrine or metabolic disease, rule out MD (by surface cytology) if pruritus, cutaneous inflammation, or non-inflammatory seborrhea are present.
- Cases of non-pruritic MD are rare, and most will be associated with hyperadrenocorticism, hepatocutaneous syndrome, zinc-responsive dermatosis, or iatrogenic immunosuppression from cancer chemotherapy.

▼ ***Key Point*** The most common presenting complaint associated with non-pruritic MD is seborrhea oleosa accompanied by a foul odor.

Canine Malassezia Otitis

- *M. pachydermatis* plays an important role in cases of ceruminous otitis externa, in which it is often highly inflammatory (see Chapter 59). However it is a normal inhabitant of 15% to 49% of healthy canine ear canals, depending upon the study reported.
- *M. furfur* and *M. obtusa* have also been isolated from dogs with otitis externa.
- As with the skin, there is no reliable smell or characteristic of otic exudate that routinely indicates an infection is associated with yeast rather than bacteria (contrary to anecdotal claims), so cytologic evaluation is essential (see "Diagnosis").
- Otitis media may also occur in which *Malassezia* is the sole infectious organism isolated (see Chapter 61). These cases result from extension of the infection through a ruptured tympanum, which may sometimes heal and therefore seal the infection within the bulla. Undiagnosed otitis media is a common underlying cause of chronic or relapsing otitis externa and must be identified and treated in order for permanent resolution of the case to occur.

Feline Malassezia Dermatitis and Otitis

- Feline MD is rare compared with canine MD.
- It may be associated with any primary pruritic disease and often causes a diffuse erythematous, scaly to waxy dermatitis. However, not all cases of MD in cats are pruritic.

- MD seems to be especially pruritic when associated with facial dermatitis and/or otitis externa in cats. Facial pruritus is one of the most common and frustrating problems encountered in feline dermatology, and the list of primary etiologies that can incite it is extensive.
- Markedly pruritic ceruminous otitis may be associated with *Malassezia* spp.
- As in dogs, *Malassezia* paronychia may be associated with waxy exudates in the claw beds and rust-colored staining of the proximal claws. The Cornish and Devon Rex breeds appear to be predisposed.
- *Malassezia* spp. may also be associated with some cases of *feline facial acne* (affecting any combination of the chin, neck, and perioral and periocular regions). Many cases are non-pruritic.
- Cats with thymoma-associated dermatosis (regional dorsal to generalized exfoliative dermatitis), may have MD that may not be pruritic.
- Cats with pancreatic or hepatobiliary carcinomas may develop a paraneoplastic alopecia of the ventrum and legs (skin has a glistening sheen). Secondary *Malassezia* overgrowth may provoke pruritus in this otherwise non-pruritic disease, but even non-pruritic cats should be screened cytologically.

ZOONOSIS

It has recently been documented in a human neonatal intensive care unit (ICU) that the zoophilic species *M. pachydermatis* can cause a similar life-threatening fungemia in humans. The source of a yeast infection was shown to be a pet dog owned by a nurse who worked in the ICU. This observation suggested that *M. pachydermatis* could represent an emerging infectious zoonotic pathogen. An epidemiologic survey conducted by my clinical research group has shown that *M. pachydermatis* can be isolated very commonly from the hands of dog owners, regardless of whether the dogs have MD or healthy skin. However, the public health significance appears to be extremely minor, considering the commonality of mechanical carriage by dog owners and the paucity of fungemia cases reported in the human literature.

DIAGNOSIS

▼ ***Key Point*** *Malassezia* organisms can be identified on animal skin by cytology, culture, histopathology, and polymerase chain reaction (PCR).

Cytology

Methods for collection include dry skin scrapings, adhesive tape stripping, cotton-tipped swabs, and direct impression smears with glass slides (also see Chapter 37).

For Dry Skin

- Scrapings and adhesive tape stripping (or direct skin impression with adhesive-coated slides) work best. With scrapings, it may be necessary to mix the material with saline and heat fix until dry (in order to adhere the material to the slide).

For Greasy Skin

- Direct impression smears allow quantification of yeast per microscopic field (as does tape stripping and adhesive-coated slides).
- Cotton-tipped swabs are useful for interdigital spaces if they are tacky, as it can be difficult to impress slides directly—especially in small-breed dogs. Adhesive tape also works nicely in tight spaces.
- For diagnosis of *Malassezia* paronychia, use the broken end of a cotton-tipped swab's wooden handle or a metal spatula to scrape the claw fold and press or roll exudate firmly onto a glass slide.
- For examination of ear exudate in dogs with ceruminous or exudative otitis externa, roll exudate in a thin layer on glass slides with a cotton-tipped swab. It is often useful to sample the skin of the concave pinna separately from the ear canal if pinnal dermatitis is present.

Preparing Samples for Microscopic Examination

- When material is applied to a glass slide, use a modified Wright's stain (such as Diff-Quik). Heat fixing of the slide prior to staining is performed by many dermatologists, but a study has shown it to be generally unnecessary.
- Examine under an oil immersion (1000×) or high-power dry (400×) field for oval or peanut-shaped (budding) yeast. Use oil immersion for more reliable identification of bacteria and yeast cells.
- When adhesive tape is used, it may be dipped in the stain, rinsed, and dried with a warm air dryer. Apply the tape to a glass slide while it is still warm and sticky for best adhesion. Some clinicians prefer wet mounts: A drop of new methylene blue stain is placed on a glass slide, and the tape strip is laid on top.

Interpretation of Cytologic Results: How Many Is Too Many?

- For skin, 1 yeast per oil immersion field (oif) is a general guideline used by many dermatologists, although the only controlled study published has suggested 1 yeast per 27 oif may be sufficient to correlate with pathologic effect.
- Normal dogs may routinely exhibit up to 5 organisms per high-dry (400×) field (roughly <2 per oif), while cats may harbor up to 12 organisms per high-dry field (roughly <5 per oif).

▼ ***Key Point*** These numbers are guidelines only. Since dogs may mount a hypersensitivity response to *M. pachydermatis,* it is possible that some indi-

viduals will suffer a pathologic effect from what would otherwise be considered a "normal" population of yeast colonizing the skin or ear canals.

Culture

Culture for *Malassezia* organisms is generally unnecessary and rarely performed.

Histopathology

This should *not* be necessary to make the diagnosis of MD if routine cytology is performed. While *Malassezia* spp. are often found on biopsies submitted for evaluation of pruritic dermatitis, histopathology cannot be relied upon to make the diagnosis of MD; loss of stratum corneum during tissue processing may yield a false-negative result.

Polymerase Chain Reaction

This technique is capable of identifying the *Malassezia* species with an extremely high degree of accuracy but is primarily used for research purposes or to monitor for point sources in epizootic outbreaks.

TREATMENT

Chose therapy based upon the distribution of the infection, the general health status of the patient, and the expectations of the pet owner in regards to time and effort commitment (relevant to topical therapy) and side effects (most relevant to systemic therapy). Diagnose and eliminate (or control) underlying diseases to prevent of recurrence. Since *M. pachydermatis* is part of the normal cutaneous microflora, complete elimination of the organism is likely to be impossible.

Systemic Therapy (Table 41-2)

▼ ***Key Point*** Unless there is a specific contraindication to using an oral antifungal drug, treat most cases of generalized and regional MD (e.g., pododermatitis) systemically. Otitis media also requires systemic therapy to reliably achieve therapeutic drug levels within the tympanic cavity. Oral ketoconazole, itraconazole, or fluconazole is most commonly recommended. Griseofulvin is ineffective against *Malassezia* spp.

Ketoconazole

- *Ketoconazole* (Nizoral, Janssen, and generics) is an imidazole antifungal with proven efficacy for canine MD. It undergoes extensive metabolism by the liver, and its use in patients with hepatic disease is contraindicated. It is also a known teratogen in dogs. Adverse effects include gastrointestinal upset (anorexia, vomiting, diarrhea), thrombocytopenia (rare), and hepatotoxicity, although none of these side effects are at all common. Hepatotoxicity is a moderate risk in cats, however, and its use in feline MD is not recommended. In aged or debilitated dogs, evaluate hepatic enzymes prior to use of ketoconazole. I do not routinely perform screening tests in young or healthy dogs. For long-term or repeated use, monitor hepatic function on a case-by-case basis as dictated by clinical signs (some dermatologists recommend monthly monitoring). Always administer this drug along with food for maximum absorption.

Itraconazole

- *Itraconazole* (Sporanox, Ortho Biotech) and *fluconazole* (Diflucan, Roerig) are triazole antifungals with less risk for hepatotoxicity than ketoconazole. Itraconazole is metabolized by the liver, while fluconazole is excreted via the kidneys. Due to cost, fluconazole is rarely chosen as a first-line treatment. Itraconazole is the treatment of choice in cats unless preexisting hepatopathy is known, in which case fluconazole should be used. Always administer itraconazole with food; feeding does not influence the absorption of fluconazole.

Table 41-2. SYSTEMIC DRUGS FOR TREATMENT OF MALASSEZIA DERMATITIS AND OTITIS MEDIA

Drug	Supplied As	Dose, Frequency, Duration	Species
Ketoconazole	200-mg tablets	5–10 mg/kg q24h × 21–28 days, or	D
		low dose regimen: 5 mg/kg q24h × 10 days, then eod × 10	D
		Pulse dose regimen for *prophylaxis:* 5–10 mg/kg for 2 consecutive days/wk	D
Itraconazole	100-mg capsules	5 mg/kg q24h × 21–28 days, or	D & C
		5 mg/kg for 2 days/wk × 3 weeks	D
	10-mg/ml of elixir	2.25–5 mg/kg q24h × 21–28 days (pulse dose not reported)	D & C
Fluconazole	50-, 100-, 150-, 200-mg tablets and oral powder for a 10-mg/ml suspension	2.5–5 mg/kg q24h × 21–28 days	D & C
Terbinafine	200-mg tablets	30 mg/kg q24h × 21–28 days	D
		30–40 mg/kg q24h × 21–28 days	C

Terbinafine

- *Terbinafine* (Lamisil, Novartis) is an allylamine antifungal with a high margin of safety for use in mammals. It is a less proven drug for MD, but based upon its ability to reduce *Malassezia* colonization on healthy basset hounds, it is likely to be effective.

Lufenuron

- *Lufenuron* (Program, Novartis Animal Health) is a benzoylphenylurea drug that disrupts chitin synthesis in the cell wall of insects and perhaps some fungi. There is no evidence at this time to suggest that this drug is effective in the treatment of MD.

Topical Therapy

▼ ***Key Point*** Topical antifungals are most useful for treatment of localized infections or as adjunctive therapy along with oral drugs. Topical antifungals are also quite valuable in the prophylaxis of chronic or relapsing MD.

- For regional or generalized disease, shampoos containing miconazole, ketoconazole, chlorhexidine, or selenium sulfide are available and have met with variable success depending upon client compliance, frequency and technique of application, and severity of disease. Conditioners containing miconazole and chlorhexidine are also available, as is lime sulfur dip. Enilconazole is available as a rinse in some countries, but not in the United States.
- For frequently relapsing cases, shampoo therapy (once to twice weekly, 10 minutes minimum contact time) may be adequate for prophylaxis.
- *Malassezia* pododermatitis and paronychia may be treated with topical therapy alone in a limited number of cases, but such therapy can be labor intensive for the client and poorly received by the patient. Success with shampooing or soaking the feet in miconazole, ketoconazole, or chlorhexidine products (minimum of 10 minutes contact time) and use of miconazole and/or chlorhexidine spray or wipes on a daily basis has been reported anecdotally. For *Malassezia* paronychia, gentle scrubbing of the claw folds with a toothbrush using miconazole shampoo has been described but is labor intensive.
- Use miconazole, clotrimazole, or ketoconazole sprays, lotions, wipes, or creams for "spot" therapy.
- Use ointments and lotions containing nystatin, thiabendazole, miconazole, or clotrimazole for otitis externa. Some products also contain glucocorticoids and antibacterials.

Immunotherapy

A commercial *M. pachydermatis* extract (Greer Laboratories, Lenoir, NC) is now available for intradermal testing and use in immunotherapy vaccines. A multicenter study is under way to determine its utility as an immunotherapeutic extract.

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Chapter 42

Dermatophytosis

Karin Muth Beale

Dermatophytosis is an infection of keratinized tissues usually caused by dermatophytes of the genera *Microsporum, Trichophyton,* and *Epidermophyton*. These organisms are keratinophilic and invade and live within the keratinized hair, nail, or skin. The majority of infections in dogs and cats are caused by three species of dermatophytes: *Microsporum canis, Microsporum gypseum*, and *Trichophyton mentagrophytes*. Other fungi are uncommon causes of dermatophytosis in pets. Dermatophytes are classified into groups based on their natural habitat as geophilic, zoophilic, or anthropophilic. Geophilic dermatophytes naturally inhabit the soil, zoophilic species are adapted to animals, and humans are the hosts for anthropophilic species. As a general rule, geophilic and anthropophilic dermatophytes tend to produce many more inflammatory lesions in animals than do the more host-adapted species.

ETIOLOGY

Microsporum Gypseum

M. gypseum is a geophilic dermatophyte that normally inhabits the soil and decomposes keratinaceous debris. However, this organism is the second most common cause of dermatophytosis in dogs in the United States, and it occasionally infects cats. *M. gypseum* is most commonly isolated from animals that spend much time outdoors. Because the organism is not specifically adapted to living on animals, it tends to incite inflammation. Lesions are commonly seen in areas with significant soil contact, such as the feet and muzzle.

Microsporum Canis

This zoophilic dermatophyte is responsible for the majority of the clinical cases of dermatophytosis in dogs. *M. canis* is the cause of approximately 98% of the cases of feline dermatophytosis. It was previously thought that cats served as the reservoir for *M. canis;* however, studies show that it is rarely isolated from healthy pet cats. The isolation of *M. canis* from a dog or cat is a significant finding, and the condition requires treatment.

Trichophyton Mentagrophytes

This zoophilic dermatophyte is the third most common cause of dermatophytosis in dogs and less commonly affects cats. *T. mentagrophytes* is the most common cause of dermatophytosis in rodents and rabbits. Pet rodents or rabbits should be considered possible reservoirs of infection. Wild rodents are commonly infected, and the infections may be clinically inapparent. Cats that hunt may be pre-disposed to acquiring this dermatophyte infection, as are dogs that dig and root in soil.

Anthropophilic Dermatophytes

Anthropophilic dermatophytes such as *Microsporum audouinii* rarely affect pets but can cause intensely inflamed lesions in animals. Zoophilic species of dermatophytes other than *M. canis* and *T. mentagrophytes,* such as *Trichophyton equinum, Trichophyton verrucosum,* and *Microsporum nanum,* may cause dermatophytosis in dogs or cats; however, such animals usually are in contact with livestock that are natural reservoirs or hosts for those organisms.

CLINICAL SIGNS

Canine Dermatophytosis

- Canine dermatophytosis is characterized by alopecia and scaling. Usually there are focal to multifocal, circumscribed, affected patches of skin.
- Hair loss, broken hairs, scaling, pustules, papules, exudation, crusting, and hyperpigmentation may be seen.
- Pruritus is variable.
- The classic lesion is a circular area of alopecia and scaling with central healing; however, the lesions may be irregular in appearance.
- Several factors influence the severity of the lesions. Young and immunocompromised animals tend to develop more extensive lesions that take longer to resolve than do those of healthy adult animals. This is because the ability to mount an effective inflam-

matory response is necessary to eliminate the infection. In addition, the pathogenicity and the species of dermatophyte affect the degree of inflammatory response.

Kerion

A kerion is a round, raised, well-circumscribed, erythematous, alopecic, nodular lesion that results when follicular rupture, furunculosis, and pyogranulomatous inflammation occur with a dermatophyte infection. The lesions have a spongy feel on palpation and will sometimes exude purulent to hemorrhagic material that may result in crust formation.

- Kerions are most commonly seen on the limbs and face of dogs. They are usually solitary and mimic histiocytomas.
- The etiology usually is *M. gypseum*.
- These lesions may be secondarily infected with *Staphylococcus intermedius*.

Generalized Dermatophytosis

Generalized dermatophytosis is uncommon in the dog.

- Characteristic findings are widespread alopecia and seborrhea with or without pruritus.
- Other lesions, similar to those of focal dermatophytosis, may also be present.
- Generalized dermatophytosis in adult dogs is often associated with immunosuppression or systemic disease.

Feline Dermatophytosis

▼ ***Key Point*** Feline dermatophytosis can occur in many different clinical forms. Consider dermatophytosis in the differential diagnosis of most feline dermatoses. Feline dermatophytosis is the most common infectious skin disease in cats.

▼ ***Key Point*** Cats of any age may be infected, but younger, older, and long-haired cats seem to be affected more frequently. Systemic disease may increase susceptibility to infection. Cats with feline immunodeficiency virus (FIV) have an increased risk of dermatophytosis.

Classic Ringworm

Ringworm lesions may be present in cats; however, the circular lesions of alopecia and scaling with central healing are less common in cats than in dogs. Crusting, scaling, and hair loss are most commonly seen. Cats may have what appears to be a localized infection when in reality the infection is generalized. This is especially true of long-haired cats.

Subclinical Infection

Adult cats may have subclinical dermatophyte infections. These cats may have minimal (e.g., a minor degree of scaling or a few broken hairs) or no apparent clinical lesions. These cats serve as an important reservoir in the spread of dermatophytosis, and culture is necessary to identify affected cats.

Miliary Dermatitis

In cats, dermatophytosis may occur as a *miliary dermatitis* that may or may not be pruritic (see Chapter 53).

Symmetrical Alopecia

Symmetrical alopecia may be caused by dermatophytosis in cats. Excessive grooming as a result of pruritus, combined with follicular inflammation, can lead to excessive hair loss in some cats.

Pseudomycetoma

- Pseudomycetoma (Majocchi granuloma) is a form of granulomatous dermatitis in the cat caused by a dermatophyte, usually *M. canis*.
- This type of lesion is almost exclusively seen in Persian cats.
- In this lesion the fungus is sequestered in the dermis but does not proliferate; a nodular, ulcerating dermatitis is the result.
- Affected cats usually have generalized dermatophytosis.

Onychomycosis

- This dermatophyte infection of the nails is seen in both dogs and cats (also see Chapter 63).
- The lesions usually are caused by *T. mentagrophytes* in dogs and *M. canis* in cats.
- The nails are dry, cracked, brittle, and frequently deformed.
- Onychomycosis very rarely affects all four feet.
- Usually there is a concurrent infection with inflammation of the nail fold, and the pads may be affected as well.

DIAGNOSIS

▼ ***Key Point*** False-positive diagnosis of dermatophytosis in animals with circular lesions of alopecia is common. Follicular infections with *Demodex* and *Staphylococcus* organisms produce similar lesions.

- Do *not* diagnose dermatophytosis solely on the basis of clinical signs. Because of the numerous clinical conditions in dogs and cats that can mimic dermatophytosis, perform specific diagnostic procedures to obtain a definitive diagnosis.

Differential Diagnoses

Canine Dermatophytosis

- In the dog, the most common cause of circular alopecia is staphylococcal folliculitis (see Chapter 38), followed by localized demodicosis (see Chapter 43).
- Follicular infections with different organisms share common reaction patterns of papules, pustules, alopecia, scaling, and crusting.
- Use diagnostic tests such as skin scrapings, surface cytology, bacterial cultures, and skin biopsies to rule out some of the more common causes of focal alopecia in dogs.
- Consider dermatophytosis in the differential diagnosis of a generalized scaling, crusting, alopecic dermatosis. A number of different conditions can cause a generalized dermatitis similar to that seen in generalized dermatophytosis in the dog (Table 42-1).
- The differential diagnosis for kerions and pseudomycetomas includes the various causes of nodular dermatitides, such as cutaneous neoplasms, staphylococcal furunculosis, and acral lick dermatitis (see Table 42-1).

Table 42-1. DIFFERENTIAL DIAGNOSIS FOR DERMATOPHYTOSIS IN DOGS

Focal to Multifocal Dermatophytosis
Demodicosis
Staphylococcal folliculitis
Abrasions
Pemphigus foliaceus/erythematosus
Zinc-responsive dermatosis
Generalized Dermatophytosis
Demodicosis
Staphylococcal folliculitis
Dermatophilosis
Pemphigus foliaceus
Cheyletiellosis
Sebaceous adenitis
Primary cornification defects
Secondary cornification abnormalities (allergic dermatoses, endocrinopathies, nutritional deficiencies, etc.)
Epidermotropic lymphoma
Kerions
Histiocytoma, mast cell tumor, other neoplasms
Staphylococcal furunculosis
Demodicosis and furunculosis
Acral lick dermatitis
Foreign bodies
Subcutaneous mycoses
Actinomycotic infections
Mycobacterial infections
Onychomycosis/Nail Fold Dermatophytosis
Staphylococcal onychitis
Demodicosis
Zinc-responsive dermatosis
Pemphigus vulgaris/foliaceus
Symmetric lupoid onychodystrophy

Feline Dermatophytosis

The list of disorders to be considered in the differential diagnosis of feline dermatophytosis is extensive and includes all causes of miliary dermatitis and symmetrical alopecia (see Chapters 52 and 53).

History

An accurate history can provide useful information regarding the possible source of infection.

- Obtain an accurate drug history. Consider the possibility of exposure to dermatophytes from other infected animals, cattery/grooming/boarding facilities, or the environment of the animal (outdoor exposure in the case of geophilic dermatophytes, the introduction of a new kitten or cat, etc.).
- Determine whether the animal has had any abnormalities suggestive of underlying systemic disease, particularly in older animals.

Physical Examination

- Look for signs suggestive of dermatophytosis. Wood's light examination, microscopic examination of glowing hairs, and cultures are recommended in the following patients:
  - Dogs with lesions characteristic of dermatophytosis
  - Dogs with generalized lesions of alopecia and scaling
  - Cats with clinical signs of dermatophytosis (hair loss, scaling, broken, frayed hairs, pruritus)
  - Cats with systemic disease or viral infections that have concurrent skin disease
  - Any cat whose owner develops lesions suggestive of dermatophytosis
  - Recently adopted or purchased cats with skin disease
- Thoroughly examine adult animals with widespread lesions, especially dogs, for signs indicative of underlying systemic disease such as hyperadrenocorticism.

Wood's Light Examination

- Use the Wood's light to screen for dermatophytosis. The light emitted may cause fluorescence of hairs infected with *M. canis*. Electric lamps are preferred over battery-operated lamps due to superior light intensity.
- Be wary of false-positive results. Scale, ointments, creams, and bacterial folliculitis may all fluoresce under the light; however, they do not give the typical apple-green fluorescence of the hair shaft seen with *M. canis* infection.
- Hairs may remain fluorescent after an *M. canis* infection has resolved. Therefore, positive fluorescence alone should not be used to confirm active infection or monitor therapy.

▼ ***Key Point*** Hairs infected with *M. gypseum* and *T. mentagrophytes* do not fluoresce an apple-green color under Wood's light, and less than 50% of *M. canis*–infected hairs fluoresce. Use the Wood's light only as a screening tool, not as a confirmatory diagnostic test.

Direct Microscopic Examination of Hair

Direct microscopic examination can provide a diagnosis of dermatophytosis within minutes if affected hairs are properly examined.

- Selection of the sample to be examined is critical.
  - Pluck hair from areas of active inflammation.
  - Broken or frayed hairs are ideal.
  - If there was fluorescence with Wood's light examination, select those individual hairs that fluoresced.
- Place the hairs to be examined on a glass slide.
  - Clear the sample to facilitate observation of spores and hyphae (Table 42-2).
  - When the specimen has been cleared, scan the slide using low magnification (10×) for abnormal hairs. Look for hairs that are frayed, swollen, and pale.
  - When you have located the hair, examine it at a higher magnification (20–40×).
- The presence of ectothrix spores surrounding the hair and of hyphae within the hair shaft is diagnostic for dermatophytosis. Ectothrix spores appear as round to oval, greenish, translucent beads (Fig. 42-1).

This technique requires some practice. A negative direct microscopic examination does *not* rule out dermatophytosis.

Table 42-2. CLEARING AGENTS USED FOR MICROSCOPIC EXAMINATION OF SPECIMENS OF HAIR

Agent	Instructions
10–20% KOH	Place several drops on the slide, apply a coverslip, and allow the slide to clear for 30 min before examining.
10–20% KOH	Follow the same procedure as above, but gently heat the slide for 15 sec, allow it to cool, and then examine it.
2 parts KOH, 1 part DMSO	Place several drops on the slide, apply a coverslip, and allow it to clear for 5 min before examining.
Chlorphenolac (50 g chloral hydrate, 25 ml liquid phenol, and 25 ml liquid lactic acid)	Place several drops on the slide, apply a coverslip, and examine immediately.

DMSO, dimethyl sulfoxide; KOH, potassium hydroxide.

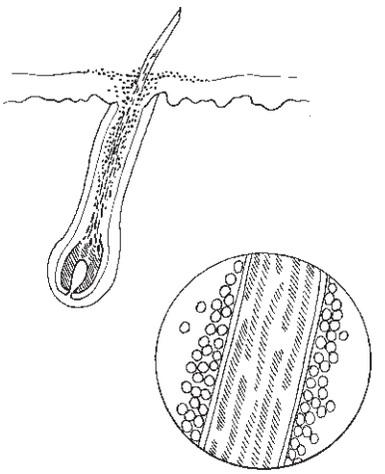

Figure 42-1. Arthrospores can be identified outside infected hair shafts (ectothrix) in animals. Fungal hyphae may be seen within infected hair shafts *(inset)*.

▼ ***Key Point*** Avoid false-positive diagnoses based on direct examination. Dermatophytes do not produce macroconidia in the tissue. Nonpathogenic fungal conidia and plant pollen are frequently mistaken for dermatophytes; these structures are darkly pigmented, whereas dermatophytes are not.

Fungal Culture

▼ ***Key Point*** Fungal culture is the most reliable and definitive method of identifying infected animals; it is the only method of identifying the species of fungi and should be performed in all suspected cases of dermatophytosis.

The ideal culture media for dermatophytes is dermatophyte test media (DTM), which is composed of Sabouraud's agar, antimicrobials to inhibit bacterial and fungal saprophyte growth, and phenol red as a pH indicator. DTM is available in screw-cap containers or in plates with DTM on one side and plain Sabouraud's agar on the other. The plates are preferred over the tubes because it is easier to obtain samples from the plates for species identification. Saprophytes are less likely to overgrow dermatophyte colonies on the plates than on the tube media. Plain Sabouraud's agar is better for evaluating colony morphology because DTM may suppress the formation of conidia and alter colony coloration.

Technique

1. Specimen collection of hair involves three steps:
   a. Clip hairs to 0.5 cm in an area of active inflammation; areas of broken, stubbly hairs of positive Wood's light fluorescence are ideal.
   b. Lightly swab the area with alcohol and allow to air-dry.

c. Gently remove the clipped hairs from the follicles; hemostats are ideal for this purpose.
2. Place hairs on the media (not deeply embedded).
3. In cases of onychomycosis, clip the proximal nail into small pieces for culture.
4. Place the sample (hairs or nail particles) in a dark environment, protected from ultraviolet light and desiccation. Maintain the cultures at a temperature between 24°C and 27°C (75°F and 81°F). Do not close the container tightly.
5. Observe the sample daily for colony growth and for a color change in the media.
6. As a general rule, dermatophytes turn DTM red simultaneously with colony growth, whereas saprophytes generally do not turn the media red until after a week or so after fungal growth commences. Therefore, inspect the culture daily.
7. Fungal colonies that are darkly pigmented (blue, green, black, or a combination) are *not* dermatophytes.

▼ ***Key Point*** Some species of fungi other than dermatophytes may turn the DTM media red within the first 7 to 10 days; therefore, microscopic examination of the mycelia is necessary to identify the fungus definitively as a dermatophyte.

Identification of Subclinically Infected Cats

- Identification of the dermatophytosis in the minimally symptomatic cat can be accomplished using a toothbrush technique. Vigorously brush the cat over the entire body with a new toothbrush.
- Tease the hair from the brush and place the collected hairs and scale onto the fungal culture media. Alternatively, the distal bristles can be cut from the brush and placed directly on the media with the attached hairs.

Identification of Dermatophyte Species from a Fungal Colony

The colony morphology in combination with the characteristic microscopic morphology allows identification of the dermatophyte species causing the infection (Table 42-3). The easiest and most practical method of observing microscopic morphology is the "acetate tape" method:

1. Gently touch a 2-cm strip of clear acetate tape to the surface of a mature culture colony (>5 days old). A colony on plain Sabouraud's agar is preferable, if available.
2. Then place the tape over a glass slide with a drop of lactophenol cotton blue or new methylene blue stain.
3. Observe the slide microscopically for identification of the dermatophyte species by conidia formation (Fig. 42-2).

Biopsy and Histopathology

Generally, it is not necessary to biopsy skin for identification of a dermatophyte infection. However, dermatophytes may be visible in hematoxylin-eosin (H&E)-stained sections and are readily detected with periodic acid-Schiff (PAS) and Gomori methenamine silver (GMS) stains. In cases of suspected dermatophyte onychomycosis, the nail itself may be submitted in 10% formalin for histopathologic evaluation.

TREATMENT

▼ ***Key Point*** Dermatophytosis is a zoonotic disease, and children and immunocompromised individuals are at increased risk; therefore, minimize exposure of people and other animals to the affected animal.

- Dermatophyte infections may be self-limiting, particularly in dogs; however, plan treatment with the goals of eliminating the infection in the animal and preventing the spread of infectious materials to other pets or people in the household.
- Treatment requires therapy for the infected pet, as well as methods to decontaminate the pet's environment.

Table 42-3. COLONY AND MICROSCOPIC MORPHOLOGY OF DERMATOPHYTE CULTURES ON SABOURAUD'S DEXTROSE AGAR

Organism	Colony Morphology	Microscopic Morphology*
Microsporum canis	The surface is cottony to woolly and white. The reverse side is yellow-orange.	Abundant spindle-shaped macroconidia with thick, spiny walls and a terminal knob are present. Six or more cells are found in the macroconidia. One-celled microconidia are uncommon.
Microsporum gypseum	The surface is flat, granular, and light tan to cinnamon in color with white mycelia. The reverse side is pale yellow to tan.	Abundant spindle-shaped macroconidia with no terminal knobs are present. Macroconidia contain up to six cells. Microconidia are uncommon.
Trichophyton mentagrophytes	The surface usually is cream-colored and powdery. The reverse side is tan to brown, or red.	Some strains produce spiral hyphae. Microconidia are numerous and often are arranged in grape-like clusters along the hyphae. Macroconidia are uncommon; if present, they are slender and cigar-shaped with smooth thin walls.

*See Figure 42-2.

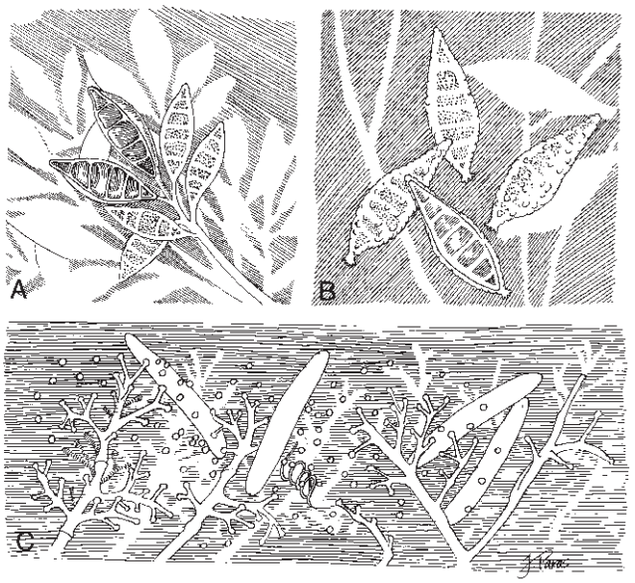

Figure 42-2. Identification of dermatophyte species from mature fungal colonies is possible by microscopically examining the conidia morphology: *A, Microsporum gypseum. B, Microsporum canis. C, Trichophyton mentagrophytes.*

- Cats are usually clinically asymptomatic prior to a mycologic cure—that is, the dermatophytes are still present after the animal is free of lesions. Thus two consecutive negative fungal cultures at 2-week intervals are necessary before the animal can be said to be cured.

▼ ***Key Point*** *Always* treat cats with dermatophytosis with systemic antifungal therapy. Dogs with localized lesions of dermatophytosis may be treated with topical therapy only; however, *always* use systemic antifungal therapy in dogs with onychomycosis, multiple lesions, or generalized lesions.

Topical Therapy

Topical Shampoo and Dip Therapy

Indications

- Topical therapy with whole-body shampoos or dips is most useful for decreasing the spread of disease, and this helps decrease the probability of the pet becoming re-infected from re-exposure to dermatophyte spores (particularly *M. canis*).
- Use topical therapy in every cat with dermatophytosis and in dogs with multifocal or generalized disease.

Clipping the Haircoat

- Clipping the haircoat is optimal, especially in cats with dermatophytosis. This helps decrease the release of infected hairs and spores into the environment.
- Clipping the coat may lead to a temporary worsening of the pet's condition by spreading the lesions. Warn the owner of this possibility.

Procedure

- Topical shampoos and dips may decrease the duration of systemic therapy and ultimately the cost of treatment.
- Few topical therapies have demonstrated antifungal activity in vivo or in vitro. Useful treatments include lime sulfur (1:16) (LymDyp, DVM Pharmaceuticals), enilconazole (10%), and miconazole shampoo. Enilconazole is not approved for use in dogs and cats in the United States. Miconazole shampoo is useful as an adjunct to systemic therapy.
- Because shampooing may spread the lesions through mechanical trauma, it would appear that the most effective topical whole-body therapy approved for use in the United States is lime sulfur. Apply the lime sulfur as a rinse, and gently sponge or pat (not rub) onto the animal. Lime sulfur dips should be applied once to twice weekly.
- If lime sulfur is used on a cat, place an Elizabethan collar after dipping to prevent ingestion of the substance. Warn owners that the dip may discolor the pet's haircoat, may dry the skin and coat, and in some cases may be irritating with repeated use.

Local Topical Therapy

- Localized topical therapy with creams and ointments containing miconazole, clotrimazole, or terbinafine seems to have limited value. Restrict use to localized lesions in dogs. This form of therapy may not speed resolution of the lesion, but it may help prevent dissemination of infective materials.
- Do not use creams and ointments in cats with dermatophytosis.

Systemic Therapy

- Systemic antifungal therapy (Table 42-4) is indicated in the treatment of all cats with dermatophytosis, dogs with generalized or multifocal dermatophytosis, and dogs and cats with onychomycosis.

Griseofulvin

▼ ***Key Point*** Griseofulvin, a fungistatic antimicrobial, is a commonly used drug in the treatment of dermatophytosis in dogs and cats.

- Absorption of the drug is enhanced when it is given with a fatty meal. Griseofulvin is available in microsize and ultramicrosize formulations in polyethylene glycol to enhance absorption so that lower doses can be used (see Table 42-4).
- Never administer griseofulvin, which is a teratogen, to pregnant animals.

Table 42-4. SYSTEMIC ANTIFUNGAL THERAPY FOR TREATMENT OF DERMATOPHYTOSIS

Drug	Brand Name (Manufacturer)	Dose/Application	Comments	Side Effects
Griseofulvin-microsize	Fulvicin U/F (Shering) Grifulvin V (Ortho)	25–50 mg/kg q24h Tablets, suspension	Not for use in cats infected with FIV	Idiosyncratic myelotoxicity, nausea, vomiting, ataxia, teratogenic
Griseofulvin-ultramicrosize	Gris-PEG (Dorsay)	5–10 mg/kg q24h Tablets	Not for use in cats infected with FIV	Idiosyncratic myelotoxicity, nausea, vomiting, ataxia, teratogenic
Ketoconazole	Nizoral (Janssen) Generic ketoconazole	10 mg/kg q24h Tablets	Not for use in cats, some strains of *M. canis* may be resistant	Gastric irritation, anorexia, nausea, idiosyncratic hepatoxicity, lightening of haircoat, teratogenic
Itraconazole	Sporanox (Janssen)	10 mg/kg q24h Capsules, suspension	Combined/continuous pulse therapy: 10 mg/kg daily for 28 days, then on alternate weeks Short-term cycle therapy: 10 mg/kg once daily for 15 days, followed by fungal culture. Cycle repeated until culture negative	Teratogenic, nausea, vomiting
Terbinafine	Lamisil (Novartis)	30–40 mg/kg once daily Tablets	May be used at this dose in combined/continuous pulse therapy or short-term cycle therapy as described above	Vomiting, nausea

- Common side effects include anorexia, vomiting, and diarrhea.
- Less common side effects, which appear to be idiosyncratic, include pyrexia, icterus, ataxia, angioedema, and myelosuppression.
- During therapy, monitor purebred cats, which may be pre-disposed to develop myelosuppression.

▼ ***Key Point*** Do not treat cats infected with FIV with griseofulvin, as they are very susceptible to toxicity from this drug and may suffer a severe, and sometimes fatal, neutropenia. Thus FIV testing is imperative before using griseofulvin in any cat.

Ketoconazole

Ketoconazole is a fungistatic imidazole derivative with broad-spectrum antifungal activity against both superficial and deep mycotic infections.

- Use this in dogs with griseofulvin-resistant dermatophytosis and for dogs that cannot tolerate griseofulvin therapy. Ketoconazole may not be effective against certain strains of *M. canis*. See Table 42-4 for the dosage.
- Because nausea and anorexia are frequently encountered in cats when using ketoconazole, and because *M. canis* may be resistant, do not use this in cats.

Itraconazole

Itraconazole is a triazole antifungal that is effective for the treatment of dermatophytosis. This is the therapy of choice for cats with dermatophytosis.

- Itraconazole is the drug of choice in FIV-positive cats.
- It is also effective in dogs; however, the expense of the drug may preclude its use in many cases.
- Itraconazole is teratogenic at high doses; therefore, do not use it in pregnant animals.
- Flexible dosing schedules (see Table 42-4) may be utilized with this drug since high levels are maintained in keratinized tissues (hair, nail, and stratum corneum).

Terbinafine

- Terbinafine is an allylamine antifungal agent that is fungicidal against dermatophytes.
- Terbinafine is well tolerated by cats and dogs. Vomiting is the most often reported side effect in pets.
- Terbinafine may be used on a daily basis (see Table 42-4) or with continuous/pulse therapy as with itraconazole.

Lufenuron

Lufenuron is used for control of pre-adult fleas. It disrupts chitin synthesis. Chitin is a component of the

fungal cell wall, and preliminary studies suggested that it may be useful in the treatment of dermatophytosis in dogs and cats. However, recent, controlled studies suggest that lufenuron will not prevent infection in exposed cats, nor will it alter the course of infection. I do not recommend the use of lufenuron for the treatment of dermatophytosis.

Antifungal Vaccine

There is a commercially available, killed vaccine for *M. canis* (Fel-O-Vax MC-K, Fort Dodge). The product insert claims its use is as an "aid in the prevention and treatment of clinical signs of disease caused by *Microsporum canis*." The vaccine is intended as an adjunct to traditional therapy, not a replacement. The insert also states that "vaccination has not been demonstrated to eliminate *M. canis* organisms from infected cats." Studies by the manufacturer indicate that there is a decrease in clinical signs in affected vaccinated cats compared with unvaccinated cats. However, there is no data to suggest that a cure is obtained faster when using this product or that this vaccine helps prevent infection in challenged animals.

Monitoring Therapy

Animals treated for dermatophytosis may appear clinically normal long before they are actually cured or culture negative. Reassess animals frequently to monitor response to therapy and to assess the need for modifications in therapy.

- Check animals on treatment at least every 3 to 4 weeks. Monitor for medication side effects.
- After 4 to 5 weeks of systemic therapy, check fungal cultures every 2 to 4 weeks depending upon clinical signs.
- Do not discontinue therapy until two negative cultures have been obtained.

PREVENTION

When planning and carrying out preventive measures, consider that dermatophyte spores can remain viable in the environment for many years.

Current Recommendations for Disinfection

The purpose of environmental disinfection is to prevent reinfection of the pet and to prevent infection of other household members. Unfortunately, many of the disinfectants that are in use today are not effective for killing dermatophyte spores. Evaluation of several different disinfectants found that only concentrated bleach and 1% formalin were 100% effective in killing spores. These products are not acceptable for routine environmental disinfection.

- Discard animal bedding, collars, brushes, and toys.
- Clean all draperies and bedding material.
- Remove and clean all furnace and air conditioning filters. Catteries or multiple cat households should consider having air ducts cleaned.
- Thoroughly vacuum floors, carpeting, and furniture to remove infected hairs. Do this at least 3 to 4 times weekly. Dust surfaces with an electrostatic dust-trapping cloth on a daily basis. Dispose of vacuum bags after each use.
- Clean surfaces that will not be damaged by the solution with a 1:10 dilution of bleach (sodium hypochlorite) on a weekly basis.
- Dispose of all grooming equipment.
- Wash hands thoroughly after handling infected animals.

Identification of the Source of Exposure

- Examine other animals in the household.
- Specific dermatophyte species that are cultured can provide helpful clues. For example, if *T. mentagrophytes* is isolated from a dog that spends most of the time indoors and there is a pet rodent in the household, brush culture the rodent for the presence of dermatophytes.
- Treat all infected animals in the household.

Preventive Measures in a Cattery

- Identify all infected animals. For best results, use the toothbrush culture technique described previously.
- Separate infected from culture-negative animals.
- Treat infected cats until tests are culture negative before reintroducing them into the general cat population.
- Disinfect cages on a regular basis and vacuum and disinfect air vents.
- Never use the same grooming equipment on both infected and culture-negative cats.
- Place all new animals brought into a cattery in isolation until culture-negative results have been obtained.

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Chapter 43

Canine and Feline Demodicosis

Sarah Colombini Osborn

DEMODEX MITES

- Every animal harbors its own host-specific species of *Demodex* mite. *Demodex* mites, in low numbers, are normal inhabitants of the stratum corneum, hair follicles, and sebaceous glands.
- Demodicosis is the disease state associated with the abnormal proliferation of *Demodex* mites.
- Demodicosis occurs commonly in dogs and less commonly in cats. The feline mite resides more superficially on the skin than the canine mite.
- The entire life cycle (25–30 days) is completed on the host. Mites cannot survive off the host for more than a couple of hours.
- Four stages of the life cycle may be demonstrated in skin scrapings: eggs, larvae, nymphs, and adults.
- Transmission of the mite occurs by direct contact during nursing in the first 2 to 3 days of life.

CANINE DEMODICOSIS

Etiology

- Although *Demodex canis* is part of the normal fauna of canine skin and is the most common mite found in cases of demodicosis, two other *Demodex* mites have recently been identified. One is a short-tailed *Demodex* mite (unnamed as yet) and the other is a long-bodied *Demodex* mite *(Demodex injai).*
- More than one type of mite may be found on some dogs.
- The mites are present primarily in hair follicles and rarely in sebaceous glands, although the short-tailed mite resides on the skin surface.
- Treatment and prognosis appear similar between the various mite species.

Pathogenesis

- The pathogenesis of demodicosis is not completely understood.
- Affected animals probably have a mite-induced immunosuppressive disorder of T cells of varying severity in which the immunosuppression is proportional to the number of mites present.
- The tendency to develop juvenile-onset, generalized demodicosis is familial. Adult-onset and localized demodicosis are not. Although the mode of inheritance is not known with certainty, an autosomal recessive mode is suspected.
- Purebred dogs have a higher incidence of demodicosis, with the Shar-Pei, West Highland white terrier, Boston terrier, and English bulldog being among the most commonly affected breeds.
- In most cases, canine demodicosis is not contagious.

Clinical Signs

▼ ***Key Point*** Characterization of demodicosis in dogs is important to both treatment and prognosis. Demodicosis is classified as: (1) juvenile-onset or adult-onset, (2) squamous or pustular, and (3) localized or generalized.

Juvenile Onset

- Onset in animals less than 2 years of age is considered *juvenile onset* in most breeds. Onset in animals greater than 2 years of age is considered *adult onset.*
- Juvenile-onset, generalized demodicosis is a familial disease, and all affected animals should be neutered. The parents and siblings of the affected animal should also be removed from the breeding population.

Adult Onset

- Adult-onset demodicosis invariably results from immunosuppression. Approximately 50% of adult-onset demodicosis cases result from exogenous or endogenous glucocorticoids (iatrogenic or spontaneous hypercortisolism).
- Diagnosis of adult-onset, generalized demodicosis is cause for a thorough workup to evaluate for underlying immunosuppressive conditions, including hypothyroidism, hypercorticism, neoplasia, and administration of immunosuppressive medications.

Localized

- Localized demodicosis is classified as less than approximately six lesions or only one body region affected. The periocular and perioral regions are most commonly affected and pruritus may be present.
- Nearly 90% of localized demodicosis cases will spontaneously resolve in young animals, while 10% will become generalized regardless of treatment.
- Localized demodicosis is not familial.

Generalized Demodicosis

- Generalized demodicosis is classified as more than approximately six lesions, involvement of two or more body regions, or involvement of two or more feet (pododemodicosis).

Squamous Demodicosis

- Squamous demodicosis presents as patchy alopecia with no pyoderma. Fine scales may be present in the affected areas and close examination may reveal comedones (plugged hair follicles).

Pustular Demodicosis

- Pustular demodicosis presents with a secondary pyoderma, with *Staphylococcus intermedius* being the most common bacterial organism involved.

Pododemodicosis

- Pododemodicosis lesions are especially susceptible to develop secondary pyoderma.

Demodex Otitis

- Demodicosis of the ear canals associated with ceruminous otitis externa occurs rarely and may result in intense pruritus.

Diagnosis

- Obtain a thorough history and physical examination.
- For dogs with adult-onset demodicosis, obtain the following:
  - Complete blood count, chemistry panel, urinalysis
  - Further testing: Screening thoracic and abdominal radiographs (for neoplasia), thyroid profile, adrenocorticotropic hormone stimulation test, or low-dose dexamethasone test
- *Deep skin scraping* is the preferred means to diagnose demodicosis. If performed properly, mites should be present on skin scrapings in nearly all affected animals.
- If skin scrapings cannot be performed due to location (eyelid, etc.) or discomfort, perform a trichogram by plucking hairs in the affected areas and examining them microscopically in the same manner as skin scrapings. This technique, however, can yield false-negative results in mildly affected dogs.

Skin Scraping Technique

- Squeeze the skin prior to and during the scrapings to facilitate mite collection.
- Apply a few drops of mineral oil to the sites that will be scraped.
- Scrape the skin in the direction of hair growth with a dull #10 scalpel blade.
- Scrape until capillary oozing occurs.
- Collect debris and blood from the site and place on a slide with mineral oil.
- Moistening the blade with mineral oil may facilitate collection of material.
- Apply a cover slip to the slide and examine microscopically under the low power objective (4×, 10×) (Fig. 43-1).
- Obtain scrapings from a minimum of four or five locations, including lesions, lip folds, and interdigital regions.
- Scrapes should be positive if the animal has demodicosis and the correct technique is employed. Exceptions are the Shar-Pei or dogs with chronic fibrotic lesions (especially of the interdigital skin) that may require biopsy.
- Quantify the number of eggs, juveniles, and adult mites from each location to determine the severity of the disease and for later evaluation of response to treatment.
- A single mite on skin scrapings may be normal, but perform multiple follow-up skin scrapings to rule out demodicosis.

Skin Biopsy

- Skin biopsy and histopathology may be indicated in the Shar-Pei or from dogs with chronic, fibrotic lesions (see Chapter 37). This is especially true of dogs with chronic pododemodicosis.

Figure 43-1. *Demodex canis.*

Treatment

Localized Demodicosis

▼ ***Key Point*** No therapy is necessary for localized demodicosis, as there is no difference in resolution rates between treated and untreated cases.

- There is no evidence that topical treatment of localized lesions prevents the disease from becoming generalized.
- If treatment of localized demodicosis is to be initiated, use topical spot treatments such as benzoyl peroxide gels, amitraz (Mitaban, Pharmacia & Upjohn) in mineral oil (1:9), or 1% rotenone ointment (Goodwinol, Goodwinol Products).
- An amitraz collar (Preventic, Virbac) may also be considered appropriate treatment for localized demodicosis.
- Topical treatment may cause increased alopecia and erythema.
- For cases of demodicosis localized to the external ear canal, amitraz in mineral oil (1:9) can be very effective (6–8 drops in the ear canal q24h).

▼ ***Key Point*** Never treat localized demodicosis with systemic or full-body topical parasiticides as it increases the potential for resistance and impairs the ability to determine if the disease would have become generalized, making neutering of the pet essential.

Generalized Demodicosis

- More than 30% to 50% of dogs less than 1 year of age with generalized demodicosis will spontaneously recover. If a dog continues to have clinical lesions beyond 1 year of age, then spontaneous resolution becomes unlikely.
- It appears that the shorter the haircoat, the better the prognosis.

▼ ***Key Point*** In cases of pustular demodicosis, always treat with appropriate systemic antimicrobial therapy as pyoderma contributes to the mite-specific immunosuppression and makes resolution of the demodicosis more difficult. Extended courses of antibiotic therapy are typically indicated (4–8 weeks).

- Medicated bathing with a benzoyl peroxide shampoo on a weekly basis is beneficial.
- Corticosteroids are contraindicated in all forms of demodicosis.

Amitraz

- Amitraz remains the only licensed product by the U.S. Food and Drug Administration for treatment of generalized demodicosis in the dog.
- The label instructions are to use a 250-ppm concentration (1 bottle in 2 gallons of water) once every 2 weeks.
- It is not an approved treatment for localized demodicosis.
- Dips may be performed at the veterinary clinic or by the owners. Be very familiar with the precautions that appear on the label instructions and the possible side effects for humans in contact with the dip (see below).

Amitraz Dip Procedure

- Keep the haircoat cut short during treatment to improve the efficacy of amitraz dips.
- Remove all crusts and bathe the entire dog with a benzoyl peroxide shampoo prior to dipping.
- The dips must be prepared fresh prior to each dip as the product looses efficacy and breaks down to more toxic products once the vial is opened.
- A 15-minute contact time is extremely important, especially on the feet and face. The dip should be sponged over the entire body area for the full duration.
- Do not rinse or towel-dry following the dip.
- Avoid getting the patient wet in between dips (i.e., prevent them from swimming, do not bathe with any shampoo, and do not allow them to be outside if it rains).
- Efficacy is increased significantly when dips are increased to once weekly, and increasing the concentration (e.g., 500 ppm) of the dips may improve efficacy. However, this is extra-label use of the product, and the potential for side effects may increase.
- Most dogs require an average of six to nine dips to achieve resolution of demodicosis—some cases may need more dips before resolution occurs.

Minimizing Side Effects of Amitraz Dips

- Depression, lethargy, and hypothermia are the most common side effects of amitraz dips. Patients should be monitored for these side effects. Less common side effects include pruritus, neurologic signs, and bradycardia.
- Especially for small-breed (e.g., Yorkshire terriers and Chihuahuas) or young dogs, dilution of the dip to half strength for the first couple of dips may help determine how the patient will tolerate the dips. The dip then needs to be increased to full strength to resolve the mites and help prevent development of resistance.
- Yohimbine (Yobine, Lloyd Labs) at 0.11 mg/kg may be used pre- and/or post-dipping to help prevent or reverse side effects of the dips.
- Amitraz shows an increasing frequency of side effects as the topical concentration increases.

▼ ***Key Point*** Do not apply the dip if you are asthmatic, diabetic, have cardiovascular disease, or are taking alpha 2-agonists.

Amitraz Collar

- Amitraz collars may be beneficial as an adjunctive treatment for generalized demodicosis or a sole treatment for localized demodicosis.
- It is not effective as the sole treatment for generalized demodicosis.

Ivermectin

- Ivermectin (Ivomec, Merial) remains an extra-label alternative for the treatment of canine generalized demodicosis. Use for those patients that do not respond to or tolerate amitraz dips.
- Obtain signed owner consent for the use of ivermectin in the pet.
- Avoid ivermectin in collies, shelties, and herding breeds, as they are very susceptible to developing signs of ivermectin toxicity.
- The target dose of ivermectin is 400 to 600 mg/kg orally once daily. Slowly increase the dose by 100 mg/kg/day to allow close monitoring for potential side effects.
- Length of treatment ranges from 60 to 120+ days.
- Every-other-day therapy has been reported to be effective, although the duration of treatment appears to be prolonged.

Ivermectin Toxicity

- Signs of ivermectin toxicity may occur in any breed, although collies, shelties, and herding breeds are most susceptible. Of collies, 30% to 40% will show adverse effects to ivermectin administration, which may prove fatal.
- Side effects include mydriasis or miosis, salivation, depression or lethargy, anorexia, vomiting, ataxia, stupor or coma, and possibly death.
- Immediately withdraw ivermectin and administer symptomatic therapy should signs of toxicity occur. There is no antidote for ivermectin toxicity.

Milbemycin

- Milbemycin oxime (Interceptor, Ciba-Geigy) is in the same drug family as ivermectin and is also *not* approved by the Food and Drug Administration for the treatment of canine demodicosis.
- It may be safer in sensitive breeds as it requires a higher dose to produce side effects.
- The recommended dose is 1 to 2 mg/kg orally once daily.
- Cure rates appear to be higher with higher dosages, and dogs with adult-onset demodicosis respond less favorably then those with juvenile-onset demodicosis.
- The tablet is easier to administer than ivermectin, especially in small dogs.
- Milbemycin has the disadvantage of being 3 to 4 times more expensive than ivermectin.
- moxidectin, another milbemycin, has also been reported to be effective in the treatment of canine demodicosis at doses of 0.2 to 0.4 mg/kg/day. This is also off-label use; only consider using when dogs cannot be treated with amitraz or the disease is resistant to amitraz.

Combination Therapy with Amitraz and Ivermectin or Milbemycin

- Daily ivermectin or milbemycin therapy combined with weekly amitraz dips results in an extremely high incidence of severe neurotoxicity.
- Once weekly administration of ivermectin with weekly or every-other-week amitraz dips appears safer but is likely no more effective than amitraz dips alone.
- Do not use combination therapy.

End Point of Treatment

- Regardless of the type of therapy selected, perform multiple deep skin scrapings prior to and every 2 to 4 weeks throughout treatment.
- Scrape the same four or five areas and record the number of eggs, juveniles, and adult mites to monitor response to treatment.

▼ ***Key Point*** Dogs will achieve clinical cure prior to parasitologic cure (skin scrape negative). Even the finding of dead mites is considered a positive scraping. Continue treatment for at least 4 weeks beyond negative skin scrapings. Premature cessation of therapy is the most common cause for recurrence of demodicosis.

- If a dog is going to relapse, most do so within the first 6 months following the cessation of therapy. The dog is only considered cured after 12 months free of disease.

Unsuccessful Treatment or Recurrence of Demodicosis

- Maintenance therapy is necessary in up to 20% of demodicosis patients. This is especially true for cases of adult-onset, generalized demodicosis in which the underlying immunosuppressive condition cannot be determined or corrected.
- Treatment options to keep the *Demodex* mite numbers under control and clinical signs to a minimum must be tailored to the patient.
- Options include amitraz dips every 2 to 6 weeks or ivermectin or milbemycin administered every other

day, once daily every other week, or the first week of every month.
- Immunostimulants such as levamisole, thiabendazole, and vitamin E have shown no effect on the resolution of canine demodicosis and are not recommended.

FELINE DEMODICOSIS

Etiology

- Feline demodicosis is caused by either *Demodex cati* (long-tailed mite) or *Demodex gatoi* (short-tailed mite).
- A third possible *Demodex* mite has also been reported.
- *D. cati* is found in hair follicles and has a similar appearance to *D. canis* in the dog. The feline mites, however, have a slimmer, elongated body compared with the canine mites.
- *D. gatoi* is a superficial mite found in the stratum corneum, with a short, broad, blunted abdomen.
- Generalized demodicosis with *D. cati* is rare, and an underlying immunosuppressive disease (diabetes, feline leukemia or feline immunodeficiency virus, hyperadrenocorticism, respiratory infection, etc.) should always be suspected in affected cats.

▼ ***Key Point*** *D. gatoi* is contagious among cats and generalized infection with this mite is not typically associated with underlying disease.

Clinical Signs

- The clinical signs of feline demodicosis are quite variable and some cats may serve as asymptomatic carriers.
- Localized demodicosis may present as a single area of alopecia and scaling, primarily affecting the periocular, head, and neck regions.
- Occasionally, the mites may be confined to the external ear canals, with ceruminous otitis externa being the only clinical sign. Large numbers of mites have also been found on skin scrapings from the ear canals of asymptomatic cats.
- Clinical signs of generalized demodicosis include multifocal to generalized alopecia, scaling, erythema, and hyperpigmentation.
- Bilaterally symmetrical alopecia can be a common clinical finding with generalized demodicosis, making differentiation from allergic dermatitis and psychogenic dermatosis difficult.
- Pruritus with *D. cati* is variable and usually minimal. Pruritus with *D. gatoi* is typically much more pronounced, with excessive grooming and subsequent alopecia being the primary presenting complaints.

Diagnosis

- Multiple superficial skin scrapings are the diagnostic tools of choice.

▼ ***Key Point*** Feline *Demodex* mites can be very difficult to find on skin scrapings (much like canine scabies), and treatment is recommended whenever feline demodicosis is suspected.

- Due to the small size and translucency of *D. gatoi,* use the 10× objective when searching microscopically for the mite. Reduce the intensity of the light to increase the contrast.
- The number of mites present in the skin appears to be dramatically reduced in those cats that are pruritic, likely due to over-grooming.
- If *D. cati* is found on skin scrapings, search for an underlying disease. Perform complete blood count, serum chemistry panel, urinalysis, and tests for feline leukemia and feline immunodeficiency virus.

Treatment

- The treatment of choice for both species of feline *Demodex* mites is lime sulfur dips (LymDyp, DVM Pharmaceuticals) every 5 to 7 days for six treatments.
- If a cat has demodicosis or lime sulfur dips are being administered as a therapeutic trial, improvement should be evident following three to four dips.
- The superficial location of the mites in the skin of cats compared with that of dogs likely accounts for the good response to lime sulfur dips.
- If *D. gatoi* is present or the mite cannot be found on skin scrapings, treat all contact cats simultaneously as some cats may serve as asymptomatic carriers of the mite.
- Treatment of localized demodicosis confined to the ear canals includes lime sulfur, ear mite preparations, and amitraz in mineral oil (1:9) applied to the ear canal.
- Do not use amitraz dips for the treatment of feline demodicosis due to the effectiveness of more benign therapy and the significant potential for side effects.
- Recent findings suggest that clinical signs of demodicosis may resolve with weekly application of selamectin (Revolution, Pfizer) but that mites are still present on skin scrapings. When application of selamectin is decreased or discontinued, the clinical signs of demodicosis recur.
- Ivermectin has not been shown to be reliably effective unless administered on a daily basis. Further clinical studies are needed to determine the most effective dosing regimen of ivermectin before this medication can be recommended as an appropriate treatment for feline demodicosis.

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Chapter

44 Scabies, Notoedric Mange, and Cheyletiellosis

Lauren R. Pinchbeck / Andrew Hillier

Sarcoptic mange, notoedric mange, and cheyletiellosis are parasitic dermatoses caused by acarine mites living on or within the skin of the host animal. Exposure to these mites and the corresponding incidence of parasitic dermatoses are closely related to environmental factors, especially animal contact and living in endemic areas. Although these mites are not completely host specific, they exhibit host preference and have zoonotic potential for causing dermatoses in humans.

Ectoparasitism is a differential diagnosis in all veterinary patients presenting with a primary problem or clinical signs suggestive of pruritus. The level of pruritus can be variable, especially among cats, and the recognition of pruritus may be underappreciated by owners. Assess parasitism prior to pursuing primary allergic diseases such as atopic dermatitis or cutaneous adverse food reaction. Parasitism is generally a curable disease, and the diagnosis of a primary allergy can only be definitively diagnosed after parasitism is ruled out.

Lesions resulting from infestation with these mites are primarily due to self trauma. In addition, lesions may be due to mechanical damage from burrowing of the mite into the superficial layers of the skin, pruritogenic substances secreted by the mite, or the hypersensitivity reaction developed against extracellular products of the mite. The variability of clinical manifestations of these dermatoses probably reflects variations in duration and intensity of the hypersensitivity reaction and variations in the capacity of the host to limit parasite multiplication.

▼ ***Key Point*** Always consider parasites in patients presenting with pruritus.

SCABIES

Etiology

- Scabies (sarcoptic mange) is a non-seasonal, intensely pruritic papulocrustous dermatosis of dogs caused by the epidermal mite *Sarcoptes scabiei* var. *canis* (Fig. 44-1). Although fairly host specific, the mite can affect cats, foxes, and humans. Sarcoptic acarosis is rare in the cat, and an underlying immunosuppressive disease (i.e., feline immunodeficiency virus infection) is likely to be concurrent and should be investigated.
- The adult mite is microscopic (200–400 µm), roughly circular in shape. It is characterized by two pairs of short legs anteriorly that bear long, unjointed stalks with suckers and two pairs of rudimentary legs posteriorly that do not extend beyond the border of the body.
- The parasite completes its life cycle (egg–larva–nymph–adult) in 12 to 21 days in tunnels and molting pockets in the stratum corneum of the epidermis. Mites burrow into the lower stratum corneum but rarely penetrate further. The female may reach the stratum spinosum as she creates the tunnel and deposits eggs.
- Although scabies mites live in the superficial layers of the skin, the mite antigen can reach the lower epidermal and dermal skin and induce a humoral and cell-mediated immune response. Dogs may develop a protective immunity after successful treatment and cure of a scabies mite infestation. Thus, subsequent reinfestation may not result in clinical signs. The exact mechanism of protective immunity is not fully understood, and its elucidation is further complicated by crossreactivity and cross-sensitization to house dust mites.
- Although the parasite is susceptible to high temperature and drying, it can live in the environment for up to 21 days under ideal environmental conditions.
- Scabies is highly contagious and is primarily transmitted by direct contact with an infested animal. Fomite and fur transmission to humans or other animals can occur via contact with grooming equipment or at kennels.
- The incubation period is highly variable and is dependent on factors such as the number of mites present, the time required for the development of hypersensitivity, and the treatments prescribed. The use of systemic corticosteroids may allow the mite population to increase more rapidly.
- Observable dermatologic changes are often out of proportion with the number of mites present on the

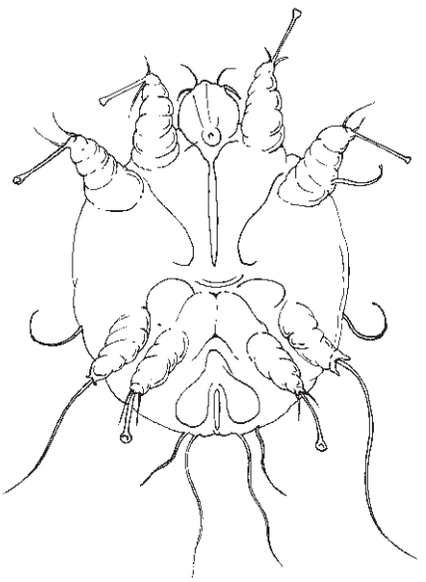

Figure 44-1. *Sarcoptes scabiei.*

animal, suggesting that cutaneous hypersensitivity to mite antigen plays an important role in the course of disease.

Clinical Signs

▼ ***Key Point*** Scabies is typically characterized by papular dermatitis and intense pruritus that is incompletely or minimally responsive to corticosteroids.

- The body sites typically involved include the ear pinnae margins, elbows, hocks, and ventral chest. Lesions and pruritus can become widespread, but the dorsum is usually spared.
- Early lesions are characterized by erythematous papular eruptions that develop thick crusts that may be yellow in color. With time, self-excoriation results in patchy to widespread alopecia, and generalized papulocrustous dermatitis develops. Hyperpigmentation and lichenification are the most dominant lesions in chronic cases due to constant self trauma at affected body sites.
- Some dogs are intensely pruritic but have few, if any, lesions other than mild erythema and occasional excoriations. Others may have less severe pruritus with many mites present (so-called Norwegian scabies).

Diagnosis

- Major differential diagnoses include cutaneous adverse food reaction (CAFR) and flea bite hypersensitivity (FBH), as these diseases can also be intensely pruritic. The distribution patterns characteristic of CAFR, FBH, and scabies can mimic each other in chronic cases, especially if secondary infections are present.
- Additional differentials to consider include cheyletiellosis, *Otodectes cyanotis* dermatitis, dirofilariasis, *Pelodora* dermatitis, atopic dermatitis, and contact dermatitis.
- *Malassezia* dermatitis and superficial pyoderma are also important differentials, and these secondary infections should be considered at the initial presentation. These infections can be intensely pruritic in animals hypersensitive to the organisms. Dermatophytosis is not usually pruritic, but it should be pursued as a differential if therapy does not resolve the clinical signs.

History

- Rapid onset of intense pruritus and rapid progression of lesions with inconsistent response to corticosteroids.
- Likely source of infection. Inquire about visits to training or boarding facilities, dog shows, dog parks, grooming parlors, etc., approximately 1 month prior to the onset of the pruritus.
- Potential exposure of the affected animal to other species known to harbor the mite, especially fox.
- Pruritic dermatitis involving dogs and humans in contact with the affected animal. The absence of pruritus in in-contact animals does not rule out the possibility of infestation.

Physical Examination

- Characteristic cutaneous lesions and typical distribution pattern as described.
- Generalized peripheral lymphadenopathy may be palpated in an affected dog.

Diagnostic Tests

- To make a definitive diagnosis, the clinician must demonstrate the presence of any life stage of the mite and/or eggs. Perform superficial skin scrapings and fecal flotation. Remember that the mite is often very difficult to find, even with multiple skin scrapings.

▼ ***Key Point*** Failure to find the mite does not eliminate the diagnosis of scabies. Always use trial therapy if the diagnosis remains in question and the degree of suspicion is high enough to justify its use.

- To obtain superficial skin scrapings, identify non-excoriated and recently affected body sites where crusted papules are visible. Avoid lesions of chronic pruritus, such as severe lichenification. Usually the

ear pinnae, elbows, hocks, and ventral thorax are best. Apply a liberal amount of mineral oil to the skin surface and scrape a wide anatomic area with a #10 scalpel blade. Transfer the collected material to a glass slide and examine under 10-power magnification and reduced light. Carefully evaluate all microscope fields for any life stage of the mite. Even finding an egg or brown, oval fecal pellets in the material is diagnostic.

▼ ***Key Point*** Obtaining multiple superficial skin scrapings, performed over wide areas of recently affected body sites, will increase the chances of finding mites.

- Of dogs with scabies and ear pinna lesions, 75% to 90% have a positive pinnal-pedal reflex. In one study, this test had a sensitivity of 81.8% and a specificity of 93.8%.
  - To perform this test, maneuver the tip of an affected ear pinna and rub it vigorously against the base of the ear for at least 5 seconds. At the same time, observe the ipsilateral hind limb. If the dog moves the limb in an attempt to scratch, the test is positive.
  - A positive reflex alone is not diagnostic, and a negative result does not rule out scabies.
- Most dogs develop a humoral antibody response between 2 and 5 weeks after infection with scabies. An enzyme-linked immunosorbent assay (ELISA) used to detect serum immunoglobulin G (IgG) antibodies to *Sarcoptes* mite antigen is available (Imovet Sarcoptic). The test has a reported diagnostic sensitivity of 83% to 92% and a specificity of 89.5% to 96%. It may be helpful in the diagnosis of canine scabies when the disease is suspected, but mites cannot be identified.
  - Send labeled serum (1 ml) on ice packs with submission form overnight to the following address:

    Attn: Dana Ambrose
    Athens Diagnostic Laboratory
    University of Georgia College of Veterinary Medicine
    Athens, Georgia 30602-7383
  - Submission forms may be downloaded from the Athens Diagnostic Laboratory website at http://hospital.vet.uga.edu/dlab/athens/access.pdf.
  - Seroconversion may take up to 5 weeks, so do not submit serum for this test in acute cases. Currently, this test is recommended only if clinical signs have been present for at least 2 weeks.
- House dust mite, a common allergen in dogs with atopic dermatitis, shares some antigens with *S. scabiei*. Patients with scabies may have positive intradermal and serum allergy test results to house dust mite allergens. Thus, rule out scabies definitively prior to making a diagnosis of atopic dermatitis and performing allergy testing.

Treatment

- Emergence of resistant strains of the *Sarcoptes* organism and an array of available commercial products make selection of parasiticides difficult. Products highly efficacious in one geographic location may be ineffective in another.
- A number of acaricidal products have demonstrated efficacy in the treatment of sarcoptic mange. Many of these products have real potential for toxicity and adverse reactions in certain breeds or species. Idiosyncratic reactions have also been reported in certain breeds at therapeutic doses.
- Initially, use a product approved and licensed by the U.S. Food and Drug Administration (FDA) for the target animal species and disease being treated. Any other application is extra-label usage of that drug. The FDA recognizes the need for extra-label usage in veterinary medicine, but you should obtain informed consent from the owner. If the FDA product cannot be used in a particular animal, attempt to use a drug that is approved for the species you are treating but for another disease.
- For scabies, treat all in-contact animals concurrently.
- Evaluate heartworm status in all dogs prior to treatment. Some topical treatments are systemically absorbed.
- Systemic therapies are emerging and proving to be efficacious in the treatment of scabies in dogs. The macrocyclic lactones ivermectin (Ivomec, Merial Animal Health), milbemycin oxime (Interceptor, Novartis Animal Health), moxidectin (Cydectin, Fort Dodge Animal Health), and selamectin (Revolution, Pfizer Animal Health) are effective.

Selamectin

- Selamectin is a novel semisynthetic avermectin produced by *Streptomyces avermitilis*. In the United States, it is approved for the prevention of canine heartworm, flea control, deworming, and the treatment of sarcoptic mange and *Otodectes cyanotis* in dogs. It is also licensed for the control of *Dermacentor variabilis* infestations. For cats, it is labeled in the United States for the prevention of dirofilaria, fleas, and *Otodectes cyanotis*. It is also used for gastrointestinal nematodes in cats. In cats and dogs, selamectin may be given at 6 weeks of age at the label dosage of 6 to 12 mg/kg applied to the skin.

▼ ***Key Point*** Selamectin (Revolution, Pfizer Animal Health) is the only product licensed by the FDA for the treatment and control of scabies.

  - Selamectin is apparently safe in collies, related breeds, and their crosses.
  - Two treatments with selamectin 30 days apart at a dose of 6 to 12 mg/kg applied to the skin on the

dorsal neck is reported by the manufacturer to be 100% efficacious for the treatment of scabies by day 60. Field and laboratory trials were comparable to a reference positive-control product. We frequently use selamectin every 14 days for two to three treatments for the treatment of confirmed or suspected scabies acarosis. This regimen would be extra-label usage. Environmental treatment may not be necessary.

Milbemycin Oxime

- Milbemycin oxime (Interceptor, Novartis Animal Health) is a macrolide antibiotic made from the fermentation of *Streptomyces hygroscopicus* and is approved for monthly heartworm prophylaxis. It is not approved by the FDA for the treatment of scabies, but it may be an alternative treatment, especially in breeds of dogs in which ivermectin is contraindicated and the FDA-approved product cannot be used.
  - Dosing regimens of either 2 mg/kg PO twice at 14-day intervals or 2 mg/kg PO at 7-day intervals for 3 to 5 weeks have been effective. Other regimens that may be effective include 1 mg/kg PO every 2 days for eight treatments and 2 mg/kg PO twice weekly for 3 to 4 weeks.
  - Accurate dosing of milbemycin oxime is essential in at-risk breeds. When administered at doses of less than 3 mg/kg, adverse effects are rare. Milbemycin is fairly well tolerated in collies and related breeds, but some dogs may be sensitive even at doses of less than 3 mg/kg. Always use caution in at-risk breeds and their crosses.
  - Lack of response to milbemycin when mites are not observed on scrapings does not necessarily rule out the disease. Reevaluate patients after the second or third treatment to look for clinical improvement. Treatment duration may need to be extended.

Ivermectin

- Ivermectin (Ivomec, Merial Animal Health) is very effective in the treatment of scabies, but it is not approved by the FDA for the treatment of scabies. Ivermectin is only licensed in the dog for the prevention of dirofilariasis at a dosage of 0.006 mg/kg PO monthly. For cats the dosage is 0.024 mg/kg PO monthly. Extra-label doses of ivermectin preparations that are marketed for use in other species are reported for the treatment of scabies.
  - A dosage of 0.2 to 0.4 mg/kg PO every 7 days for three to four treatments or SC every 14 days for two to three treatments is effective.
  - Any dog may have an idiosyncratic reaction to ivermectin. Some recommend a step-up dose regimen to identify dogs that are sensitive. Do not administer to collies, Shetland sheepdogs, Old English sheepdogs, Australian shepherds, or their crosses.
  - Adverse reactions to ivermectin may include tremors, ataxia, mydriasis, stupor, coma, and death. As there is no known antidote for ivermectin toxicity, only supportive therapy (fluids, parenteral nutrition) is available.
  - The 0.5% pour-on preparation of ivermectin is effective at 0.5 mg/kg applied topically to the dorsum twice 14 days apart. This may be considered if a large number of dogs must be treated. Systemic absorption must be considered, and the same precautions should be taken.

Fipronil Spray

- A 0.25% fipronil spray (Frontline Spray; Merial Animal Health) at a dose of 3 ml/kg applied every 21 days for three treatments has been safe and effective in 4-week-old puppies. Decreased pruritus was recognized 1 week after the first application. It has also been used effectively as a sponge-on preparation in dogs when applied at a dose of 6 ml/kg applied twice 7 days apart. These treatments would be extra-label usage. Recently, use of this product has been recommended only for early cases of scabies or for use in pets for which alternative products are contraindicated.

Dips

- Dips traditionally were routine in the treatment of scabies. Although less commonly used today, dips may be indicated in certain situations. Clip the hair when the dog has medium to long hair or a dense coat. When scale and crust are present, bath with a keratolytic shampoo prior to dipping. Treat the entire coat; spot treatment is ineffective.
- Dips known to be effective include the following:
  - *Lime sulfur* (LymDyp, DVM Pharmaceuticals): A 2.5% to 5% solution every 5 to 7 days. It is the safest dip for young animals or sick and debilitated patients. The animal may appear worse after the first treatment but will likely be 50% to 75% improved after the second application. Reevaluate after the third dip and continue treatment until the dog is asymptomatic and negative skin scrapings are obtained. The foul odor and potential for staining light haircoats, fabrics, paints, metal, and jewelry make lime sulfur less appealing. These problems are not significant once the coat is dry. Staining of the pet's haircoat is temporary, and the discoloration and associated dry skin resolve once treatment is discontinued.
  - *Amitraz* (Mitaban, Pfizer Animal Health): A 0.025% solution applied 3 times 14 days apart. This treatment would be extra-label usage. A response is usually seen after the second application. Care and appropriate precautions must be taken in applying the dip. Do not use amitraz in toy breeds, pregnant or nursing bitches, or puppies less than 3 months

of age. Inform owners of side effects and signs to monitor for at home after dip application. Have the dip performed by trained personnel in a setting where the animal can be monitored for side effects after the application. Yohimbine and atipamezole are antidotes.

Other Treatments

- Doramectin at a dose 0.2 mg/kg SC or IM administered once.
- Moxidectin 1% injectable at a dosage of 0.2 to 0.25 mg/kg PO or SC every 7 days for 3 to 6 weeks. Side effects of this medication may include urticaria, angioedema, and ataxia. Side effects seem to occur more frequently when administered subcutaneously, so the oral route is preferred.
- These treatments would be extra-label usage.

Treatment Principles

- Treat all dogs in contact with the affected animal. Do not allow affected and in-contact animals to socialize with other dogs or travel where there may be fur-bearing animals.
- Cats may be reservoirs but do not usually need to be treated. If there are cats in the household, treat with selamectin every 2 to 4 weeks while the affected dogs in the household are being treated.
- Mites die after a few days when off the host, but general cleanup of the environment and application of a parasiticide containing permethrin may be beneficial when a number of animals are affected (e.g., a kennel or pet shop). Environmental treatment may prevent reinfestation from point sources. Consider environmental treatment if there is a poor response to parasiticidal therapy in proven cases or in recurrences.
- If a therapeutic trial does not result in the reduction and subsequent resolution of clinical signs within 3 to 4 weeks, reassess the animal for other causes of pruritus (most notably infection and allergic dermatitis) and pursue further diagnostics.

NOTOEDRIC MANGE

Etiology

- Notoedric mange (feline scabies) is an intensely pruritic, crusting dermatosis of cats caused by the sarcoptiform mite, *Notoedres cati* (Fig. 44-2). The mite may also infest dogs, fox, and rabbits and may cause transient lesions in humans.
- Notoedric mange is uncommonly diagnosed, but it may be endemic in a few localities.
- This obligate parasite is a burrowing mite similar to *S. scabiei,* and the life cycle is approximately 17 to 21 days.

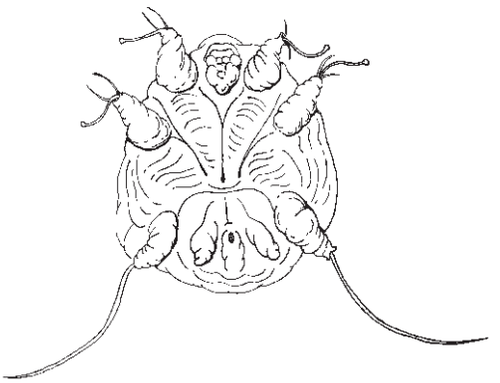

Figure 44-2. *Notoedres cati.*

- In comparison to *S. scabiei* var. *canis, N. cati* is smaller; has medium-length, unjointed sucker-bearing stalks on the legs; and has more body striations. The major differentiating characteristic is the dorsally located anus in *N. cati.*

▼ ***Key Point*** Notoedric mange is highly contagious and is usually transmitted by direct contact.

- It commonly affects entire litters and all in-contact adult cats in cattery situations. Characteristically, it is a disease of adult cats, but it may present as a fulminating dermatitis in kittens.
- *N. cati* survive for only a few days off the host, but fomite transmission should be considered in cases that do not respond to therapy.
- The exact pathogenesis of notoedric mange is unknown, but the intense pruritus and inflammation may be due to the proximity of the burrowing tunnels to the nerve endings in the skin.

Clinical Signs

- Classically, the ear pinnae, head, and neck are the affected body sites.
- Initially there are erythematous papular eruptions on the medial aspect of the pinnae as the mites burrow between hair follicles. The papules may have a well-defined center representing the location of the burrow.
- Lesions can then spread rapidly to the head, neck, perineum, and feet. This distribution is consistent with the grooming and nesting behaviors of most cats. The abdomen, flanks, base of tail, and inner thighs become affected with time.
- As the disease progresses, the affected body sites become thickly crusted. The intense pruritus results in self-excoriation that leads to alopecia and lichenification. A matted haircoat may be noted in medium- and long-haired cats.
- Persistent self-trauma can lead to secondary infection.
- Peripheral lymphadenopathy is usually present.

Diagnosis

- Diagnosis is suggestive if there is a compatible history, intense pruritus, and characteristic distribution of lesions. Definitive diagnosis can only be made by finding mites on superficial skin scrapings.
- Differential diagnoses include both primary and secondary causes of pruritus in cats. Other parasitic dermatoses such as *Otodectes cyanotis* dermatitis and cheyletiellosis can have similar clinical signs. CAFR, FBH, and atopic dermatitis are allergic diseases that should remain differentials until the appropriate therapeutic and diagnostic trials are completed. Infectious diseases such as dermatophytosis can present with lesions that mimic notoedric mange but are not normally intensely pruritic infections. Perform fungal cultures at the initial evaluation to rule out dermatophytosis early. Cats with autoimmune diseases may present with papulocrusting dermatitis, so include pemphigus foliaceus, pemphigus erythematosus, and systemic lupus erythematosus on the differential list, although these diseases are typically not associated with pruritus.

Diagnostic Tests

- Diagnostic tests include superficial skin scrapings and fecal flotation to look for ova or ingested adult mites.
- Superficial skin scrapings are examined using the 10-power objective with reduced light as for scabies.

▼ ***Key Point*** In contrast to scabies, large numbers of mites are typically found on affected animals with superficial skin scrapings. Cats that are hypersensitive may have severe clinical signs but very few mites. Asymptomatic carriers may be detected in a multi-cat environment. The absence of pruritus in in-contact cats does not rule out the possibility of *N. cati* infestation.

- Consider a therapeutic trial to provide supportive evidence for a diagnosis of notoedric mange, although definitive diagnosis can only be made by demonstrating the live mites. The best areas to scrape are lesions on the ears and face.

Treatment

- Concurrently treat all in-contact animals due to the possibility of asymptomatic and transiently infested carriers.
- Reevaluate cats every 14 days and repeat superficial skin scrapings at each visit to determine the treatment end point.

Dips

- Dips have been the traditional mode of therapy.
  - Sedation may be necessary for safe handling of the cats during treatment.
  - Clip medium- to long-haired cats.
  - Bathe cats with a keratolytic shampoo before dipping to loosen and remove adherent surface crusts.
  - Place an Elizabethan collar after dipping to prevent ingestion of the substance.
- Dips that may be effective include the following:
  - *Lime sulfur* (LymDyp, DVM Pharmaceuticals): 2% solution applied every 5 to 7 days for 6 to 8 weeks. This is the safest dip for young kittens or sick and debilitated animals. Continue dips until there is resolution of the clinical signs and negative superficial skin scrapings.
  - *Amitraz* (Mitaban, Pfizer Animal Health): 0.025% solution applied once and repeated in 2 weeks. This treatment would be extra-label usage. Use extreme caution in cats.

Systemic Therapy

- *Selamectin* (Revolution, Pfizer Animal Health) is effective at a dose of 6 to 12 mg/kg applied to the skin on the dorsal neck 1 to 2 times 30 days apart. This treatment would be extra-label usage.
- *Ivermectin* (Ivomec, Merial Animal Health) is effective at a dosage of 0.3 mg/kg PO every 14 days for three treatments. It has also been used at dosages of 0.2 to 0.3 mg/kg SC every 14 days for two to three treatments and 0.4 mg/kg SC on a single occasion. These treatments would be extra-label usage. Use extreme caution in cats.
- Recently, *doramectin* was used for the treatment of notoedric mange in five cats. The use of doramectin has been studied in ruminants and swine. Doramectin has the same spectrum of activity as ivermectin, but the plasma half-life is twice as long. The longer plasma half-life is due to the oil formulation and the non-polar structure of the ivermectin ring. These features may provide residual activity during treatment, and a single dose may therefore be used.
- Doramectin at a dose from 0.2 to 0.3 mg/kg SC administered once is effective. Precise dosing may be difficult with the 1% solution. This treatment would be extra-label usage. Use extreme caution in cats.
- Because the mite does not persist long off the host, a single thorough cleaning of the environment is all that is usually necessary. One application of a parasiticide in a cattery where multiple animals are infested with the mite is helpful, but treatment with an acaricidal compound is not mandatory.

CHEYLETIELLOSIS

Etiology

- Cheyletiellosis (*Cheyletiella* dermatitis) is a highly contagious, variably pruritic, and dorsally distributed papulocrustous or scaling dermatosis caused by the

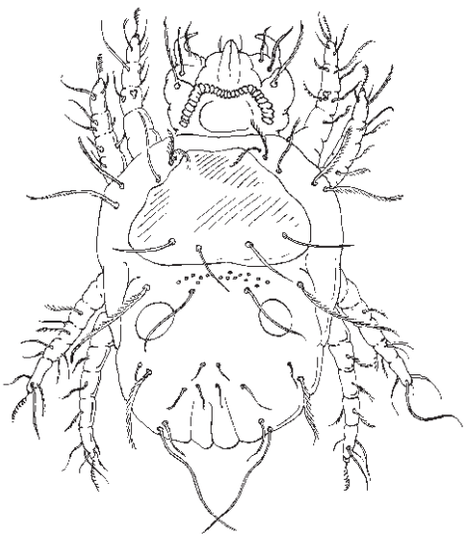

Figure 44-3. *Cheyletiella yasguri.*

surface-dwelling mites *Cheyletiella yasguri* (dog) (Fig. 44-3), *C. blakei* (cat), and *C. parasitovorax* (rabbit).

- The cheyletiellidae are obligate parasites that are not strictly host specific and may travel freely to various host species, including humans. Humans in contact with animals carrying *Cheyletiella* spp. may become transiently infected and develop a pruritic papular dermatitis of the arms, abdomen, or chest.
- *Cheyletiella* mites are large (500 µm × 350 µm) and saddle-shaped. They can be identified by prominent hook-like accessory mouthparts (palpi). All four pairs of legs extend beyond the body margin and bear terminal combs, not claws.
- They have been found on cats, dogs, foxes, rabbits, squirrels, and poultry.
- The entire life cycle (egg–larva–nymph–adult) is spent on the host and is completed in approximately 3 to 6 weeks. Female mites may live free of their hosts for as long as 10 days.
- *Cheyletiella* spp. are non-burrowing epidermal mites that dwell on the skin surface. In the keratin layer, they reside in pseudotunnels they create, and they periodically pierce the skin to feed on tissue fluids (lymph).
- Cheyletiellosis is highly contagious, especially between young animals, and is zoonotic. Transmission is typically by direct contact, but indirect transmission via fomites may be as important. Eggs attach to hair, and hair shed into the environment can be a source for reinfestation.
- In some animals, the intensity of the pruritus and severity of lesions are out of proportion with the low number of mites present, theoretically suggesting a hypersensitivity reaction to the mite or mechanical irritation. The excessive scale may be due to the mite's burrowing, but, more likely, the significant scale is the result of a host defense mechanism. Epidermal cell turnover will increase in response to an insult to the epidermal barrier.

Clinical Signs

- The hallmark of cheyletiellosis is excessive scaling and associated pruritus. A crusting or papular dermatitis may also characterize the disease. The haircoat may be greasy. Cats may have a papulocrustous eruption (miliary dermatitis).
- Dorsal truncal distribution is typical in dogs and cats, but a generalized distribution may occur. Puppies tend to be affected over the caudal dorsum initially, and the lesions then spread up the back to the head.
- Pruritus is highly variable, ranging from absent to constant. Asymptomatic carriers can also exist. Introduction of a susceptible pet into the household may be the first indication that there is a carrier animal.

▼ ***Key Point*** The most common clinical presentation of cheyletiellosis is a puppy or kitten recently acquired from a pet shop, kennel, or cattery with a pruritic, dorsal papulocrustous or scaling dermatosis.

Diagnosis

- The variability in clinical presentation, along with the difficulty of finding the mite, can make cheyletiellosis a challenging condition to definitively diagnose. Its prevalence is probably underappreciated, especially when pets are on flea control products year-round.
- Differential diagnoses include all diseases that cause pruritus and/or scale. Other mite infestations such as sarcoptic mange, notoedric mange, and pediculosis are included. Consider allergic diseases and include FBH, CAFR, and atopic dermatitis. Superficial pyoderma and *Malassezia* dermatitis are also differentials. All causes of seborrhea and miliary dermatitis in the cat are additional differentials.
- Rule out *Cheyletiella* before making a diagnosis of idiopathic seborrhea or a primary keratinization disorder. This is especially important in pets that frequent grooming, day-care, or boarding facilities.
- Suspect cheyletiellosis based on the following:
  - The nature and distribution of the cutaneous lesions, as previously described.
  - Exposure of the patient to other animals just prior to the onset of clinical signs.
  - Involvement of in-contact animals and humans. Clinical signs in affected humans are often characteristic (pruritic papules with central necrosis) and may be the only evidence that the animal in the household is infested.
- Consider cheyletiellosis in every pruritic cat. In addition, consider cheyletiellosis in every cat presented with miliary dermatitis and symmetrical alopecia.

- Make a definitive diagnosis by demonstration of the mite or egg on the animal. Mites are usually present in high numbers, but occasionally they can be difficult to detect. The absence of mites does not rule out this disease when there are compatible clinical signs.

Diagnostic Tests

- Several diagnostic tests may be needed. Techniques used to demonstrate the mite or its eggs include the following:
  - *Direct examination* of the surface of the skin and haircoat using a magnifying lens. The mites are very large; hence the name "walking dandruff."
  - *Flea combing* is the most reliable method for finding mites in both symptomatic and asymptomatic patients. Comb the entire coat for several minutes. Brushing the collected material onto a dark background may facilitate recognition of mites. If no mites are found at the initial diagnostic appointment, instruct the owner to similarly brush the coat of the pet several times a day for several days and collect the material in a container for examination at the clinic.
  - *Superficial skin scrapings* performed as previously described for scabies and notoedric mange. In animals with thick coats, clip an area so that the affected hair and skin can be visualized and sampled.
  - *Adhesive acetate tape* (Scotch tape) *preparation* is the classic diagnostic test; however, it only samples a small area. If used, sample several sites. Press a small piece of tape repeatedly over affected hair and skin. Place the tape strip onto a glass slide with a few drops of mineral oil.
  - *Potassium hydroxide (KOH) digestion.* Mix epidermal material collected with flea combing with 10% KOH and heat for 10 to 20 minutes. Centrifuge with a saturated sugar solution and examine microscopically under 40-power magnification.
  - *Fecal flotation.* Double centrifugation with a standard sucrose solution may be performed to examine feces for ova and ingested mites. This may provide supportive evidence for the diagnosis of cheyletiellosis in pets with low mite numbers.

▼ ***Key Point*** The most effective diagnostic techniques for cheyletiellosis are the acetate tape preparation and the collection of epidermal debris with a flea comb.

- In some cases, the mite or its eggs cannot be demonstrated, and a therapeutic trial is indicated. Such trials can only definitively rule out cheyletiellosis.

Treatment

- Although *Cheyletiella* mites appear to be susceptible to most insecticides, they may be extremely difficult to eradicate. Treatment of the patient, all in-contact animals, and the premises is mandatory. Successful treatment plans are 6 to 8 weeks in duration.
- There are no veterinary products specifically licensed by the FDA for the treatment of cheyletiellosis in dogs or cats.
- Flea shampoos, powders, foams, and sprays have not been efficacious as sole therapies for cheyletiellosis. Historically, organophosphates, carbamates, and amitraz have been advocated. However, there are newer treatments that provide an effective and safer alternative.
- Dips traditionally were routine in the treatment of cheyletiellosis and may still be indicated in certain situations. Clip the hair when the animal has medium to long hair or a dense coat. When scale and crust are present, bathing with a keratolytic shampoo prior to dipping is beneficial. The entire coat must be treated; spot treatment is ineffective.

Treatments for cheyletiellosis that have been effective include the following:

- *Lime sulfur* (LymDyp; DVM Pharmaceuticals) as a 2% solution applied as a dip every 7 days for six to eight treatments. Lime sulfur can be used safely in kittens, puppies, pregnant or lactating animals, or debilitated animals.
- Weekly *pyrethrin sprays* or L-pyrethrin dips diluted according to label instructions. Products used on cats should be approved for use in this species and should always be diluted according to the label instructions.
- *Amitraz* (Mitaban, Pfizer Animal Health) as a 0.025% solution applied as a dip every 14 days for four treatments. This treatment would be extra-label usage. Use extreme caution in cats. Monitor as described for scabies.
- *Ivermectin* (Ivomec; Merial Animal Health) at a dosage of 0.2 to 0.3 mg/kg PO every 7 days or SC every 14 days for 6 to 8 weeks in dogs and cats.
  - This treatment would be extra-label usage. Consider risks of adverse reaction, and have the owner give informed consent. Due to the low cost, ivermectin may be appealing if there is a kennel or multi-pet environment. Consider safer alternatives first.
  - Evaluate heartworm status before administration.
  - Do not administer to herding breeds such as collies, collie crosses, Shetland sheepdogs, Old English sheepdogs, or Australian shepherds. Any patient can show clinical signs of ivermectin toxicity, so careful patient monitoring is indicated. Clinical signs of toxicity include vomiting or diarrhea, mydriasis, depression, persistent lethargy, ataxia, tremors, ptyalism, recumbency, excitability, stupor, coma, and death.
  - Administration of the bovine 0.5% alcohol-based ivermectin (Ivomec Pour-On for cattle, Merial Canada) applied topically to the interscapular skin.

This was recently reported in cats using a dose of 0.5 mg/kg (0.1 ml/kg). Four to six treatments may be required. This treatment would be extra-label usage.

- *Fipronil spray,* 0.25%, at a dose of 3 ml/kg or the 10% concentrated solution (Frontline Spot-on Dog, Merial Animal Health) applied every 30 days for two to three treatments. Frontline Plus (Merial Animal Health) should be similarly effective. This treatment would be extra-label usage.
- *Selamectin* (Revolution, Pfizer Animal Health). For cheyletiellosis, apply every 30 days for three treatments. This treatment would be extra-label usage. We routinely use selamectin every 2 weeks for three treatments in adult cats and dogs.
  - Selamectin is reportedly safe in ivermectin-sensitive collies.
- *Milbemycin oxime* (Interceptor, Novartis Animal Health) at a dosage of 2 mg/kg PO every 7 days in dogs. Treatment may take 9 weeks. The efficacy of milbemycin oxime has not been demonstrated in cats. This treatment would be extra-label usage.
- Clean and spray the animal's quarters and bedding with a residual insecticide appropriate for killing adult fleas. Discard any bedding or grooming supplies that cannot be effectively cleaned to prevent fomite-mediated reinfestation. Launder washable fabrics at 55°C and then treat. Professional exterminators may be required. Perform frequent vacuuming with disposal of the collected material.
- Treat all in-contact animals throughout the treatment period and reevaluate the affected animals at regular intervals to assess for mites and eggs. Continue treating for 2 to 4 weeks beyond resolution of clinical signs and pruritus and until a negative examination for mites and eggs has been made.
- Treat the environment every 2 weeks with a premise spray appropriate for killing fleas. In addition, the car may need to be treated if the pet rides in the vehicle. Treat any visiting fur-bearing mammals.
- Client compliance is central in the effective resolution of *Cheyletiella* dermatitis and environmental contamination. If a treatment failure is suspected, first ensure that all instructions were followed as prescribed. Always ask the clients if they are able to perform rinses or dips at home. Alternatively, these can be performed in the hospital by trained technicians.

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Chapter 45

Flea Allergy Dermatitis

Craig E. Griffin

Flea allergy dermatitis (FAD) is a hypersensitivity reaction to one or more components of fleas, especially allergens in flea saliva. Several types of hypersensitivities, such as cutaneous basophil hypersensitivity, immunoglobulin E (IgE)-mediated immediate hypersensitivity, late-onset IgE reactions, and delayed-type hypersensitivity, can occur alone or in combination. The hypersensitivity reactions cause inflammation leading to pruritus and the generation of most of the lesions.

In most geographic areas, FAD is still a common cause of skin disease in dogs and cats. During the summer it is often the most common disease seen by the small animal practitioner and is a common reason for exacerbation of pruritus in patients with concurrent FAD and atopic dermatitis. In some areas, and when indoor infestations occur, FAD may be non-seasonal. The advent of newer, more effective flea control products has been both beneficial and detrimental to clinical practice. The new products have greatly minimized the impact of FAD in many practices and allowed much more effective flea control. At the same time, many clients utilizing these products no longer believe fleas can be the cause of disease. Thus, establishing the diagnosis and client acceptance of the diagnosis is more troublesome, as clients do not see fleas but FAD is still occurring.

Atopic dermatitis or adverse food reactions ("food allergy") may occur in combination with FAD, and occasionally all three reactions will be present in one patient. The prevalence of FAD in patients with atopic dermatitis is generally higher; up to 80% of dogs with atopic dermatitis that are exposed to fleas were reported to have FAD.

ETIOLOGY

- *Ctenocephalides felis* is the species that usually infests both dogs and cats. *Pulex irritans* and less commonly *Ctenocephalides canis* may be responsible in some areas.
- Investigations with purified flea saliva led to the discovery of several antigens, and one named Cte f 1 has been cloned. Eighty percent of clinical flea-allergic dogs have an IgE response to Cte f 1, making this a major allergen involved in the pathogenesis. It is not the only allergen, and some flea-allergic dogs do not react to Cte f 1, nor do all have IgE-mediated disease.

Important Flea Life Stages

Effective control of flea populations and prevention of exposure to adult fleas requires an understanding of many aspects of the flea life cycle and biology. Adult fleas only represent a small percentage of the total flea population. Eggs, larvae, and pupae make up the vast majority.

Larval Stage

- Larvae are positively geotactic and negatively phototaxic and therefore migrate deep into carpets and under furniture.

Pupal Stage

- Of the pre-adult stages, the pupal stage is most troublesome.
- This stage is most resistant to environmental changes, such as low humidity, and is also most resistant to environmentally applied insecticides, partly due to their location deep in the carpet. The pupa's external sticky cocoon attracts a coating of environmental debris that also helps protect the developing adult inside the cocoon from insecticides.
- The pre-emerged adult flea inside the cocoon will wait for optimal environmental and local host factors before emerging. Emergence of the adult from the cocoon may be delayed up to 5 months and can be responsible for pet owners seeing young adult fleas even after environmental therapy. Delayed emergence and resurgence of fleas after effective use of environmental insecticides has been termed the *pupal window.*

Newly Emerged Adult Fleas

- The newly emerged adult flea will rapidly find its host in response to stimuli such as positive phototaxis, carbon dioxide, body heat, light changes from movement, and negative geotaxis.

- Even residual types of environmental insecticides and insect growth regulators (IGRs) are not rapid enough in killing fleas to prevent these newly emerged adults from finding their host. The time necessary for even effective topical or systemic therapies to eliminate all the developing stages from an enclosed environment has been termed the *developmental window*. As a result of these pupal and developmental windows, owners may see emerging young adult fleas and feel that the products are not beneficial, leading to poor compliance or premature termination of treatments that would eventually be effective.

Other Environmental Sources of Fleas

Other environmental sources for newly emerged or mature adult fleas must also be considered.

- *C. felis* commonly infest opossums, raccoons, skunks, coyotes, foxes, and some rodents. Areas outdoors frequented by these other hosts will keep flea populations present in locations that pets may frequent, exposing the pet to more fleas.
- In these circumstances, even the use of the newer topical or systemic flea-killing products may not prevent clinical allergy from occurring. As the products with the most rapid killing effect take 4 to 6 hours to kill newly emerged adult fleas, enough of these newly emerged fleas (or fleas from other environmental sources) may be present to keep significant disease occurring for days. Thus, active FAD may be present even though an infestation in the pet's home environment may be prevented.

CLINICAL SIGNS

- Pruritus is the primary clinical sign, which the owner may observe as chewing (as if eating corn on the cob), rubbing, rolling, or scratching. Cats may groom excessively or pull out their hair. Severe chewing may lead to excessive wear of the incisor and canine teeth.
- Primary lesions are papules and erythematous macules in dogs and focal crusted erosions or papules (miliary eczema) in cats. Exudation and crusting may be seen.
- Secondary lesions result from the chronic inflammation and pruritus-induced trauma and include alopecia, excoriations, broken hairs, dry hair, scaling, hyperpigmentation, and lichenification.

Pattern of Involvement

Lesions are localized to areas of flea bites, and distant lesions and significant disease from one flea bite is unlikely. Generalized disease does not occur without generalized biting.

- Involvement of the tail-base and dorsal lumbar region has been shown to be highly discriminant for the diagnosis of FAD. The caudal thighs, groin, and abdomen are frequently affected, although less severely than the dorsal lumbar region. In chronic and severe cases, there is extension of the lesions cranially on the trunk.
- Ear disease, otitis externa, perioral lesions, and pododermatitis (especially of the front paws) are usually not seen and are highly discriminant for a diagnosis other than FAD. When these signs are present in a dog suspected of FAD, they suggest either that flea allergy is not present or that flea allergy is present with a concurrent disease, such as atopic dermatitis or food adverse reaction.
- Cats with FAD commonly have miliary crusts in the cervical as well as the dorsal lumbar region. Lesions may be limited to the abdomen and groin or cervical area.

Secondary Problems

Secondary problems that may occur often represent focal sites of infection; foci of severe trauma, possibly from the itch-scratch cycle; or a different pathologic reaction.

- Acute moist dermatitis (hot spots), acral pruritic nodules, eosinophilic plaques, and eosinophilic granulomas may be seen in dogs and cats.
- Superficial or deep pyoderma may develop, especially in animals repeatedly treated with corticosteroids.
- Animals with superficial pyoderma will present with pustules, crusted papules, or circular spreading rings of crust over erythematous erosions, lichenified plaques, or papules.
- Deep pyoderma may be present as furuncles, hemorrhagic bullae, fistulous tracts, crusted ulcers, and proliferative pruritic nodules.

DIAGNOSIS

FAD is diagnosed presumptively in pruritic animals with typical patterns of involvement. Flea involvement that may be determined by finding fleas, flea feces, or a history of possible exposure to fleas is supportive of the diagnosis. In cases with no direct evidence of fleas, response to flea control is used as evidence that fleas were present. Always consider the presence of coexistent allergies as they are frequently overlooked.

▼ ***Key Point*** The most definitive diagnosis of FAD requires typical lesions, a typical pattern, a positive intradermal or in vitro test to Cte f 1 (flea antigen), and a complete response to effective flea control.

History

- Identify typical patterns of involvement and seasonality compatible with fleas.

- A history of otitis externa or paw licking suggests that other or concurrent allergies are present.
- Obtain information regarding the number and type of pets, housing, the type of floor covering, current pesticide use, and client concerns regarding the use of pesticides.
- Possible sources of exposure to fleas should also be investigated. A history of cats living in the same environment also has a positive correlation with a diagnosis of FAD. Investigate how much time is spent outside, the type of outdoor environments the pet has access to, and the possible presence of stray or feral cats as well as opossums and other wildlife.
- A history of prior favorable response to flea control also supports a diagnosis of FAD. Adverse food reaction is one of the few differential diagnoses for the lesions and pattern of involvement seen in FAD, and a gastrointestinal history (bowel movements, borborygmus, flatulence, etc.) may be helpful in this regard.

Physical Examination

- Examine for fleas or flea dirt in longhaired animals by brushing the pet over white paper; in shorthaired animals, flea combing may be helpful.
- Closely examine areas of involvement typical for other allergies (see Chapters 46 and 47) for evidence of coexisting disease.
- Closely examine the dorsal lumbar area for papules, which are the primary lesions seen in canine FAD.
- Carefully palpate the skin in cats; this is important because the typical small, crusted papules (miliary crusts) often are more easily felt than seen.
- Shave the haircoat to allow closer observation of the lesions.
- Examine for lymphadenopathy in cats, a common finding in chronic FAD.

Dermatopathology

Dermatopathology is not specific (but may be suggestive) with FAD. Superficial, mixed perivascular dermatitis with eosinophils is typical in FAD, and occasionally intraepidermal eosinophilic microabcesses may be seen; these changes may be seen in other allergic dermatoses. Typically, histopathology is not necessary in the diagnosis of FAD.

Intradermal Testing

Intradermal testing with 1/1000 wt/vol flea antigen (Greer Labs) has been documented as a reliable test for diagnosing FAD when evaluated at all possible reaction times.

- Positive reactions may occur in 15 minutes (immediate), 6 to 8 hours (late onset), or 24 to 48 hours (delayed).
- A positive test indicates that flea hypersensitivity is present, but it does not document that all clinical signs are related to fleas, that is, there may be subclinical hypersensitivity.
- A negative test at all observation times usually indicates (approximately 90%) that flea allergy is not present.
- False-negative results may occur if glucocorticoids and antihistamines are not properly withdrawn before testing.

Serum In Vitro Testing

Recent advances have led to an in vitro test that is valuable in the diagnosis of FAD (Heska Corporation). This test utilizes a recombinant flea salivary antigen.

- A positive test is strongly correlated with FAD.
- A negative test does not preclude a diagnosis as some dogs and cats react to a different allergen or have FAD by other allergic mechanisms.

Response to Therapy

A favorable response following parasiticidal therapy directed against fleas is helpful in making a diagnosis of FAD. It does not eliminate the diagnosis of coexisting diseases.

TREATMENT

FAD is best treated by eliminating exposure to the flea allergen (i.e., effective flea control). When a complete flea control program is used, more than 90% of cases can be controlled without additional treatment. Raising the allergic and pruritic thresholds by treating coexistent problems also may be helpful. In cases in which adequate flea control cannot be achieved, blocking the allergic reaction with systemic therapy is required.

Decrease Allergic Load (Flea Control)

Modern flea control utilizes a variety of chemicals directed at many different parts of the flea life cycle (Table 45-1). Many products are typical insecticides in that they kill adult fleas. In the flea-allergic dog that gets exposed to adult fleas, the speed of kill becomes relevant because the longer fleas live on the FAD pet, the more bites and allergens the pet is exposed to. Repellent activity is especially beneficial for decreasing allergen exposure. It is believed, although not yet proven, that permethrin (a known mosquito repellent) may also have some repellent activity against adult fleas. IGRs do not kill adult fleas and do not prevent biting, but they interfere with the development of eggs into larvae or pupae by mimicking insect juvenile hormone. The two available in the United States are methoprene and pyriproxyfen. The insect development inhibitor (IDI),

Table 45-1. CHEMICALS USED FOR FLEA CONTROL

Chemical Name	Example of Brand/ Manufacturer	Main Area Used and Stage Targeted	Treatment Regimen	Advantages	Disadvantages
Borates	Dustmite and Flea Control/Aveho Biosciences Rx for Fleas/ Fleabusters	Environment, ingests and desiccates larvae.	Wettable powder sprayed on or added to carpet shampooer. Powder applied and brushed into carpets.	Long-term effects, safety.	Powder can be messy, and both are labor intensive to apply.
Fipronil	Frontline/Merial	Dogs and cats topical, adulticide.	Monthly topical spot application spreads over body and spray.	Rapid kill.* Shown to resist depletion by shampooing or water.	Cannot be applied more often than monthly. External insecticide.
Fipronil/ methoprene	Frontline Plus/ Merial	Dogs and cats topical, adulticide and IGR.	Monthly topical spot application spreads over body.	Rapid kill. One product delivers integrated flea control.	As above, and IGR not photostable.
Imidacloprid	Advantage/Bayer	Dogs and cats topical, adulticide.	Monthly up to weekly topical spot application spreads over body and spreads local into environment where pets sleep.	Rapid kill. More frequent application can make it more effective in FAD dogs and cats.	Expense when used more often than monthly. External insecticide.
Imidacloprid/ permethrin	Advantix/Bayer	*Dogs only.* Two types of adulticide, possible repellent.	Monthly topical spot application.	As above, plus integrated flea control and suspected to have flea repellent effect.	As above. *Not for cats.*
Lufenuron	Program/Novartis Animal Health	Dogs and cats oral or injectable. IDI larvae.	Oral for dogs and cats, and long-acting injection for cats.	Systemic very effective for whole month and not affected by topical therapy. No external drug.	Not adulticidal and not as effective for FAD as sole therapy in dogs and cats that spend much time outdoors.
Methoprene	Various	Dogs and cats topical, systemic, and environment. IGR to multiple stages.	Varies on delivery system and what is treated.	Effective against multiple stages with large margin of safety.	UV susceptibility limits environmental use.
Nitenpyram	Capstar/Novartis Animal Health	Dogs and cats oral, adulticide.	Oral systemic therapy. To maintain levels, q24h in cats and q48h in dogs.	Extremely rapid kill† and safe to use daily makes it most effective as trial therapy and short-term prevention. No external insecticide on pet.	Short half-life limits long-term use due to expense.
Permethrin	Multiple	Dogs only most formulations. Topical and environment.	Varies with product type and where applied.	Suspected repellent effect makes particularly useful for FAD-affected dogs. UV resistant. Longer effect than pyrethrin.	Most products not allowed on cats, and ones allowed must be low concentration.
Pyrethrin	Various shampoos and spray	Topical and environmental products, adulticide.	Apply up to daily to pets or environment.	Rapid kill and large safety margin makes it useful on puppies, kittens, and environment where it is allowed when many other products are not.	Short residual action and rapid UV degradation.
Pyriproxyfen	Various	Dogs and cats topical and environment. IGR multiple stages.	Varies with form and use.	Photostable, so longer-term effect.	Concern for effect on other insects since long-term environment persistence.
Selamectin	Revolution/Pfizer	Dogs and cats topical.	Monthly topical administration, which is absorbed systemically.	Rapid kill. Not readily washed off for long. Broad spectrum, so multiple-use product.	Expense if only use is for fleas. Although rapid kill, some suggest still slower than other rapid kill.

*Rapid kill means over 90% of fleas applied to the pet's haircoat are killed in 24 hours or less.
†Extremely rapid kill is over 90% of fleas killed in 4–6 hours.
FAD, flea allergy dermatitis; IDI, insect development inhibitor; IGR, insect growth regulator; UV, ultraviolet.

lufenuron inhibits chitin synthesis and also prevents the development of larvae.

Complete flea control requires treating the affected pet, other pets in the same environment, and the pet's environment. Modern product developments have totally changed the approach to flea control in the last few years (see Table 45-1). Compliance and flea control success have greatly improved because of long-acting, total-body protection that can be achieved with topical focal spot applications, systemic therapy from monthly oral or topical spot formulations, and improved flea collar technology. These products have made the use of flea shampoos, dips, and sprays for on-pet use obsolete for long-term flea control. Pyrethrin shampoos may still be used to rapidly remove fleas in infested puppies, kittens, or adults when quick elimination of fleas on a pet is required. However, they are not routinely recommended as compliance and efficacy are less than newer products.

Resistance to some flea products has been seen in the past. The cat flea has been described as the most resistant of the flea species, and to more types of products. Integrated pest management decreases the probability of this developing to the newer products now being used extensively. The international imidacloprid flea susceptibility monitoring program developed an in vitro assay to test for the development of flea resistance. Evaluations of natural strains of fleas from around the world have not yet detected any resistance.

Compliance is still a key component of a successful flea control program. Even the newer products require regular use to prevent the development of viable eggs from being laid. Therefore, to assure that the flea life cycle is broken, owners must be diligent about proper application of these products at correct intervals. This involves the use of different ingredients or techniques on pets and in the environment. In severely infested environments, effective control may take 4 to 8 weeks to achieve. Once flea control is achieved, clients may find that only one or two aspects of flea control are sufficient for maintenance, but the long-term use of an integrated pest control plan is optimum.

▼ ***Key Point*** The optimum control will utilize integrated pest management as the most effective way to eliminate multiple stages of the flea life cycle and decrease the chance that resistant strains of fleas will develop.

Environmental Treatment for Indoor Areas

Because the majority of flea eggs, larvae, and pupae are located in the environment, it is essential to treat environmental areas. Treatment of indoor areas is critical when the affected animal spends most of the time indoors. This is the habitat that can be controlled most effectively. The main life stages being targeted are the larvae and eggs.

- These stages are mainly found in carpets and cracks or spaces in flooring. Most tile, linoleum, and smooth wood floors do not readily support flea development. Therefore, treatment can be applied to carpeted areas, pet bedding, and upholstered furniture that pets have access to.
- Since larvae are mobile and negatively phototaxic, treatment under furniture and behind doors is an important aspect of control.
- Hand-held application is preferred for making sure products reach the important areas.
- Vacuuming, especially with vacuums that have beater bars, is also helpful in decreasing the number of eggs and larvae. The cleaner bags should be removed following vacuuming to prevent any fleas from returning to the environment.
- Treat linoleum and tile floors by frequently mopping with routine disinfectants.

Insect Growth Regulators

The newer systemic and topical formulations with IGRs for rapid adult kill in under 24 hours are also very helpful in keeping an indoor environment flea free (see Table 45-1). Imidacloprid has also been shown to be transferred to treated pets bedding and is an effective ovicidal and larvacidal agent if the bedding is not laundered. IGR-containing products that have residual effects and bind to the pets hair are likely to also have an environmental effect.

Borate Products

In houses in which floors are primarily carpeted, borate products are most effective, lasting up to 1 year. They are also safe, with no reported toxicity.

- An electrostatically charged sodium polyborate powder (Rx for Fleas, Fleabusters) is applied as a powder and brushed into carpets and pet-exposed furniture.
- Disodium octaborate tetrahydrate (Dustmite and Flea Control, Aveho Biosciences) is a wettable powder that once mixed with water is sprayed on. It may also be added to carpet shampooers or steam cleaners providing excellent penetration to deeper carpet fibers.

Permethrin or Pyrethrin Combined with Insect Growth Regulators

Another alternative is spraying all carpeted surfaces and furniture that pets have access to with permethrin or with pyrethrin in conjunction with an IGR.

- Effective products include methoprene, permethrin, phenothrin (Vet Kem Siphotrol Plus II House Treatment, Wellmark), pyriproxyfen, pyrethrin and permethrin (Virbac Knockout ES Area Treatment,

Virbac), and tetramethrin with pyriproxyfen (Ectokyl IGR Pressurized Spray, DVM Pharmaceuticals).
- Frequency of use varies with products selected, but in general these IGR combinations last at least 1 month.

Environmental Treatment for Outdoor Areas

Treat outdoor pens and similar enclosures weekly for 3 weeks and then monthly.

- A liquid application of chlorpyrifos, permethrin, or diazinon is preferred.
- Although helpful in long-term control, granular and microencapsulated insecticides have been less beneficial for obtaining initial control.
- Pyrethrins are safe and have minimal environmental impact, but weekly applications are required as they have no residual activity.
- The IGR pyriproxyfen is photostable and therefore a useful adjunct to outdoor therapy when used with adulticides.
- Consideration should also be given to areas that are occupied by both pets and wildlife that may carry fleas, for example, under trees that may harbor opossums or raccoons.

Treatment of Unaffected Pets

Treat unaffected animals in the same environment with adulticidal and/or insect development inhibitor flea products that lack flea repellent effects.

- Regular use of the topical adulticides fipronil or imidacloprid or of lufenuron helps prevent unaffected animals from contributing to reintroduction of fleas into the home environment. Combination products or combining IGR products will improve environmental control of population levels and is an integrated pest control strategy.
- In cases in which topical treatments are not wanted by owners or pets react, systemic products such as lufenuron or collars may be helpful.
- Use an approved flea collar with at least an IGR on cats that cannot be treated with topical spot applications, dips, sprays, or foams.

Treatment of Affected Pets

Treat affected animals with an adulticidal product and repellents as frequently as allowed for these products.

- The new topical adulticides, fipronil, imidacloprid, and selamectin, have been shown to be efficacious for treating FAD in dogs and cats, even when environmental treatment is not done. Fipronil in the spray formulation appears to be more efficacious than the spot application and is preferred for the affected pet if client compliance is not a problem.
- Nitenpyram is the most rapid flea-killing systemic product available, with the drawback of a short half-life. This means there is duration of only 1 day in cats and 2 days in dogs. It may be used when pets are known to be going into areas where fleas may be present. It is also helpful as a trial therapy to see if flea control is effective and help establish FAD as the diagnosis.
- The newest generation products have improved these products by combining another topical agent that works by another mechanism. Fipronil is combined with an IGR methoprene and imidacloprid is combined with an adulticide and repellent permethrin. Repellent activity for mosquitoes has been documented; effectiveness for repelling fleas is still to be determined.
- Permethrin is toxic for cats and cannot be used on cats. Use water-based pyrethrin spray for cats, and for dogs use either pyrethrin or permethrin sprays (Duocide LA, Allerderm/Virbac) that contain a repellent. Apply daily if approved for such use.

Increase Allergic/Pruritic Threshold

- Control concurrent allergic diseases such as atopic dermatitis and food allergy.
- Treat secondary pyoderma, which often increases pruritus, with systemic antibiotics (see Chapter 38).
- Eliminate dry skin by use of baths, moisturizing sprays or rinses, and fatty acid supplements.
- Remove other irritants or allergens on the skin surface, which may aggravate inflamed skin, by frequently bathing the animal. Use this option cautiously with most topical treatments, although fipronil and imidacloprid and selamectin still have efficacy if bathing is 48 hours from application time. Selamectin is absorbed systemically, excreted in epidermal secretions, and replenished, although bathing may temporarily decrease surface levels. Do not bath for 48 hours following application.

Block Allergic Reactions

A variety of systemic drugs may be used to alter the allergic reaction. This approach is often used at the beginning of the flea control program and to break the itch-scratch cycle. Resort to long-term use of systemic drugs only when clients cannot effectively control fleas. This most often occurs with outdoor or roaming pets, especially cats.

Glucocorticoids

- Topical triamcinolone 0.015% spray (Genesis spray, Virbac) has been shown to be effective in the management of experimentally induced FAD and has been effective in some clinical cases.
- Systemic glucocorticoids are often effective. Initially, use prednisone or prednisolone, 1 to 2 mg/kg PO q12–24h, to stop the pruritus associated with FAD.
- Use either oral triamcinolone acetonide (Vetalog, Fort Dodge), 0.25 to 0.5 mg/kg q12–24h, or methyl-

prednisolone (Medrol, Pfizer), 0.8 to 1.6 mg/kg q12–24h, if polyuria, polydipsia, or polyphagia associated with prednisone or prednisolone is unacceptable to the client.
- When pruritus is controlled, change to an alternate-day program and then taper to the lowest effective dose.

Cyclosporine

Although not approved for FAD, some dogs with FAD have responded well to this new treatment for atopic dermatitis. Relative effectiveness compared to glucocorticoids is not known. Atopica (Novartis) at 5 mg/kg q24h has been effective with fewer side effects than glucocorticoids.

Antihistamines

Antihistamines are infrequently effective for FAD. They may be used in conjunction with glucocorticoids and have a synergistic effect that makes possible a reduction in the glucocorticoid dose.

- Diphenhydramine HCl, 2 mg/kg PO q8h; hydroxyzine HCl or pamoate, 2 mg/kg PO q8h; doxepin HCl, 1 to 2 mg/kg PO q12h; or clemastine, 0.05 to 0.1 mg/kg q12h PO may be useful in dogs.
- Chlorpheniramine may be helpful in dogs at a total dosage of 2 to 6 mg PO q8–12h. It is especially useful in cats at a total dosage of 2 mg PO q12h.

Fatty Acid Supplements

Fatty acid supplements containing omega-3 fatty acids and dihomogammalinolenic acid alone rarely control FAD. However, they may be helpful in controlling concurrent atopy, alleviating dry skin, and modulating the production of inflammatory mediators. These effects may raise the pruritic/allergic threshold and have a synergistic effect with other treatments, allowing a reduction in the glucocorticoid dose.

Allergen-Specific Immunotherapy

Allergen-specific immunotherapy (ASIT), previously referred to as hyposensitization with standard allergens and protocols, has not been shown to be efficacious in studies. However, ASIT has been reported to be occasionally effective in individual cases, but it is not considered cost effective for most clients, considering the low level of efficacy. A recent trial with flea salivary antigen did show efficacy in a blinded, controlled trial, suggesting that if done in type I allergic dogs with the exact allergen they tested positive to, then this form of therapy may be beneficial. This is not commercially available at this time.

PREVENTION

Prevention is achieved by long-term continuation of a flea control program. Long-term treatment may not have to be as complete or as frequent as the initial treatment program. Another option is to use prevention by anticipating increases in flea population and increasing the use of parasiticidal therapy just before the onset of environmental conditions favoring these increases.

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Chapter 46

Atopic Dermatitis

Andrew Hillier

Atopic dermatitis (AD) is a genetically predisposed inflammatory and pruritic allergic skin disease with characteristic clinical features. It is associated most commonly with immunoglobulin E (IgE) antibodies to environmental allergens: dust mites (house dust and storage mites), pollens (trees, grasses, and weeds), mold spores, danders, insects (moth, cockroach, etc.), and other miscellaneous allergens.

In dogs, this results in skin disease in most cases, with occasional concurrent involvement of other organ systems. Cats generally develop dermatitis as well, but they may also develop asthma-like respiratory tract disease in association with IgE antibodies to environmental allergens. However, the link between feline asthma and AD is uncertain.

ETIOLOGY

AD is a classic example of an IgE-mediated, type I hypersensitivity reaction. Patients may have hypersensitivity to one, a few, or many allergens. AD is a complex skin disease, and a state of "cutaneous hyperreactivity" often exists. The following factors may contribute to clinical disease:

- Environmental allergens
- Staphylococcal pyoderma
- *Malassezia* (yeast) dermatitis
- Concurrent flea allergy or food allergy
- Irritants such as chemicals, plants, and medications
- Temperature and humidity
- Local skin factors such as dry skin, excoriations, etc.

Recognition of factors contributing to disease in each individual patient is critical in the development of successful treatment strategies. As there is a *summation of effects* (added effects of multiple stimuli), elimination of some of the most significant stimuli may reduce the skin inflammation below the patient's *pruritic threshold* (the point at which pruritic stimuli induce skin disease and pruritus) without a need to address all factors that may be contributing to the pruritus.

Incidence in Dogs

AD is a common skin disease that affects 10% to 15% of the dog population. Data from 52 general practices in the United States documented that AD was diagnosed in 8.7% of all canine patients and in 21.6% of all dogs presented with skin or ear disease. In regions where fleas are not a significant problem, AD is likely the most common allergic disease of dogs and cats.

Age and Sex Predilection

- *Age at onset:* Clinical signs are first seen between the ages of 6 months and 3 years in the majority of dogs. AD will rarely develop for the first time once animals are over 7 years of age.
- *Sex predilection:* None known.

Breed Predilection

AD can affect dogs of *any breed* as well as mixed-breed dogs.

- *High-risk breeds:* Beauceron, Boston terrier, boxer, Cairn terrier, Chinese Shar-Pei, cocker spaniel, Dalmatian, English bulldog, English setter, fox terrier, golden retriever, Irish setter, Labrador retriever, Labrit, Lhasa apso, miniature schnauzer, pug, Scottish terrier, Sealyham terrier, West Highland white terrier, wirehaired fox terrier, and Yorkshire terrier.
- *Low-risk breeds:* Dachshund, Doberman pinscher, German shepherd, German short-haired pointer, and poodle.

Seasonal Incidence

Typically, AD is seasonal in nature initially, but the majority of dogs progress over a period of years to develop non-seasonal (year-round) disease. However, many dogs with non-seasonal AD have seasonal exacerbations due to pollen allergies or concurrent flea allergy dermatitis.

Incidence in Cats

There is no reported sex or breed predilection, although Abyssinian cats were suggested in one review to have a higher incidence of AD. The age of onset of clinical signs is similar to dogs.

CLINICAL SIGNS

AD should be considered a differential diagnosis in any dog with the following:

- Pruritus
- Recurrent staphylococcal or *Malassezia* dermatitis
- Otitis externa

Pruritus

Pruritus is the initial and most outstanding clinical sign of AD in dogs and cats. Pruritus is mild to moderate in most cases but may become severe in some chronically affected dogs. It is responsive to glucocorticoid therapy, at least initially.

- The pruritus in AD typically involves one or more of the following body locations:
  - *Face*—Especially periocular, muzzle and chin
  - *Ears*—Most commonly the ear canal but sometimes also the ear pinna and skin at the base of the ear
  - *Ventrum*—Including the neck, axilla, abdomen, and groin
  - *Distal limbs*—Including the carpal and tarsal area, digits, and interdigitally
- Other locations sometimes affected include the perineum and the flexural surface of the elbows and hocks.
- Pruritus may become generalized with chronicity or when a secondary infection is present.

Staphylococcal and Malassezia Dermatitis

AD in dogs is commonly complicated by recurrent staphylococcal pyoderma (see Chapter 38) and *Malassezia* yeast dermatitis (see Chapter 41).

- Both infections contribute to the skin disease and pruritus. Once the infections are treated and resolved, pruritus is usually diminished, sometimes significantly. However, residual pruritus typically remains—a strong clue to a primary underlying allergic dermatitis. Rarely, treatment of the secondary infection leads to resolution of the pruritus as well—these patients only have pruritus when the infection flares and is active.
- Staphylococcal infections tend to involve the trunk, while *Malassezia* infections are more frequently found in the ventral neck, interdigital area, and nail folds. Either infection may become generalized.

Otitis Externa

Otitis externa is common in dogs with AD—one study reported that 86% of cases had otitis. One or both ears may be affected.

- Early cases have mild erythema of the ear pinna and ear canals. As the disease progresses, hyperplasia of the epithelium and ceruminous exudation usually develop.
- Most frequently, allergic otitis becomes complicated by secondary bacterial and yeast infections (see Chapter 59).

Skin Lesions

There is currently debate about the skin lesions that typify AD (assuming that secondary infections are not present).

- Some dogs with AD have no primary lesions, while others may have a macular to papular dermatitis (i.e., a rash).
- Chronic self-trauma as a result of the allergic inflammation eventually leads to secondary lesions such as alopecia, lichenification, hyperpigmentation, and seborrhea. The most important aspect of these lesions is whether their location on the body is typical for AD. Similar secondary lesions are seen in other pruritic but non-allergic dermatoses; however, the lesions are not in the locations on the body that are associated with AD.

Clinical Signs in Cats

Pruritus is the hallmark of the disease in cats as well. However, the other characteristics of AD in cats do not mimic the disease in dogs very closely.

- Pruritus due to AD in cats may manifest as *symmetric alopecia, miliary dermatitis,* or one of the *eosinophilic granuloma complex lesions.* These cutaneous reaction patterns may also be observed in cats with non-atopic pruritic skin disease as well (see Chapters 52 and 53 for differential diagnoses).
- Secondary bacterial or yeast infections and otitis are less common than in dogs but may be present in some atopic cats and must be considered part of the diagnostic workup.

DIAGNOSIS

The diagnosis of AD in dogs and cats is based on the following:

- Typical historical features
- Presence of characteristic clinical signs
- Exclusion of other differential diagnoses

Differential Diagnoses

The following are the most significant differential diagnoses that need to be considered.

Seasonal Disease

- Flea allergy dermatitis
- Insect bite hypersensitivity

Non-seasonal Disease

- Food allergy
- Scabies
- Contact dermatitis

Diagnostic Approach

Use the following three-step approach in patients with suspected AD.

Step 1

- Diagnose and treat secondary infections.
- Diagnose and treat concurrent flea allergy.
- Diagnose and treat scabies.

Step 2

- Confirm that secondary infections, flea allergy, and scabies have been ruled out.
- Determine that residual pruritus is still present.
- If pruritus is seasonal and flea allergy has been ruled out, the patient has AD.
- If pruritus is non-seasonal, perform a food trial to rule out food allergy (see Chapter 47).

Step 3

- If pruritus resolves with a food trial, the likely diagnosis is food allergy, and it is confirmed when pruritus recurs with a challenge trial using the former diet.
- If partial response occurs with a food trial, a combination of food allergy and AD is likely.
- If no response occurs with a food trial, the patient has AD.

Allergy Testing

Perform allergy testing only after a diagnosis of AD has been made and when allergen-specific immunotherapy (ASIT) is anticipated in the treatment plan. The true utility of allergy testing is in the selection of allergens for ASIT.

▼ ***Key Point*** Do not use allergy testing as the basis for diagnosis of AD.

Both intradermal tests (IDTs) (or skin tests) and serum allergy tests (SATs) detect the presence of allergen-specific IgE. A positive allergy test indicates the presence of excessive amounts of IgE to an allergen and may be associated with the following:

- Subclinical hypersensitivity (and not causing disease)
- Clinical allergy (and leading to AD)

Correlation with Seasons

The clinical significance of a positive allergy test can only be ascertained once all other possible causes for the dermatitis have been ruled out and if the positively reacting allergens are known to be in high quantities at the time of year that the individual patient has exacerbations of skin disease (i.e., correlation of seasons of the allergens and the disease in the patient). Thus, once the result of the allergy test is available, it is essential to review the patient's history to consider the seasonal or non-seasonal nature of the disease and the patient's environment. In general, allergens may be categorized as follows (there may be significant geographic variation):

- *Non-seasonal*—House dust mites *(Dermatophagoides farinae, Dermatophagoides pteronyssinus),* storage mites *(Tyrophagus putrescentiae, Lepidoglyphus destructor),* cockroach, moth, danders/epidermals, indoor molds *(Penicillium, Aspergillus, Rhizopus, Mucor)*
- *Spring*—Tree pollens
- *Summer*—Grass pollens, outdoor molds *(Alternaria, Cladosporium)*
- *Fall*—Weed pollens, outdoor molds

Intradermal Versus Serum Allergy Tests

- Neither type of test has been proven to be more accurate than the other, although IDTs have been regarded the "gold standard." Both tests, if performed appropriately, may provide useful information.
- I prefer to perform both tests in all patients with AD where ASIT is anticipated. However, it is not essential and the results of either test will provide clinically useful information in many patients.
- There are numerous laboratories that perform serum allergy tests. It should be emphasized that none of the commercially available serum allergy tests has been proven to be more accurate than any other in peer-reviewed publications. The following factors should be considered when choosing an SAT:
  - Scientific basis of the assay
  - Published results of studies using these assays
  - Laboratory's involvement in allergy research
  - Quality and efficiency of the service
  - Availability of qualified technical staff for consultation
  - Cost
  - Recommendations from experts
  - Personal experience

Allergy Screening Test

- A simple, rapid screening test is available for in-clinic use by veterinarians (Allercept E-Screen, Heska).
- It is important to realize that this test does not screen for allergy (i.e., clinical disease) but does screen for the presence of above-normal levels of IgE to major allergens.
- This screening test has good predictive value for the likely result of the full and complete regional panel. Thus, if the screening test is positive, then there is a high likelihood of at least one positive reaction on the full panel. Similarly, if the screening test is negative, it is unlikely that there will be a positive reaction on the full panel.

Interpretation of a "Positive" Intradermal or Serum Allergy Test

Indicative of AD is when the positively reacting allergens are known to be present in the environment at the time of year when the patient has skin disease or has exacerbations of skin disease.

Interpretation of a "Negative" Intradermal or Serum Allergy Test

Consider the following interpretations for negative allergy test results:

- The patient does not have AD—Reconsider other differential diagnoses.
- The alternative type of allergy test may be more informative (i.e., an IDT if an SAT was performed, or vice versa).
- Drug interference—Glucocorticoids and antihistamines may interfere with an IDT, while an SAT is reportedly unaffected (however, a small percentage of dogs on glucocorticoids may have a less-than-optimal SAT).
- Time of year—The best results with an IDT are often seen at the end of the patient's allergy season, while the best results of an SAT are often seen at the peak of the patient's allergy season.
- Allergens of significance for the patient were not tested—This may be the case in a small percentage of dogs. Most IDTs and SATs include all known major allergens.
- A small percentage of dogs with AD never have positive allergy tests (may be the equivalent of intrinsic AD in humans).

TREATMENT

Current treatment options for AD include the following:

1. ASIT
2. Anti-inflammatory therapy
3. Antimicrobial therapy
4. Allergen avoidance

General Treatment Guidelines and Overview

The choice of treatment options to institute in the individual patient will depend on the following:

- Nature and intensity of clinical signs
- Presence of flare factors (pyoderma, yeast dermatitis, otitis, etc.)
- Patient acceptance of repeated topical, oral, or injectable treatment
- Owner willingness to accept time, effort, and expense of treatment

Thus, there is no "cookbook formula" for treatment of AD in all patients as these factors differ between patients. Most patients can be successfully controlled with a combination of treatments.

1. Antimicrobial therapy:
   - Use antibiotics for active infections and prophylactically.
2. Flea control:
   - Use flea control whether the patient is flea allergic or not.
3. ASIT:
   - Recommend ASIT in *all* cases of AD unless the clinical signs are very mild (i.e., easily controlled with anti-inflammatory therapy without side effects) or have a very limited season.
4. Crisis management during therapeutic trials:
   - Use "crisis busting" prednisone, 0.5 to 1.0 mg/kg q24hrs for 3 days only.
5. Initial therapy (best for dogs with mild disease):
   - ASIT
   - Hypoallergenic or moisturizing shampoo as often as possible
   - Omega-3 fatty acids once daily for 3 months
   - Antihistamine trial—Try two or three for 10 days each
   - Topical lotion or spray for localized areas once daily (preferably with residual activity, such as leave-on conditioners)
6. If poor response to initial therapy or moderate disease is present:
   - Reconsider ASIT
   - Topical triamcinolone spray for 3 weeks
   - Temaril-P (loading then taper)
   - Prednisone loading then taper (methylprednisolone if unacceptable mineralocorticoid side effects from prednisone)
   - Topical tacrolimus for focal areas of severe pruritus
7. If still poor response or severe disease is present:
   - *Refer* the case to a dermatologist!
   - Reconsider the diagnosis
   - Reconsider ASIT
   - Cyclosporine
   - E-collars, T-shirts, body suits

Allergen-Specific Immunotherapy

ASIT (also known as hyposensitization or desensitization) is the practice of administering gradually increasing quantities of an allergen extract to an allergic subject to ameliorate the symptoms associated with subsequent exposure to the causative allergen. Allergens are given by subcutaneous injection in increasing doses up to a maintenance dose or a patient-determined maximum dose.

Indications

- All dogs and cats with non-seasonal AD.
- Dogs and cats with seasonal AD where anti-inflammatory therapy is ineffective, associated with unacceptable side effects, or unsustainable.
- ASIT should not be reserved only for severe cases of AD; that is, it is not a last resort treatment. Limited evidence suggests better efficacy in younger dogs with AD that do not have advanced skin disease.

Efficacy

- True efficacy of ASIT has not been studied in randomized controlled clinical studies.
- Generally, it appears that between 60% and 75% of patients will have 50% improvement in their clinical signs with ASIT.
- As a general guideline for pet owners, one-third of patients have an excellent response, one-third have a good response, and one-third have a poor or no response.
- Owners must understand that it will likely be a number of months (usually 2–6 months and possibly as long as 12 months) before improvement is seen.
- The efficacy of ASIT in cats has not been established but is likely to be similar to that in dogs.

Protocols

- A wide range of protocols for ASIT exists. Generally, a loading phase (increasing concentrations of allergen over a period of weeks to months) is followed by a maintenance phase (once the maximum concentration of allergen has been reached).
- No particular protocol has been proven to be more effective than another. I recommend following the protocol that is supplied by the dermatologist or laboratory performing the allergy test.
- Current studies are evaluating *rush immunotherapy,* where the loading phase is very rapid (increasing concentrations of allergen administered every 30 to 60 minutes in a hospital environment) and the maintenance phase is reached within 24 to 48 hours. Whether rush immunotherapy is as effective (or more effective) than conventional immunotherapy is unknown. There may be a potential for increased risk of adverse reactions (anaphylaxis in particular) with this protocol.

Recheck Evaluations on ASIT

Studies have indicated that as many as 40% to 50% of pet owners discontinue ASIT without consulting their veterinarian. This is likely due to a lack of communication concerning the expectations and the time necessary before a response is seen. Recheck at least after 3 and 12 months of ASIT. Evaluate for the following:

- Recurrence of skin infections.
- Control of concurrent diseases (e.g., flea allergy dermatitis).
- Changes in pruritus at the time of each injection: If there is a temporary (a few days to a week or two) increase in pruritus, the dose may be too high; a temporary decrease in pruritus may indicate that the injection needs to be given more frequently.

Anti-inflammatory Therapy

Drugs used for symptomatic control of AD are categorized as follows (see Table 46-1).

Drugs with Weak Evidence of Efficacy

- Widely recommended and used
- Generally safe and inexpensive
- Highly effective in a few patients but ineffective in the majority of patients

Drugs with Fair Evidence of Efficacy

- Effective in about 50% of patients
- Limited number of studies with low numbers of subjects (await further evaluation)

Drugs with Strong Evidence of Efficacy

- Effective in a majority of patients
- Higher risk of significant side effects
- May be more expensive

Drugs Used to Treat Atopic Dermatitis

Consider the following comments and specific recommendations for the drugs listed in Table 46-1.

Antihistamines

- Try each for a 7- to 10-day trial.
- Failure to respond to one antihistamine does not predict failure to respond to other antihistamines.

Tricyclic Antidepressants

- I typically use tricyclic antidepressants (TCAs) for patients that are "highly strung"—the anxiolytic effect may be of benefit in these patients.
- Doxepin may be effective because of potent antihistaminic effects.

Table 46-1. PHARMACOLOGIC AGENTS USED FOR THE SYMPTOMATIC CONTROL OF CLINICAL SIGNS OF ATOPIC DERMATITIS IN DOGS

Drugs with Weak Evidence for Efficacy in Treatment of AD			
Antihistamines	Diphenhydramine	Benadryl/generics	2 mg/kg q8h
	Hydroxyzine	Atarax/generics	2 mg/kg q8h
	Chlorpheniramine	Chlortrimeton/generics	0.2–0.5 mg/kg q8h
	Clemastine	Tavist/generics	0.1 mg/kg q12h
	Cyproheptadine	Periactin/generics	1 mg/kg q12h
Tricyclic antidepressants	Doxepin	Generics	1–2 mg/kg q12h
	Amitriptyline	Elavil	1 mg/kg q12h
Fatty acids	Omega-3 fatty acids	Generic fish oil caps	180 mg EPA/5 kg q24h
		3V Caps HP	Label instruction
Topical moisturizers	Moisturizers	Various	As often as possible
		HyLyt EFA	
Topical anti-inflammatory drugs	Various: Pramoxine hydrocortisone oatmeal, diphenhydramine	Various	Daily–weekly
Drugs with Fair Evidence for Efficacy in Treatment of AD			
Tacrolimus		Protopic	Every 24 hours
Topical triamcinolone		Genesis spray	q12h for 1 week, then q24h for 1 week, then q48h
Misoprostol		Cytotec	3–6 µg/kg q8h
Pentoxifylline		Trental/generics	10–15 mg/kg q8–12h
Drugs with Strong Evidence for Efficacy in Treatment of AD			
Glucocorticoids	Prednisone	Generics	Crisis buster: 1 mg/kg q24h for 3 days Long term: 1 mg/kg q24h for 7 days, taper to <0.5 mg/kg q48h
	Methylprednisolone	Medrol	0.8 mg/kg q24h for 7 days, taper to <0.4 mg/kg q48h
Calcineurin inhibitors	Cyclosporine	Atopica	5 mg/kg q24h for 30 days, taper to q48–72h

AD, atopic dermatitis; EPA, eicosapentaenoic acid.

Fatty Acids

- Both omega-6 (vegetable oils) and omega-3 (fish oil and flaxseed oil) have been recommended.
- I prefer omega-3 fatty acids for anti-inflammatory effects.
- Omega-6 fatty acids may be of benefit in restoration of the lipid barrier.

Topical Moisturizers

- A lipid barrier defect has been documented in dogs with AD.
- Restoration of the lipid barrier may prevent penetration of allergens, infectious agents, and irritants.
- The use of moisturizers with frequent bathing (daily to weekly) may have the added benefits of "clearing" the skin of allergens, infectious agents, and irritants.
- I prefer the HyLyt EFA (DVM Pharmaceuticals) products as they contain omega-6 fatty acids along with the moisturizers.

Topical Anti-inflammatory Drugs

- There are numerous topical medications with added anti-inflammatory agents (oatmeal, local anesthetics, glucocorticoids, antihistamines, etc.).
- I prefer leave-on conditioners with glucocorticoids or local anesthetics (e.g., ResiCort and ResiProx, Virbac).

Tacrolimus

- Useful for treatment of localized areas of pruritus.
- Available as an ointment (Protopic 0.03% and 0.1%, Fujisawa—the higher concentration is preferable). Each tube of ointment is expensive, but if used only on focal lesions, it may last a few months.

Topical Triamcinolone

- Useful if large areas are to be treated
- Preferable to systemic glucocorticoids
- Genesis spray (Virbac)

Misoprostol

- Limited reports indicate that it may be of benefit in some patients, but I have no experience with this agent.

Pentoxifylline

- I have found this to be beneficial in only a few patients.
- Use the higher dose (15 mg/kg) at least q12h, and preferably q8h.

Glucocorticoids in Dogs

- Unfortunately, some AD patients are "steroid dependent."
- In this case, try Temaril-P (Pfizer) at label doses. The tablet is a combination of an antihistamine (trimeprazine) and glucocorticoid (prednisolone). Typically, less glucocorticoid is necessary to control AD with Temaril-P than with glucocorticoids alone.
- I frequently use a "crisis-busting" dosage of prednisone (1 mg/kg for 3 days only) in dogs when severe exacerbations of pruritus occur.
- If prednisone is necessary long-term, aim for a maintenance dosage of <0.5 mg/kg q48h.
- There is rarely a need for long-acting depot injectable glucocorticoids in dogs. Although they are often effective initially, reasons to avoid these include the risk of serious side effects, the development of bacterial infections of the skin and lower urinary tract, and the possibility of adult-onset demodicosis.

Glucocorticoids in Cats

- For cats, dexamethasone is my preferred oral glucocorticoid. The crisis-busting dosage is 0.5 to 1.0 mg once daily for 3 days. If maintenance dexamethasone is necessary, aim for <0.25 mg/kg every 3 to 4 days.
- Depot injectable glucocorticoids (e.g., methylprednisolone acetate, Depo-Medrol, or triamcinolone, Vetalog) may be acceptable in cats for temporary remission of pruritus in cats with seasonal disease.

Cyclosporine

- Cyclosporine may be as effective as glucocorticoids for the control of AD in dogs and cats.
- I prefer a dosage of at least 5 mg/kg q24h on an empty stomach.
- Treat for a minimum of 30 days before assessing the response.
- Side effects are common, including vomiting (30% of cases), diarrhea (20% of cases), gingival hyperplasia, hypertrichosis, and pyoderma.
- The drug is very expensive and is likely to be most commonly used in smaller-breed dogs and cats to treat refractory or severe disease.

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Chapter

47 Food Hypersensitivity

Stephen D. White

Adverse reactions to foods have been well documented in small animals. The terms *food allergy* and *food hypersensitivity* have been used interchangeably in the human and veterinary medical literature to describe clinical signs induced by food ingestion in which there are demonstrable or highly suspected immunologic reactions. The terms *food intolerance* and occasionally *food sensitivity* have been used when an immunologic etiology is unlikely or has not been established. Although the causes of abnormal reactions to ingested foods have not been well established in small animals, food hypersensitivity and food allergy are the terms commonly used. I prefer the former as being more accurate in describing an abnormal response of the immune system. Allergies to inhalant aeroallergens cause atopic dermatitis (see Chapter 46).

ETIOLOGY

- The exact mechanisms of food hypersensitivity have not been delineated in dogs and cats. Reactions to food have been noted in dogs and cats that could be termed immediate (i.e., hypersensitivity type I, occurring within minutes to hours after ingestion) or delayed (i.e., type IV, occurring within hours to days of ingestion). Recent reports (Ishida et al., 2003 and 2004) lend credence to both IgE- and cell-mediated mechanisms. A spontaneous canine model of IgE-mediated food hypersensitivity has been developed (Jackson and Hammerberg, 2002). However, documentation of the mechanisms involved in the development of food hypersensitivity in pet animals is still lacking.
- In dogs, the most common confirmed dietary allergens are beef, soy, dairy products, and cereal. Other allergens reported include cheese, chicken, chicken eggs, lamb, and chocolate.
- In cats, beef, milk, and fish are the most common dietary allergens. I have identified fish as an offending allergen in 50% of cats with food hypersensitivity.
- The vast array of foodstuffs used in commercial pet foods, as well as variable processing methods, probably accounts for the large numbers of allergens reported. Any dietary protein, even in small (mg) quantities may be the cause of food hypersensitivity.
- Food contaminants such as pathogenic bacteria and toxins, food additives such as tartrazines, and vasoactive amines such as tyramine in cheese have all been implicated or suspected as mimicking food hypersensitivity in humans. Their importance in small animals is unknown and is likely to be low.

CLINICAL SIGNS

▼ ***Key Point*** Although the age of onset is variable, predisposition is noted for young dogs (≤1 year of age). Owners seldom relate the onset of clinical signs to any change in diet.

- No sex predilections have been noted in dogs or cats with food hypersensitivity. Terriers and Siamese cats may be predisposed. Clinical signs are variable.
- Pruritus is the most common sign in dogs; rarely, nonpruritic animals are reported. The pruritus is often distributed similar to that for atopic dermatitis (i.e., feet, ears, face, and axillae) and these two diseases are clinically virtually indistinguishable if the pruritus is non-seasonal (year-round). The pruritus may be severe from very early in the disease. Animals with food hypersensitivity have been described as having glucocorticoid-resistant pruritus; however, this should not be regarded as a feature of food hypersensitivity as some animals are responsive to glucocorticoid administration.
- Cutaneous lesions noted in dogs include papules, erythema, epidermal collarettes, pododermatitis, seborrhea, and otitis externa. Rarely, sloughed or cracking claws may be caused by food hypersensitivity.
- In cats with food hypersensitivity, clinical signs include generalized pruritus, miliary dermatitis, facial and head pruritus, pruritic angioedema-urticaria, eosinophilic plaque, eosinophilic ulcer, mural folliculitis, and erythema.
- Gastrointestinal signs (vomiting, diarrhea) have also been noted (see Chapters 67 and 69). These may be more common than previously thought. Dogs in par-

ticular may show signs suggestive of colitis. In cats, food hypersensitivity has been manifested as lymphocytic-plasmacytic enteritis or colitis.
- Neurologic signs (epileptiform seizures, malaise) and respiratory distress (asthma-like syndromes) occasionally have been reported.
- Multiple organ involvement is uncommon.

DIAGNOSIS

Suspect food hypersensitivity in the following situations:

- Non-seasonal occurrence of pruritic skin lesions
- Recurrent pyoderma and yeast infection and recurrent otitis
- Lack of response to steroidal or other anti-inflammatory drugs in dogs and cats, although efficacy of corticosteroids in controlling pruritus does not rule out a diagnosis of food hypersensitivity
- Lack of response to progestational drugs in cats

Laboratory Findings

There are no consistent laboratory findings in small animals with food hypersensitivity. Peripheral eosinophilia may or may not be present.

Histopathologic Findings

Histopathologic findings are nonspecific and nondiagnostic, usually characterized by perivascular dermatitis with neutrophils or mononuclear cells predominating and variable secondary suppurative changes. Tissue eosinophilia is uncommon but has been reported. Histopathology is rarely needed as part of the diagnostic workup in cases of suspected food hypersensitivity.

Intradermal Testing

Intradermal skin testing with food extracts usually has been unrewarding in humans and small animals, possibly owing to changes in composition of the allergen with digestion or to improper dilution of the test allergen.

Serologic Diagnostic Tests

Serologic diagnostics using the radioallergosorbent test (RAST) or the enzyme-linked immunosorbent assay (ELISA) for reaginic antibodies in humans correlate with history and provocative exposure tests in over 50% of cases reported. However, the data from two studies, one utilizing RAST (White and Mason, 1990) and one utilizing the ELISA test (Jeffers et al., 1991), have shown that these tests are of no value in small animals. Most commercial laboratories that perform serologic allergy testing offer tests with "food panels." I do not use these tests as an aid in the diagnosis of food hypersensitivity and recommend that clinicians should not do so at this point in time.

▼ ***Key Point*** The most valid and most often recommended method for diagnosis of food hypersensitivity is the restricted ("hypoallergenic" or "elimination") test diet.

Restricted Diet Test

Home-Prepared Diets

- An appropriate restricted diet generally contains one protein and one starch. These must be based on avoidance of previously fed dietary ingredients, including snacks, treats, table scraps, cat food, and flavored medications. Remember that dogs living in households with cats tend to have been exposed to fish through their consumption of either cat food or cat feces. I often start dogs on home-cooked diets with pork and potatoes, although pinto beans and potatoes may also be used. Based on non-exposure, rabbit, duck, and tuna are also options. I have also used "exotic" foods like elk when feasible. Other than fresh water, nothing else should be fed to the dog during the restricted diet trial. This means that vitamins and chewing toys must be eliminated and that flavored medications (such as certain ectoparasite and endoparasite preventatives and vitamin supplements) should be replaced by other, equally effective non-flavored preparations. Protein-flavored toothpaste should be replaced by the malt-flavored variety. Because the restricted diet is not a balanced one, owners should be warned that the dog may lose weight, develop a "dull" haircoat or scaling, or be hungrier than usual.
- In cats, pork and tapioca pudding (the latter prepared with water, not milk) is usually palatable.
- Restricted diets should be free of colorings, preservatives, and flavorings. Do not give palatable medications, such as certain heartworm preventatives (substitute another type of heartworm preventative for the duration of the diet), and omit all vitamin and mineral supplements.
- Do not use vegetables during the trial as a treat unless you are certain that the animal has never been exposed to that vegetable. I am aware of at least two dogs that were allergic to carrots, and a dog has been reported with an allergic response to tomato.

Commercial Limited-Antigen Diets

- Owners may be unable or unwilling to cook for their pet for the time period needed. In such cases, commercially available limited-antigen diets may be used.
- For dogs these would include Purina LA (salmonid); Iams FP (fish and potato) and KO (kangaroo and oats); IVD duck, venison, whitefish, or rabbit plus potato; Hills D/D (duck or fish and rice); or Waltham fish and rice.
- For cats these would include IVD duck, venison, or rabbit plus green pea; Hills D/D feline; or Iams lamb and barley.

- Commercially prepared pet foods, including diets containing no preservatives and diets marketed as "natural," are *not* adequate test diets. These products do not meet the criteria for a true restricted test diet because of the many foodstuffs they contain and the processing of these ingredients.
- Use of a commercially prepared diet will give an approximately 90% chance of determining a food allergy; however, none of these diets will work for all animals, and failure of an animal to improve on such a diet may warrant trying another one or a home-cooked diet in another trial.

Hydrolyzed Protein Diets

- Another option for animals who already have been fed many foods, or whose dietary history is unknown, is the use of hydrolyzed protein diets, in which the protein source is hydrolyzed to small molecular weights, thus avoiding the body's "immunologic radar." Such foods for dogs include Purina HA (hydrolyzed soy and corn starch), Hills Z/D Ultra (hydrolyzed chicken and chicken liver and corn starch), and Hills Z/D Low allergen (hydrolyzed chicken and chicken liver and potato). For cats I have used Hills feline Z/D Low allergen (hydrolyzed chicken and chicken liver and rice protein) or Purina HA (not yet available at the time of writing of this chapter).

Concurrent Medical Therapy

- Occasionally, an animal may be presented to the clinician with pruritus so severe that administration of oral corticosteroids is justified while the diet is in progress. Administer prednisone or prednisolone, 0.5 to 1.0 mg/kg PO q24h, for 10 to 14 days, and then stop. Continue the diet for a minimum of 2 weeks beyond discontinuation of the medication in order to properly evaluate response to diet.
- Identification, treatment, and resolution of secondary bacterial and yeast infections are critical if the clinician is to be able to evaluate the response to the restricted diets.

Interpreting Results

- Clinical improvement is observed in most animals within 24 hours to 4 weeks after starting the restricted diet. It may take longer than this for complete resolution of pruritus.
- In my experience, 8 weeks is a reasonable length of time in which to expect some improvement. Improvement is best defined as a reduction of pruritus (or other clinical signs if pruritus is absent).
- If only partial improvement is noted, the diet may not have been given long enough for full effectiveness.
- Alternatively, evaluate the restricted diet's content and consider a change (e.g., substitute potatoes for rice).
- Consider other, concurrent hypersensitivities, such as fleas and atopic dermatitis. Literature reports indicate that approximately 30% of dogs with food hypersensitivity have concurrent atopic dermatitis; in these patients, residual pruritus is to be expected and is associated with the atopic dermatitis.

TREATMENT

Once improvement is noted, several treatment alternatives are open to the clinician.

- Challenge the animal with its original diet in order to substantiate the diagnosis. A recurrence of clinical signs is usually seen within 72 hours of initiating the dietary challenge, but it may take as long as 2 weeks, particularly when a hypersensitivity to cereals is involved.
- This rechallenge procedure is particularly important when the clinical improvement with the restriction test occurred over the course of a change in season, as this may cause a decreased exposure to environmental aeroallergens; that is, pollens may have led to improvement in a pet with atopic dermatitis, rather than improvement from the change in diet.
- If clinical signs recur with the original diet and food hypersensitivity is confirmed, then revert back to the restricted diet. Once clinical signs have resolved again, add individual foodstuffs to the restricted diet at 5- to 10-day intervals until a balanced diet is achieved or the offending allergen(s) is discovered.
- Many owners are unwilling to exacerbate a clinically improved animal or separate various components of foods to determine potential allergens. Instead, they are more interested in achieving a balanced, less expensive diet as soon as possible.
- Once the diagnosis of food hypersensitivity is confirmed, if the pet's restricted diet has been homemade, the diet may be changed to one of the commercially available limited-allergen diets mentioned in the previous section (see "Restricted Diet Test"). If the new diet is not tolerated, most animals show a recurrence of clinical signs within 72 hours, although a few pets may take longer.
- If the animal cannot tolerate a commercial diet, use a home-prepared diet consisting of a protein and carbohydrate source supplemented with vitamins, minerals, and, for cats, 60 to 100 mg of taurine daily. Supplementation with 0.5 teaspoon of clam juice per day, recommended by some, is *not* adequate taurine supplementation. For further information on additive-free supplements for homemade hypoallergenic diets, see the article by Roudebush and Cowell (1992). Consultation with a veterinary nutritionist is strongly advised in the formulation of home-prepared diets.

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Chapter

48 Immune-Mediated Dermatoses

Karen Helton-Rhodes

Immune-mediated dermatoses are relatively uncommon diseases in domestic animals. This group may be divided into autoimmune and immune-mediated categories according to immunopathogenesis.

- Autoimmune diseases include the pemphigus complex, bullous pemphigoid, mucous membrane pemphigus, and uveodermatologic syndrome (Vogt-Koyanagi-Harada syndrome). These are characterized by a specific antibody-mediated or cell-mediated immune response directed against a normal component of the skin or body.
- Immune-mediated dermatoses include systemic lupus erythematosus and cutaneous (discoid) lupus erythematosus. In these diseases, antigen-antibody complexes are formed and then deposited in various locations (vessel walls, glomeruli of the kidney, or basement membrane zone of the skin). This deposition of immune complexes may then trigger an inflammatory response that results in tissue destruction.
- Vasculitis can be either autoimmune or immune mediated, depending on the underlying etiology.

PEMPHIGUS COMPLEX

The pemphigus complex of diseases includes pemphigus foliaceus, pemphigus erythematosus, pemphigus vulgaris, pemphigus vegetans, panepidermal pustular pemphigus, paraneoplastic pemphigus, and drug-related pemphigus.

▼ ***Key Point*** Pemphigus foliaceus is the most common autoimmune skin disorder in dogs and cats.

- Pemphigus erythematosus is considered a variant of pemphigus foliaceus. It may have clinical and histopathologic features of lupus erythematosus and is therefore considered a "crossover" between the pemphigus and the lupus erythematosus complexes.
- Pemphigus vegetans is an extremely rare variant of pemphigus vulgaris that is distinguished clinically from the other autoimmune diseases by the production of lesions that are vegetative (i.e., proliferative) rather than pustular or ulcerative.

Etiology

The exact cause or stimulant for the production of the pemphigus antibody is unknown. Theories involve either abnormal immune regulation or abnormal antigen stimulation.

- A virus spread by an insect vector has been proposed as the initial stimulus. This theory gains support from an endemic form of pemphigus (fogo selvagem) in humans in South America.
- Genetic factors may be equally important as there are breed predilections for the disease.
- In humans, once formed, the antibody binds with components found in the core of the desmosome (desmoglein I or plakoglobin). Desmosomes function as attachment areas between keratinocytes of the skin. This binding stimulates plasminogen activators (i.e., serine proteases), which subsequently cause the conversion of plasminogen to plasmin.
- The production of plasmin causes the disruption of the desmosome attachments and therefore a loss of keratinocyte adhesion. This loss of adhesion between adjacent cells is called *acantholysis,* and the individual cells are termed *acantholytic cells.*
- All of the diseases in the pemphigus complex appear to have the same immunopathogenesis, but the target protein will vary depending on the type of pemphigus. The location of the bulla or separation within the epidermis differs; for example, pemphigus foliaceus has a more superficial bulla than pemphigus vulgaris.

Clinical Signs

Pemphigus Foliaceus

- Breeds that are predisposed include Akitas, chow chows, bearded collies, dachshunds, Doberman pinschers, schipperkes, and rottweilers.
- Lesions consist of erythematous macules that progress rapidly to a pustular phase and then appear as a dry,

yellow crust. These lesions may be limited to the pinnal, perioral, periocular, dorsal muzzle, nasal planum, and/or nail bed regions, or they may be generalized. Although pustules are the primary lesions, these are uncommonly seen and the clinician is more typically presented with a crusting dermatitis.
- Animals may present with marked hyperkeratosis (scaling) or crusting of the foot pads with or without nail bed involvement. The nails usually are normal.
- Cats commonly exhibit a marked paronychia that appears as a thick "cheesy" core of exudate when the nails are extruded manually.
- Mucocutaneous and oral lesions are rare.
- Pruritus is variable—the appearance of lesions precedes the pruritus (in contrast to allergic dermatoses, where pruritus is the first clinical sign).

Pemphigus Erythematosus

- Pemphigus erythematosus is a rarely recognized variant of pemphigus foliaceus.
- Collies appear to be at risk (this disease is one of several differential diagnoses for "collie nose").
- Lesions are similar to those of pemphigus foliaceus but are limited to the face.
- Some animals may show depigmentation of the planum nasale.

Pemphigus Vulgaris

- Lesions are characterized as vesicobullous eruptions that rapidly ulcerate, leaving thick crusts.
- Lesions may be primarily mucocutaneous in location or generalized.
- Onychomadesis (loss or shedding of the nails) and foot pad ulcerations are common.
- Ulceration of the oral cavity may be an initial presenting sign in over 50% of cases and is eventually present in 90% of cases. Drooling and difficulty in eating may be presenting signs.
- Pruritus and pain are variable.

Pemphigus Vegetans

- Pemphigus vegetans is an extremely rare variant of pemphigus vulgaris.
- Lesions usually are generalized rather than mucocutaneous.
- Lesions are vegetative (proliferative) or verrucous (wart-like).

Panepidermal Pustular Pemphigus

- Lesions are limited to the face.
- Pustules are found at all levels within the epidermis and follicular epithelium.
- Lesions are short-lived pustules that rupture and form a thick, adherent crust.

Paraneoplastic Pemphigus

- Rare form of pemphigus recognized in association with canine lymphoma and one case of Sertoli cell tumor.
- Oral cavity is often affected.

Drug-Related Pemphigus

- Pemphigus may be drug induced or drug triggered.
- The drug-induced form often resolves when the medication is withdrawn, while the drug-triggered form usually requires immunosuppressive therapy.
- Trimethoprim-sulfa is the most common drug associated with pemphigus.
- Feline cases are associated with itraconazole, methimazole, and lime sulfur dips.

Diagnosis

▼ ***Key Point*** Histopathologic examination of skin biopsies gives the most valuable diagnostic information. Obtain at least three biopsies of the freshest pustules, vesicles, or bullae or from the edge of an ulcerated lesion.

- In all of the pemphigus complex diseases, the complete blood count (CBC), serum biochemical profile, and urinalysis are non-diagnostic.
- Anti-nuclear antibody (ANA) tests are positive at low titers in 50% of pemphigus erythematosus patients, but in other forms of pemphigus the ANA tests are generally negative.

▼ ***Key Point*** False-positive ANA titers may be seen in animals with pemphigus, rheumatoid arthritis, idiopathic thrombocytopenia, autoimmune hemolytic anemia, thyroiditis, endocarditis, cancer, hepatotoxicity, feline leukemia, feline infectious peritonitis, dirofilariasis, demodicosis, and flea allergy dermatitis; they even may be seen in clinically normal animals.

Pemphigus Foliaceus

- Direct smear of an intact pustule or surface beneath a thick crust reveals numerous acantholytic cells.
- Histopathologic findings include subcorneal and/or intragranular pustules with acantholytic cells.
- Direct immunofluorescent antibody (IFA) tests and direct immunoperoxidase staining (IPS) tests are positive, with intercellular staining of immunoglobulin and/or complement in the upper one-third of the epidermis.

▼ ***Key Point*** IFA is positive in only 50% of autoimmune cases, whereas IPS is very sensitive and is positive in 95% of confirmed cases.

- IPS is not very specific; positive results are obtained in 73% of animals with pyoderma, 67% with dermatophytes, 50% with demodicosis, and 100% with scabies. Also, IPS is positive with the immunoreactant immunoglobulin G in an intercellular pattern in biopsies obtained from normal canine planum nasale and foot pads. IFA is positive with the immunoreactant immunoglobulin M in a basement membrane zone pattern in 75% of normal canine nasal biopsies and 45% of biopsies of normal foot pads, thus yielding false-positive results.

▼ ***Key Point*** Indirect pemphigus titers using serum are unreliable in dogs and cats.

Pemphigus Erythematosus

- Direct smears are similar to those of pemphigus foliaceus.
- ANA tests are positive, with low titers, in 50% of cases.
- Histopathologic findings include subcorneal and/or intragranular pustules, hydropic degeneration of the basal cell layer, and dyskeratotic cells.
- IFA and IPS are positive (see the preceding section), with staining in the intercellular pattern with or without concurrent staining in the basement membrane zone.

Pemphigus Vulgaris

- Direct smears are similar to those of pemphigus foliaceus.
- Histopathologic findings include suprabasilar pustules with acantholysis.
- IFA and IPS are positive (see "Pemphigus Foliaceus"), with intercellular deposition of immunoglobulin or complement in the lower one-third of the epidermis.

Pemphigus Vegetans

- Direct smears are similar to those of pemphigus foliaceus.
- Histopathologic findings include intraepidermal acantholytic eosinophilic microabscesses with significant surface crusting and verrucous vegetations and papillomatous proliferations.
- IFA and IPS are positive (see "Pemphigus Foliaceus"), with an intercellular staining pattern.

Panepidermal Pustular Pemphigus

- Histopathology findings include sterile pustules involving the subgranular layers of the epidermis and outer root sheath of the hair follicle, suppurative crusts with acantholytic cells, irregular epidermal hyperplasia, and a superficial perivascular and interstitial inflammatory response.

Paraneoplastic Pemphigus

- Histologic lesions appear to be a mixture of pemphigus foliaceus (PF), pemphigus vulgaris (PV), and erythema multiforme.
- Autoantibody targeted appears to be different than those recognized in PF and PV (desmoplakin II and a 190 kDa protein).

Drug-Related Pemphigus

- Most cases resemble pemphigus foliaceus.

Differential Diagnoses

The major differential diagnoses for pemphigus foliaceus include the following.

Generalized Pustular Crusting

- Bacterial pyoderma (it is essential to rule out pyoderma before making a diagnosis of pemphigus foliaceus based on negative cytology, negative culture, and poor response to antibiotics)
- Dermatophytosis
- Demodicosis
- Cutaneous drug reaction
- Dermatophilosis
- Subcorneal pustular dermatoses
- Sterile eosinophilic pustulosis

Pedal Lesions

- Superficial necrolytic dermatitis
- Systemic lupus erythematosus/discoid lupus erythematosus
- Zinc-responsive dermatoses
- Contact dermatitis
- Digital hyperkeratosis

Nasal or Facial Lesions

- Bacterial pyoderma
- Dermatophytosis
- Demodicosis
- Cutaneous drug reaction
- Dermatomyositis
- Pemphigus erythematosus
- Discoid lupus erythematosus

Treatment

General Considerations

Management is similar for each of the diseases in the pemphigus complex.

▼ ***Key Point*** The goal in treating autoimmune skin diseases is to keep the condition in satisfactory remission on a "safe" dose of medication. It is better for the animal to have a few remaining lesions on low-dose alternate-day glucocorticoids than to have normal skin on high daily doses of glucocorticoids.

- For initial therapy, choose prednisone. If the response is poor, add a chemotherapeutic agent such as azathioprine to the protocol.
- For more rapid and complete resolution of clinical signs with less resistance to therapy, start with a regimen of prednisone and an adjunctive chemotherapeutic drug.
- Maintain medications at a high dose until clinical signs have resolved at least 75% to 85%, then gradually decrease dosages while monitoring for exacerbation of disease.
- Taper either the prednisone or the chemotherapeutic agent first, depending on side effects noted.
- Another option is to alternate the dosage reductions of the two medications until there is complete remission and therapy is no longer necessary or until the minimum dosage of drug needed to control the disease is found.
- Initially, monitor CBC and platelet count every 2 weeks. After the disease is controlled and the level of medication is being tapered, gradually decrease the frequency of monitoring to every 1 to 2 months. Evaluate periodic (every 3–6 months) urine cultures for occult lower urinary tract infections.
- It is typically very difficult to induce remission of lesions without the initial use of glucocorticoids.

Prednisone as a Single Therapeutic Agent

- Prednisone, 1 to 2 mg/kg PO q12h (dogs) or 1 to 3 mg/kg PO q12h (cats).
- Use in conjunction with over-the-counter sunscreens and topical glucocorticoids and/or topical tacrolimus (see later section).
- Treatment of choice for pemphigus erythematosus.

Prednisone with Azathioprine

- Prednisone, 1 to 2 mg/kg PO q12h in combination with azathioprine (Imuran, Burroughs-Wellcome), 1 to 2 mg/kg PO q24–48h (dogs).
- Treatment of choice for pemphigus foliaceus, pemphigus vulgaris, and pemphigus vegetans when lesions are advanced.
- Side effects of azathioprine include vomiting, diarrhea, pancreatitis, dermatitis, anemia, bone marrow suppression, and hepatotoxicity.
- Monitor CBC and platelet count every 3 to 4 weeks.

▼ ***Key Point*** Do not use azathioprine in cats because of idiosyncratic reactions characterized by severe, non-responsive leukopenia and thrombocytopenia most pronounced in feline leukemia virus– and feline immunodeficiency virus–positive cats.

Prednisone with Chlorambucil

- Prednisone, 1 to 2 mg/kg PO q12h in combination with chlorambucil (Leukeran, Burroughs Wellcome), 0.2 mg/kg PO q24–48h.
- Treatment of choice for pemphigus complex in small dogs and all cats when lesions are severe.
- Toxicity from this protocol is mild and includes vomiting, anorexia, and diarrhea (usually resolves when the dosage is changed from a daily to an alternate-day regimen), as well as a mild, gradual, and rapidly reversible myelosuppressive effect.
- Monitor CBC and platelet count every 2 weeks.

Tetracycline and Niacinamide

- Used for mild or localized cases.
- Tetracycline has anti-inflammatory properties affecting complement activation, antibody production, chemotaxis, prostaglandin synthesis, lipases, and collagenases.
- Niacinamide inhibits mast cell degranulation and phosphodiesterase.
- Adverse reactions include vomiting, diarrhea, anorexia, and increased serum liver enzymes.
- In dogs with >10-kg body weight, give 500 mg of each drug q8h (higher doses have been used in some large- and giant-breed dogs).
- In dogs with <10-kg body weight, give 250 mg of each drug q8h.
- Clinical response may take 1 to 3 months; then taper the medication dose according to clinical response.

Cyclosporine

- Cyclosporine blocks regulatory proteins that upregulate activation genes of T-helper inducer and cytotoxic cells.
- The clinical response is variable in autoimmune and immune-mediated diseases.
- Give 5 mg/kg/day PO without food (2 hours before and after dosing).
- May be used with glucocorticoids if needed.
- Side effects include vomiting, diarrhea, anorexia, weight loss, hepatotoxicity, gingival hyperplasia, involuntary shaking, hirsutism, and papillomatosis.
- Use caution when using in conjunction with other drugs that influence the hepatic microsomal isoenzyme P450 system (e.g., ketoconazole)—use half the dose of cyclosporine to avoid toxicity.
- Monitor the serum chemistry panel every 3 months.
- Cyclosporine is very expensive, especially in medium- to large-breed dogs. As the reported success rate of this therapy is not very high, it should be regarded as a distant choice of treatment.

Tacrolimus (Topical)

- 0.1% topical formulation
- Often used for pemphigus erythematosus and discoid lupus erythematosus but in focal cases only, especially involving the face

Dapsone

- Dapsone (Jacobus) is rarely used for pemphigus and may be combined with glucocorticoids.
- Dapsone decreases complement activation, antibody production, lysosomal enzyme synthesis, and neutrophil chemotaxis.
- Dosage is 1.0 mg/kg q8h; use for *dogs only*.
- Lag phase of 4 to 8 weeks.
- Side effects include anemia, neutropenia, thrombocytopenia, hepatotoxicity, gastrointestinal signs, neuropathies, and cutaneous drug eruptions.
- Monitor CBC, platelet counts, serum chemistries, and urinalysis every 3 weeks for the first 4 months.

Sulfasalazine

- Sulfasalazine (Azulfidine, Pharmacia) is rarely used for pemphigus and may be combined with glucocorticoids.
- Sulfasalazine has anti-inflammatory properties.
- Dosage is 10 to 40 mg/kg q8h; consider it for cases with marked neutrophilic component.
- Monitor as for dapsone and check tear production (keratoconjunctivitis sicca is common side effect).

Gold Therapy

- Aurothiomalate (gold salts) (Myochrysine, Merck) is rarely used, and no published reports exist regarding its effectiveness in animal patients.
- Prednisone, 1 mg/kg PO q12h, also may be needed until remission is achieved.
- Gold therapy is suitable for both dogs and cats; however, results appear to be much better in cats.
- Auranofin (Ridaura, SmithKline Beecham), an oral form of gold salts, has been tried in a limited number of cases but needs further investigation for use in dogs and cats.
- Side effects include thrombocytopenia, aplastic anemia, toxic epidermal necrolysis, stomatitis, nephrotic syndrome, hepatotoxicity, dermatitis, and pancreatitis. Eosinophilia may herald toxicity.
- Monitor CBC, platelet count, and urinalysis every 2 weeks during the first 3 months of treatment and a serum chemistry panel monthly.

Prognosis

- The prognosis for control of pemphigus foliaceus is fair to good.
- If glucocorticoids cannot be administered, then the prognosis is poor to guarded.
- It is important that the clinician always remember the following:
  - The drugs are more likely to kill the patient than the disease.
  - 100% control of all lesions is not always necessary.

SUBEPIDERMAL BLISTERING DERMATOSES

This category includes bullous pemphigoid, mucous membrane pemphigoid, and epidermolysis bullosa acquisita.

Etiology

The immunopathogenesis of bullous pemphigoid and mucocutaneous pemphigoid involves antibody production directed against the hemidesmosomes located in the lamina lucida (BPA II/ collagen type XVII) region of the basement membrane zone of the skin. The complement cascade is then activated, causing the release of components C3a and C5a, which triggers mast cell degranulation. Mast cell mediators attract inflammatory cells that release lysosomal enzymes, resulting in tissue destruction and subepidermal blisters. The target antigen for epidermolysis bullosa acquisita is the anchoring fibrils of the lamina densa (type VII collagen).

Clinical Signs

Bullous Pemphigoid

- This is a relatively uncommon autoimmune dermatosis.
- Collies, Doberman pinschers, and Shetland sheepdogs may be predisposed.
- Clinical signs and lesions mimic those of pemphigus vulgaris.
- Vesicles and bullae of bullous pemphigoid are more stable than those seen with pemphigus, most likely due to the depth of the lesion.
- Oral cavity lesions are common and occur in 80% of cases, but they are not usually the initial presenting clinical sign. Cutaneous or mucocutaneous vesicobullous lesions generally precede oral cavity involvement.
- Pruritus and pain are variable.

Mucous Membrane Pemphigoid (Cicatricial Pemphigoid)

- This is relatively common, accounting for half of the reported subepidermal blistering diseases.
- Common in the German shepherd breed; no age or sex predilection.
- Transient vesicles that rapidly evolve into erosions, ulcers, and crusts.
- Lesions concentrate around the oral cavity, nasal planum, eyes, ear canals, genitalia, and anus.
- Oral mucosal lesions are common and are often present from the outset of disease.

Epidermolysis Bullosa Acquisita

- This is extremely rare. It is mostly seen in young dogs and is clinically similar to bullous pemphigoid.

- Great Danes appear to be at a greater risk than other breeds.
- Lesion is deeper in the skin since the anchoring fibrils (type VII collagen) of the lamina densa are the target antigen.

Diagnosis

- Direct smears are negative for acantholytic cells because this disease does not affect intercellular adhesion.
- CBC, serum biochemical profile, and urinalysis are non-diagnostic.
- ANA test is negative.
- Histopathologic findings include a subepidermal cleft or bulla with a lichenoid infiltrate of neutrophils and/or eosinophils.
- IFA and IPS are positive (see under "Pemphigus Foliaceus"), with a linear band of staining along the basement membrane zone.

Treatment

Therapeutic options for subepidermal blistering diseases are the same as those available for the pemphigus (see "Treatment" under "Pemphigus Complex").

UVEODERMATOLOGIC SYNDROME

This disease is also known as the Vogt-Koyanagi-Harada (VKH) syndrome.

Etiology

The exact immunopathogenesis of VKH syndrome is unknown. In humans, circulating lymphocytes from patients with VKH syndrome show significant cytotoxic activity against P-36 human melanoma cells. The factors responsible for the cellular hyperactivity against melanin-containing cells have not been determined. Deficiency of T-suppressor cells, viral inducement of immunologic abnormality, and genetic factors have all been implicated.

Clinical Signs

- Akitas, Samoyeds, and Siberian huskies appear to be predisposed.
- In humans, three phases have been recognized:
  - *Meningoencephalitic phase*—Fever, malaise, headache, nausea, vomiting, and tinnitus
  - *Ophthalmic phase*—Photophobia, uveitis, and blindness
  - *Dermatologic phase*—Leukoderma (acquired lack of skin pigment) and leukotrichia (acquired lack of hair pigment)
- Dogs appear to exhibit primarily the ophthalmic and dermatologic phases.
- Dermatologic lesions (leukoderma, leukotrichia) affect primarily the nose, lips, foot pads, eyelids, and anus.
- Erosions and ulcerations may or may not be present in conjunction with leukoderma.

Diagnosis

- Direct smears are negative.
- CBC, serum biochemical profile, and urinalysis are non-diagnostic.
- ANA test is negative.
- Histopathologic findings include a histiocytic interface dermatitis with pigmentary incontinence (histiocytes contain fine melanin granules).
- IFA and IPS are negative.

Treatment

- Treatment is similar to that for the pemphigus (see "Treatment" under "Pemphigus Complex").
- VKH syndrome is very difficult to control and usually requires high levels of prednisone and azathioprine.
- Ocular changes usually dictate the therapeutic course. For treatment of uveitis, see Chapter 136.

LUPUS ERYTHEMATOSUS COMPLEX

This includes discoid lupus erythematosus (DLE), systemic lupus erythematosus (SLE), exfoliative cutaneous lupus erythematosus (ECLE), vesicular cutaneous lupus erythematous (VCLE), and canine lupoid onychitis (CLO).

Etiology

The exact immunopathogenesis of this group of diseases is unknown. Antigen-antibody complexes are produced and subsequently lodge in small vessels and the basement membrane zone of the skin (SLE and DLE) and in various organ systems (SLE). Genetic factors, T cell defects, B cell hyperactivity, hormonal alterations, and viral inducement of antigen-antibody complex formation have all been implicated. (See Chapter 24 for more information about SLE.)

Clinical Signs

Discoid Lupus Erythematosus

- Collies, Shetland sheepdogs, German shepherds, and Siberian huskies are predisposed.
- There are no internal manifestations of disease except in very rare "potential" crossover cases that, in time, become more consistent with SLE.
- The initial lesion is an area of depigmentation or erythema that slowly progresses to loss of the normal cobblestone appearance of the nasal planum and eventual development of erosions, ulcers, and crusts.

- The planum nasale is the area most commonly affected, although lesions have been noted on the eyelids, lips, foot pads, and concave surface of the pinnae and in the oral cavity.
- Profuse hemorrhage may occur following minor trauma to the planum nasale.
- Sunlight exacerbates the lesions and may play a role in the pathogenesis of DLE.

Systemic Lupus Erythematosus

- Collies and Shetland sheepdogs are predisposed.
- SLE is a multiorgan disease with dermatologic manifestations in 32% to 54% of cases.
- Cutaneous signs associated with SLE include ulcerative stomatitis, seborrhea, mucocutaneous ulceration, foot pad ulceration, panniculitis (lupus profundus), urticaria, and purpura.
- Non-cutaneous signs of SLE (see Chapter 24) include polyarthritis, fever, glomerulonephritis, hemolytic anemia, thrombocytopenia, polymyositis, neurologic signs, pleuritis, myocarditis, and lymphadenopathy.

Exfoliative Cutaneous Lupus Erythematosus

- This hereditary disease (autosomal recessive) is also known as *lupoid dermatosis* of German shorthaired pointers. It usually occurs in the first year of life.
- It is characterized by localized to generalized scale with follicular casting and alopecia. Pruritus is minimal. The course may wax and wane.
- Dogs may also have blood dyscrasias, joint disease, and features of sebaceous denitis.

Vesicular Cutaneous Lupus Erythematosus

- This is also known as *ulcerative dermatosis* of collies and Shetland sheepdogs and was previously thought to be a variant of dermatomyositis. It has an adult onset.
- Lesions are annular, polycyclic, and serpiginous (wavy, indented) ulcerations and are located primarily in the inguinal and axillary regions.

Canine Lupoid Onychitis

- This is primarily a disease that affects the claw with "lifting" of the nail due to separation from the basement membrane. Lesions may also affect the tail and planum nasale.
- Dogs rarely experience associated pain and seem to be more comfortable once the nail has fallen off.
- The nail will often remain misshapen and fail to form a more normal appearing nail.
- Pyonychia is absent.

Diagnosis

Discoid Lupus Erythematosus

- Direct smears are non-diagnostic.
- CBC, serum biochemical profile, and urinalysis are non-diagnostic.
- ANA test is positive in 5% of cases of DLE. This may indicate those animals with the potential for conversion to SLE that therefore should be closely monitored.
- Histopathologic findings include a lichenoid interface dermatitis composed primarily of lymphocytes and plasma cells, thickened basement membrane zone, hydropic degeneration of the basal cell layer, apoptotic keratinocytes in the lower layers of the epidermis, pigmentary incontinence, and excess of dermal mucin.
- IFA and IPS are positive, with a granular or rough band of immunoglobulin and/or complement deposited at the basement membrane zone.

Systemic Lupus Erythematosus

- Direct smears are non-diagnostic.
- CBC, serum biochemical profile, and urinalysis may show a variety of abnormalities, depending on the non-cutaneous organs involved (see Chapter 24).
- ANA test is positive in 85% to 90% of cases.
- The negative titers in 10% to 15% of ANA tests may be a laboratory "fault" because of the current inability of most laboratories to test for extractable nuclear antigens.
- The lupus erythematosus cell preparation is unreliable and not routinely used in veterinary medicine.
- Histopathologic findings include epidermal and dermal lesions similar to those seen in DLE and may include leukocytoclastic vasculitis and mononuclear panniculitis.
- IFA and IPS are positive, with a band of staining at the basement membrane zone of the skin and involved dermal and subcutaneous vessels.

Exfoliative Cutaneous Lupus Erythematosus

- Histopathology reveals hyperkeratosis, basal cell degeneration, and apoptotic epidermal cells, as well as features of sebaceous adenitis.

Vesicular Cutaneous Lupus Erythematosus

- Histopathology reveals an interface dermatitis and folliculitis composed predominantly of lymphocytes with vesiculation of the dermal-epidermal junction.

Canine Lupoid Onychitis

- This is a clinical diagnosis. Histopathology is rarely diagnostic.

Treatment

Lupus Erythematosus Complex

- To treat SLE, give prednisone, 1 mg/kg PO q12h.
- Systemic glucocorticoids are rarely necessary in DLE; thus, only use them in severe DLE that is unresponsive to other therapies.

- Apply topical glucocorticoids to the planum nasale. This may be the only form of corticosteroid needed to treat and control mild cases.
- Topical tacrolimus (Protopic 0.03% or 0.1%) may be beneficial.
- Apply topical sunscreens to the planum nasale during periods of sun exposure.
- Administer vitamin E 400 IU PO q12h. Give 2 hours before or after a meal.
  - Vitamin E has a 30- to 60-day lag phase, and therapy usually is maintained for the life of the dog.
  - No side effects have been reported in dogs. Problems noted in humans include thrombophlebitis, hypertension, fatigue, cardiac disease, and diabetes mellitus.
- Tetracycline and niacinamide in combination may be effective. In dogs over 10 kg, the initial dosage is 500 mg of each drug PO q8h, and in dogs under 10 kg, the dosage is 250 mg of each drug PO q8h. Once response is noted, the dosage can be decreased to q12h and then to q24h. Side effects include anorexia, vomiting, and diarrhea.
- Severe cases may require the use of azathioprine, as described for the pemphigus complex (see "Prednisone with Azathioprine").
- Gold salts are contraindicated in SLE because of the potential for both the drug and the disease to produce glomerulonephritis.
- In severe cases of anemia and thrombocytopenia, splenectomy may be indicated (see Chapter 25).
- Trental (pentoxifylline) has been helpful in rare cases, especially for lupoid onychitis.
- Essential fatty acid supplementation may be used as an adjunct therapy for all of the disorders.

VASCULITIS

Etiology

- Most of the recognized vasculitic syndromes are caused by deposition of immune complexes within vessel walls. Complement components are then activated and act as chemoattractants for neutrophils. Neutrophils infiltrate the vessel wall and release lysosomal enzymes such as elastase and collagenase, which damage the vessel wall. Thrombosis, occlusion, hemorrhage, and necrosis may develop. Blood flow turbulence and hydrostatic tension may also play a role in the immunopathogenesis of vasculitis.
- Inciting causes of vasculitis are varied and include allergic diseases, bacterial and viral infections, drug reactions, chemicals, neoplasia, SLE, rickettsial diseases, polyarteritis nodosa, rheumatoid arthritis, and cold hemagglutinin disease. (See Chapter 153 for more information on vasculitis.)

Clinical Signs

- Vasculitis is a polysystemic disease.
- Dermatologic signs include petechiae, ecchymoses, hemorrhagic bullae, ulcerations, urticaria, and edema.
- Non-cutaneous signs are similar to those described for SLE.

Diagnosis

- Direct smears are non-diagnostic.
- Diascopy, the application of a glass slide pressed to an erythematous lesion, may help rule out vascular fragility. The lesion clears if the erythema is due to vascular dilatation but remains if hemorrhage or vascular leakage has occurred.
- CBC, serum biochemical profile, and urinalysis changes are dependent on the underlying etiology and on the target organ system.
- ANA test is negative unless SLE is the underlying cause of the vasculitis.
- Histopathologic findings include leukocytoclastic vasculitis, fibrinoid degeneration of vessel walls, thrombosis, and endothelial swelling.
- IFA and IPS may be positive in early lesions, with immunoglobulin and complement detected in and around vessel walls. Affected animals have high levels of circulating immune complexes and low levels of complement.

Treatment

- Treatment is similar to that described for the pemphigus (see "Treatment" under "Pemphigus Complex").
- Do not use glucocorticoids if there is an infectious etiology.
- Dapsone (Jacobus), 1 mg/kg PO q24h, may be used in cases of idiopathic neutrophilic vasculitis.

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Chapter 49

Necrotizing Skin Diseases

Gail A. Kunkle

Necrotizing dermatitis refers to those skin conditions in which there is death of tissue. With many cases of necrotizing dermatitis, eschar (slough) formation and ulceration is often the visible clinical sign, and it occurs when there is cell death, especially within the epidermis and the hair follicles. In other necrotizing skin diseases, the tissue destruction may arise in the dermis or even from compromise of deeper vessels. In these cases the first clinical signs may be discoloration, swelling, or coolness to the skin followed later by cutaneous ulceration. Causes of necrotizing skin disease are categorized in Table 49-1.

▼ ***Key Point*** Dependent on the depth of necrosis or the percentage of surface area which is ulcerated, necrotizing dermatoses can be life-threatening.

An overview of necrotizing dermatitis will be presented in this chapter, followed by discussion of the specific diseases that cause the disorder.

CLINICAL SIGNS

Necrotizing skin diseases are characterized clinically by well-defined areas of devitalized skin (eschar), which may vary from pinpoint sized to involving of a large portion of the skin surface. The area may be discolored, ranging from dark red to purple to yellow to black. There may be swelling and even gas production within the tissues. In time, the devitalized skin develops into a thick adherent crust, revealing deep ulceration if removed. Common sequelae are systemic signs of toxicity.

PRINCIPLES OF DIAGNOSIS

Significant necrosis of the skin is a dermatologic emergency and may result in death; thus, initiate the diagnostic approach to necrotizing skin disease as quickly as possible.

Early identification of an underlying cause and specific treatment generally allows a better clinical outcome. The diagnostic approach should be as thorough as possible from the outset to increase the chance of a definitive diagnosis.

▼ ***Key Point*** Specific diagnosis is best made by routine histopathology from representative primary skin lesions and/or tissue samples adjacent to necrosis, in conjunction with a careful history and thorough physical examination.

History

- Identify or exclude several of the potential causes of necrotizing dermatoses.
- Record a thorough drug history and take note of environmental factors.
- Record a careful timetable of events in addition to the owner's description of the earliest cutaneous lesions and their temporal relationship to any noted systemic signs.

Physical Examination

- Thoroughly examine all of the skin, including the inside of the ears, the oral cavity (and other mucosal surfaces), and haired as well as non-haired skin.
- Note any primary lesions.
- Look for secondary lesions and for evidence of how they may have developed.
- Palpate all peripheral lymph nodes for enlargement.
- Take the body temperature.
- Perform a general physical examination, including examination of the eyes, auscultation of the thorax and palpation of the abdomen, to evaluate for systemic signs.

Serum Biochemical Profile, Urinalysis, and Complete Blood Count

- Evaluate these in animals with systemic signs such as anorexia, fever, and depression. This minimum database may even be justified in animals with extensive necrotizing dermatitis but without overt clinical signs of systemic disease.
- Use these as baseline information when progressive disease is suspected.

Table 49–1. CLASSIFICATION AND CAUSES OF NECROTIZING DERMATOSES

Category	Cause
Vasculitis	Sepsis Systemic infectious disease Drug-induced Neoplasia Immune-mediated Focal (rabies vaccination) Post-vaccination ischemic dermatopathy Dermatomyositis Idiopathic
Neoplasia	Squamous cell carcinoma (see Chapter 30) Mast cell (see Chapter 28) Lymphoma (see Chapter 27) Lymphatoid granulomatosis Other tumors (see Chapter 30)
Drug-induced	Antibiotics Biologicals Barbiturates Phenylbutazone Gold salts
Toxic epidermal necrolysis	Drug-induced Systemic disease
Erythema multiforme	Neoplasia Idiopathic
Superficial necrolytic dermatitis	Glucagonoma Hepatopathy
Environmental	Contact irritant Snake bite Spider bite Radiation Burns Frostbite Decubitus ulcers
Immune-mediated	Systemic lupus erythematosus (see Chapter 24) Bullous pemphigoid (see Chapter 24) Pemphigus complex (see Chapter 24) Cold agglutinin disease Vasculitis Vesicular cutaneous lupus erythematosus
Infectious	Bacterial cellulitis (see Chapter 38) Deep fungal infection (see Chapter 40)
Vascular compromise	Thrombovascular necrosis Mechanical occlusion Diabetes mellitus (see Chapter 34)

Tests for Systemic Immune-Mediated Diseases

- When clinical signs suggest systemic disease, perform antinuclear antibody (ANA) testing of serum to assess the presence or absence of antibodies directed against multiple nuclear antigens.
- Other immune tests such as Coombs testing and cryoglobulin identification may be indicated in cases in which specific diseases are suspected.
- See Chapter 24 for further discussion of testing for systemic immune-mediated diseases.

Skin Biopsy

- Skin biopsy is usually a critically important diagnostic tool in necrotizing skin diseases (see Chapter 37). Sampling of early primary lesions is most likely to be rewarding. When vasculitis is suspected, obtain deep wedge biopsies for diagnosis—deep tissue may not be obtained if only punch biopsy tissue specimens are collected.
- Collect lesions that are primary eruptions and/or skin immediately adjacent to necrotic skin.
- Use formalin as a fixative and obtain representative tissue samples from various types of lesions. A pathologist familiar with dermatopathology often can determine if systemic or topical disease is present.
- Most pathologists now use formalin-fixed tissue for immunohistochemistry for the presence of antibody. However, absence of antibody does not rule out autoimmunity as a cause.

Skin and Blood Cultures

- Evaluate the patient for infection by culturing the skin for bacterial (aerobic and anaerobic) and fungal agents.
- For systemic diseases, blood cultures may be indicated.

Other Diagnostic Evaluations

- Evaluate rickettsial serum titers and other disease-specific hematologic tests as indicated.
- Perform liver function tests (pre- and post-prandial serum bile acids) and abdominal ultrasound (to evaluate the liver and pancreas) to assess a suspected case of superficial necrolytic dermatitis.
- Radiography and ultrasonography are useful if cutaneous lesions are suspected to be secondary to malignancy or systemic disease.
- In rare cases, response to therapy or removal of a suspected inciting drug confirms the diagnosis.

PRINCIPLES OF TREATMENT

▼ ***Key Point*** Therapy is most effective when a specific cause is identified; treatment can then be focused on the elimination or modification of the underlying cause.

Cutaneous necrosis is best managed aggressively with treatment directed against a definitive cause. If there is a possibility that drugs are implicated, discontinue all drugs until a definitive or probable diagnosis is established. Secondary infection is likely and best treated with a broad-spectrum antibiotic (preferably one that the patient has not previously received). Toxins associated with tissue necrosis can have systemic effects; therefore, debride tissues and flush frequently with sterile

saline. When the cause cannot be identified, supportive care is the mainstay of treatment. Hydration and provision of a high-quality protein diet are important aspects of therapy.

SPECIFIC NECROTIZING DERMATOSES

Vasculitis/Vasculopathy

Etiology

Vasculitis is an inflammatory process that occurs within blood vessel walls and that can lead to necrosis of the vessels and subsequent death of the adjacent tissue. Histopathologic evidence of vasculitis can be subtle and transient. When surrounding tissues suggest vascular compromise or there is vessel wall damage without cells, many pathologists refer to this as vasculopathy. Acute cutaneous vasculitis is most likely to result in necrotizing skin signs including hemorrhage (ecchymoses or purpura), hemorrhagic bullae, necrosis (eschar), and punched out ulcers. Hemorrhage can be confirmed clinically by diascopy (the skin remains discolored when pressure is applied with a glass slide. In comparison, erythema blanches under pressure). Chronic vasculitis or cell-poor vasculitis (vasculopathy) is more likely to present with ischemic changes such as alopecia, scaling, hyperpigmentation and some erythema. Both often involve the ears, tail tip, face, and extremities. Cutaneous vasculitis and vasculopathies are rarely primary in the dog. The list of secondary causes is quite extensive; for prognosis and treatment purposes it is useful to separate these into infectious and non-infectious etiologies. In spite of an extensive search for an underlying cause, many cases are idiopathic.

Non-immunologic Causes

- Necrotizing vasculitis can be seen with a variety of infections caused by bacteria, viruses, disseminated fungi, and tickborne organisms such as Rickettsia rickettsii. Bacteria may directly invade the vessel walls, especially with sepsis. Other infections such as E. coli can produce toxins that result in specific signs of vasculopathy as seen in the cutaneous and renal glomerular vasculopathy of greyhounds.
- Neoplasia can result in vessel wall necrosis through toxin production or direct invasion of the vessel wall by neoplastic cells.
- Specific drugs can induce lesions of vasculitis in animals; the antifungal drug, itraconazole, at a dosage of 5 mg/kg q12h PO has been observed to cause vasculitis in some dogs.

Immunologic Causes

- With autoimmune disease immune complex deposition may occur in vessel walls. Antibodies or cytotoxic cells may attack components of the vessel walls in other connective tissue conditions.
- Focal cutaneous vasculitis has been reported at the site of rabies vaccination. This is usually a deep panniculitis, and the cutaneous clinical sign most often is alopecia instead of necrosis. Similar lesions may develop later at sites distant from the site of vaccination.
- Post-vaccination ischemic dermatopathy and familial dermatomyositis in the acute stages may exhibit erosions or ulcerated lesions on the extremities in association with vasculitis. However, in the majority of these cases the signs are more chronic and are evidence of a vasculopathy.

Clinical Signs

- Vasculitis signs usually consist of necrosis and ulceration. These commonly occur on the pressure points, foot pads, pinnae, and extremities. Mucocutaneous ulcerations may be present as well as fever, lymphadenopathy, anorexia, and depression. Acute signs are more often necrotic or erosive lesions whereas chronic signs may show alopecia and scarring.

Treatment

- Vasculitis/vasculopathy is best managed by treatment of the underlying disease. Unfortunately, a specific cause of vasculitis/vasculopathy cannot be identified in a significant number of cases.
- If sepsis or generalized bacterial, fungal, or rickettsial disease is identified, treat the infectious agent.
- If the vasculitis is drug induced, discontinue the offending drug immediately. Corticosteroids at anti-inflammatory dosages (prednisone or prednisolone, 1.1 mg/kg q12–24h PO) are advocated by some for the management of drug-induced vasculitis.
- If immune complexes are being deposited in vessel walls, give immunosuppressive doses of glucocorticoids (2–4 mg/kg q12–24hr PO) or other drugs.
- Corticosteroids may be beneficial in some cases of vasculitis/vasculopathy. Other cases are self-limiting. In some, alternative treatments may be beneficial. Pentoxyfylline (10–15mg/kg q8h PO) has a wide range of properties, few side effects, and can be used for successful management in idiopathic cases. Dapsone (Avlosulfone, Jacobus) (dogs only) as well as sulfasalazine reportedly have been effective. The initial dosage of dapsone is 1 mg/kg q8–12h PO; when the disease is controlled, gradually reduce the dosage. Both of these drugs have potential side effects, and should be used accordingly.

Neoplasia-Related Skin Necrosis

- Neoplasia can cause skin necrosis and cutaneous ulceration through a variety of mechanisms. As mentioned previously, neoplasia can cause vasculitis.

Through release of necrosis factors generated by tumor cells, there may be local death of tissues. Also, the encroaching growth of a rapidly advancing lesion may cause circulatory compromise, leading to cutaneous tissue necrosis. There are several neoplastic conditions that may result in dermal necrosis, including cutaneous lymphoma.

Clinical Signs

- Clinical signs depend on the type and location of the tumor as well as the stage of the disease. In epidermotropic lymphoma and in some cases of cutaneous lymphoma, ulceration and necrosis of the tissues at the mucocutaneous junctions and inside the oral cavity may be seen with or without well-defined tumors. In other cases of cutaneous lymphoma, multifocal cutaneous necrotic lesions may occur without mucocutaneous lesions. In lymphomatoid granulomatosis (angiotropic lymphoma) neoplastic cells are noted around and within the walls of vessels with the result of ischemic necrosis.

Treatment

- Neoplasia treatment depends on the type of tumor, its potential for metastasis, and its biologic behavior. Surgical resection is indicated for solitary lesions. Treatment of other tumors should be based on current recommendations for the individual type of neoplasia. (See Chapters 27–30.)

Drug-Induced Necrosis

- Drug-induced necrosis of the skin followed by ulceration may occur with various drugs. Hypersensitivity may be responsible in many of these cases, but proving this can be difficult. Vesiculobullous drug eruptions may precede ulceration, and purpura may occur before there is apparent tissue death.

Clinical Signs

- Drug-induced necrosis of the skin can cause a wide variety of clinical signs and can mimic almost any condition.
- When this is due to a systemically administered drug, the cutaneous lesions frequently start out focally but rapidly progress to generalized. *Fixed drug eruption* is an exception to this because on subsequent exposures it always occurs in the same local area. Fixed drug reaction can result in focal ulceration. Most drug eruptions begin with generalized erythroderma or erythematous macules, followed by vesiculation and then necrosis or ulceration of the skin. These eruptions may occur during the first exposure to a drug. If they occur with first exposure, they do not usually develop clinically until after 5 to 7 days of drug administration.
- Drug reactions to topically applied drugs can occur if the animal has an idiosyncratic reaction or, more often, if prior exposure has induced hypersensitivity. Contact allergic dermatitis can be the result of a topical drug, and extensive ulceration can occur, especially if the diagnosis is not made early.

Treatment

- For treatment of drug-induced necrosis, discontinue the offending drug immediately. New lesions may continue to develop after discontinuation of the drug. If the adverse effects resolve and are known to be dosage dependent, resume therapy at a much lower dosage if the primary disease mandates continuation of the drug. In most instances, it is preferable to substitute a different drug and to avoid giving the suspect drug to the animal in the future. The efficacy of corticosteroids, both at immunosuppressive and at anti-inflammatory levels, for drug reactions is highly controversial. Assess each case individually for potential advantages and disadvantages.

Toxic Epidermal Necrolysis and Erythema Multiforme

Toxic epidermal necrolysis (TEN) and erythema multiforme (EM) are both necrotizing skin diseases most often caused by drugs. These conditions may also be the result of systemic diseases such as cholangiohepatitis, hepatic necrosis, and endocarditis. Other etiologies include infections, immune-mediated diseases, neoplasia, and idiopathic causes. Although they may have similar etiologies, the histopathology and clinical course of TEN and EM are often quite separate. Some of the drugs that have been implicated in TEN and EM in dogs and cats include levamisole, penicillins, cephalosporins, sulfonamides, gold salts, 5-fluorocytosine, and antiserum.

Toxic Epidermal Necrolysis

- TEN may mimic EM in its early signs, but it is a much more serious disease. The histological lesion of TEN is full thickness coagulative necrosis of the epidermis which may extend into the hair follicles. In early lesions and prior to secondary infection the dermis is not necrotic and inflammation is minimal. In this way TEN can be differentiated from chemical or thermal injuries if the lesions are biopsied early.

Clinical Signs

- Eventually full-thickness necrosis and sloughing of the skin occur, often involving large areas of skin. The clinical appearance can mimic a burn. There may be a positive Nikolsky sign in which normal-appearing skin can be separated away from the underlying dermis with firm manual pressure. The patient usually shows systemic signs of malaise and fever.

▼ ***Key Point*** Because of the extensiveness of TEN, it is crucial to pursue an early diagnosis and to eliminate the inciting cause as quickly as possible while providing aggressive supportive therapy.

Treatment

- Toxic epidermal necrolysis represents a true dermatologic emergency. Immediately discontinue any suspect drugs and search for systemic disease or neoplasia. Once full-thickness necrosis of the skin begins, start aggressive supportive care with intravenous (IV) fluids such as lactated Ringer's solution to replace estimated fluid loss. Keep affected tissues clean and debrided; and cover with a topical cream such as silver sulfadiazine (Silvadene, Marion) to decrease evaporation from large denuded areas. Secondary infection can result in sepsis and hypoproteinemia may be a concern when large areas are affected. Corticosteroids (prednisone or prednisolone, 2.2 to 4.4 mg/kg q12h PO initially, and then taper the dosage) are recommended by some, especially early in the course of the disease.
- The prognosis is guarded, and in spite of removal of the causative agent or disease, TEN can continue to progress and may be fatal.

Erythema Multiforme

- EM tends to be less severe than TEN. Histological examination generally shows single cell necrosis of epidermal cells at all levels of the epidermis. There often is an inflammatory infiltrate noted, even in early lesions. Occasionally, in more severe forms of EM, there can be an overlap of the histopathological findings with a confluence of cells dying, mimicking TEN.

Clinical Signs

- Multifocal clinical lesions may appear papular, macular, vesicular, bullous, or target-like, with central areas of redness surrounded by an erythematous ring. Cutaneous lesions usually progress to multifocal ulcerations and these are often in arciform or polycyclic conformations. Mucocutaneous areas are generally affected.

Treatment

- Erythema multiforme is treated by discontinuation of any potential causative drugs as soon as possible and giving supportive care. Symptoms may continue for several days past withdrawal of the offending agent, and pain and scarring may occur.
- The prognosis for survival is better if the primary causative condition is not life-threatening.
- Although not as serious a disease as TEN, the initial prognosis for EM is guarded. The disease is progressive in some dogs and difficult to control in others.

Superficial Necrolytic Dermatitis

- Superficial Necrolytic Dermatitis (SND) *(necrolytic migratory erythema [NME], metabolic epidermal necrosis [MEN], and hepatocutaneous syndrome)* is an uncommon canine skin disease which is a manifestation of a poorly defined error in metabolism. The histologic picture is similar to glucagonoma syndrome in humans. The histopathological findings include a marked parakeratotic epidermis with inter- and intracellular edema, keratinocyte degeneration in the upper epidermis, and hyperplastic basal cells, forming a characteristic "red, white, and blue" histological lesion diagnostic for this syndrome.
- In a recent retrospective study affected SND dogs had a high frequency of chronic phenobarbital usage administered for idiopathic epilepsy. Liver enzyme values, especially alkaline phosphatase, are often elevated.
- Some cases (<10% of cases reported in the literature) have had glucagonomas (i.e., endocrine tumor of the pancreas similar to the disease in humans).
- Mean plasma amino acid concentrations for dogs with SND reportedly are lower than normal dogs or dogs with hepatitis, some amino acids are <20% of the normal values. A metabolic hepatopathy with increased hepatic catabolism of amino acids is hypothesized as the cause of this syndrome, but the exact metabolic etiology is still undefined.

Clinical Signs

- The clinical findings in SND are erythema, crusting, exudation, and ulceration of the skin of the footpads, mucocutaneous junctions, and pressure points. Classically there is crusting, ulceration, and fissuring of the footpads with some patients being reluctant to walk due to pain. Although this condition may clinically mimic EM, the footpad lesions are more suggestive of SND. Systemic SND signs are quite varied and may include clinical signs of concurrent diabetes mellitus and/or hyperadrenalcorticism.

Treatment

- Treatment with dietary supplementation of protein (high protein diets or egg yolks) or amino acid supplements (e.g., Promod 1 scoop/10 kg), fatty acids, and zinc have generally not been rewarding. Intravenous solutions of amino acids (e.g., Aminosin 500 ml weekly) have caused transient improvement in some cases.
- There is frequently a secondary bacterial and/or yeast infection of the lesions (especially interdigitally). Recognition and control of the infection (topical and systemic antimicrobial therapy) provides significant benefit (and temporarily improved quality of life) to some dogs although the primary disease will progress.

- The medium- to long-term prognosis is generally poor, and an outcome of euthanasia is common, often due to the painful feet of the patient. The reported mean survival time from diagnosis is less than 6 months, but some dogs live for months with waxing and waning of their symptoms.

Environmental Injury of the Skin

Environmental factors can cause necrosis and ulceration of the skin. The clinical signs of environmental injuries of the skin vary depending on the specific etiology and location of exposure.

Contact Irritant Chemicals

- Contact irritant chemicals can caustically burn or necrose the skin after topical exposure. The list of primary irritants is extensive and includes soaps, detergents, insecticidal sprays, fertilizers, and caustics such as strong acids or alkalies. Medications and hypertonic solutions delivered extravascularly can also result in necrosis of the underlying tissue and the skin.

Clinical Signs

- Lesions of cutaneous necrosis can occur wherever the skin was exposed to the irritant. Usually the feet, scrotum, and ventral abdomen are involved if the animal walked or lay down on the causative agent. The muzzle or oral cavity may be involved if the animal tried to remove the compound by licking.

Treatment

- Treatment requires removal of the irritant followed by supportive care.

Snake Bite

- Snakes, including pit vipers (copperhead, cottonmouth, and rattlesnake) and coral snakes, produce venoms that alter the integrity of blood vessels, blood cells, and coagulation; affect the nervous system; and result in necrosis at the site of envenomation.
- Snake bites most frequently occur during the warmer months in geographic areas with an indigenous population of venomous snakes.

Clinical Signs

- The face and extremities are the common sites of involvement. Initial signs are localized soft tissue swelling that spreads rapidly. Local hemorrhage occurs, followed by necrosis of tissue and sloughing.

Treatment

- Treatment of snake bite varies with the severity of the clinical signs, location of the bite, type of snake, and length of time since the bite. Initially, immobilize the lesion and keep the patient quiet. Application of tourniquets is controversial, as is glucocorticoid therapy. When polyvalent antivenom (Antivenin, Fort Dodge) is indicated, give one vial slowly IV as soon as possible after the bite and repeat injections as necessary. Monitor the patient closely for anaphylaxis. Broad-spectrum antibiotics are generally indicated because both anaerobic and aerobic infections are often sequelae to the bite. Keep the lesions clean and debride wounds regularly.

Spider Bite

- Spiders (e.g., brown recluse and brown spider) cause necrotizing skin lesions by injection of a potent dermonecrotic toxin into the tissue when they bite. The enzymes in the venom and the immunologic response of the host both play a role in dictating the clinical response.
- These toxins can continue to damage the surrounding tissue for an extended time after the bite.

Treatment

- Excise the bite wound if the lesion is identified early as a bite from one of these spiders.
- Corticosteroids and antivenom do not appear to reduce local necrosis.
- When systemic signs are present, corticosteroids combined with supportive care are beneficial. Intravascular hemolysis and renal failure are possible sequelae.

Radiation Injury

- Radiation injuries may be acute or chronic, and necrosis and ulceration of the tissue can occur days to weeks after exposure.
- Radiation injury occurs in the anatomic area previously exposed to radiation.

Clinical Signs

- The clinical signs include erythema of the skin, moist desquamation, pigmentation or change in hair color, and loss of hair.

Treatment

- Treat acute radiation damage with gentle topical cleansing, followed by topical creams. Use medications to control pain as needed.
- Chronic radiation injury and areas of cutaneous atrophy caused by acute damage may later necrose and slough. This condition usually is progressive. Supportive care is the primary treatment.

Burn Injury

- Burn injuries can result from heat, sun, flames, scalding liquids, friction, and electricity. The history usually identifies the source of injury.

- Burns can cause significant necrosis and loss of skin. Depending on the depth of the burn, necrosis may involve only the epidermis or may extend deeper into the tissues.

Clinical Signs

- Clinical signs usually include pain, erythema, and eschar formation with full-thickness burns. Deeper burns may result in shock, electrolyte and protein disturbances, and life-threatening secondary bacterial infection.

Treatment

- Treat burns according to their depth (partial- or full-thickness) and extent over the body. Apply intensive and aggressive topical therapy in severe cases. Give medications such as morphine to control pain. Cleanse, debride, and cover burns with an antibacterial cream (e.g., Silvadene or Marion) (see Chapter 56 for management of open wounds). Fluid replacement and protein supplementation are important. Because secondary bacterial (e.g., Pseudomonas) infection is common, systemic broad-spectrum antimicrobial drug therapy is essential. Skin grafts may be necessary for extensive full-thickness burns (see Chapter 57).
- The prognosis depends on the extent of the surface area involved.

Frostbite

- Frostbite occurs when exposure to environmental cold results in vasoconstriction so severe that the effects are not totally reversible on rewarming of the tissues.

Clinical Signs

- Frostbite most often results in necrosis and sloughing of the tips of the ears or tail. In the dog, the scrotum can also be affected. Debilitated animals are more susceptible because of immobility and poor circulation.

Treatment

- Frostbite-affected animals usually are presented long after the damage has occurred, and supportive care with debridement may be necessary. In early cases, rapidly rewarm the tissues in water heated to 40–42°C. Whirlpool therapy can be helpful. Medication for pain may be necessary. If self-trauma can be minimized, the lesions are best left uncovered. Administer systemic antibiotics to manage secondary infection.

Decubitus Ulcers

- Decubitus ulcers are a form of vascular compromise related to environmental conditions, characterized by loss of soft tissue cushion over bony prominences.
- Decubitus ulcers usually are secondary to pressure necrosis in recumbent animals.

Clinical Signs

- Pressure points, especially stifles, elbows, hocks and hips, are common sites. These lesions are well demarcated, with full-thickness necrosis usually extending to the underlying musculature.

Treatment

- Decubitus ulcers are best treated by making the patient ambulatory, but if this is not possible, then supportive care is required. Clean and rotate the patient often. Soft bedding or a water mattress is useful. Keep ulcerated areas free of fecal and urine contamination. If possible, cover affected areas with clean dressings. Tie-over bandages are very useful for these lesions (see Chapter 56). A wide variety of agents are available for topical use. In some cases, surgical debridement and reconstruction are indicated (see Chapter 56).

Immune-Mediated Dermatoses

- Immune-mediated dermatoses are one group of conditions that may present with substantial areas of cutaneous necrosis. In general these diseases have blister (or pustule) and cleft formation, followed by separation within the viable skin. Ulceration and erosion then occur as this portion of the skin dies and lifts off.
- Autoimmune diseases that affect the skin include systemic diseases, such as systemic lupus erythematosus, cold agglutinin disease, and immune-mediated vasculitis, and the more cutaneous conditions of bullous pemphigoid and pemphigus complex. These are discussed elsewhere (see Chapter 24).

Clinical Signs

- Immune-mediated dermatoses usually cause acute lesions that may include vesicles, bullae, ulcers, hemorrhagic nodules, and erosions. The mucocutaneous junctions may be involved. The animal is generally middle-aged or older and may have systemic signs. See Chapter 24 for discussion of autoimmune diseases.

Treatment

- Treatment depends on the type of immune-mediated disease and the severity and extent of the lesions. Initially, give systemic corticosteroids at immunosuppressive dosages (prednisone or prednisolone at 2.2 to 4.4 mg/kg q12–24h PO for dogs; approximately twice that dosage for cats). Other immunosuppressive drugs such as azathioprine (Imuran, Burroughs-Wellcome) [dogs only], cyclophosphamide (Cytoxan,

Bristol-Myer), and chlorambucil (Leukeran, Burroughs-Wellcome) may be necessary in severe or refractory cases.

Infection-Induced Necrosis

- Infection from deep bacterial or fungal invasion can lead to local areas of cellulitis or abscessation and subsequent necrosis of surrounding tissues.
- Both streptococcal and staphylococcal infections n the dog can result in a rapidly progressing deep necrotizing fasciitis. Although staphylococcus can produce exfoliative toxins that result in a more superficial peeling of the skin (staph scalded skin syndrome), staphylococcus and streptococcus can produce exotoxins similar to those that produce toxic shock syndrome in humans.

Clinical Signs

Canine patients with necrotizing fasciitis will have intense pain, swelling, and necrosis of the fascia, fat and overlying skin. These patients can rapidly deteriorate and die if aggressive treatment is not elected.

- Embedded foreign bodies may result in central necrosis of the tissue due to release of neutrophilic enzymes. The lesion ruptures and drains externally at the most necrotic site.
- Infection can also cause sepsis and vasculitis resulting in necrolytic dermatitis.

Treatment

- Treat by administering systemic antimicrobial agents against the offending etiologic agent, based on culture and sensitivity testing. Establish and maintain local drainage.

Vascular Compromise

- Vascular compromise can occur whenever there is interruption of the normal circulation to an area of tissue. This is involved in many of the aforementioned conditions and also can be the result of a thrombus, vasculopathy, or mechanical or pressure constriction (e.g., elastic bands).
- There is a unique thrombovascular problem in some dachshunds that affects the dependent portion of the aural pinnae.
- In diabetes mellitus, vasculopathies may occur rarely in the extremities of dogs and cats. In these cases a chronic ulcerated lesion on an extremity usually fails to heal even with symptomatic treatment.

Clinical Signs

- Vascular compromise can lead to sloughing or ulcerated lesions. In mechanical occlusion of the circulation, the necrotic lesion is distal or beneath the obstruction. For example, an elastic band tightened around the tail over time causes underlying tissue death and sloughing of the distal tail.

Treatment

- Treat vascular compromise based on the etiology and the location of the necrosis. In thrombovascular necrosis of the ears, resect all affected tissue. When mechanical occlusion causes incomplete circulation to the tissue, remove the mechanical device. In diabetes mellitus, the optimal approach to the vasculopathy is to carefully monitor and control the diabetes.

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Chapter 50

Keratinization Defects

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PRIMARY DEFECTS OF KERATINIZATION

Primary defects of keratinization are dermatoses that are manifested clinically by localized or generalized excess scale formation. The scale may be formed from the interfollicular epidermis or may emanate from hair follicles as comedones and follicular casts. Histologically, the most striking abnormalities involve the keratinizing structures of the body including the epidermis, hair follicle outer root sheath, and hair cuticle.

▼ ***Key Point*** Cutaneous scaling of dogs is a very common clinical sign. In most cases, it is not due to a primary keratinization defect but is secondary to other dermatologic diseases. Common conditions causing secondary scaling include demodicosis, scabies, cheyletiellosis, atopic dermatitis, adverse food reaction ("food allergy"), flea allergy, pyoderma, yeast infection, dermatophytosis, hypothyroidism, hyperadrenocorticism, sex hormone abnormalities, pemphigus foliaceus, mycosis fungoides, and environmental influences. The veterinarian must determine whether the scaling is secondary to one of these conditions or associated with a primary keratinization defect. A primary keratinization defect is never diagnosed until the secondary causes of scaling have first been considered.

In this chapter, an overview of the etiology, clinical signs, diagnosis, and treatment of keratinization disorders is presented, followed by a description of each specific disease.

Etiology

- For most of the diseases classified as primary keratinization defects, the pathophysiology is unknown. For others, the cause is known and the primary pathophysiology involves a defect in the keratinizing epithelium or the cutaneous glandular function.

Clinical Signs

- Disorders of keratinization are characterized clinically by mild-to-severe dry, waxy, or greasy scales. Some degree of "seborrheic odor" may be associated with the skin condition. Because hair follicles and glandular structures may also be involved, it is not unusual to see comedones and follicular casts. Comedones are blackheads resulting from dilation of hair follicles with keratin plugs. Follicular casts are tightly adherent scales around hair shafts, giving the so-called candle wax appearance. Common secondary findings include alopecia, inflammation, crusts, pruritus with secondary excoriations, and pyoderma. Secondary *Malassezia* colonization may also be associated with primary and secondary causes of scaling, especially with greasy scales.

▼ ***Key Point*** Primary keratinization defects are usually hereditary and appear during the first 2 to 3 years of life. A breed incidence for these disorders is known. An observant owner usually indicates that the scaling was present before the development of secondary signs.

Diagnosis

No specific laboratory test exists for definitive diagnosis of a primary keratinization disorder. A combination of factors is used, including age of onset, breed, history, diagnostic elimination of more common secondary causes of scaling, findings on histologic examination of skin biopsies, and response to therapy.

▼ ***Key Point*** Skin biopsy is the most important diagnostic tool for primary keratinization defects (see Chapter 37). Biopsy results not only help make a definitive diagnosis but also help rule out dermatoses associated with secondary scaling.

Take several biopsies from lesions of various ages. Send samples to a veterinary pathologist who specializes in dermatopathology.

Treatment

After a definitive diagnosis of a primary keratinization defect is established, warn owners that the condition is most likely controllable but not curable.

▼ ***Key Point*** Some type of topical and systemic treatment will probably be needed for the remainder of the patient's life.

▼ ***Key Point*** It is imperative to treat any secondary bacterial and/or yeast infections before a decision is made on the type of specific treatment that will be needed for the primary keratinization disorder.

PRIMARY IDIOPATHIC SEBORRHEA

Primary idiopathic seborrhea is the most common chronic keratinization disorder encountered in dogs. Predisposed breeds include cocker spaniels, English springer spaniels, West Highland white terriers, basset hounds, Irish setters, German shepherds, dachshunds, Doberman pinschers, Chinese Shar-Peis, and Labrador retrievers.

Etiology

- In cocker spaniels and Irish setters, at least part of the pathophysiology of scale formation involves hyperproliferation of basal epidermal keratinocytes.

▼ ***Key Point*** Many dogs with primary idiopathic seborrhea will have concurrent dermatoses that contribute to the severity of the cutaneous scale and inflammation.

For example, it is not unusual to see a seborrheic cocker spaniel with concurrent allergic dermatosis and secondary pyoderma and/or yeast dermatitis. When these conditions are diagnosed and treated properly, the remaining scale caused by the primary seborrhea is much less severe and easier to control.

Clinical Signs

- Depending on the breed, clinical signs may range anywhere from dry scaling (seborrhea sicca), to greasy scaling (seborrhea oleosa), to scaling and greasiness with inflammation and pruritus (seborrheic dermatitis), and any combination of these clinical abnormalities on the same animal. Breeds affected with the seborrhea sicca form of idiopathic seborrhea include Doberman pinschers, Irish setters, German shepherds, and dachshunds. Breeds most predisposed to the seborrhea oleosa form include cocker spaniels, English springer spaniels, basset hounds, West Highland white terriers, Chinese Shar-Peis, and Labrador retrievers.

Diagnosis

- A definitive diagnosis of primary idiopathic seborrhea requires a number of different supporting factors, including age of onset, breed, history, diagnostic elimination of secondary causes of scaling, and findings on histopathologic examination of skin biopsy specimens.
- The most important aspect of the diagnostic plan is a full investigation for secondary causes of scaling. The primary differentials are allergic dermatitis, scabies, dermatophytosis, demodicosis, bacterial folliculitis, *Malassezia* dermatitis, hypothyroidism, and vitamin A–responsive dermatosis. Additional differentials in Doberman pinschers are color-dilution alopecia and adult-onset follicular dysplasia.
- Biopsy samples are usually characterized by orthokeratotic and parakeratotic hyperkeratosis, follicular hyperkeratosis, and dyskeratosis. Often, the follicular abnormalities are more impressive than are the changes in the surface epidermis.

Treatment

Topical Therapy

- As in most primary keratinization disorders, the treatment goal in primary idiopathic seborrhea is to control scale formation, not to cure the disease. Moisturize the skin and haircoat when dry scaling is present. This task is accomplished with twice-weekly moisturizing hypoallergenic shampoos (HyLyt EFA, DVM Pharmaceuticals; Allergroom, Virbac; Micro Pearls Advantage Hydra-Pearls, EVSCO) and frequent moisturizing rinses (HyLyt EFA Bath Oil Coat Conditioner, DVM Pharmaceuticals; Humilac, Virbac) after each shampoo.
- When dry scaling is severe and some keratolytic activity is needed, the treatment usually consists of sulfur and salicylic acid shampoos (SebaLyt and SeboRex, DVM Pharmaceuticals; Sebolux, Virbac; Micro Pearls Advantage SebaMoist and SebaHex, EVSCO) followed by moisturizing rinses. Dietary supplementation with an omega-6 and omega-3 essential fatty acid combination is also beneficial (e.g., DermCaps, DVM Pharmaceuticals).
- Use keratolytic and keratoplastic degreasing shampoos to control the scale and odor associated with seborrhea oleosa. Effective topical agents include coal tar (NuSal-T, DVM Pharmaceuticals; T-Lux, Virbac; LyTar, DVM Pharmaceuticals; Allerseb-T, Virbac), benzoyl peroxide (OxyDex and Sulf OxyDex, DVM Pharmaceuticals; Pyoben, Virbac; Micro Pearls Advantage Benzoyl Plus, EVSCO), and selenium sulfide (Selsun Blue, Ross). If significant bacterial and/or yeast infections are playing a major role in the greasy scaling dermatitis, it is better to use an antibacterial and antifungal shampoo combination (Malaseb Shampoo, DVM Pharmaceuticals;

KetoChlor Shampoo, Virbac) alone or alternated with one of the keratolytic degreasers.

Systemic Therapy

- The synthetic retinoid etretinate (Tegison, Roche) had been effective for idiopathic seborrhea in cocker spaniels, springer spaniels, Irish setters, golden retrievers, and mixed-breed dogs at 1 mg/kg PO q24h. Etretinate has been replaced by acitretin (Soriatane, Roche) at a dosage from 0.5 to 1.0 mg/kg PO q24h. Response is seen within 2 months and consists of decreased scale, odor and pruritus, and softening and thinning of seborrheic plaques. Some dogs have been maintained without signs of toxicity over several months on alternate-day therapy.

▼ ***Key Point*** The synthetic retinoids are associated with teratogenicity. Do not use in breeding animals, and warn clients about the serious potential risks from accidental human ingestion. Other potential side effects include keratoconjunctivitis sicca; leg and joint pain; and mild elevations in cholesterol, triglycerides, and liver enzyme levels. These are usually reversible on discontinuation of therapy or lowering the dosage. Perform Schirmer tear tests and liver panels every 2 to 4 weeks initially and then every 3 months during maintenance therapy. Unfortunately, the synthetic retinoids are prohibitively expensive for most owners.

- Calcitriol (Rocalcitrol, Roche) has been effective for idiopathic seborrhea in cocker spaniels at 10 ng/kg PO q24h. Give the medication as far removed as possible from the main meal of the day to decrease the possibility of hypercalcemia. Response is seen within 2 to 3 months. Continue treatment for life with monitoring of calcium and parathyroid hormone levels.
- Cyclosporine (Atopica, Novartis) at a dosage from 5 to 10 mg/kg PO q24h has been effective for some dogs with severe idiopathic seborrheic dermatitis. It is suspected that these dogs may be those with a strong allergic component to their disease.
- A 7- to 10-day course of prednisone or prednisolone at an anti-inflammatory dose may occasionally be needed during periods of severe inflammation and pruritus in dogs with seborrheic dermatitis.

VITAMIN A–RESPONSIVE DERMATOSIS

Vitamin A–responsive dermatosis is a rare, nutritionally responsive scaling disorder of primarily cocker spaniels. Similar syndromes have been reported in other breeds, including miniature schnauzers, Labrador retrievers, and Chinese Shar-Peis in Europe.

Etiology

This condition is not a systemic vitamin A deficiency but probably represents a local deficiency in the epidermis, a problem with uptake in the skin, a disorder of cutaneous utilization, or a positive pharmacologic effect of high doses on the epidermis.

Clinical Signs

- Vitamin A–responsive dermatosis has clinical signs consisting of refractory generalized scaling, dry haircoat with easy epilation, prominent comedones, and hyperkeratotic plaques with large "fronds" of keratinous material protruding from the follicular ostia. The plaques are usually on the ventral and lateral thorax and abdomen, but the neck and face may also be involved. Other clinical features include a rancid odor from the skin, ceruminous otitis externa, and varying degrees of pruritus. Gordon setters have a dorsal pruritic papular dermatitis that responds partially to antibiotic treatment, but relapses without vitamin A supplementation.

Diagnosis

- Vitamin A–responsive dermatosis is characterized clinically by an early age of onset of refractory generalized scaling with ventral follicular hyperkeratosis and hyperkeratotic plaques with large "fronds" of keratinous material protruding from the follicular ostia in cocker spaniels. Gordon setters have a dorsal pruritic papular dermatitis that responds partially to antibiotic treatment but relapses without vitamin A supplementation.
- The major diagnostic differentials for this condition include primary idiopathic seborrhea, zinc-responsive dermatosis, generic dog food dermatosis, sebaceous adenitis, and superficial necrolytic dermatitis.
- A more definitive diagnosis can be made with skin biopsy findings consisting of marked follicular hyperkeratosis and very distended follicular ostia, mild orthokeratotic hyperkeratosis of the epidermis, and mild irregular epidermal hyperplasia. Even with classic clinical and histologic findings, a definitive diagnosis can be confirmed only by response to supplementation with vitamin A.

Treatment

- Treat patients with vitamin A–responsive dermatosis with 625 to 800 IU/kg PO q24h of vitamin A. Improvement is seen within 4 to 6 weeks, complete remission is obtained by 10 weeks, and treatment is needed for life. Vitamin A at this dosage is well tolerated in dogs; therefore, no clinicopathologic monitoring is necessary. Keratolytic shampoos containing benzoyl peroxide have excellent follicular flushing activity. Twice-weekly treatment helps remove keratinous debris from follicles and hastens recovery.

ZINC-RESPONSIVE DERMATOSIS

Etiology

- *Zinc-responsive dermatosis* is a rare, nutritionally responsive scaling disease of several breeds of dogs, especially Alaskan malamutes and Siberian huskies. The incidence of this disease seems to be decreasing.

Clinical Signs

Zinc-responsive dermatosis is typically divided into the following two clinical syndromes:

- *Zinc-responsive dermatosis of Siberian huskies and Alaskan malamutes* is the first syndrome. It is also reported in American Eskimo dogs, Samoyeds, Doberman pinschers, and Great Danes. Alaskan malamutes have a genetic defect affecting zinc absorption from the intestines. Thus, the condition may occur even while the dog is on a well-balanced commercial diet. Zinc-responsive dermatosis may be precipitated by stress, estrus, and gastrointestinal disorders affecting absorption. Diets high in calcium and phytate (plant-derived protein especially high in cereals) may also precipitate the disorder by binding zinc in the gastrointestinal tract. A condition resembling zinc-responsive dermatosis has been described in dogs fed nutritionally incomplete generic dog food.
  - Lesions usually develop in dogs before puberty or in young adulthood. They include alopecia, erythema, scaling, and crusting involving the face, head, scrotum, and legs. Lesions often encircle the mouth, chin, eyes, ears, prepuce, and vulva. Thick crusts may be found on the elbows and other pressure points of the body. The foot pads may be hyperkeratotic. The haircoat is generally dull and dry.
- *Zinc-responsive dermatosis of rapidly growing puppies* on zinc-deficient diets or oversupplemented with vitamins and minerals, especially calcium, is the second syndrome. It is also seen with diets high in phytate. Commonly affected breeds include Great Danes, Doberman pinschers, beagles, German shepherds, German shorthaired pointers, Labrador retrievers, and Rhodesian ridgebacks. In addition to scaling and crusting, these dogs exhibit secondary infections, lymphadenopathy, depression, and anorexia. The most obvious cutaneous lesions involve the head, elbows, other joints, and foot pads.

Diagnosis

- Zinc-responsive dermatosis is diagnosed clinically by early age of onset, dietary history, breed, and physical examination findings. A firmer diagnosis is made with skin biopsy results of a marked, diffuse surface and follicular parakeratotic hyperkeratosis and a hyperplastic superficial dermatitis. A definitive diagnosis can be confirmed only by response to dietary zinc supplementation. Important diagnostic differentials for this syndrome include demodicosis, dermatophytosis, pemphigus foliaceus, generic dog food dermatosis, and superficial necrolytic dermatitis.

Treatment

- Treatment of zinc-responsive dermatosis depends on the specific syndrome.
  - The first syndrome of zinc-responsive dermatosis usually responds to zinc sulfate at 4.5 mg/kg (elemental zinc dose) PO q24h or divided q12h with food. A better alternative is zinc methionine at a dosage of 1 to 3 mg/kg (elemental zinc dose) PO q24h because it is better absorbed in dogs and causes less gastrointestinal upset. Correct dietary imbalances (e.g., high calcium and phytate, generic diets). Symptoms resolve rapidly, but lifetime therapy is usually needed. Zinc may cause vomiting, in which case lower the dose and give the medication with food.
  - The second syndrome in puppies usually responds over time to dietary corrections alone. However, recovery may be hastened by supplementation as discussed for the first syndrome. Some puppies may need supplementation until maturity.

EPIDERMAL DYSPLASIA

Epidermal dysplasia is an extremely severe keratinization disorder reported only in West Highland white terriers.

Etiology

- It may be a genetic keratinization abnormality or a severe inflammatory or hypersensitivity reaction associated with atopic dermatitis, adverse food reaction, or infections such as *Malassezia pachydermatis*.

Clinical Signs

- Epidermal dysplasia of West Highland white terriers develops in either sex, usually during the first year of life. Clinical signs begin with erythema and pruritus of the ventrum and extremities. These rapidly progress to a generalized disorder ("armadillo disease") with severe erythema and pruritus, alopecia, hyperpigmentation, lichenification, lymphadenopathy, greasy skin and haircoat, rancid odor, ceruminous otitis, and secondary bacterial infection. Some dogs have secondary *Malassezia pachydermatis* colonization of the surface and infundibular keratin, which may contribute to the severity of the disease.

▼ ***Key Point*** Secondary staphylococcal and *Malassezia* infections may be associated with any of the primary and secondary causes of scaling. Always

look for the presence of bacteria and yeast with skin cytologic examination (see Chapter 37).

Diagnosis

- Epidermal dysplasia is diagnosed clinically by early age of onset of severe ventral erythema and pruritus rapidly progressing to chronic lesions in West Highland white terriers. This diagnosis is supported by skin biopsy findings consisting of hyperplastic perivascular dermatitis with epidermal abnormalities, including hyperchromasia, excessive keratinocyte mitosis, crowding of basilar keratinocytes, epidermal "buds," loss of epidermal cell polarity, and parakeratosis. Budding yeast organisms and gram-positive cocci may also be found in surface and infundibular keratin.
- The principal diagnostic challenge in these dogs is to determine if the condition is caused by epidermal dysplasia, some other pruritic skin disease, or a combination. Primary diagnostic differentials that must be considered include atopic dermatitis, adverse food reaction dermatitis, scabies, and primary idiopathic seborrhea. Evaluate all of these by appropriate testing or response to therapy in the diagnostic workup.
- A definitive diagnosis of epidermal dysplasia can be made only with characteristic clinical and histologic findings and elimination of other diagnostic differentials. Another challenge is to determine how much secondary bacterial infection or *Malassezia* colonization is contributing to the severity of the clinical condition. This can only be assessed by evaluating response after treatment with appropriate topical and systemic antimicrobial agents.

Treatment

- Epidermal dysplasia has generally been thought to be nonresponsive to medical therapy. However, this observation has changed with the realization that most of these dogs manifest the syndrome secondary to allergies and skin infections, especially yeast.
- In patients with secondary *Malassezia* colonization, there may be significant improvement in pruritus and skin condition with ketoconazole (Nizoral, Janssen), 5 to 10 mg/kg PO q24h, or itraconazole (Sporanox, Janssen), 5 mg/kg PO q24h, and twice-weekly application of a topical antifungal shampoo. Alternate-day or twice-weekly pulse dosing with the systemic antifungal agents may be used after initial treatment for long-term control of redevelopment of the infection.
- Similar to what was described above for dogs with idiopathic seborrhea, cyclosporine (Atopica, Novartis) at a dosage of 5 to 10 mg/kg PO q24h has been effective because of the strong allergic component associated with this disease.

LICHENOID-PSORIASIFORM DERMATOSIS

Etiology

- *Lichenoid-psoriasiform dermatosis* is an extremely rare, probably inherited, keratinization defect reported only in English springer spaniels.

Clinical Signs

- Clinical signs include non-pruritic, erythematous, lichenoid papules and plaques involving the pinnae, external ear canal, preauricular and periorbital skin, lips, prepuce, and inguinal region. Chronic cases have papillomatous-type lesions, which may involve the face, ventral trunk, and perineum. A more generalized distribution of greasy scales and crusts may also be present.

Diagnosis

- Lichenoid-psoriasiform dermatosis is diagnosed clinically by early age of onset of refractory, plaque-like lesions involving the face, ears, and ventrum in English springer spaniels. Perform skin scrapings and fungal culture to rule out demodicosis and dermatophytosis.
- The definitive diagnosis is based on skin biopsy results. Histologic examination reveals lichenoid dermatitis (i.e., a band of mononuclear cells in the superficial dermis) with psoriasiform epidermal hyperplasia, intraepidermal microabscesses, and Munro microabscesses. Advanced lesions may show papillated epidermal hyperplasia and papillomatosis.

Treatment

- Lichenoid-psoriasiform dermatosis is a waxing and waning dermatitis. Minimal responses usually follow medical therapy with most antibiotics, low-dose glucocorticoids, vitamin A, levamisole, dapsone, autogenous vaccines, and topical antiseborrheic agents. Cephalexin may be helpful when secondary pyoderma is present. Prednisone at 2.2 mg/kg PO q24h has improved lesions in some cases but has not resulted in complete remission.

SCHNAUZER COMEDO SYNDROME

Etiology

- *Schnauzer comedo syndrome* is a follicular keratinization defect of miniature schnauzers characterized clinically by multiple comedones along the dorsal midline of the back. The etiology is probably genetic because of the exclusive occurrence in miniature schnauzers. A developmental defect may affect the hair follicle, leading to abnormal keratinization, comedo forma-

tion, follicular plugging and dilation, and secondary bacterial folliculitis.

Clinical Signs

- Schnauzer comedo syndrome usually develops in young adult dogs. Clinical signs include crusted, papular comedones (blackheads) along the dorsal midline of the back from the neck to the tail. In the early stages and in mild cases, lesions are difficult to see through the haircoat but are more easily palpated as "bumps" down the back. Animals with advanced disease frequently have secondary bacterial folliculitis and, rarely, furunculosis. The lesions may be accompanied by pruritus and pain. The infection leads to alopecia, with a "moth-eaten" appearance to the coat. The condition is chronic—for the life of the dog. Dogs with advanced disease should be evaluated for hypothyroidism and hyperadrenocorticism.

Diagnosis

- Schnauzer comedo syndrome is characterized clinically by dorsal follicular comedones in miniature schnauzers.
- Diagnostic differentials include demodicosis, dermatophytosis, and bacterial folliculitis. Obtain a complete drug history in miniature schnauzers with comedo syndrome. Glucocorticoids are comedogenic, and long-term administration may precipitate or worsen the condition. Older miniature schnauzers with endogenous Cushing disease and hypothyroidism may develop dorsal comedones. Confirm the diagnosis by skin biopsy, which shows dilated hair follicles filled with keratinous debris. Dilated or cystic sebaceous or apocrine glands, folliculitis, perifolliculitis, or furunculosis may be found.

Treatment

Topical Therapy

- The majority of cases of schnauzer comedo syndrome can be controlled with periodic application of benzoyl peroxide shampoos (OxyDex, DVM Pharmaceuticals; Pyoben, Virbac) to flush follicles and control secondary bacterial folliculitis. A combination benzoyl peroxide and sulfur shampoo (Sulf OxyDex, DVM Pharmaceuticals) is especially effective because of enhanced keratolytic activity. Benzoyl peroxide gels (OxyDex Gel, DVM Pharmaceuticals; Pyoben Gel, Virbac) are helpful to remove tightly adherent comedones. Gentle agitation with a mildly abrasive sponge (Buff-Puff, Johnson & Johnson) helps mechanically remove adherent comedones. Systemic antibiotics for a minimum of 3 weeks are indicated to control secondary staphylococcal folliculitis.

Systemic Therapy

- If there is no response to topical therapy, the synthetic retinoid isotretinoin (Accutane, Roche), 1 to 2 mg/kg PO q24h, has been very effective. Rapid response is seen within 3 to 4 weeks. After lesions resolve, most dogs can be maintained in remission without signs of toxicity on alternate-day therapy.

ICHTHYOSIS

Etiology

- *Ichthyosis* is an extremely rare, congenital keratinization defect of dogs, especially terriers, characterized by very severe scaling of the skin and foot pads. Lamellar ichthyosis results in severe scaling with moderate to marked hyperkeratosis and a thickened granular layer histologically. It may be an autosomal recessive trait in dogs (as it is in humans), although the exact genetics have not been studied.

Clinical Signs

- Ichthyosis is reported most commonly in terriers and terrier crosses. In most cases, the entire body is covered with tightly adherent, fine, white scales, some of which may appear as feathered keratinous projections. Extensive alopecia, hyperpigmentation, and lichenification may occur. Large quantities of waxy adherent scales may also be produced, especially in the flexural creases and intertriginous regions. Severe foot pad hyperkeratosis may be present with the margins more severely involved.

Diagnosis

- Canine ichthyosis is diagnosed clinically by congenital, severe cutaneous scaling and foot pad hyperkeratosis in terriers. Skin biopsy and histologic findings confirm the diagnosis. They include increased mitotic activity in the basal keratinocytes, prominent stratum granulosum, severe laminated orthokeratotic hyperkeratosis, vacuolated keratinocytes in the superficial epidermis, and follicular hyperkeratosis and plugging.
- Because of the congenital nature of this disorder, it is rarely confused diagnostically with other keratinization defects. However, if its presence at birth cannot be firmly established, the diagnostic differentials include zinc-responsive dermatosis, nasodigital hyperkeratosis, primary idiopathic seborrhea, canine distemper virus, pemphigus foliaceus, lupus erythematosus, hypothyroidism, generic dog food dermatosis, and superficial necrolytic dermatitis.

Treatment

Topical Therapy

- Topical therapy is helpful, including warm water soaks to help remove scales, antiseborrheic shampoos (SebaLyt, DVM Pharmaceuticals; Sebolux, Virbac), antiseborrheic gels (KeraSolv, DVM Pharmaceuticals; Retin-A, Ortho) for locally severe lesions, lactic acid as a total body rinse or spray (Humilac, Virbac; Micro Pearls Humectant Spray, EVSCO), and a combination rinse of 75% propylene glycol and 25% humectants (Humilac, Virbac). Topical therapy other than shampoos is used twice daily until the scale and odor are controlled and then is used as often as necessary for maintenance.

Systemic Therapy

- Excellent results have been obtained with isotretinoin (Accutane, Roche) at a dosage of 1 to 2 mg/kg PO q24h. Remission occurs usually within 8 to 12 weeks, although it may take up to 6 months. Some dogs can be maintained on alternate-day therapy.
- The long-term prognosis for ichthyosis is poor because of the severe scale formation and the continual therapy that will be needed for the entire life of the patient.

SEBACEOUS ADENITIS

Etiology

- *Sebaceous adenitis* is an inflammatory disease process directed against the sebaceous glands of the skin. Predisposed breeds include standard poodles, Akitas, Samoyeds, and vizslas. The pathophysiology is unknown but may include an inherited defect of sebaceous gland development, immune-mediated sebaceous gland destruction, a primary follicular keratinization defect with obstruction of sebaceous ducts and inflammation, and abnormal lipid metabolism affecting sebaceous secretions and keratinization.

Clinical Signs

- Sebaceous adenitis has two different clinical presentations related to coat length as follows:
  - Long-coated breeds, such as standard poodles, Akitas, and Samoyeds, have non-pruritic patchy or symmetrical alopecia with excess scale formation and dull, brittle hairs. Specific areas include the dorsal planum of the nose, top of the head, dorsal neck and trunk, tail, and pinnae. Advanced lesions include tightly adherent silver-white scales, follicular casts, matted hair, and secondary bacterial folliculitis.
  - Short-coated breeds, such as Vizslas, have circular areas of alopecia and scaling of the head, ears, trunk, and extremities. These areas may enlarge and eventually coalesce into serpiginous patterns or diffuse alopecia.

Diagnosis

- A tentative clinical diagnosis of sebaceous adenitis is made based on breed, history, and clinical findings. The definitive diagnosis is based on skin biopsy specimens revealing nodular granulomatous to pyogranulomatous inflammation at the level of the sebaceous glands. Advanced lesions are characterized histologically by a complete loss of sebaceous glands with periadnexal fibrosis.

Treatment

- Response to therapy for sebaceous adenitis depends on the stage and severity of the disease. Immunosuppressive dosages of glucocorticoids may be effective very early in the course of the disease when severe inflammation is present.
- Isotretinoin (Accutane, Roche) at 1 mg/kg PO q12–24h may be effective in refractory cases, especially in short-coated breeds. After remission is obtained, the goal is to gradually decrease the dosage to 1 mg/kg PO q48h. Cyclosporine (Atopica, Novartis) has also been used in refractory cases at 5 mg/kg PO q12h.
- Topical therapy with sprays or rinses consisting of 75% propylene glycol and 25% humectants (Humilac, Virbac) is helpful when applied once daily. Other therapy consists of essential fatty acid dietary supplements, antiseborrheic shampoos and emollients, antibiotics, and antibacterial and follicular flushing shampoos.

IDIOPATHIC NASODIGITAL HYPERKERATOSIS

Etiology

- *Idiopathic nasodigital hyperkeratosis* is a primary keratinization disorder characterized by excess keratin accumulation on the planum nasale, foot pads, or both. It is most commonly seen in cocker spaniels and English springer spaniels, although any breed may be affected.

Clinical Signs

- Idiopathic nasodigital hyperkeratosis may have focal or diffuse lesions characterized by tightly adherent, thick accumulations of keratin on the nasal planum, foot pads, or both. This material is usually extremely dry and may be accompanied by cracks, fissures, erosions, and ulcers. Severe foot pad involvement may result in pain and lameness.

Diagnosis

- Idiopathic nasodigital hyperkeratosis is diagnosed by finding nasal and/or digital hyperkeratosis without evidence of other concurrent diseases. Consider all diseases that may cause the lesions. Unfortunately, the list is long and includes canine distemper virus, pemphigus foliaceus, pemphigus erythematosus, lupus erythematosus, nasal solar dermatitis, hypothyroidism, zinc-responsive dermatosis, generic dog food dermatosis, and superficial necrolytic dermatitis. Pemphigus foliaceus, superficial necrolytic dermatitis (hepatocutaneous syndrome), and lupus erythematosus are the most common causes of nasal and digital hyperkeratosis.
- Perform extensive diagnostic tests only when the condition is severe or when clinical signs suggest that one of the other more serious diseases listed previously is present.

▼ ***Key Point*** Idiopathic nasodigital hyperkeratosis is merely cosmetic for most dogs and requires neither extensive diagnostic workup nor treatment.

- When warranted, perform a complete diagnostic evaluation including a good history, complete blood count (CBC), serum biochemical profile, thyroid evaluation with baseline thyroxine and a thyroid-stimulating hormone level, and biopsy for histologic evaluation. Histopathologic findings are most helpful in ruling out the diagnostic differentials. Abnormalities for idiopathic nasodigital hyperkeratosis are nonspecific and consist of irregular epidermal hyperplasia with severe orthokeratotic and parakeratotic hyperkeratosis.

Treatment

- Medical treatment of idiopathic nasodigital hyperkeratosis includes hydration of the hyperkeratotic tissue by water soakings or wet dressings followed by application of petrolatum jelly as an occlusive agent to help seal moisture into the stratum corneum.
- Although simple hydration may be adequate for mild lesions, more severe hyperkeratosis requires a topical agent with keratolytic activity. A gel containing salicylic acid, lactic acid, and urea (KeraSolv Gel, DVM Pharmaceuticals) is helpful, as is topical 0.025% or 0.01% tretinoin gel (Retin-A, Ortho). Apply the gel q12h until the condition is controlled, then use as needed for long-term maintenance. Irritation may be a problem, especially with tretinoin. Corticosteroid and antibiotic ointments, creams, or gels may be needed when severe inflammation or secondary infection is present.
- When very severe projections of keratin are present, especially on foot pads and causing lameness, they may be surgically removed by trimming the dead tissue with scissors.

CANINE EAR MARGIN DERMATOSIS

Etiology

- *Canine ear margin dermatosis* is a rare, idiopathic keratinization defect characterized by greasy plugs that adhere to the skin and hairs of the pinnae of the ears in a bilaterally symmetrical pattern. This dermatosis occurs primarily in dachshunds but is also occasionally seen in other breeds with pendulous ears. (See Chapter 58 for a discussion of pinnal diseases.)

Clinical Signs

- Canine ear margin dermatosis has greasy plugs adhering tightly to the skin surface and hair shafts on the pinnal margins. Alopecia may develop with time. Pruritus is usually absent. In severe untreated cases, a progression to ulceration and necrosis has been reported that is due to thrombosis of capillaries that supply blood to the pinnal margins. This condition may result in severe scarring and fissures.

Diagnosis

- Canine ear margin dermatosis is tentatively diagnosed in the early stages when only scale is present by breed and clinical signs alone. Perform skin scrapings and fungal culture to rule out scabies (a consideration only if pruritus is present), demodicosis, and dermatophytosis. Skin biopsy findings reveal prominent orthokeratotic and parakeratotic hyperkeratosis. However, biopsy is unnecessary and the ear margin is a difficult part of the body from which to remove tissue.
- When the condition has progressed to ulceration and necrosis, the number of differential diagnoses to consider is more extensive and includes lupus erythematosus, pemphigus complex, cutaneous vasculitis, dermatomyositis, cold agglutinin disease, frostbite, drug reactions, and lymphoreticular neoplasms. Diagnostic procedures to differentiate these diseases include CBC, serum biochemical profile, urinalysis, skin biopsy for routine histologic examination and direct immunofluorescence, Coombs testing, and antinuclear antibody testing.
- Skin biopsy specimens reveal necrosis and ulceration. Some sections may demonstrate vascular thrombosis. However, the changes are nonspecific and may be seen with many of the diagnostic differentials. Therefore, all of the suggested diagnostic tests are recommended to eliminate the differentials and to establish a definitive diagnosis of canine ear margin dermatosis.

Treatment

- The mild scaling form of ear margin dermatosis is usually controllable but rarely curable with topical

therapy. Periodic use of an antiseborrheic shampoo to remove the scales and waxy accumulations is all that is needed to control the mild form of the condition. Helpful agents include sulfur and salicylic acid (SebaLyt, DVM Pharmaceuticals; Sebolux, Virbac) and benzoyl peroxide (OxyDex, DVM Pharmaceuticals; Sulf OxyDex, DVM Pharmaceuticals; Pyoben, Virbac). A topical glucocorticoid cream may be needed in severe unresponsive cases or in those with severe inflammation.

- The advanced ulcerative and necrotic stage may be responsive to pentoxifylline (Trental, Hoechst Marion Roussel) at a dosage of 10 to 15 mg/kg PO q8–12h if there is a component of vasculitis present.

SUPPLEMENTAL READING

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Chapter 51

Sex Hormone and Endocrine Look-alike Dermatoses

Linda A. Frank

▼ ***Key Point*** Bilaterally symmetrical alopecia sparing the head and extremities is usually associated with an endocrine cause such as hypothyroidism or hyperadrenocorticism; however, this same pattern of alopecia is seen with sex hormone dermatoses and various other dermatoses described in this chapter.

The differential diagnoses for an "endocrine" pattern of alopecia (other than hypothyroidism and hyperadrenocorticism) include sex hormone aberrations, follicular arrest (Alopecia X), cyclic flank alopecia, pattern baldness, and post-clipping alopecia. In addition, more generalized non-inflammatory alopecias may be associated with follicular dysplasias and telogen defluxion.

SEX HORMONE DERMATOSES

Etiology

Sex hormones are produced primarily from cholesterol by the zona reticularis of the adrenal cortex and by the gonads. Sex hormones are also produced in the tissues by peripheral conversion. Sex hormone dermatoses are uncommon in the dog and are attributed to an overproduction of one or more of the sex hormones. This overproduction may arise endogenously from the adrenal glands or gonads or exogenously from administration of a hormone product. The alopecia results from the effects of hormones on the hair follicle, inhibiting the normal cyclic pattern of hair growth.

Hyperestrogenism

- The source of excess estrogen production is from cystic ovaries, ovarian granulosa cell tumors, or testicular tumors (especially Sertoli cell tumors). Iatrogenic estrogen supplementation (such as for treating urinary incontinence) can also be a source.
- Estrogen inhibits initiation of anagen, the hair growth phase.

Hyperandrogenism

- The source of excess androgen production is from testicular tumors (e.g., interstitial cell tumors, seminomas) and possibly from adrenal tumors.
- Hyperandrogenism is uncommonly associated with alopecia in dogs. Excess androgen is more often associated with hyperplasia and hypersecretion of the sebaceous and circumanal or hepatoid glands.

Hyperprogesteronism

- An endocrine pattern of alopecia caused by a progesterone-secreting Sertoli cell tumor was reported in one dog.
- Progesterone may bind to glucocorticoid receptors, thus blocking hair growth.
- Progesterone may also cross with testosterone receptors, resulting in either down-regulation or up-regulation of the receptors.

Clinical Signs

▼ ***Key Point*** The classic endocrine pattern of alopecia is a bilaterally symmetrical *diffuse* alopecia sparing the head and extremities caused by non-inflammatory endocrine dermatoses. Focal or patchy alopecias are more likely caused by inflammatory dermatoses, such as pyoderma, demodicosis, or dermatophytosis.

Hyperestrogenism

Cutaneous Signs

- These dogs often present with bilaterally symmetrical alopecia sparing the head and extremities. The alopecia may begin in the perineal, inguinal, and flank regions and then progress to involve the entire trunk.
- Comedones may be seen in the inguinal region.
- The coat may have a generalized dry or oily seborrhea.
- Hyperpigmentation may be seen as diffuse pigmentation in the areas of alopecia, or it may appear as macular lesions with a ventral distribution.

- In male dogs, a clinical sign highly suggestive of excess estrogen production is linear preputial dermatosis that appears as a narrow strip of hyperpigmentation along the ventral midline from the prepuce toward the scrotum.

Female Reproductive Signs

- The nipples and vulva may be enlarged, similar to a normal heat cycle.
- The heat cycles may be abnormal, especially persistent or irregular estrus.

Male Reproductive Signs

- The testes may be palpably abnormal.
- The nipples may enlarge, similar to what occurs in females.
- Males may attract other male dogs.

Other Signs

- Hyperestrogenism can cause serious bone marrow suppression and aplastic anemia.

Hyperandrogenism

- Intact male dogs are most commonly affected. Testes are palpably normal in most cases, but a testicular tumor may be identified.
- Hyperandrogenism is only rarely associated with alopecia.
- Typical lesions include perianal gland hyperplasia, resulting in a "donut" ring around the anus. This can result in anal sac impaction.
- Generalized seborrhea oleosa is a presenting sign in some dogs.
- Local hyperplasia of the supracaudal gland may appear as alopecia and seborrhea of the dorsal aspect of the tail approximately one-third the distance from the tail base.

Hyperprogesteronism

- Bilaterally symmetrical alopecia sparing the head and extremities has been attributed to elevated progesterone in one dog.

Diagnosis

Suspect sex hormone dermatoses in dogs that have typical clinical signs after routine diagnostic testing has ruled out the more common causes of endocrine alopecia, such as hypothyroidism or hyperadrenocorticism (see Chapters 31 and 33). In intact dogs, the resolution of clinical signs in response to neutering confirms the diagnosis. In neutered dogs with sex hormone dermatosis, adrenal testing is required.

Diagnosis of Gonadal Causes in Intact Dogs

- In intact animals, the excess sex hormone is most likely gonadal in origin. Measure baseline concentrations of estradiol, progesterone, and testosterone to establish a presumptive diagnosis. If any of these hormones is *substantially* increased out of the normal range, then there is good reason to suspect this is causing the dermatosis.
- Use diagnostic imaging, especially ultrasonography, to identify gonadal tumors.
- Evaluate a complete blood count to assess bone marrow status when hyperestrogenism is suspected.
- Confirm the diagnosis based on resolution of clinical signs in response to neutering or ovariohysterectomy.
- The intact animal may also respond to treatment with an antagonistic hormone, such as androgen to treat hyperestrogenism; however, this approach is not recommended since the primary cause of the sex hormone imbalance is a gonadal tumor.

Diagnosis of Adrenal Tumors

- Adrenal tumors have been associated with abnormal sex hormone production; thus, in neutered dogs with clinical signs suggestive of a sex hormone dermatosis, the excess sex hormones are most likely arising from the adrenal glands.
- Perform abdominal ultrasonography to identify adrenal tumors.
- Measure the serum concentration of the sex hormones as well as cortisol, before and after adrenocorticotropic hormone (ACTH) stimulation, to identify *substantial* increases in one or more of these adrenal hormones. Hyperandrogenism sometimes occurs concurrently with hypercortisolemia. To perform the ACTH stimulation test, obtain baseline and, 1 hour post-ACTH, serum samples. ACTH is administered at 5 µg/kg IV. The serum samples need to be frozen and mailed overnight to the following address: Clinical Endocrinology Service, 2407 River Drive, Rm A105 Veterinary Teaching Hospital, University of Tennessee, Knoxville, TN 37996-4543 (telephone: 865-974-5638).

Skin Biopsy

A skin biopsy may support the diagnosis of a sex hormone imbalance; however, the findings are nonspecific. The biopsy can only document the presence of a non-inflammatory alopecia accompanied by hairs that are not cycling (typical endocrine histopathology pattern). This is not specific for endocrine disease; it also is seen in many of the endocrine "look-alike" alopecias discussed in the later sections of this chapter.

▼ ***Key Point*** A biopsy result indicating an endocrine pattern of alopecia simply means that there is no inflammation to explain the alopecia, the thickness of the dermis and epidermis is normal to decreased, and the hairs are in telogen phase (not cycling). Think of this as a non-inflammatory pattern of alopecia that can be associated with endocrine or endocrine look-alike dermatoses rather than strictly an endocrine pattern of alopecia.

Treatment

- If the dog is intact, the treatment of choice is neutering.
- Under certain circumstances, treatment using an antagonistic hormone may result in resolution of clinical signs; however, this is not recommended since surgical excision is a preferable treatment for gonadal tumors.
- If the abnormal sex hormones are arising from adrenal hyperplasia, treatment with mitotane may abolish the hormone-secreting tissue and result in resolution of clinical signs (treatment of hyperadrenocorticism is described in Chapter 33).
- If there is an adrenal tumor, surgery is the treatment of choice (see Chapter 33).

ENDOCRINE LOOK-ALIKE DERMATOSES

Various dermatoses with an endocrine pattern of alopecia include Alopecia X, pattern baldness, cyclic flank alopecia, and post-clipping alopecia. Endocrine alopecia caused by hypothyroidism (see Chapter 31) and hyperadrenocorticism (see Chapter 33) is seen more commonly than the endocrine look-alike causes of alopecia.

▼ ***Key Point*** Endocrine look-alike dermatoses cannot be definitively diagnosed without first ruling out hypothyroidism and hyperadrenocorticism.

Alopecia Associated with Follicular Arrest (Alopecia X)

Etiology

- This disease is also known as adrenal hyperplasia-like syndrome, growth hormone-responsive alopecia, biopsy-responsive alopecia, pseudo-Cushing's syndrome, and other names.
- The pathomechanism of the disease is unknown. A defect in anagen initiation of the hair cycle at the level of the follicle is suspected. The role that adrenal steroid hormone intermediates play in this disease is currently under debate.

Clinical Signs

- This is most commonly seen in the "plush-coated" breeds such as Pomeranians, malamutes, huskies, chow chows, Samoyeds, keeshonds, and American Eskimo dogs and in miniature poodles.
- This occurs in adult male and female dogs between 1 and 10 years of age irrespective of neuter status.
- The dog presents with the typical endocrine pattern of alopecia. Initially there is loss of guard hairs that progresses to complete alopecia of the neck, tail, rump, perineum, caudal thighs, and ultimately trunk.
- The skin may become intensely hyperpigmented in areas of alopecia.

Diagnosis

- First rule out other endocrine dermatoses such as hypothyroidism, hyperadrenocorticism, and sex hormone dermatosis.
- A biopsy will categorize the alopecia as non-inflammatory (endocrine pattern) and rule out conditions such as sebaceous adenitis or folliculitis as causes of the alopecia.
- There is no confirmatory diagnostic test.

▼ ***Key Point*** With few exceptions, histopathology cannot differentiate among various endocrine dermatoses and cannot be used to definitively diagnose Alopecia X.

Treatment

- This is a "responsive dermatosis." Several treatment approaches can produce hair regrowth, but unfortunately, this is seldom permanent. Many dogs lose their hair again during subsequent hair cycles.
- If the dog is intact, neutering results in hair regrowth in some cases.
- Melatonin (3 mg q12h for small dogs and 6–12 mg q12h for large dogs) results in some degree of hair growth in approximately half of the cases. Because this treatment is very safe, it is currently recommended as a first approach to treating dogs with Alopecia X after neutering. The only contraindication is treating dogs with diabetes mellitus, as melatonin may cause insulin resistance.
- Mitotane results in hair regrowth in some cases. The recommended dosage is lower than that used for hyperadrenocorticism (25 mg/kg, PO, q24h or divided q12h for 5–7 days, then divided twice weekly for maintenance).
- Testosterone results in hair regrowth in some dogs. Adverse effects of this treatment can include cholangiohepatitis or aggressive behavior.
- When the condition was thought to be growth-hormone related, treatment with growth hormone resulted in hair regrowth. Unfortunately, growth hormone can result in diabetes mellitus and is difficult to obtain.

Cyclic Flank Alopecia

Etiology

- This is a seasonal truncal alopecia that occurs primarily during periods of decreasing day length. Therefore, the hair loss usually occurs during the winter to spring months, although this can be quite variable. The condition appears to be more prevalent in the northern states and Canada, possibly due to shorter day lengths.
- The condition may recur yearly, sporadically, or never again. The actual mechanism of the alopecia is not known.

Clinical Signs

- Breeds predisposed to this condition include Airedales, boxers, and English bulldogs, but the condition has been reported in many different breeds.
- The age of onset is usually between 1.5 and 4.5 years.
- The condition occurs in intact or neutered dogs of either sex.
- Dogs present with alopecia of the flanks and/or lateral thorax that is usually symmetrical. The alopecia can progress to involve the thoracolumbar region. The alopecia is usually more delineated than that seen with hyperadrenocorticism; however, early in the condition, the haired regions of the flank may appear diffusely thinned.
- The skin in the alopecic areas is often hyperpigmented. Hyperpigmentation on the bridge of the nose is occasionally associated with this condition.

Diagnosis

- First rule out endocrinopathies such as hypothyroidism and hyperadrenocorticism.
- Biopsy is often helpful. Characteristic findings, in addition to a non-inflammatory pattern of alopecia, include follicular keratosis with deformed ("witch's foot") follicles and variable melanization of sebaceous glands and ducts.

Treatment

- Melatonin may shorten the duration of the alopecia and prevent its recurrence. Use the same dosage as for Alopecia X (see the preceding section).

▼ ***Key Point*** Melatonin is a useful treatment for many of the endocrine look-alike alopecias.

Pattern Baldness

Etiology

- This is a tardive hypotrichosis in dogs that usually begins at less than 1 year of age and progresses throughout their lives.
- The pathomechanism is unknown, but a genetic defect is suspected.

Clinical Signs

There are four patterns of alopecia that can be included in this category.

Pinnal Alopecia of Dachshunds

- Pinnal alopecia of dachshunds occurs most commonly in male dogs.
- The alopecia affects both pinnae and is usually first noticed when the dog is less than 1 year of age.
- The alopecia is progressive, with the pinnae becoming hyperpigmented and "leathery" in texture over time.

Caudal Thigh Alopecia of Greyhounds

- Greyhounds frequently develop alopecia of the caudal thighs (bald thigh syndrome).
- This occurs in young to middle-aged adults, irrespective of sex or neuter status.

Ventral and Caudal Thigh Alopecia of Various Breeds

- Ventral and caudal thigh alopecia is frequently seen in dachshunds and Boston terriers. Other breeds including whippets and Italian greyhounds may also be affected.
- The alopecia is usually first noticed when the dog is less than 1 year of age.

Patterned Alopecia of Portuguese Water Dogs and American Water Spaniels

- Portuguese water dogs and American water spaniels may develop a patterned alopecia of the ventral neck, caudomedial thighs, and tail.
- This is usually first noticed when the dogs are less than 1 year of age.

Diagnosis

- Pattern alopecia (baldness) is usually diagnosed based on signalment and clinical signs.
- Because of the young age of onset, endocrinopathies are unlikely. However, hypothyroidism and hyperadrenocorticism should be ruled out in greyhounds with alopecia of the caudal thighs since this tends to develop at a later age.
- Biopsies may help differentiate pattern alopecia from "endocrine" alopecia if taken early in the disease process. Hair follicles and adnexa are decreased in size (miniaturized) with small anagen hair bulbs still present. Later in the course of disease, there is a decrease in the number of hair follicles and adnexa, and few, if any, anagen hair bulbs remain.

Treatment

- There is no known treatment for canine pattern alopecia.

- Interestingly, some respond to melatonin (see the "Alopecia X" section), suggesting that the alopecia may be associated with hair cycle arrest, similar to the other endocrine look-alikes discussed.

Post-Clipping Alopecia

Etiology

- Failure to regrow hair following clipping is a common sequel to the "summer cut" and surgical site preparation. Possible explanations for this include an arrest of the cycling hair follicle due to the clipping or surgical procedure or the clipping of the coat during a normal telogen phase of the hair cycle in dogs with very seasonal growth phases.
- It may be seen more frequently with clip sites of epidural anesthesia.

Clinical Signs

- Delayed hair regrowth is seen at clipped areas. This tends to be most noticeable over the trunk, causing it to be easily confused with endocrine dermatoses.
- Many times some hairs have regrown within the alopecic area while the rest remain inactive.

Diagnosis

- History of a recent clip and clinical signs are highly suggestive of this condition.
- Because endocrinopathies may be associated with lack of hair regrowth following clipping, it is important to rule out hypothyroidism and hyperadrenocorticism.
- Biopsy supports a non-inflammatory cause of the alopecia. Biopsy may show telogen arrest with all hairs in telogen. In some cases the biopsy is very similar to normal-haired areas of the same dog, suggesting that the dog's hair growth cycle was in a normal resting phase. The biopsy may show anagen hairs, indicating that hair regrowth has started.

Treatment

- This condition is self-limiting and does not require treatment. Hair usually grows back within 1 year, especially after the dog completes a heavy shedding cycle.
- Melatonin appears to help stimulate hair regrowth, although controlled studies have not been done (see the "Alopecia X" section for dosages).

Follicular Dysplasias

Follicular dysplasias include color dilution alopecia and black hair follicular dysplasia.

Etiology

- This condition appears to be congenital and/or genetic.
- The pathomechanism of the alopecia is unknown; however, it may involve defective melanization and/or a hair defect.

Clinical Signs

Color Dilution Alopecia

- Color dilution alopecia is seen in dogs with diluted haircoat colors such as blue Doberman pinschers or fawn Irish setters. It also occurs in Yorkshire terriers. Any breed of dog with a color dilution can in theory have this condition.

Black Hair Follicular Dysplasia

- In black hair follicular dysplasia, the alopecia is restricted to the black-haired areas of the coat. This condition is usually seen in piebald dogs (dogs with large patches of white and black) throughout the coat, although it has also been seen in black Doberman pinschers.
- Alopecia occurs in dogs less than 3 years of age and progresses. Seborrhea and pyoderma are often associated with areas of alopecia.

Diagnosis

- Suspect this condition when alopecia is restricted to a specific color region of the haircoat.
- Microscopic examination of the hair (trichogram) is useful only in dogs with color dilution alopecia. This reveals large and irregular melanin aggregates within the hair shaft resulting in distortion and breakage of the shaft.
- Histopathology is useful for both conditions, revealing abnormal melanin clumping within the hair shafts and periadnexally within the dermis.

Treatment

- Symptomatic treatment of seborrhea and pyoderma is essential.
- There is no known treatment to reverse the clinical alopecia. There are anecdotal reports of partial response to retinoids and melatonin.

Telogen Defluxion

Etiology

- Illness or severe stress causes abrupt cessation of anagen and synchronizes hair follicles into the telogen (resting) stage of hair growth.
- Telogen hairs synchronously shed in 1 to 3 months as the new anagen hair cycle begins.

Clinical Signs

- Hairs begin to shed in abnormal amounts, resulting in alopecic patches, usually 1 to 3 months following a stressful incident or illness.

- Hairs epilate easily. The skin appears otherwise healthy with no evidence of pyoderma or inflammation.

Diagnosis

- Suspect telogen defluxion based on history and clinical signs.
- A trichogram of the epilated hairs will confirm that all hairs are in telogen.
- Biopsy will support a non-inflammatory alopecia and either confirm all hairs to be in telogen or reveal early regrowth of a new wave of anagen hairs.

Treatment

- Telogen defluxion is self-limiting, and hair eventually regrows normally without treatment.

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Chapter 52

Feline Symmetrical Alopecia

Vicki J. Scheidt / Andrew Hillier

Alopecia is defined as the absence of hair from skin areas where it is normally present. Feline symmetric alopecia (FSA) is a cutaneous reaction pattern with many possible etiologies; FSA should not be a final diagnosis, and it is important to determine the primary cause for the most appropriate therapy to be instituted.

In order to properly define the clinical problem and formulate an appropriate list of differential diagnosis, it is helpful to further categorize alopecia as follows:

- Whether the alopecia is self-induced (i.e., a result of pruritus) or not
- Distribution of lesions (body locations involved, localized or generalized)
- Duration (permanent or transient)
- Degree (partial or complete)

Alopecia in the cat, whether symmetric or asymmetric, is most often associated with varying degrees of pruritus and skin reactivity depending on the underlying disease.

▼ ***Key Point*** Although self-trauma (pruritus) due to underlying inflammatory skin disease is the most common cause of FSA, visible skin inflammation may be minimal or absent, even in cases of severe pruritus and alopecia.

NORMAL SHEDDING OF HAIR

In animals, the haircoat aids in thermal regulation, protects the skin, and has important aesthetic qualities. Cats are fastidious and spend a great deal of time grooming their coats. Normal grooming behavior aids in hair removal and normal shedding. However, when grooming becomes excessive, it may accentuate hair damage and skin disease. It may be difficult for some owners who are inexperienced in the grooming behavior of cats to be able to distinguish between normal grooming and excessive grooming due to pruritus.

Hair follicles have specific cycles of growth (anagen) and rest (telogen) that are primarily stimulated by changes in the photoperiod and to a lesser extent by temperature. From winter to late spring in temperate climates, minimal hair growth occurs and the thick winter coat is shed. Therefore, cats that live outside in colder climates may shed excessively in late spring and develop a transient thinning of the coat (hypotrichosis). Secondary hairs undergo a growth phase in the fall and winter that results in the thick, heavy coat needed for colder temperatures. Seasonal changes are less dramatic in tropical regions or in environments with artificial lighting (e.g., cats confined indoors). Under these conditions, a small amount of hair loss may occur continuously.

ETIOLOGY OF ALOPECIA

Multiple factors play a role in normal hair follicle development and growth (Table 52-1). Absence or changes in one or more of the factors can alter the normal hair growth process and result in alopecia. The underlying causes of FSA can vary depending on the area or region of the body affected. This chapter focuses on the causes of FSA that are primarily confined to the trunk (dorsum, perineum, caudal thighs, flanks, ventral abdomen, and thorax). The underlying causes of FSA affecting the trunk region have been classified into those that are associated with self-trauma or pruritus (e.g., licking or scratching) and those that are nonpruritic (Table 52-2).

▼ ***Key Point*** Determine whether pruritus and concurrent skin inflammation are present when formulating a differential diagnosis for FSA in the cat.

Self-induced (Pruritic) Alopecia

Allergic dermatitis and parasitic infestations are the most common causes of self-induced alopecia. Other cutaneous reaction patterns associated with allergic and parasitic dermatoses are feline miliary dermatitis (see Chapter 53) and eosinophilic granuloma complex lesions (see Chapter 53). Allergic causes of self-induced alopecia in cats typically do not have as strong a regional distribution (i.e., involvement of specific body locations) as is the case in dogs.

Table 52-1. INTERNAL AND EXTERNAL FACTORS INFLUENCING HAIR FOLLICLE GROWTH AND DEVELOPMENT

Internal Factors	External Factors
Genetic	Nutritional
Hormonal	Infectious
Immunologic	Bacterial
Neoplastic	Fungal (dermatophytes)
Stress	Parasitic
	Physical (traumatic)
	Chemical (toxins, drug therapy)

Table 52-2. CAUSES OF FELINE SYMMETRIC ALOPECIA OF THE TRUNK

Self-induced (Pruritic)	Non–self-induced (Nonpruritic) (All Rare)
Allergic dermatoses	Feline endocrine alopecia
Food allergy	Sex hormone-related
Atopy	Hyperthyroidism/hypothyroidism
Flea allergy	Hyperadrenocorticism
Demodicosis	Systemic disease
Dermatophytosis	Diabetes mellitus
Otodectic mange	Renal disease
Notoedric mange	FeLV and FIV
Bacterial skin infection	Telogen effluvium/anagen defluxion
Yeast *(Malassezia)* skin infection	Paraneoplastic alopecia
	Thymoma
Psychogenic alopecia	
Intestinal parasite hypersensitivity (rare)	
Chronic cystitis (rare)	

Flea Infestation and Flea Allergy Dermatitis

When associated with mild pruritus and minimal dermatitis, fleas can cause a symmetric alopecia of the dorsum, proximal tail, flanks, perineum, and ventral abdomen. Although a similar presentation can be seen in cats with flea allergy dermatitis, the alopecia and pruritus are much more severe in flea-allergic cats, and they typically have concurrent skin lesions (miliary dermatitis) along the dorsum, tail base, and ventral abdomen (see Chapter 45). Some flea-allergic cats do not have involvement of the typical body locations as mentioned; other body locations maybe involved, and flea allergy dermatitis should remain a differential diagnosis for cats with pruritus and alopecia even if the typical body locations are not involved.

Fleas and/or their feces are usually present on examination. However, in some cases the fleas and feces are removed during the excessive grooming (fleas may be found on fecal flotation in these cases) and the absence of fleas or flea feces should *not* rule out the possibility of flea allergy dermatitis.

Food Allergy

Food allergy in cats is associated with non-seasonal pruritus and a variety of clinical presentations, including FSA. The skin lesions and severe pruritus may be generalized or confined to the face and ears or trunk. Alopecia, whether diffuse or symmetric, results from excessive pruritus triggered by an allergic reaction to specific food items ingested (see Chapter 47). Stubbled or broken hairs, with or without concurrent focal erythema, papules, and crusting (miliary dermatitis), are usually present. Food allergy should be considered a differential diagnosis in any cat with non-seasonal pruritus and alopecia.

Feline Atopic Dermatitis

Atopic dermatitis in cats may be associated with seasonal or non-seasonal alopecia and pruritus (see Chapter 46). Similar to that seen in feline food allergy, the alopecia is secondary to pruritus and is associated with broken or stubbled hairs and concurrent skin lesions. The alopecia may be generalized or confined to the head and neck or distal extremities. Food allergy and atopic dermatitis are virtually indistinguishable on clinical examination in cats with non-seasonal pruritus.

Dermatophytosis

This is a common cause of localized or generalized alopecia in cats (see Chapter 42). Fungal organisms invade the hair shaft and grow downward but do not penetrate the mitotic region of the hair. Alopecia is not permanent unless the follicle is destroyed by secondary inflammation. A wide spectrum of clinical presentations can be seen with feline dermatophytosis, including the asymptomatic carrier state, particularly in longhaired cats. Classically, the alopecia is focal to diffuse with small numbers of fractured or stubbled hairs and mild epidermal erythema and scaling. The majority of dermatophyte infections in cats are caused by the zoophilic fungus *Microsporum canis*. Pruritus is variable in dermatophytosis and when present is typically mild and rarely moderate to severe.

Demodicosis

Demodicosis is an uncommon cause of alopecia in cats (see Chapter 43). The pathogenesis of feline demodicosis is reported to be similar to that described in the dog and caused by either *Demodex cati* (follicular mite) or *Demodex gatoi* (skin surface mite). *D. cati* is a normal inhabitant of feline skin, which under favorable conditions proliferates in hair follicles. Lesions consist of focal to diffuse alopecia, erythema, scaling, and crusts that may be localized and self-limiting or generalized. In some cases, these lesions may mimic feline endocrine alopecia. Generalized demodicosis due to *D. cati* infestation is usually associated with an underlying immunosuppressive disease, such as feline leukemia virus

(FeLV), feline immunodeficiency virus (FIV), diabetes mellitus, or neoplasia.

A pruritic, symmetric alopecia of the trunk caused by *D. gatoi* has been described in cats. Other body locations may occasionally be affected.

Otodectic Mange

Otodectes mites are the most common cause of otitis externa in cats (see Chapter 59). Otodectic mites can live on the skin surface and infrequently cause a symmetric alopecia over the lower back and tail base. Concurrent otitis externa may or may not be present. The degree of pruritus is variable.

Notoedric Mange

Notoedres mites cause a severely inflammatory and pruritic dermatitis involving the head, pinna, and neck in particular. Typically, miliary dermatitis is seen, but FSA may be an uncommon manifestation of infestation with this mite.

Bacterial Infection (Pyoderma)

Bacterial infection (usually staphylococci bacteria) is usually secondary to underlying primary disease, for example, allergic dermatitis, parasitic infestations, or endocrinopathy. Secondary bacterial skin infections are far less common in cats compared with in dogs. However, occasional cats may have a secondary bacterial infection that will mask response to flea control or food trials if not detected and treated to resolution.

Yeast (Malassezia) Dermatitis

Similar to bacterial infections, yeast dermatitis is usually a secondary problem associated with primary skin disease (allergy, parasites, endocrine, etc.) and is also far less common in cats compared with dogs. However, when present, yeast infections may induce moderate to severe pruritus in their own right, even when the underlying primary disease is non-pruritic (e.g., endocrine). Once again, failure to detect and resolve yeast skin infections will make it difficult to appreciate response to flea control, food trials, immunotherapy, etc.

Psychogenic Alopecia

This condition is often an enigma. Alopecia develops because the cat excessively licks, bites, or pulls out hair from those areas normally groomed (perineum, ventral abdomen, flank). In most cases, a stressful event such as moving to a new surrounding, being hospitalized or boarded, loss of a favorite companion, or introduction of a new pet or person (baby) into the environment precipitates the disease. Psychogenic alopecia is most common in nervous or "high-strung" cats, such as Siamese, Abyssinian, or black-colored cats. Typically, the areas affected are regions the cat can easily lick, such as the dorsal lumbosacral region, tail, medial and caudal thighs, ventral abdomen, flanks, and perineum. Partial to complete alopecia and stubbled hairs are observed, and concurrent skin changes (e.g., erythema, erosions, exudation, and crusting) are rare.

▼ ***Key Point*** As with most psychogenic conditions, it is critical to rule out the more common and likely pathologic causes of FSA before a diagnosis of psychogenic alopecia can be confirmed.

Non–self-induced (Nonpruritic) Alopecia

Feline Endocrine Alopecia

This is a disease of unknown cause. It is presumed to result from hormonal imbalances or deficiencies based on the positive response observed following treatment with specific hormones. The condition is characterized by non-pruritic, symmetric hair loss on the perineum, ventral abdomen, and caudal or medial thighs. Although the alopecia may spread to the flanks, lateral thorax, and proximal tail, the dorsum is usually spared. A thinning of the hair, rather than complete baldness, with normal, non-inflamed skin is the classic presentation. Feline endocrine alopecia primarily affects neutered females and males. However, this syndrome has been reported in intact cats.

Significant controversy exists regarding the relationship of hypothyroidism to feline endocrine alopecia. Affected cats usually have normal baseline serum thyroxine (T_4) levels; however, serum T_4 levels at 6 hours following stimulation with thyroid-stimulating hormone (TSH) have been low compared with TSH stimulation results in normal cats. These findings suggest that some cats with feline endocrine alopecia may have a low thyroid reserve.

Some cats with hyperthyroidism may develop truncal alopecia, although typically the skin lesions of hyperthyroidism are uncommon and more often associated with a dull, greasy, lusterless haircoat.

Feline hyperadrenocorticism is rare; however, spontaneous and iatrogenic Cushing disease can produce FSA of the trunk or pinnae associated with thin hypotonic skin.

Telogen Effluvium

This is a syndrome in which the anagen cycle is shortened and a wave of hairs simultaneously enters the resting phase. Conditions associated with physiologic stress (e.g., fever, shock, pregnancy and lactation, malnutrition, adverse drug reactions, or a severe debilitating disease) can precipitate rapid shedding in animals. The resultant alopecia can be partial to complete, localized or generalized, and usually non-pruritic. Affected hairs are easily epilated by friction or grooming.

Anagen Defluxion

This is a syndrome in which there is a sudden interruption of growth of anagen hairs, causing deformity

and fragility of the hair, which is then subject to breaking, and leading to alopecia. Causes of anagen interruption may include severe disease and fever. A wave of hair loss occurs shortly after the precipitating event.

Systemic Disease

Diffuse, symmetric, or asymmetric hair loss in the cat can be caused by systemic disease. Hair follicles are sensitive to pathologic and physiologic changes resulting from systemic diseases, such as end-stage kidney disease, chronic hepatitis, diabetes mellitus, and viral infections (FeLV, FIV). The degree of pruritus and skin lesions associated with the alopecia is variable.

CLINICAL SIGNS

- FSA is either self-induced (pruritic) (a direct result of the cat excessively licking or pulling the hair out) or non-pruritic (hair follicles fall out independently). The finding of stubbled or broken hairs suggests self-trauma. However, invasion of organisms, such as dermatophytes, into the hair shaft can also produce fractured or stubbled hairs. A trichogram (examination of hairs under low-power microscopy) may help demonstrate broken hair shafts or fungal elements.
- A history of frequent vomiting of hairballs or hair in the feces (or hair impaction of feces) may also support the possibility of self-induced alopecia and excessive grooming.
- Excoriations, erosions, and/or ulcerations in conjunction with stubbled hairs usually imply that the hair loss and skin changes are self-inflicted. These lesions may also be secondary manifestations of a primary vesicular or bullous disease; however, these lesions are usually associated only with rarely seen dermatoses.
- Pruritic or self-inflicted alopecia that is responsive to systemic corticosteroid therapy suggests an underlying allergic or parasitic etiology. Alopecia that is responsive to systemic progestational therapy, however, may have a hormonal, an allergic, or a psychogenic basis.
- Cats that are nervous, poorly adjusted, or high strung are more likely to develop excessive grooming behavior (e.g., psychogenic alopecia) and subsequent alopecia.
- Systemic signs (e.g., anorexia, vomiting, weight loss, polydipsia, polyphagia, or polyuria) may be present when the alopecia is associated with either a primary systemic disease (e.g., renal disease or diabetes mellitus) or a secondary hormonal imbalance (e.g., iatrogenic Cushing disease).

DIAGNOSIS

▼ ***Key Point*** FSA can be classified as either self-induced (pruritic) or non-pruritic based on the history and gross appearance of the haircoat and skin. The goal of diagnostic evaluations is to identify the underlying disease.

When self-induced alopecia is suspected but not supported by history and physical findings, preventing the cat from licking the body, using an Elizabethan collar continually for 2 to 4 weeks, is often conclusive. In such cases, obtain baseline diagnostic tests first (e.g., skin scrapings and fungal culture).

History

Evaluate for pruritus, the general psychological state of the cat, environmental changes that preceded the alopecia, past and current hormonal status of the cat, concurrent systemic signs, and possible nutritional or therapy-related causes.

Physical Examination

Perform a thorough examination of the integument and all internal organ systems.

- Examine hair shafts and follicles from affected areas, grossly and microscopically, for structural abnormalities (e.g., fractures, bulges, and constrictions). Telogen hairs plucked from the skin have a fusiform appearance and a dry, white, club-shaped root on gross or microscopic examination. In contrast, growing or anagen hairs have a blunt end that is glistening, pigmented, and surrounded by a root sheath.
- Examine the skin in both alopecic and normal areas for primary (erythema, papules) and secondary (crusts, scale, hyperpigmentation) lesions. Note the thickness and elasticity of the skin.
- Search for external parasites (fleas and flea dirt—use a flea comb over the entire trunk).
- Note abnormalities in other organ systems.

Diagnostic Tests

Tests for Bacteria and Yeast

- Perform *skin surface cytology* (see Chapter 37) to check for bacterial and yeast secondary infections.

Tests for Mites

- Perform *deep skin scrapings* to rule out *D. cati* infestations.
- Perform *superficial or surface skin scrapings* to rule out *D. gatoi, Otodectes cyanotis, Notoedres,* or other external mite infestations.
- Collect *ear smears* from cats with concurrent otitis externa or those with a history of recurrent otodectic mange (ear mites).

Tests for Dermatophytes

- Perform *fungal culture* to identify a dermatophyte infection. Examine affected hairs with an ultraviolet light (Wood's lamp). Approximately 50% of the cases of *M. canis* fluoresce. Use hairs that fluoresce an apple-green color, both for culturing and for microscopic examination for fungal spores or hyphae, using a clearing agent (KOH). Refer to Chapter 42 for details concerning the diagnosis of dermatophytosis.

Allergy Testing

- In cats with non-seasonal FSA, institute an *elimination diet* trial (see Chapter 47). The diagnosis of food allergy is confirmed with amelioration of the pruritus and/or excessive licking during a 4- to 8-week diet trial and recurrence of signs following provocative exposure to the original diet or offending antigen.
- Perform *intradermal skin testing* or *in vitro allergy testing* for flea and environmental allergens in cats with a history of seasonal (spring to fall) and non-seasonal pruritus, especially if there is a history of response to systemic corticosteroid therapy. Correlate positive reactions with the history of allergen exposure and seasonality.

Flea Control

- Appropriate flea control (see below) should be instituted in any cat with FSA involving any body location, but especially if the caudal dorsum, tail base, perineum, caudal or medial thighs, ventral abdomen, and/or inguinal regions are involved.

Skin Biopsy

- Skin biopsy of affected and unaffected areas is helpful in evaluating the growing stages of hair follicles and in identifying any concurrent follicular inflammation—whether infectious, parasitic, or allergic. (See Chapter 37 for skin biopsy technique.)

▼ ***Key Point*** Histopathology of affected skin is not usually helpful in making a specific diagnosis. Most often the pathologist will be able to indicate if there is a primary inflammatory or primary endocrine disease, at best. Thus, histopathology is typically of little benefit in the workup of FSA.

Endocrine Tests

- Obtain *baseline serum thyroid hormone* levels or perform a *TSH stimulation test* in cats with non-pruritic alopecia and histopathologic findings consistent with an endocrine-based alopecia. A TSH stimulation test is superior to serum baseline T_4 levels for diagnosing hypothyroidism in the dog and cat and is the test of choice (see Chapter 31).
- Perform an *adrenocorticotropic hormone (ACTH) stimulation test* in cats with non-pruritic alopecia and concurrent polyuria, polydipsia, polyphagia, lethargy, pendulous abdomen, and/or thin, easily torn skin to rule out iatrogenic or naturally occurring hyperadrenocorticism (see Chapter 33).

Ancillary Laboratory Tests

- Perform a *complete blood count, serum biochemical profile,* and *urinalysis* in cats with symmetric alopecia and concurrent systemic signs (e.g., fever, depression, anorexia, and polyuria-polydipsia) to identify any underlying primary disease (e.g., diabetes mellitus) or adverse reaction to previous therapy (e.g., iatrogenic Cushing disease resulting from prolonged systemic corticosteroid or progestational therapy).
- The finding of peripheral eosinophilia in a cat with seasonal or non-seasonal pruritus and/or licking is suggestive of an allergic or parasitic dermatitis.
- Perform *FeLV and FIV tests* in cats with generalized demodicosis, non-healing skin infections, or protracted systemic signs (see Chapters 6 and 7).

TREATMENT

FSA is often managed with "scientific neglect" during the early stages when hair loss is mild and pruritus is absent. However, if the alopecia progresses or is observed to be self-induced, pursue an underlying cause and prescribe appropriate treatment. Determine from the onset whether the hair loss is due to self-induced behavior (licking, chewing, hair pulling) or to an underlying, non-pruritic disease (hormonal, systemic disease). Many cats are "closet lickers"; therefore, the owners may not observe excessive licking or chewing. In such cases, applying an Elizabethan collar for 2 to 4 weeks can be very helpful in identifying whether or not the cat is actually licking the hair out. Chronic cases of FSA that are associated with secondary skin changes and pruritus often require symptomatic treatment with anti-inflammatory agents during the initial stages of the diagnostic workup. Avoid prolonged corticosteroid therapy until the primary etiology has been identified and appropriately treated.

Specific Therapy

Hypoallergenic Diet

Feed a hypoallergenic diet to cats with symmetric alopecia caused by a dietary allergy (see Chapter 47). Many cats are finicky eaters and will not eat home-cooked diets. Pureeing the foods often increases the palatability of home-cooked diets. Use a daily multiple mineral-vitamin supplement when home-cooked diets are used for a prolonged period. Several commercial diets are well tolerated by food-allergic cats, including canned

Response Formula LB/Feline (Eukanuba Veterinary Diets) and canned or dry Limited Diets Feline/venison and green pea/rabbit and green pea (Innovative Veterinary Diets).

Immunotherapy

Allergen-specific immunotherapy (ASIT) (hyposensitization) has been reported to be an effective treatment for feline atopic dermatitis (see Chapter 46). In a recent study, Halliwell found an improvement of at least 50% in 42 cats with various dermatologic manifestations of feline atopic dermatitis following ASIT. The percentage of response for each dermatologic manifestation varied, ranging from 60% to 94%.

Flea Control

Flea control is a critical part of the management of feline flea allergy and infestation. Currently, there are several topical and/or systemic products available for use in cats and dogs that are so effective that environmental treatment is often not necessary (see Chapter 45). Lufenuron (Program, Novartis), given orally at a dosage of 10 to 15 mg/kg once a month, prevents the synthesis of chitin, which is needed for normal flea development. Eggs laid by fleas that feed on treated cats or dogs fail to hatch, and new larvae fail to molt. It has no affect on adult fleas. In contrast, topical solutions containing imidacloprid (Advantage, Bayer), fipronil (Frontline Top Spot, Rhone Merieux), or selamectin (Revolution, Pfizer), when applied once a month to the skin surface, kill adult fleas before they have a chance to lay eggs, eliminating the need for concurrent environmental flea treatment. For rapid elimination of fleas, oral nitenpyram (Capstar, Novartis) may be useful.

Antibacterial and Antiyeast Therapy

If a secondary bacterial infection is present, a 3-week course of antibiotics is essential. Commonly prescribed antibiotics include cephalexin (generics) (22 mg/kg twice daily) and amoxicillin/clavulanic acid (Clavamox, Pfizer) (13.5 mg/kg twice daily).

In the case of secondary yeast infections, systemic itraconazole (Sporanox, Janssen) at 5 mg/kg once daily is usually effective at eliminating the infection.

For both secondary bacterial and yeast infections, topical therapy with chlorhexidine +/− miconazole (e.g., Malaseb, DVM Pharmaceuticals) provides additional useful adjunctive therapeutic support. If the secondary infection is localized, topical therapy alone may be adequate.

Antifungal Therapy

Clinical management of feline dermatophytosis includes clipping and cleansing of the affected areas, generalized topical antifungal therapy, isolation and appropriate sanitation, and systemic antifungal therapy (griseofulvin, ketoconazole, itraconazole) in severe generalized cases. Refer to Chapter 42 for details concerning the treatment of feline dermatophytosis.

Miticidal Therapy

- Apply miticidal solutions containing 2% lime sulfur (LymDyp, DVM Pharmaceuticals) once weekly for six treatments for FSA caused by *D. cati* or *D. gatoi*.
- Treat FSA caused by otodectic mange with topical or systemic ivermectin (Ivomec, MSD Agvet) at a dosage of 0.2 to 0.4 mg/kg PO or SC weekly for 4 to 6 weeks or with application of selamectin (Revolution, Pfizer) to the back of the neck every 2 weeks for three treatments. Because of the contagious nature of *O. cyanotis,* both the affected cat and all contact animals are treated for 4 to 6 weeks with a miticidal otic preparation or ivermectin.

Antiinflammatory Therapy

Use antiinflammatory drugs in cats with symmetric alopecia and concurrent pruritus that are suspected of having an underlying allergic disease (e.g., food allergy, atopic dermatitis, or flea allergy). Short-term treatment with systemic antihistamines or corticosteroids may be used during the initial stages until the causative allergen is identified (diet trial, intradermal or serum allergy testing) and is eliminated or appropriately controlled (hypoallergenic diet, immunotherapy, flea control).

Systemic Antihistamines

Compared with systemic corticosteroid use, systemic antihistamine use is generally not as effective in controlling pruritus in cats. Chlorpheniramine maleate, given at 2 mg/cat q12h PO, can be an effective treatment in cats with pruritus of an unknown or idiopathic nature. We have found hydroxyzine hydrochloride, given at 10 mg/cat q12h PO, to be effective for control of pruritus in cats with feline atopic dermatitis.

Fatty Acid Supplements

DVM Derm Caps (DVM Pharmaceuticals), 0.11 ml/kg q24h PO, are occasionally effective in controlling pruritus in cats when given alone or in combination with an antihistamine (chlorpheniramine, hydroxyzine). However, 4 to 8 weeks may be required before improvement is noted.

Systemic Corticosteroids

Corticosteroids are very effective in the management of pruritus in cats. Cats require much higher doses than dogs to suppress or control pruritus of an allergic nature. Compared with other species, cats appear to be more resistant to the harmful side effects of systemic corticosteroid therapy and the development of

iatrogenic Cushing disease. Administer dexamethasone at a dosage of 0.25 to 1.0 mg/cat once daily with a taper to 2 to 3 times weekly, or prednisolone at a dosage of 2 mg/kg q24h PO for 7 to 14 days with a taper to an alternate-day schedule, and gradually taper to the lowest effective dose. Methylprednisolone acetate (Depo-Medrol, Upjohn) given at a dose of 4 to 5 mg/kg or 20 mg/cat SC is also effective when administered every 2 to 3 weeks. When giving repeated corticosteroid injections (Depo-Medrol) every 2 to 3 weeks, do not exceed four treatments at this interval. If pruritus persists, it is imperative to find the underlying disease or look for alternative treatments.

Systemic Progestational Compounds

These compounds have been used for years to treat various feline skin diseases, including FSA, both pruritic (e.g., atopy and psychogenic alopecia) and non-pruritic (e.g., feline endocrine alopecia). In cats, progestational compounds such as megestrol acetate (Ovaban, Schering-Plough) are immunosuppressive and have potent anti-inflammatory activity. They exhibit a wide spectrum of actions and side effects. Serious side effects in the cat include decreased spermatogenesis, pyometra, mammary gland fibroadenomatous hyperplasia and mammary neoplasia in both male and female intact and neutered animals, permanent or transient diabetes mellitus, adrenocortical suppression, and various behavioral abnormalities (e.g., polyphagia with subsequent weight gain, polyuria, polydipsia, and lethargy). The oral dosage in cats is variable and starts with an induction dose of 2.5 to 5 mg per cat q24h for 5 days, decreases to every other day, and is tapered to 2.5 to 5 mg every 5 to 7 days for 1 to 2 months.

▼ ***Key Point*** Progestational compounds are not approved for use in cats. Because of this and their numerous side effects, they are administered only as the last choice.

Hormonal Therapy

Hormonal therapy has been successfully used in the cat to treat non-pruritic, FSA that is associated with normal-appearing skin and classified as endocrine in origin. Although various hormones have been effective in the treatment of feline endocrine alopecia, relapses are common and intermittent lifelong therapy is often necessary.

Combined Estrogen and Testosterone

These have been used successfully in both neutered male and female cats with feline endocrine alopecia. Repositol testosterone (12.5 mg/cat) and repositol diethylstilbestrol (0.625 mg/cat) are given IM separately or in combination. Although hair regrowth is usually present by 6 weeks, relapses are common. Side effects, including signs of estrus in females, aggressive behavior or urine spraying in males, and hepatobiliary disease in both, have been reported following androgen and/or estrogen therapy.

Thyroid Hormone

Supplemental thyroid hormone has been found to be effective in cats with feline endocrine alopecia, despite normal serum baseline thyroid levels. Sodium levothyroxine is effective at a dosage of 0.05 to 0.1 mg q12–24h PO. Sodium liothyronine (Tertroxin, Glaxo) given at 50 µg q12h PO has been reported to produce complete hair regrowth in 73% of cats treated (Thoday, 1989).

Progestational Compounds

These compounds can be effective in the management of feline endocrine alopecia. Megestrol acetate (2.5–5.0 mg/cat PO once every other day for 1–2 months) is preferred over repositol progesterone due to potential side effects of the latter in cats.

Adrenalectomy

Either unilateral or bilateral adrenalectomy is the treatment of choice for naturally occurring hyperadrenocorticism in the cat (see Chapter 33). Discontinue and avoid future treatment with systemic corticosteroids and progestational compounds in cats with iatrogenic hyperadrenocorticism.

Antianxiety Drugs and Tranquilizers

These drugs can be used in conjunction with behavior modification to treat cats with stress-induced symmetric alopecia or psychogenic alopecia. Because response to systemic antianxiety medication is variable in cats and requires much patience and effort on the part of the owner, identification and removal (if possible) of the predisposing cause is crucial. Use these drugs as adjunctive therapy to behavioral modification. The main goal is to calm the cat and eventually discontinue the antianxiety medication.

- Examples include clomipramine, alprazolam, fluoxetine, and amitriptyline.

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Chapter 53

Miliary Dermatitis and Eosinophilic Granuloma Complex

Wayne S. Rosenkrantz

Miliary dermatitis (MD) and eosinophilic granuloma complex (EGC) are extremely common cutaneous reaction patterns in the cat. The term *miliary* is a descriptive one, and it implies that the papules and crusts characteristic of the syndrome resemble millet seeds. The term *eosinophilic granuloma* is also descriptive of a group of lesions affecting the skin and oral cavity of the cat. The three clinical histologic syndromes included in this complex are eosinophilic ulcer, eosinophilic plaque, and eosinophilic (collagenolytic) granuloma.

ETIOLOGY

▼ ***Key Point*** MD and EGC are neither final diagnoses nor pathognomonic for any one disease. Many etiologies exist for both reaction patterns. The ability to control or cure chronic or recurrent cases is dependent on pursuing the underlying cause. The two conditions share similar etiologies and therefore are discussed together in this chapter.

Underlying causes or predisposing factors for MD and EGC (Table 53-1) include (1) allergies, (2) parasites, (3) infectious diseases, and (4) miscellaneous conditions.

Allergies

Allergies to biting insects (e.g., fleas, mosquitoes, and flies), foods, environmental allergens, and rarely contact substances (irritants and allergens) have been associated with MD in the cat. With the exception of contact allergies, all of these reactions have also been associated with EGC. In particular, flea and other biting insect hypersensitivities have been emphasized as etiologies in EGC.

Parasites

Parasites, such as fleas, *Demodex, Cheyletiella, Notoedres,* chiggers, *Otodectes,* lice, cat fur mites, and endoparasites, have been associated with MD. Fleas have also been implicated in EGC as a cause of a hypersensitivity reaction. These parasites also produce lesions in MD by way of a hypersensitivity reaction. Refer to the respective chapters concerning these various parasites for additional information.

Infectious Diseases

Infectious causes for both entities include bacterial infections and dermatophytosis. In EGC, viral infections are an additional consideration and for MD consider *Malassezia* (yeast) infections (see Chapter 41).

- The most common bacteria isolated in both entities include *Staphylococcus,* hemolytic *Streptococcus, Pasteurella,* and *Bacteroides* species. Presence of bacteria on cytology and positive clinical response to a variety of antibiotics in both MD and EGC gives support to a bacterial etiology. Although secondary bacterial infections are uncommon in cats (less common than in dogs), their role in disease and contribution to clinical signs is easily overlooked.
- The major dermatophyte species isolated from cats is *Microsporum canis* (see Chapter 42). This dermatophyte can produce MD, but it can also be found on cats without MD. This dermatophyte is rarely isolated from EGC lesions, and its significance in this complex is questionable.

Miscellaneous Causes

Miscellaneous conditions causing MD include genetic factors, immune-mediated diseases, drug reactions, nutritional factors, epitheliotropic lymphoma, and idiopathic causes. Genetic factors, immune-mediated disease, and idiopathic causes have received attention as etiologies in EGC.

- *Hereditary (genetic) factors* have been implicated based on reports of offspring from affected cats, which have developed similar MD or EGC lesions.
- *Immune-mediated disorders,* such as pemphigus foliaceus, can produce MD-like lesions. Immune-mediated disease has not received much consideration in EGC, although antiepithelial antibodies

Table 53-1. ETIOLOGIES OF MILIARY DERMATITIS AND EOSINOPHILIC GRANULOMA COMPLEX

	Miliary Dermatitis	Eosinophilic Granuloma Complex
Allergies		
Flea allergy	++++	++++
Mosquito and biting fly hypersensitivity	+	+++
Food allergy	+++	+++
Atopic dermatitis	+++	+++
Contact allergy	+	
Parasitic Diseases		
Fleas	+++	++
Cheyletiella	++	
Notoedres	++	
Chiggers (trombiculiasis)	++	
Otodectes	++	
Lice (pediculosis)	++	
Demodicosis	+	
Cat fur mite	+	
Endoparasites	+	
Infectious Diseases		
Bacterial infections	+++	+++
Dermatophytosis	+++	+
Viral infections		+
Miscellaneous Conditions		
Genetic causes	++	++
Immune-mediated diseases	+	+
Drug reactions	+	+
Nutritional disease	+	
Neoplasia	+	++
Idiopathic causes	+++	+++

+, Rare cause of syndrome; ++, Uncommon cause of syndrome; +++, Frequent cause of syndrome; ++++, Major cause of syndrome.

(immunoglobulin G) have been documented in cats with eosinophilic ulcers.

- *Drug reactions* can mimic any skin disease. Cases of drug-induced MD lesions have been seen but are rare. Drug-induced EGC lesions are questionable; however, some of the dorsal cervical eosinophilic ulcerative lesions can be due to injection-site reactions.
- *Nutritional factors* related to fatty acid or biotin deficiencies have been reported in the older literature as causes of MD. Such deficiencies are unlikely in cats on commercial, well-balanced diets.
- *Cutaneous neoplasms* (squamous cell carcinoma, mast cell tumor, lymphoma) can mimic MD and/or EGC.
- *Idiopathic forms* exist for both MD and EGC. Such cases most likely reflect the inability to identify one of the aforementioned diseases. Undefined allergic reactions may account for a number of these idiopathic cases.

CLINICAL SIGNS

Miliary Dermatitis

- The lesions of MD are usually small erythematous papules (1–2 mm) that develop into crusts. Secondary lesions result from self-trauma and produce alopecia, erosions, excoriations, and acute pyotraumatic dermatitis. The distribution can be localized to a specific area or generalized. The dorsal lumbosacral, cervical, and inguinal areas are the most common sites affected.
- Additional physical signs that may be noted in MD include the following:
  - Peripheral lymphadenopathy of the inguinal lymph nodes
  - Personality changes such as depression and hiding
  - Pain or twitching over affected sites
  - Concurrent lesions of EGC

Eosinophilic Granuloma Complex

The lesions of EGC are variable and are classified into three types.

Eosinophilic Ulcer

- *Eosinophilic ulcer* (indolent, rodent, and lip ulcer) is a well-circumscribed, red-brown to yellow, ulcerated lesion most commonly found on the upper lip of the cat. The lesions are generally non-painful and non-pruritic.

Eosinophilic Plaque

- *Eosinophilic plaque* is a well-circumscribed, raised exudative lesion that is highly pruritic and generally found on the abdomen or inguinal region. This lesion is the most common form of EGC in cats with concurrent MD.

Eosinophilic Collagenolytic Granuloma

- *Eosinophilic collagenolytic granuloma* is seen primarily in young cats and is a well-circumscribed, raised, erythematous to yellow linear, papular, or nodular lesion. It is most commonly found in a linear pattern (linear granuloma) over the caudal thighs and in a nodular pattern on the lower lip and in the oral cavity. Other sites include the bridge of the nose, chin, lips, pinnae, footpads, paws, and perianal region.

DIAGNOSIS

History

History helps identify seasonal allergies, such as flea and other insect hypersensitivities, atopic dermatitis, and

chiggers. A history of pruritus with MD lesions is more typical of parasitic and allergic hypersensitivity disorders.

Physical Examination

Physical examination can also help narrow the differential diagnosis in both MD and EGC by identification of the specific lesion and by the body location of the lesions.

Miliary Dermatitis

The distribution of MD lesions favors some etiologies over others:

- Dorsal distribution (especially the lumbosacral area) favors flea hypersensitivity. Cheyletiellosis can also have a dorsal distribution.
- When the head and neck are affected, consider notoedric mange, otodectic mange, food allergy, atopic dermatitis, pyoderma, or pemphigus foliaceus.

Eosinophilic Granuloma Complex

The distribution of EGC lesions is less helpful in limiting the differential diagnoses.

- Nasal and pinnal forms of eosinophilic collagenolytic granuloma tend to support the diagnosis of insect bite reactions (i.e., mosquito and black fly).
- Eosinophilic plaques on the abdomen and inguinal region suggest the diagnosis of flea hypersensitivity.
- Pruritic cervical EGC lesions are more commonly seen in food allergy, atopic dermatitis, bacterial infection, or injection-site reactions.

Minimum Database

- *Skin scrapings, Scotch tape preparations,* and *combings of hair and dander* for fleas and mites are very important in the initial MD diagnostic evaluation.
- *Skin cytology* can be of value to determine the presence of infectious organisms and inflammatory cells. Skin cytologic specimens are obtained by fine-needle aspirate of the lesion, by touching a glass slide to the lesion, or by surface scraping of the lesion (see Chapter 37). Tissue eosinophilia suggests the diagnosis of parasitic and allergic disorders.
- *Dermatophyte culture* is the best way to rule out a dermatophyte as the cause of MD (see Chapter 42).

Bacterial Culture

Bacterial culture and sensitivity tests, performed from an intact pustule, bulla, furuncle, or skin biopsy sample, can give additional information on etiology and choice of correct antibiotic for therapy. Bacterial culture is necessary if initial empirical antibiotic therapy has failed and a bacterial infection is still suspected.

Routine Blood Tests

- *Complete blood counts* may reveal peripheral eosinophilia associated with parasitic and allergic disorders, especially flea allergy. Peripheral eosinophilia tends to be seen in most cases of eosinophilic plaque and in many cases of eosinophilic collagenolytic granuloma, especially with oral lesions.
- *Serum biochemical analysis* helps rule out other concurrent medical problems.
- *Viral testing* for feline leukemia virus and feline immunodeficiency virus are recommended in recurrent cases of MD and EGC (see Chapters 8 and 9). Results of both chemistry and viral screens will influence treatment and prognosis.

Skin Biopsy

Dermatopathology is one of the most important diagnostic tests performed. Findings may support the clinical assessment, suggest additional diagnoses, provide a specific diagnosis, and rule out differential diagnoses (such as neoplasia with EGC lesions). With EGC, specific histologic patterns have been associated with the three clinical entities:

- *Eosinophilic ulcer* is usually characterized by a chronic ulcerative suppurative dermatitis. In some cases histopathology may reveal eosinophilic collagenolytic dermatitis with palisading granulomatous inflammation.
- *Eosinophilic plaque* is characterized by marked intercellular edema (spongiotic dermatitis) and tissue eosinophilia. Surface crusting with degenerating inflammatory cells with focal areas of erosions, ulceration, or necrosis are not uncommon. This is similar to what is seen histologically in some MD lesions.
- *Eosinophilic collagenolytic granuloma* is characterized by eosinophilic collagenolytic dermatitis with palisading granulomatous inflammation.

Allergy Testing

Food Elimination Diets

A food elimination diet is the only way to accurately rule out food allergy (see Chapter 47). Such a diet consists of a protein source that the cat does not or has not eaten routinely.

- The common choice is lamb baby food, but ham baby food, home-cooked chicken, turkey, fish, rabbit, and other protein sources have been provided successfully (see Chapter 47). If baby food is used, feed a product that does not contain onion powder (i.e., Beech-Nut products) to avoid potential for Heinz body anemia.
- Alternative commercially available diets include Hills (Feline z/d), Innovative Veterinary Diets (rabbit or venison with green pea), Waltham (Hypoallergenic

HP), Royal Canin (Sensitivity VR and RD) and Eukanuba (Response LB) diets. The elimination diet is fed strictly for 6 to 8 weeks.

Intradermal Allergy Testing

Intradermal testing (IDT) helps demonstrate hypersensitivity to insect and environmental allergies. Allergy testing in the cat is more difficult to perform and interpret than in the dog. Testing is, therefore, best done by an experienced veterinary allergist (see Chapter 46).

Serum In Vitro Allergy Testing

Serum in vitro allergy testing (SIAT) has improved significantly in the cat. I have had results comparable to skin testing using a liquid-phase enzymo-immunometric assay (Veterinary Allergy Reference Laboratory; Pasadena, CA) for selecting antigens for allergen-specific immunotherapy (ASIT).

▼ ***Key Point*** Positive allergy test results (IDT or SIAT) should not form the basis for a diagnosis of atopic dermatitis—positive results will help confirm the clinical diagnosis of atopic dermatitis and are essential in the selection of allergens for inclusion in immunotherapy. Allergy tests have not been shown to be useful in the diagnosis of food allergy in cats.

TREATMENT

▼ ***Key Point*** Many forms of therapy have been described for both MD and EGC. The best long-term management is achieved when a definitive diagnosis of the underlying cause has been established and specific therapy for that disease is prescribed.

Avoidance of Inciting Etiologies

Avoidance strategies are commonly used for flea bite hypersensitivities, other ectoparasitic hypersensitivities, food hypersensitivities, epithelial allergens (feathers, cat, dog, or human dander) or mold allergies and most recently for house dust mite (HDM) hypersensitivities.

Control of House Dust Mites

In my practice, HDM *(Dermatophagoides farinae)* is the most common non-seasonal allergic reaction seen in the feline.

- HDM detection can be performed by using an in-home swipe test on any textile surface (MITE-T-Fast Allergen Detection System, Aveho Biosciences). In many cases testing is not necessary and treatment can be based upon the presence of a positive allergy test or a strong clinical suspicion.
- Although treatment options for environmental allergen and mite reduction (Allerase and Dustmite, Aveho Biosciences) are available, their efficacy has not been determined in the feline. However, I commonly recommend the use of environmental control based on positive experiences seen in HDM allergy in the canine.
- In addition to treating the premises, it is also recommended to install a room air conditioner and dehumidifier in the bedroom if the home does not have central air conditioning. Lowering humidity reduces the number of mites, as well as mold and other allergens.
- It is also recommended to use wood, vinyl, or leather furniture instead of upholstery furniture; vacuum frequently; avoid pet foam beds; and wash all bedding materials in hot water (>130°F) weekly.

Glucocorticoid Therapy

This therapy can be tried in first-time cases of MD and EGC. In chronic recurrent cases, alternative therapy is given based on information from an appropriate workup. Even with proper workup, refractory allergies or idiopathic cases of both MD and EGC may require long-term glucocorticoid therapy. A variety of glucocorticoids can be tried.

- Methylprednisolone acetate (Depo-Medrol, Pfizer) at 4 mg/kg IM is a commonly used, and often efficacious, long-acting injectable glucocorticoid. Cases of refractory EGC may need three injections at 2-week intervals. In general, after remission, do not use methylprednisolone acetate more often than every 3 months.
- As an alternative to methylprednisolone acetate, give anti-inflammatory doses of prednisolone or methylprednisolone at 2.2 mg/kg PO q24h for resolution of lesions. Decrease the dose to 1 to 2 mg/kg PO q48h for maintenance.
- Some cases can be successfully managed with initial injections of methylprednisolone acetate and then maintained with oral prednisone, prednisolone, or methylprednisolone at a dosage of 1 to 2 mg/kg PO q48h.
- Other oral glucocorticoids can be tried in refractory cases. Use triamcinolone at a dosage of 0.4 to 0.6 mg/kg PO q24h, then tapering to 0.2 to 0.3 mg/kg PO q48h–72h for maintenance; or use dexamethasone at a dosage of 0.25 to 0.75 mg PO q24h, then tapering to 0.25 to 0.125 mg q48h–72h for maintenance.
- Use intralesional triamcinolone (Vetalog, Squibb) in refractory EGC lesions at a dose of 1 to 4 mg injected intralesionally.

Antihistamine Therapy

Antihistamines can be tried in atopic dermatitis, flea allergy, and idiopathic MD and EGC:

- Chlorpheniramine, 2 to 4 mg PO q12h, appears to be the most effective antihistamine in cats and has fewer sedative or excitatory side effects, although results are not as good as with glucocorticoids.
- Other antihistamine choices are the following:
  - Cyproheptadine (Periactin), 2 to 4 mg PO q12–24h
  - Amitriptyline (Elavil), 10 mg PO q12–24h
  - Trimeprazine (Temaril), 0.5 to 1 mg/kg q8–12h
  - Cetirizine (Zyrtec), 5mg/cat q12h
  - Fexofenadine (Allegra), 10mg/cat q12h
  - Hydroxyzine hydrochloride or pamoate, 10 mg PO q12h

Food Allergy Management

After determining that a cat has a food allergy, manage with a balanced home-cooked diet or a commercial diet that is tolerated (see Chapter 47).

Allergen-Specific Immunotherapy

ASIT, based on in vitro or in vivo testing, is becoming more promising in cases of EGC and MD in which atopic dermatitis is the underlying cause. Currently, SIAT is my preferred method of allergy testing in the cat. In a limited number of cases, ASIT can manage recurrent EGC and MD lesions (see Chapter 46). Flea immunotherapy has had little benefit in controlling flea allergy in the cat. Protocols are similar to those in dogs.

Parasiticidal Therapy

Because parasites directly or indirectly, via a hypersensitivity reaction, contribute to the lesions in MD and EGC, the control of parasites on the pet and in the environment is extremely important. Integrated strategies for flea control are described in Chapter 45. Treatment of *Notoedres* and *Cheyletiella* is described in Chapter 44.

Antimicrobial Therapy

Use antibiotic therapy for primary or secondary infections in both MD and EGC. Initially, select antibiotics empirically based on cytologic findings. In chronic cases, culture and sensitivity results are employed. Therapy for dermatophytosis is described in detail in Chapter 42. Antibiotics for empirical therapy are listed here; continue treatment for a minimum of 2 weeks and 10 days past clinical cure:

- Trimethoprim-potentiated sulfas, 30 mg/kg PO q12h.
- Cefadroxil (Cefa-Drops, Fort Dodge), 20 mg/kg PO q12h.
- Amoxicillin-clavulanate (Clavamox, Pfizer), 12 to 15 mg/kg PO q12h.
- Clindamycin (Anirobe, Pfizer), 5 to 10 mg/kg PO q12h.
- Fluoroquinolones (occasionally); for example, enrofloxacin (Baytril, Bayer), 2.5 to 5 mg/kg PO q24h, or marbofloxacin (Zeniquin, Pfizer), 2.5 mg/kg PO q24h. Dosages greater than 5 mg/kg should be avoided with enrofloxacin due to the potential development of a rare idiopathic blindness syndrome.

Immunomodulating Therapy

Drugs that either stimulate or suppress the immune response have been tried with EGC. Chlorambucil (Leukeran, Glaxo Wellcome), 0.1 to 0.2 mg/kg PO q48h, or aurothiomalate (Myochrysine, Merck), 2 mg/kg IM weekly, may be used in refractory EGC. Both drugs have long lag phases before response is seen and can create side effects (e.g., bone marrow suppression) that should be monitored.

Interferon alpha-2a (Roferon, Hoffman La Roche) has also been tried in refractory EGC cases at a dose of 30 IU/cat PO once daily for 7 days on a one-week-on/one-week-off schedule, with limited success.

Cyclosporine and Tacrolimus

Cyclosporine (Atopica or Neoral oral suspension, Novartis) and tacrolimus (Protopic topical preparations 0.03% and 0.1%, Fujisawa USA) are immunosuppressant agents that have been used extensively in human medicine, primarily to prevent organ transplant rejection. However, I have used these drugs occasionally in the treatment of EGC and MD allergy-induced cases.

- Both drugs are activated by binding to specific intracellular receptors, called immunophilins. They inhibit calcium-dependent pathways, particularly affecting the enzymatic action of calcineurin, resulting in blocking of regulatory proteins that activate T-helper inducer and cytotoxic cells. Many cytokines are affected, especially interleukin-2 (IL-2).
- Cyclosporine is given at 5 mg/kg PO q24h. It may take up to 6 weeks to completely evaluate responses.
- Currently, due to the much greater potency and potential toxicity of tacrolimus and lack of adequate dosing regimes, systemic administration is not recommended and only topical use is recommended. Tacrolimus can be used topically to lesions on a daily basis, and if effective, responses should be seen within 7 to 10 days.
- Both drugs appear to be well tolerated in the cat with gastrointestinal symptoms, the major side effect from oral cyclosporine or ingestion of topically applied tacrolimus.

Progestational Therapy

Progestational compounds have been advocated for treating both MD and EGC. Most veterinary dermatologists do not use or recommend these products because of their potential for severe side effects. They are not approved for use in cats. With the effectiveness of other forms of therapy, progestational drug therapy is undesirable because of the potentially severe and

life-threatening side effects (including pyometra, diabetes mellitus, and mammary neoplasia).

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Chapter

54 Surgery of Intertriginous Dermatoses

Jamie R. Bellah

Intertriginous dermatoses are surface pyodermas that are associated with skin folds. Chronic skin apposition results in friction, minor trauma, and poor air circulation along with a moist environment conducive to colonization and infection by bacteria and yeasts.

▼ ***Key Point*** Inflammation and exudates associated with skin fold pyoderma cause pain, pruritus, and malodor. Conservative treatment is only palliative. Resolution of these conditions can be accomplished only by surgery.

ETIOLOGY

Normal skin defense mechanisms are as follows:

- Intact epidermis and stratum corneum
- Sebum that contains antibacterial and antifungal fatty acids
- Skin microflora that may secrete antibiotic-like substances

Skin fold pyoderma is classified as a surface pyoderma. (See Chapter 38 for a complete discussion of pyoderma.)

- Bacteria and yeasts remain on top of the skin.
- Warm, moist environment within recess of the skin fold allows colonization by *Staphylococcus intermedius* or *Malassezia pachydermatis.*
- Other infecting organisms include *Streptococcus, Escherichia coli, Pseudomonas, Proteus,* and *Candida.*
- Surface bacteria and yeasts act on trapped secretions and sebum, producing breakdown products that are irritating and odoriferous.
- Superficial skin erosions and inflammation result.
- Self-trauma and obesity tend to worsen the condition.

Locations, characteristics, and breeds associated with intertriginous dermatoses include the following.

Facial or Nasal Fold

- Frequently associated with secondary ulcerative keratitis
- Brachycephalic breeds: Pekingese, English bulldog, pug, French bulldog, Boston terrier
- Persian cats

Lip Fold

- Common in dogs with excessive mandibular labial tissue, such as spaniels, Saint Bernard, Irish setter, Newfoundland, golden retriever, and Labrador retriever.
- Redundant lip fold is usually located behind the mandibular canine tooth.
- Can be bilateral.
- Causes severe halitosis.
- May occur after partial mandibulectomy or maxillectomy if a skin fold is created during wound closure.

Body Fold

- Usually affects obese or Chinese shar-pei dogs.
- With shar-pei puppies, body folds become less redundant with growth but persist on the head and face.
- May occur in female dogs or cats along the abdominal midline if mammary glands or body fat creates a skin fold.
- Moist seborrhea predisposes the animal to body fold pyoderma.
- Pendulous cervical skin may result in body fold pyoderma, especially if generalized skin disease exists.
- Folds left after surgery (i.e., total ear canal ablation) or created by surgery may result in residual fold pyoderma.

Vulvar Fold

- Most common in older, obese, spayed female dogs and rarely cats.
- Seen in younger dogs with infantile vulvas.
- Accumulation of urine and vaginal secretions occur.

▼ ***Key Point*** Chronic or relapsing urinary tract infection is commonly secondary to vulvar fold pyoderma and recessed vulva.

Tail Fold ("Screw Tail")

- Common in English bulldog, pug, Boston terrier, and schipperke breeds.
- Also seen in Manx cats.
- Caused by redundant skin around the tail and the corkscrew conformation of the terminal coccygeal vertebrae.
- A full-thickness ulcer may be present in the skin under the ventrally deviating tail. This can be very painful and uncomfortable for affected dogs.
- Contamination by fecal flora causes fulminating pyoderma.
- Self-trauma and scooting exacerbate the condition.

PREOPERATIVE CONSIDERATIONS

- Conservative treatment, including clipping hair from the skin fold and cleansing with dilute antibacterial solutions, medicated soaps, antiseborrheic shampoos, astringents, and topical and systemic antibiotics, is palliative only.
- Medical treatment may be advisable before surgery in some animals to lessen the amount of wound exudate and to lower bacterial numbers at the time of surgery (see Chapter 38).
- In the presence of severe infection (i.e., tail fold pyoderma), use a perioperative antimicrobial (e.g., cephalosporins) to help prevent a postoperative wound infection.
- When show animals are affected, counsel the owner with regard to the expected postoperative appearance and consult breed requirements for show.
- Perform urine culture and treat urinary tract infection prior to vulvar fold excision.

SURGICAL PROCEDURES

Objectives

- En bloc excision of the skin fold and associated pyoderma
- Wound closure without excessive tension
- Resolution of wound infection

Equipment

- Standard general surgical pack.
- Suture material appropriate for infected wounds (e.g., polydioxanone for subcutaneous tissues and monofilament nylon for skin).
- Bone-holding forceps aid manipulation of the tail during caudectomy for screw tail.
- Bone-cutting forceps or Gigli saw for caudectomy.
- Penrose drains (most commonly for screw tail excision).
- Sterile skin marking pen

Technique

1. Facial or Nasal Fold Excision

a. Position the animal in ventral recumbency.
b. Protect the eyes with an ophthalmic ointment during preparation and surgery.
c. Clip hair from the facial skin folds and ventral eyelids sufficient to drape an appropriate margin around the fold to be excised.
d. Plan and mark (with sterile marking pen) the boundaries of the incision so that removal of too much skin is avoided. Skin is needed for closure without tension (Fig. 54-1*A*).
e. With two paired incisions, excise enough of the facial fold to alleviate the recess created by the fold and to eliminate any chance of hair contacting the eye.

▼ ***Key Point*** Stay at least 1 cm from the medial canthus of the eye, and avoid lacrimal structures and large vessels in the region.

f. Undermine skin edges gently and carefully, if required.
g. Close in two layers using fine (3-0 or 4-0) absorbable suture for subcutaneous tissue and fine monofilament suture for skin closure (Fig. 54-1*B*).

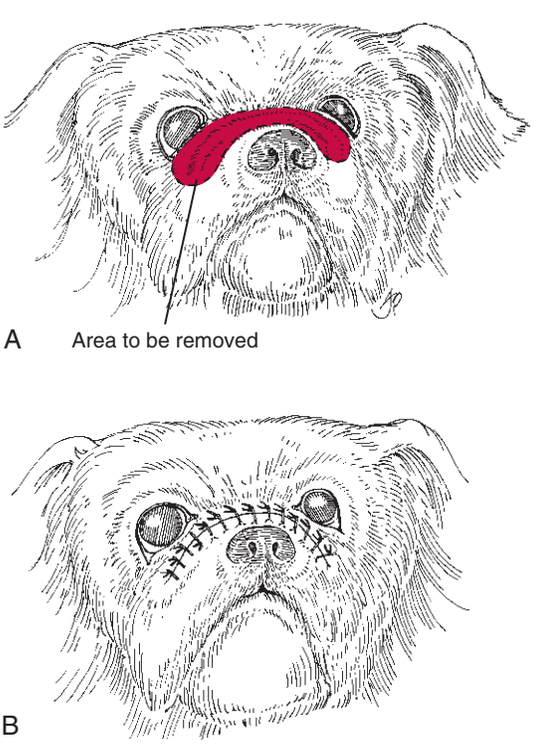

Figure 54-1. Facial fold excision. *A,* Incision boundaries (dotted lines) are planned so that enough skin for closure without tension remains. *B,* Final suture pattern.

h. Cut the suture ends short so that they do not contact the cornea.
i. Alternatively, use an intradermal pattern using fine absorbable suture, eliminating the need for suture removal.

2. Lip Fold Excision (Cheiloplasty)

a. Position the animal in dorsal recumbency.
b. Clip and prepare the skin over the mandible from its rostral tip to the mandibular angle (Fig. 54-2*A*).
c. Make an elliptical incision around the lip fold, and remove the entire fold and infected region (Fig. 54-2*B*).
d. It is very rare that the mucosal surface of the lip needs to be incised.
e. Try to avoid incising the underlying muscles of the lip.
f. Close the incision in two layers using fine absorbable suture for subcutaneous tissue and fine non-absorbable suture for skin (Fig. 54-2*C*).
g. Close the buccal mucosa, if incised, with fine, interrupted absorbable sutures.

3. Body Fold Excision

a. Position the dog so that optimal access to the body fold to be removed is accomplished.
b. Prepare the skin wide enough so the fold can be excised in its entirety.
c. Make two incisions parallel to the fold near its base, being certain to leave sufficient skin for closure.
d. Closure is done in two layers using fine absorbable suture for subcutaneous tissues and interrupted non-absorbable sutures for skin apposition.
e. Mastectomy (see Chapter 29) may be required to resolve body fold pyoderma that has resulted from rolls of abdominal fat or from pendulous mammary tissue.

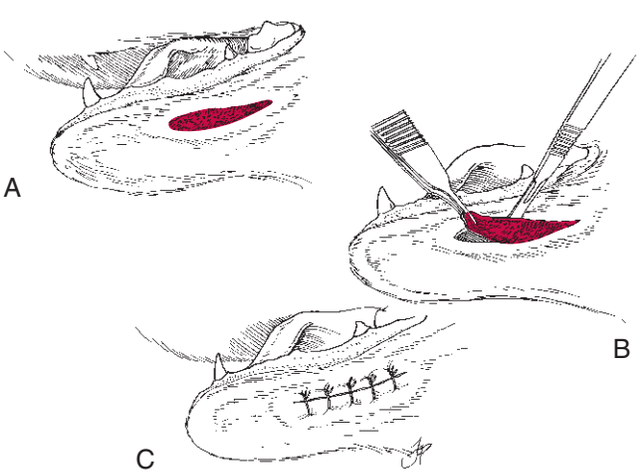

Figure 54-2. Lip fold excision (cheiloplasty). *A,* Preparation of skin. *B,* Excision of fold. *C,* Closure pattern.

4. Vulvar Fold Excision (Episioplasty)

a. Place the animal in ventral recumbency with the perineal region at the end of the table. If the rear legs are draped over the end of the table, be sure to pad them sufficiently.
b. Express the anal sacs, and place a purse-string suture around the anus.
c. Prepare the perivulvar region for aseptic surgery.
d. Mark the proposed skin incision. Make an elliptical incision around the base of the vulvar fold, then undermine and remove the incised area of skin (Fig. 54-3*A*).
e. Starting with the most dorsal suture, place simple, interrupted cuticular sutures equidistant from one another around the incision to approximate the wound margins (Fig. 54-3*B*). This step helps determine if adequate skin and subcutaneous fat have been removed.
f. Close the skin in two layers using fine absorbable suture for subcutaneous tissue and fine non-absorbable sutures for skin (Fig. 54-3*C*).
g. Remove the purse-string suture.

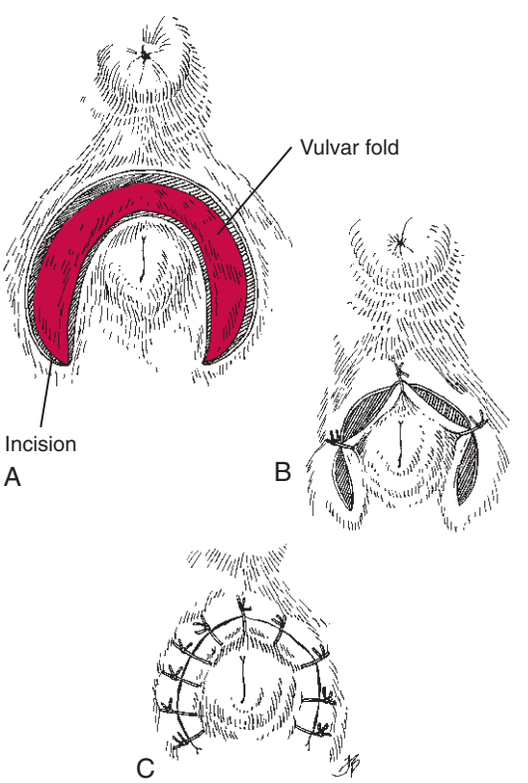

Figure 54-3. Vulvar fold excision (episioplasty). *A,* Incision pattern around the base of the vulvar fold. *B,* Simple sutures approximate the wound margin. *C,* Suture pattern.

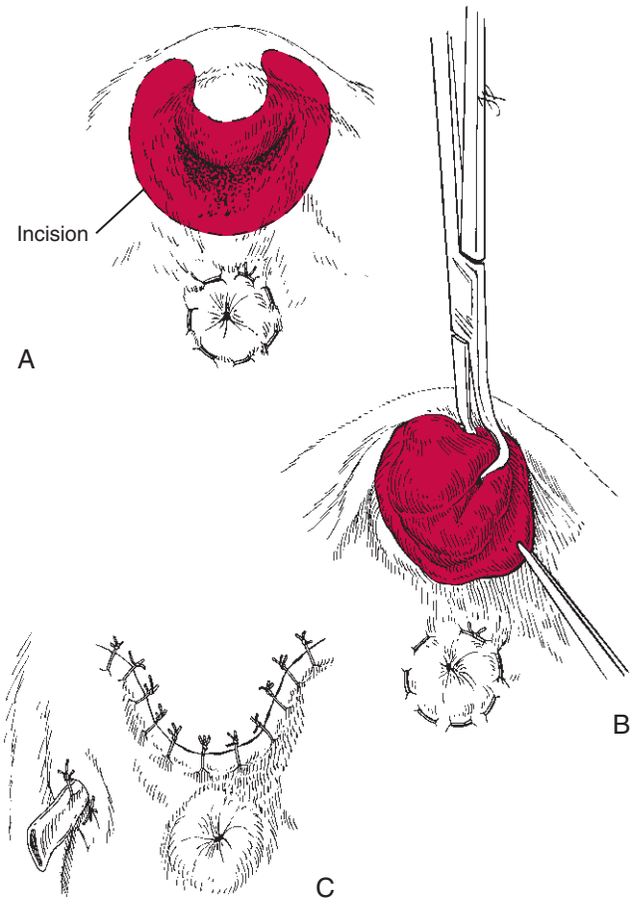

Figure 54-4. Tail fold excision and caudectomy. *A,* Place a purse-string suture around the anus, and incise the tail fold region as shown. *B,* Manipulate the tail with tail-holding forceps. *C,* Wound closure pattern and drain.

5. Tail Fold Excision and Caudectomy

a. Place the animal in ventral recumbency with the perineum facing the end of the table. A frog-leg position is used for this procedure.
b. Express the anal sacs, and place a purse-string suture around the anus.
c. Clip the entire perineum and tail-head region.
d. It is difficult to clip hair from the fold region adequately; therefore, give an antimicrobial drug perioperatively.
e. Make an incision around the tail and tail fold. Skin dorsal to the tail may be preserved and aids in cosmetic skin closure (Fig. 54-4*A*).
f. Attempt to dissect around the tail and skin fold without penetrating the fold.
g. Sometimes, because ventral deviation of the tail causes full-thickness erosion through the skin and en bloc excision cannot be performed, layered debridement must be done.
h. Manipulate the tail using bone-holding forceps (Fig. 54-4*B*).
i. Incise coccygeal and levator ani muscular attachments.
j. Using a Gigli wire or bone-cutting forceps, transect the tail rostral to its ventral deviation.

▼ ***Key Point*** Be careful during transection of the tail not to traumatize the rectum, which is just ventral to the tail base. The rectum may not be easily seen because of overlying muscle and granulation tissue associated with the ulcerated wound that sometimes underlies the ventrally deviated tail.

k. Liberally flush the surgical site with sterile saline.
l. Use several interrupted absorbable sutures to close dead space.
m. Place Penrose drains at this time, if necessary.
n. Close the wound in two layers, using fine absorbable sutures for subcutaneous tissues and fine non-absorbable sutures for skin apposition (Fig. 54-4*C*).
o. Remove the purse-string suture.

POSTOPERATIVE CARE AND COMPLICATIONS

Postoperative Care

- Prevent self-trauma (place an Elizabethan collar).
- Antimicrobial therapy may be given, based on culture and sensitivity testing, if deemed necessary.
- Keep oral incisions free of food and saliva by gentle cleansing.
- Keep perineal incisions clean, and remove fecal contamination.
- Remove Penrose drains in 3 to 5 days.
- Reassess urinary tract infection after vulvar fold excision (episioplasty) by reculture of the urine 2 to 3 weeks postoperatively.

Complications

- Self-trauma
- Wound infection
- Dehiscence
- Ectropion (aggressive facial fold removal)
- Insufficient skin fold removal (relapse of pyoderma)

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Chapter 55

Management of the Traumatic Wound by Primary Closure

Mark W. Bohling / Steven F. Swaim

Following proper initial management of a traumatic wound by debridement and lavage, the wound may be closed. Sufficient viable tissue must be present to allow closure without excessive tension. Wounds may be closed by primary closure, delayed primary closure, or secondary closure. See Chapter 56 for a discussion of open wound management.

ANATOMY

- Dogs and cats have abundant skin on the trunk and neck but a sparsity of skin on the distal limbs, tail, ear, and rostral areas of the head.
- Direct cutaneous vessels run parallel to the skin's surface and supply the subdermal plexus of the skin. See Chapter 57 for more details regarding blood supply to the skin.
- Some areas of the body have panniculus musculature underlying the skin. The skin's blood supply runs both superficial and deep to this musculature.
- Other areas of the body have loose areolar fascia deep to the dermis in which vasculature is located, and in other areas the skin is closely associated with underlying fascia.

PREOPERATIVE CONSIDERATIONS

▼ ***Key Point*** If a traumatically induced wound is to be closed, it is imperative that the tissues be viable and clean enough that wound healing can progress uneventfully. Perform adequate debridement and lavage.

- Perform a thorough physical examination and appropriate diagnostic tests on all traumatized animals to rule out associated injuries.
- Perform primary closure when:
  - The animal is in good condition.
  - A short time (6–12 hours) has elapsed since injury.
  - Minimal contamination and tissue trauma have occurred.
  - Adequate debridement and lavage have been done.
  - Adequate hemostasis has been attained.
- Perform delayed primary closure when:
  - Wounds show evidence of heavy contamination, purulent exudate, residual necrotic or questionable tissue, edema, erythema at the wound margins, lymphangitis, and skin tension.
  - Local infection has been controlled by staged debridement, lavage, topical and/or systemic antibiotics, and appropriate bandages. This is usually 3 to 5 days after wounding.
- Perform a secondary closure when:
  - The wound is in the reparative stage of healing at presentation, with a healthy bed of granulation tissue and evidence of epithelialization.
  - The wound has disrupted and has subsequently developed a healthy bed of granulation tissue.
  - It has been necessary to leave the wound open for longer than 5 days to control infection (see Preoperative Considerations, Delayed Primary Closure, Local Infection Control).

SURGICAL PROCEDURES

Primary or Delayed Primary Closure without Tension

Objectives

- Close the wound.
- Provide drainage if necessary.

Equipment

- Standard general surgical pack
- Undyed polyglactin 910, polyglecaprone, dyed or undyed polydioxanone, 2-0 to 4-0 (Vicryl, Monocryl, or PDS II; Ethicon, Somerville, NJ.) and polypropylene or nylon, 2-0 and 3-0 (Prolene or Ethilon, Ethicon, Somerville, NJ.)
- Wound lavage solution of 0.05% chlorhexidine diacetate or gluconate (Nolvasan Solution, Fort Dodge, IA. or ChlorhexiDerm Disinfectant, DVM Pharmaceuticals, Miami, FL.)

Technique

1. Pack the wound with sterile surgical sponges moistened with physiologic saline, or with water-soluble sterile lubricant (K-Y Jelly, Johnson & Johnson, New Brunswick, NJ.) or water-soluble sterile lubricant that contains chlorhexidine gluconate (Surgilube, E. Fougera & Co., Mellville, NY.)
2. Prepare the area around the wound for aseptic surgery.
3. Remove the wound packing or sterile lubricant.
4. Lavage the wound frequently with sterile isotonic fluids (or a solution of 0.05% chlorhexidine diacetate or gluconate) during surgery along with removal of devitalized tissue and debris as indicated.
5. Use as few simple interrupted absorbable sutures as necessary to close dead space in deep layers of the wound.
6. Be careful not to entrap major vessels or nerves in the sutures.
7. Place a drain (Penrose drain, or a closed suction drain [Jackson-Pratt]) if there is any possibility of residual dead space and/or wound drainage.
8. Place a simple continuous suture in the subcutaneous tissue at the wound edge using absorbable suture material.
9. Close the skin with non-absorbable simple interrupted sutures.

Postoperative Care and Complications

- Postoperative care
  - Place absorbent surgical sponges over the suture line, with extra sponges over the end of a Penrose drain.
  - Apply an absorbent secondary wrap to the area, followed by an outer wrap of porous adhesive tape.
  - Change the bandage every second or third day if there is no concern about possible complications. Change the bandage daily if there is concern about possible complications and/or a drain has been placed. The amount and nature of drainage should be assessed at each bandage change.
  - Remove the drain and discontinue bandaging when the drainage becomes minimal and is the same in quantity at successive bandage changes.
  - Remove the skin sutures 7 to 10 days postoperatively.
- Complications: Hematoma, seroma, or infection may result from improper wound evaluation, debridement, lavage, closure, or drain management.

Primary, Delayed Primary, or Secondary Closure with Tension

Objectives

- Close the wound.
- Relieve tension on the skin edges.
- Provide drainage if necessary.

Equipment

- See equipment under Primary or Delayed Primary Closure *Without* Tension.

Technique

1. The general techniques for closure of wounds with tension are the same as those for primary or delayed primary closure without tension (see previous section), with the exception of suture pattern (see tension-relieving suture patterns discussed subsequently).
2. Wounds that are in the reparative stage of healing with healthy granulation tissue and epithelialization.
   a. Excise epithelium from the edge of the wound, leaving healthy granulation tissue in the center.
   b. Gently clean the surface of the granulation tissue with 0.05% chlorhexidine solution (Fig. 55-1).
3. Gently undermine the skin surrounding the wound.
   a. Undermine bluntly, using Metzenbaum scissors, leaving some loose areolar connective tissue on the dermis or undermine beneath panniculus musculature if present.
   b. Undermine sharply with scissors or scalpel blade in areas where skin is closely associated with the underlying fascia.

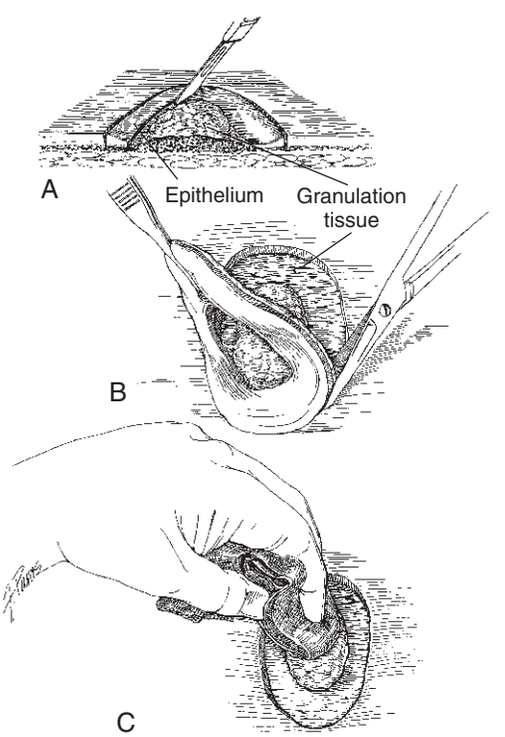

Figure 55-1. Preparation of a wound in the reparative stage of healing for secondary closure. *A,* Incising the epithelium. *B,* Removing the epithelium. *C,* Cleaning the surface of the healthy granulation tissue.

▼ ***Key Point*** Leave large identifiable blood vessels (i.e., direct cutaneous blood vessels) intact when undermining. Use good judgment when manipulating recently traumatized skin to avoid added insult to skin vasculature, which could result in skin slough.

4. One of the following tension-relieving suture patterns may be used to close the wound.
   a. Place "walking" sutures (our choice for closing wounds under tension) with absorbable material in staggered parallel rows, with bites oriented perpendicular to the wound edges to help preserve blood supply. Begin just in front of the plane where undermining stopped. Place a simple continuous subcuticular absorbable suture along the wound edge before skin closure with non-absorbable simple interrupted sutures (Fig. 55-2).
   b. Place an absorbable intradermal continuous horizontal mattress suture to appose the skin edges. This can be reinforced with non-absorbable simple interrupted skin sutures (Fig. 55-3).

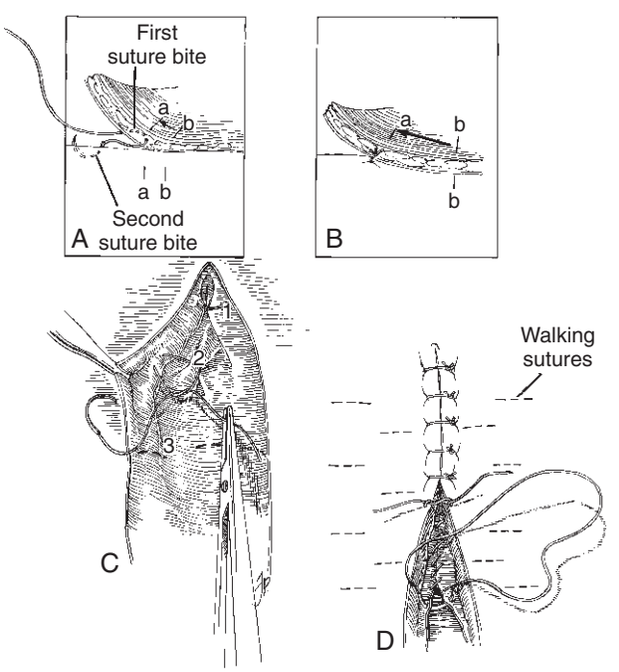

Figure 55-2. "Walking" sutures. *A,* Placing first and second suture bites. Segment of skin to be stretched (from a to b). *B,* Tying a "walking" suture advances the skin toward the center of the wound (a to b increased). *C,* "Walking" sutures placed in rows. 1, Walking suture tied; 2, placing a walking suture; 3, areas where bites will be taken for a walking suture *(broken lines). D,* Placing a simple continuous subcuticular suture along the wound edge, and simple interrupted skin apposition sutures. Broken lines are buried walking sutures. (After Swaim SF: The repair of the skin: Techniques of plastic and reconstructive surgery. *In* Bedford PGC, ed.: Atlas of Canine Surgical Techniques. Oxford: Blackwell Scientific Publications, 1984, p 49; and Swaim SF, Henderson RA: Small Animal Wound Management, 2nd Ed. Baltimore: Williams & Wilkins, 1997, p 154.)

   c. Place non-absorbable vertical mattress sutures near the wound edge over segments of Penrose drain. Use simple interrupted non-absorbable sutures to appose skin edges (Fig. 55-4).
   d. Place non-absorbable "far-near-near-far" or "far-far-near-near" sutures in the order of their names to act as apposition and tension sutures (Fig. 55-5).
   e. Preplace non-absorbable stent sutures deep to the wound tissues prior to closure of the wound. These sutures are then tied over a roll of surgical

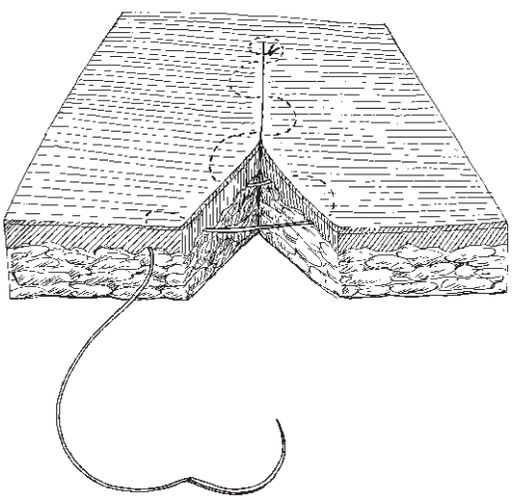

Figure 55-3. Intradermal sutures. Using 3-0 or smaller absorbable suture material in a continuous pattern, place intradermal sutures with each bite being passed horizontally. (Redrawn from Scardino MS, Swaim SF, Henderson RA, Wilson ER: Enhancing wound closure on the limbs. Compend Contin Educ 18:919, 1996.)

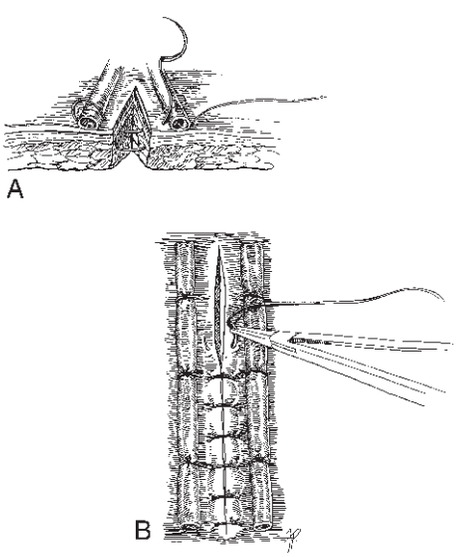

Figure 55-4. Vertical mattress tension sutures. *A,* Vertical mattress sutures placed over Penrose drains. *B,* Simple interrupted skin apposition sutures used with tension sutures.

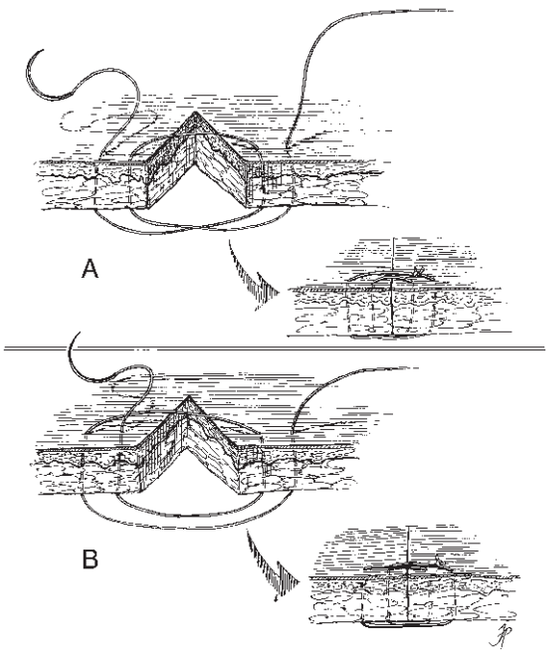

Figure 55-5. Combination apposition and tension sutures. *A,* "Far-near-near-far" sutures. *B,* "Far-far-near-near" sutures. (After Swaim SF, Henderson RA: Small Animal Wound Management, 2nd Ed. Baltimore: Williams & Wilkins, 1997, p 165.)

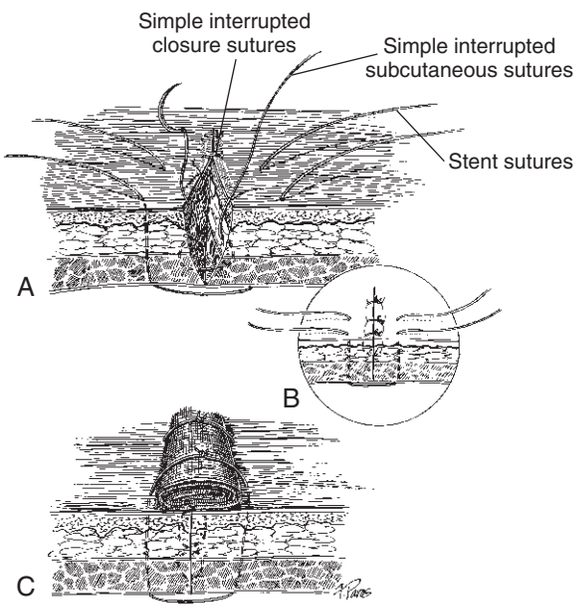

Figure 55-6. Stent sutures. *A,* Preplace stent sutures deep to the wound tissues. *B,* Wound tissues are closed. *C,* Tie stent sutures over a roll of gauze or rolled towel.

sponges or a rolled towel to act as a tension suture as well as to obliterate dead space (Fig. 55-6).

f. Place nonabsorbable Lembert sutures in the skin adjacent to the wound the day before surgery. The sutures are tied under tension. The following day, the "presutures" are removed and the wound is closed using the prestretched skin (Fig. 55-7).

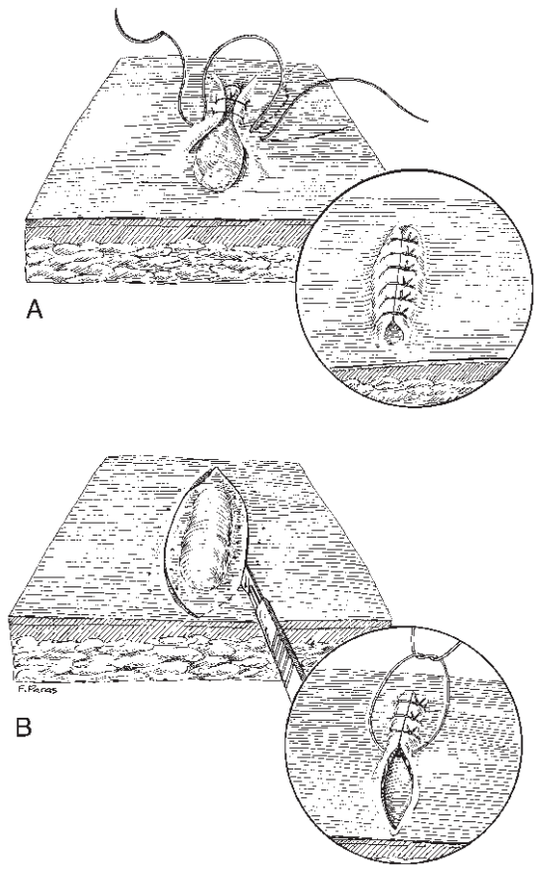

Figure 55-7. Presutures. *A,* The day before surgery, suture the skin adjacent to the lesion over the lesion using a Lembert suture pattern. *B,* The following day, remove the presutures and excise the lesion. *Inset,* Close the resulting defect or wound using the stretched skin made available by the presutures. (Redrawn from Scardino MS, Swaim SF, Henderson RA, Wilson ER: Enhancing wound closure on the limbs. Compend Contin Educ 18:919, 1996.)

g. On wounds that cannot be closed, or to help prevent further wound edge retraction, place a monofilament non-absorbable intradermal continuous horizontal mattress suture. The ends are left untied and a button and two fishing weights (split shot) are placed on each end of the suture. Traction is placed on each free suture end daily to advance the edges toward each other. Two new split shots are placed on the suture adjacent to the button after each tightening to hold the edges under tension and advance them toward the wound center (Fig. 55-8). Use "environmentally friendly" (tin) split shots to prevent lead toxicity in case the patient should chew at the wound site and swallow the split shots.

h. Another technique for closing wounds that are under considerable tension is the "pulley" suture (Fig. 55-9). This is a 4-bite buried interrupted

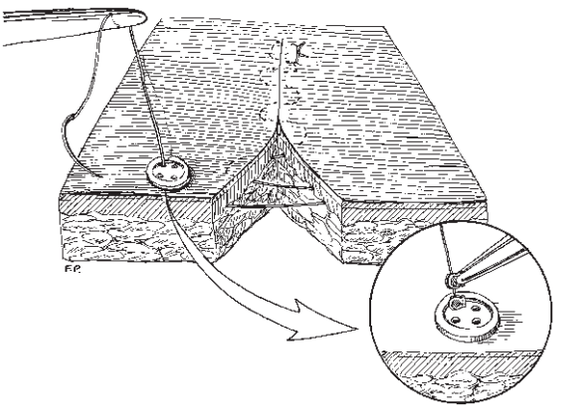

Figure 55-8. A half-buried horizontal mattress suture starts the suture at one end. Then advance the suture as an intradermal horizontal mattress suture with each bite slightly advanced. On the final bite, pass the needle through the entire thickness of the skin and through a hole in a sterile button. After the wound edges are advanced as far as possible, use two split shots to hold the suture tight (see *inset*). (Redrawn from Scardino MS, Swaim SF, Henderson RA, Wilson ER: Enhancing wound closure on the limbs. Compend Contin Educ 18:919, 1996.)

pattern with bites engaging the deep layer (underside) of the dermis. A monofilament absorbable suture such as PDS is used, in sizes 3-0 or 2-0. Multiple bites produce a mechanical advantage, like a pulley, that reduces the tension required to close the wound.

5. Use one of the following relaxing incisions for additional tension release.
   a. Make unilateral or bilateral bipedicle flaps when undermining does not provide enough relaxation for wound closure. Make an incision parallel to the wound's long axis but slightly curved toward the wound, with the width of the created flaps being equal to the wound width. Use absorbable "walking" sutures to advance and tack the flaps in place and a regular or tension-relieving suture pattern to suture the skin. Close the defects that resulted from moving the flaps (Fig. 55-10).
   b. Make unilateral or bilateral simple relaxing incisions as in creating a bipedicle flap. Move the flaps and suture in place as with bipedicle flaps. Do not close the defects that remain from moving the flaps, but leave them to heal as open wounds (Fig. 55-11).

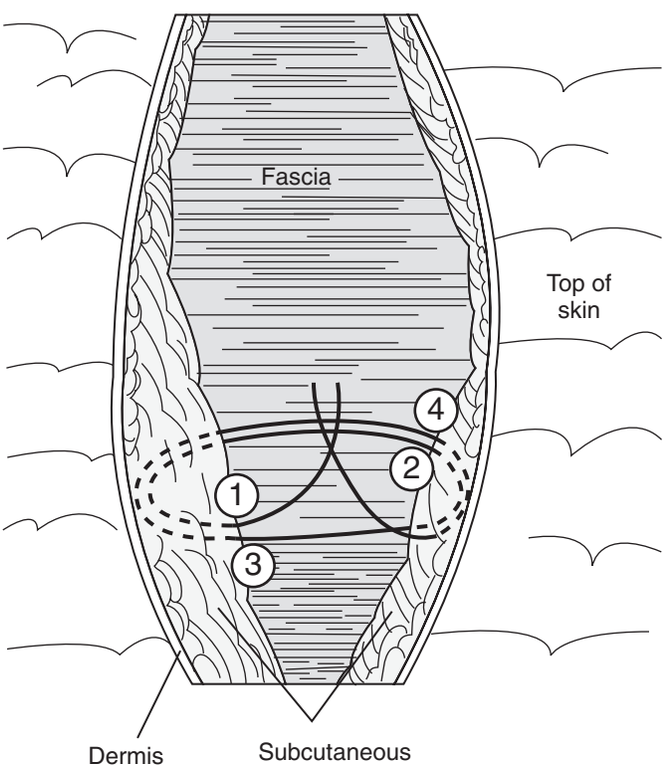

Figure 55-9. Pulley suture. This is the same as a "buried" simple interrupted suture, except that four suture bites (two on each side of the incision) are taken instead of two, creating two loops through the tissue instead of the usual single one. All bites are placed in the deep layer (underside) of the dermis to provide solid purchase in the tissue for closure against tension.

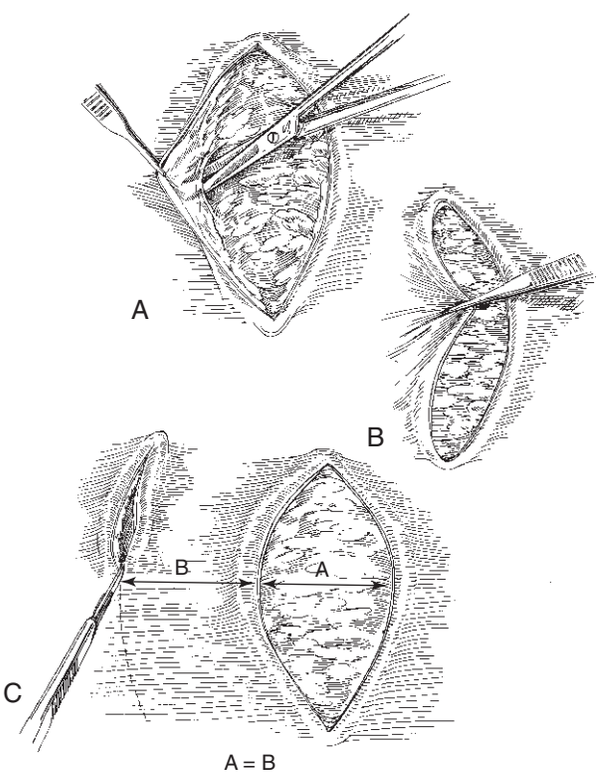

Figure 55-10. Unilateral bipedicle flap. *A,* Undermining the skin on the side of defect from which the flap will come. *B,* Checking to see if undermining provided sufficient skin for wound closure. *C,* Making an incision to create a bipedicle flap. Wound and flap width are equal (A = B).

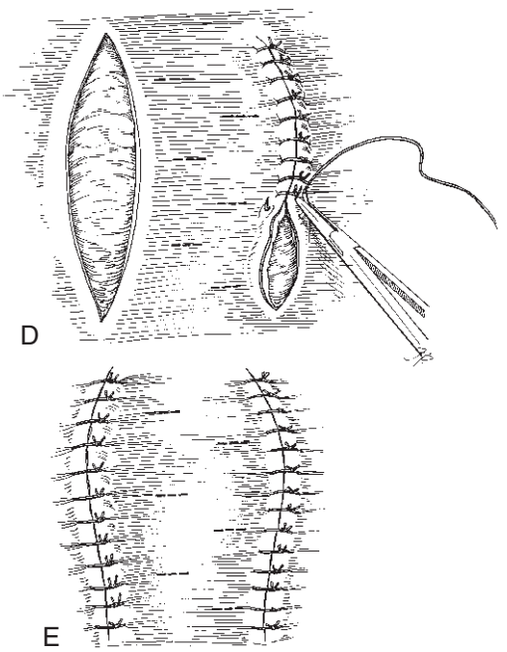

Figure 55-10, cont'd *D,* Flap being sutured into position after walking sutures have advanced it *(broken lines). E,* Donor site sutured. (After Swaim SF, Henderson RA: Small Animal Wound Management. 2nd Ed. Philadelphia: Williams & Wilkins, 1997, p 176.)

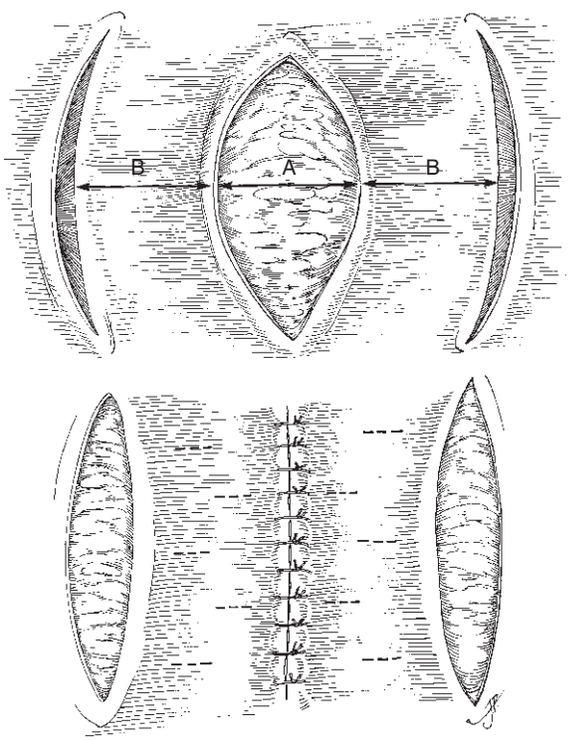

Figure 55-11. Bilateral simple relaxing incisions. *Top,* One bipedicle flap has been created on each side of the wound, with flaps equal in width to the defect width (A = B). *Bottom,* After undermining and moving the flaps with walking sutures *(broken lines)* to close the wound, leave the relaxing incision defects to heal as open wounds. (After Swaim SF, Henderson RA: Small Animal Wound Management. 2nd Ed. Philadelphia: Williams & Wilkins, 1997, p 177.)

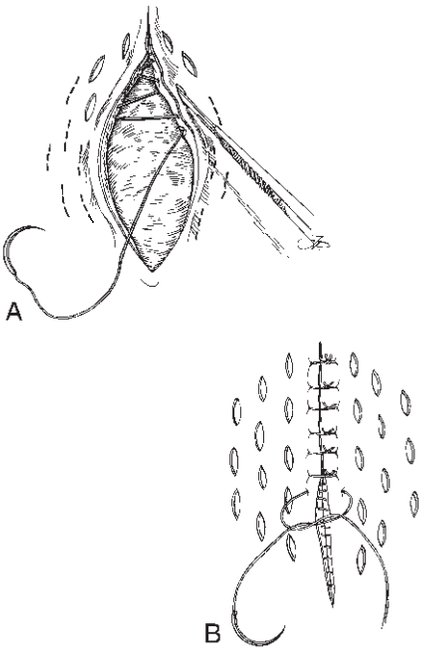

Figure 55-12. Multiple punctate relaxing incisions. *A,* Make parallel staggered rows of incisions as needed on both sides of a wound while a simple continuous intradermal suture is placed and tightened. *B,* Final wound apposition with simple interrupted sutures. (After Swaim SF, Henderson RA: Small Animal Wound Management. 2nd Ed. Philadelphia: Williams & Wilkins, 1997, pp 189–190.)

c. Make multiple, punctate, relaxing incisions 1 cm long and 0.5 cm apart in parallel, staggered rows bilaterally, as needed to allow wound closure as a simple continuous intradermal absorbable suture is placed and tightened. Final skin apposition is with simple interrupted, non-absorbable sutures (Fig. 55-12).
d. Design and incise a 60-degree equal angle, equal limb-length Z-plasty adjacent to the wound with the central limb of the Z in the direction in which relaxation is needed. After undermining the skin edges and Z-plasty flaps, close the wound using regular or tension sutures. Suture the Z-plasty flaps into their new positions (Fig. 55-13).
e. Make a V-shaped incision adjacent to the wound with the point of the V away from the wound. After undermining the resulting skin flap, use absorbable walking sutures to advance and tack the flap in place. A regular or tension suture pattern is used to suture the original skin defect. Close the V with simple interrupted non-absorbable sutures, beginning at the ends. When tension develops, close the remainder of the defect, beginning at the point of the V to form a Y-shaped suture line (Fig. 55-14).
f. Many traumatic wounds result in a large circular or nearly circular skin defect, especially after debridement is completed. Closure of these

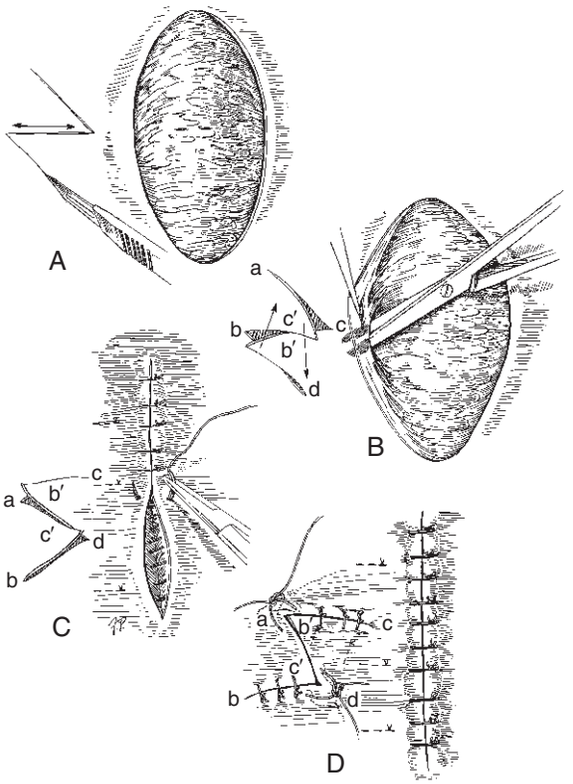

Figure 55-13. Z-plasty as a relaxing incision for wound closure. *A,* Make a 60 degree equal-angle, equal-limb-length Z-plasty designed adjacent to a wound, with the central limb in the direction relaxation is needed. *B,* Z-plasty has been cut. Undermine Z-plasty flaps and adjacent skin (*arrows* indicate Z-plasty flap transposition). *C,* Closure of the defect with automatic transposition of Z-plasty flaps. *D,* Suturing the Z-plasty flaps into their new positions. (After Swaim SF, Henderson RA: Small Animal Wound Management. 2nd Ed. Philadelphia: Williams & Wilkins, 1997, p 186.)

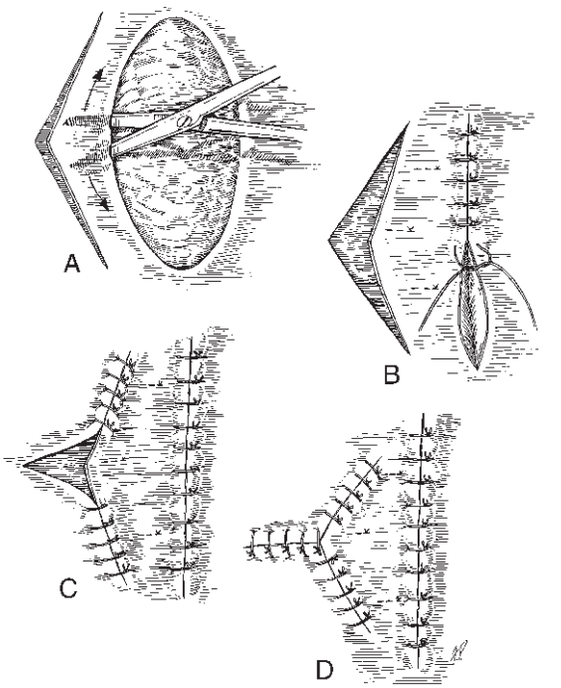

Figure 55-14. V-to-Y plasty relaxing incision. *A,* Make a V-shaped incision adjacent to the defect with point of the V away from the defect. Undermine skin between the defect and incision. *B,* Closure of the defect with walking sutures holding the flap in position *(broken lines). C,* Closure of the V-shaped incision, beginning at the ends. *D,* Closure of the stem of the Y. (After Swaim SF, Henderson RA: Small Animal Wound Management. 2nd Ed. Philadelphia: Williams & Wilkins, 1997, pp 181–182.)

defects can be problematic, particularly when they are located on a limb or other location lacking abundant adjacent skin for closure. The combined-V closure (Fig. 55-15) is often useful for such situations. Two V-shaped flaps, with width and length equal to the radius of the defect, are created as equilateral triangles. The central axis of the triangles is 45 degrees from the long axis of the wound along the line of greatest skin tension. The skin flaps are made by incising only two sides of the triangles, forming two V-shaped incisions with their points directed towards the long axis of the wound. After the flaps are incised and undermined, they are transposed and the flap tips are tacked into position. When the flap tip is sutured to the side of the circular defect, the original circular defect is converted into smaller, irregular fusiform defects. These defects are closed with simple interrupted sutures, beginning with a suture in the center of the defect to divide its length in half and continuing to divide the defect in half with each subsequent suture; this ensures an even approximation of skin over the unequal sides of the defect.

6. Drains to prevent dead space are generally not needed in wounds sutured under tension, especially if open relaxing incisions have been made.

Postoperative Care

- Bandaging is similar to that for postoperative care of wounds closed without tension. Do not remove "walking" sutures and absorbable intradermal continuous horizontal mattress sutures. Remove vertical mattress tension sutures after 3 to 4 days. Remove "far-near-near-far" and "far-far-near-near" sutures at about 10 days. Remove stent sutures after 7 to 10 days, and remove presutures within 24 hours after their placement. The adjustable horizontal mattress suture (see Fig. 55-8) may be left in place and tightened daily for several days to a week.
- Prevent self-mutilation of wounds with an Elizabethan collar or other device such as a cervical collar (Bite Not Products or Jorgensen Laboratories) or side braces, as necessary.

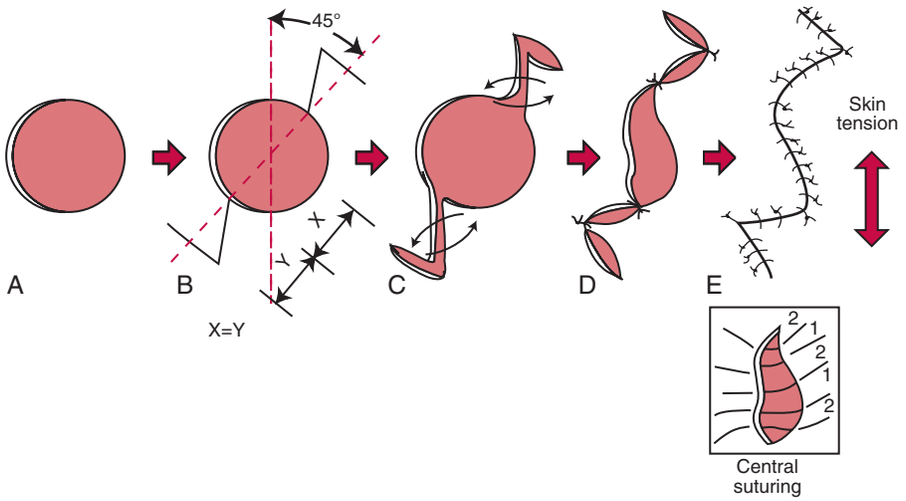

Figure 55-15. Combined-V closure of a circular skin defect. *A,* Circular defect. *B,* V-shaped flaps oriented 45 degrees off and pointing toward the line of greatest tension. Flap width (y) equals radius of the defect (x). *C,* Arrows showing transposition of the flaps. *D,* Flap tips sutured into place, creating a series of irregular fusiform defects. *E,* The completed closure. Skin from each V-shaped flap closes half of the original circular defect. *Inset,* Central suturing technique. A suture is placed at the center of each defect, subdividing it into smaller and smaller defects until it is closed. (First sutures = 1, subsequent sutures = 2.) (After Swaim SF, Henderson RA: Small Animal Wound Management. 2nd Ed. Philadelphia: Williams & Wilkins, 1997, p 266–67.)

Postoperative Complications

- When vertical mattress tension sutures are applied, there may be areas of pressure necrosis of the skin near the wound edge under the Penrose drain segments.
- Simple relaxing incisions may result in a wound equal in size to the closed wound.
- Large and numerous multiple punctate relaxing incisions may result in good tension relief but may jeopardize the blood supply to the skin between incisions with a resultant slough. Utilizing the minimum number of incisions needed for wound closure will reduce the risk of this complication; this is achieved by placing a single row of punctate relaxing incisions at a time and checking wound tension after each row is placed.
- Skin closed too tightly around a limb may result in a "biologic tourniquet," with edema and hypothermia distal to the closure site. Skin closed too tightly around the thorax may result in impaired respiration. Consider suture removal to release the tension in such cases.

SUPPLEMENTAL READING

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Chapter

56 Management of the Open Wound

David W. Knapp

Open wound management is a method of treatment which should be considered when immediate primary wound closure is not possible. Wound healing is a complicated biologic process involving inflammatory, debridement, reparative, and maturation phases. When managing a wound in an open fashion, one or all of these biologic phases may come into play. To employ open wound management techniques successfully requires a thorough understanding of the phases of wound healing. For more comprehensive descriptions of basic wound healing, see other texts. As a large percentage of wounds are associated with traumatic events, the following material is focused on traumatic wounds and skin defects. However, the same principles may be applied to defects created by surgical excision of tumors, restrictive scar tissue, or dysfunctional tissues. The goal of wound management is to restore normal anatomy and function to the patient, when possible. Reconstruction of open wounds using skin flaps or grafts is discussed in Chapter 57.

ETIOLOGY OF OPEN WOUNDS

- Vehicular trauma resulting in lacerations and/or degloving injuries or shear forces creating a devascularized section of skin
- Bite wounds resulting in lacerations, punctures, or shearing/tearing defects
- Gunshot, stab injuries, or other forms of penetrating wounds
- Skin loss due to abscesses or embolic vascular events
- Burns resulting from thermal, electrical, chemical, and radiation injury
- Large defects resulting from surgical excision of lesions, especially tumors
- Defects created by circumferential restrictions such as casts, bandages, or choke collars caught in long haired pets, or full thickness defects (i.e., decubital ulcers)

PREOPERATIVE CONSIDERATIONS

Indications

Consider leaving a wound open as a method of treatment in the following situations:

- Grossly contaminated wounds. Consider the "golden period" of 8 hours from time of injury. Wounds are classified as clean (surgically created), clean contaminated (minimal contamination, which can be effectively removed) and contaminated (gross contamination with obvious foreign material).
- Wounds with established infections.
- Wounds with large skin losses or excessive tissue trauma, particularly wounds with questionable vascular supply and tissue viability or incomplete debridement. These wounds will have impaired host local defense systems and are more susceptible to infection if closed prematurely.
- Wounds with inadequate adjacent tissue available for closure. Wounds on the distal extremities and around the face often fall into this category.
- Wounds that would result in increased tension or excessive dead space if closed primarily.
- Wounds that have failed previous closures.
- Temporary wound management while awaiting results of orthopedic or neurologic diagnostics.
- Temporary wound management before grafting techniques, the use of skin expanders or skin stretchers, or while awaiting microscopic examination of wound margins following tumor excision.

Advantages of Open Wound Management

- Provides ability for continual debridement through surgical, mechanical, or chemical means.
- Provides for optimal wound drainage when compared with primary closure combined with other methods of drainage.

- Provides access for daily wound lavage when indicated.
- Provides for daily wound inspection to evaluate progress and to adjust treatment as indicated.

Disadvantages of Open Wound Management

- Labor-intensive, requiring more time and effort on the part of the veterinarian and owner.
- More expensive due to hospitalization and repeated bandage changes, often requiring anesthesia or sedation and tranquilization.
- The wound must be protected from further injury caused by exposure or self-mutilation.
- Increased risk of nosocomial or ascending infection.
- Protein loss from large wounds with excessive drainage.
- May result in increased healing time and prolonged discomfort for the patient.

INITIAL WOUND MANAGEMENT

Patient Evaluation

- Evaluate and treat as needed for concurrent life-threatening injuries, particularly hypovolemic shock, thoracic and/or abdominal trauma, and cerebral edema or hemorrhage.
- Evaluate for concurrent orthopedic or neurologic trauma (e.g., fractures, ligamentous or tendinous injuries, spinal cord injuries, or peripheral nerve damage). If necessary, obtain radiographs when the patient is stable.
  - Orthopedic. Orthopedic injuries are common and may be located at the wound site or distant from the open defect. Evaluate for fractures and ligamentous injuries in all cases of trauma-related wounds. Carefully palpate the long bones and joints for pain and stability and obtain radiographs when indicated. Stress views may be necessary to evaluate joint stability.
  - Neurologic. Assess neurologic injury through deep and superficial pain perception and motor function. It is uncommon for neurologic limb dysfunction to result from an injury to the lower portions of an extremity since most nerve function originates from higher segments.
- Evaluate wounds involving the extremities for vascular, orthopedic, and neurologic involvement. Any defect that is full circumference will likely create severe vascular compromise.
- Evaluate wounds of the thorax and abdomen for potential involvement of the deeper thoracic, peritoneal, and retroperitoneal cavities. If exploring and/or debriding a thoracic wound, always be prepared to assist in ventilation if pneumothorax is created.

▼ ***Key Point*** Vascular compromise may lead to loss of the limb; therefore, tissues distal to the wound should be carefully assessed. Several days may be required to fully appreciate the extent of vascular injuries. Shear and tearing injuries of the skin and subcutaneous tissues of the trunk may also result in delayed tissue necrosis and eventual loss.

- Patient factors to consider which affect wound healing are age, nourished verses malnourished, concurrent metabolic diseases such as diabetes, hyperadrenocorticism and uremia, hypoproteinemia, anemia, hepatic disease, and obesity. Immunocompromised patients are at greater risk of developing infections.
- Wound factors affecting management and healing include foreign material such as dirt, plant material, suture or surgical implants, wound exudates, bacteria/infection, and vascularity.

Initial Wound Evaluation

- Analgesic or anesthetic drugs (if necessary) aid in the evaluation and treatment of the wound, especially if extensive debridement and lavage are required (see Chapters 2 and 6). In cases where general anesthesia may not be safe and sedation alone is not completely effective, consider administering epidural analgesia to provide for a more comfortable and cooperative patient. Local blocks may also be helpful in certain circumstances. Always consider intravenous postoperative analgesia, during the recovery from surgical procedures, then as needed to facilitate comfort and management of the patient. Consider placing transdermal fentanyl patches for hospitalized patients. Continued wound management may require repeated use of analgesics or anesthesia, usually diminishing in use as the wound progresses through the healing stages.
- Use sterile gloves and instruments to help prevent further bacterial contamination.
- Consider the following during the initial evaluation:
  - The extent of tissue damage to both soft and osseous structures. Closely evaluate the vascular integrity of the wound.
  - The degree of contamination or probability of existing infection. Consider the time lag between the traumatic event and the presentation of the patient to the hospital.
  - The feasibility of successful primary closure.
  - If a limb is involved, the feasibility of the leg becoming functional again.
  - The anticipated time required as well as the expense to the owner.
- Obtain bacterial cultures in advance of wound debridement and lavage. Select antibiotics based on culture and sensitivity results. If necessary, a broad spectrum antibiotic may be used while awaiting culture results.

- If active bleeding is encountered, controlling hemorrhage is best accomplished with direct pressure or isolation and ligation of the vessel. Avoid placing tourniquets, which will result in increased circulatory compromise of an area already suffering decreased vascular perfusion.

Clipping and General Cleaning

Protect the wound from loose debris and hair during the initial preparation and clipping of the adjacent area. Use a sterile water-soluble gel to cover the defect, cover with saline moistened surgical sponges, or sterile towel clamps, sutures, skin staples, or wound clips to provide an economical and efficient temporary closure. Clip a generous margin surrounding a truncal wound or the expected bandaged portion of a limb and scrub with an antiseptic soap or solution.

Cleansing the Wound

Lavage Solution

The ideal lavage solution is sterile, non-irritating, non-cytotoxic, normothermic, and isotonic. Of available solutions, warmed sterile isotonic saline best meets these criteria. Lactated ringers solution may also be used.

- The use of antibiotic or antiseptic solutions for wound lavage is controversial. There is evidence for both beneficial and detrimental effects. Controversy exists between in vitro versus in vivo studies and the antibacterial versus the cytotoxic effects of varying concentrations of chlorhexidine and povidone-iodine solutions. Use a 0.5% to 1.0% chlorhexidine solution due to its broad-spectrum and extended residual activity.
- Tap water is an economical alternative to other commonly used sterile solutions, even though it does not meet all criteria for an ideal lavage solution. When large volumes are anticipated, tap water may be the most practical irrigation solution. Due to the hypotonic nature of distilled or sterile water, their use in lavage is not recommended.
- Effective lavage often depends more on the copious volume of fluid rather than the contents of the solution. The effect of lavage is to loosen and flush away from the wound any foreign material, damaged, necrotic or free tissue, wound exudates, and bacteria.
- Do not scrub the wound, which results in increased tissue damage due to mechanical trauma. Trauma to the tissue will result in increased inflammation, delayed healing, and increased risk of infection.

Lavage Delivery Systems

Delivery systems are categorized based on pressures at which the lavage solution is applied to the wound.

- *High-pressure systems* (e.g., Water Pik) deliver solutions at pressures near 60 psi. Advantages are their ability to dislodge debris and bacteria. A potential disadvantage is the possibility of driving bacteria into tissues near wound margins resulting in microabscessation.
- *Medium-pressure systems* deliver solutions at pressures near 7 to 8 psi, which has been shown to be effective in dislodging foreign material and bacteria without risk of driving bacteria into the wound. Such a system can be developed by using a 35-ml syringe and an 18-gauge needle. Systems which combine the syringe and needle with a three way stop cock and intravenous tubing will speed the process.
- *Low-pressure systems* are ineffective at dislodging bacteria and debris. Such systems include a syringe without a needle, a bulb syringe, and tap water delivered directly from the faucet.
- Removal of lavage solution from the wound by suction, very light pressure on gauze sponges placed over the wound, or gravity avoids dilution of opsonins necessary for phagocytosis.

Debridement

▼ ***Key Point*** Surgical debridement is the most effective method for removal of dead or devitalized tissue.

- Inspect and palpate questionable tissues to determine tissue viability. Signs suggestive of non-viable tissue include the following:
  - Black, bluish-black, or a shiny white discoloration (especially if there is a distinct demarcation between abnormal and normal color)
  - Lack of bleeding at wound margins
  - Texture is leathery to touch or skin is very thin and no pain sensation is detectable.
  - Skin temperature is cool.
  - Hair is easily epilated.
- Other methods of tissue viability determination include transcutaneous oxygen (PO_2), transcutaneous carbon dioxide (PCO_2), and ultrasonic Doppler flow detection. The use of intravenous dyes is not a reliable method of evaluation.
- Reddish discoloration or severe edema is not necessarily indicative of non-viable tissue. Such tissue should be managed conservatively in the initial treatment period.
- During each surgical debridement it is best to maintain a conservative approach, leaving critical tissue of questionable viability while surgically excising only confirmed non-viable tissue. Resect contaminated or devascularized fat to decrease the risk of bacterial propagation. Use a scalpel rather than scissors to decrease additional trauma to the wound. Preserve vessels, nerves, and tendons. Remove any devascular-

ized bone to prevent sequestra formation or delay of granulation tissue bridging the wound.
- Daily mechanical debridement may be accomplished when the primary layer of the bandage is removed. In cases of continued necrosis and tissue loss, repeated surgical debridement may be necessary in addition to the routine bandage changes.
- Chemical debridement is an enzymatic removal of devitalized tissue, while selectively sparing viable structures. Such treatments may be irritating to the healing wound bed.

Bandaging

Open wound management, in most cases, requires the use of some form of bandage.

Functions of the bandage include:

- Coverage of the wound to maintain cleanliness and control wound environment
- Provide support
- Decrease swelling/edema
- Control bleeding
- Reduce potential dead space

These bandages are composed of primary, secondary, and tertiary layers. If immobilization or support is indicated, splints of metal, plastic, or fiberglass may be incorporated between the secondary and tertiary layers. A comfortable bandage will increase the probability that it will be well tolerated by the patient. Use an Elizabethan collar when patients attempt to chew or remove the bandage.

Primary Contact Layer

The primary or contact layer of the bandage is that portion of the bandage applied directly over the wound.

When selecting a dressing consider the following properties:

- Facilitates removal of exudates
- Hinders secondary infection
- Maintains moisture at the wound surface
- Permits gaseous exchange
- Creates minimal wound trauma when removed

Dressings may be adherent or non-adherent. The primary layer is also defined as either semiocclusive or occlusive. A semiocclusive dressing permits oxygen to move across the dressing as well as exudates to move away from the wound surface and into the secondary layer. Occlusive dressings function to maintain moisture at the wound surface. The primary layer should remain in contact with the wound surface, even during movement.

The primary layer may serve to:

- Debride
- Facilitate removal of wound exudates
- Deliver medication
- Provide a protective layer over the wound

Adherent Dressings

- Adherent dressings are defined by their condition on application and removal and can be classified as wet-to-wet, wet-to-dry, and dry-to-dry. Wet dressings aid in the movement of viscous exudates away from the wound and into the secondary layer, while dry dressings adhere to necrotic tissue and debris, producing mechanical debridement when removed.

▼ ***Key Point*** *Wet-to-dry* dressings are the most frequently employed method in the early management of open wounds. These dressings allow for effective removal of exudate and mechanical debridement.

The fluid dilutes the exudates, facilitating its transfer into the secondary layer of the bandage. To apply a wet-to-dry dressing, soak sterile cotton gauze sponges in sterile saline or antiseptic solution, hand squeeze to remove excess solution, and place the sponges in contact with the wound bed, being sure to pack all recesses of the wound. Remove the dressings at 12- to 24-hour intervals, permitting the gauze to dry and adhere to necrotic tissue and debris which then provides mechanical debridement on removal of the gauze sponges. Rewetting the dried sponge with sterile saline may reduce patient discomfort during bandage removal. Continue wet-to-dry dressings only as long as mechanical debridement or excessive viscous exudate removal is necessary.

- *Wet-to-wet* dressings are used for wounds requiring removal of viscous exudates only, with no removal of necrotic tissue or debris necessary. Place sterile cotton gauze sponges soaked in sterile saline or another lavage solution in contact with the wound bed. The secondary layer is a non-absorbent material, which aids in maintaining a wet primary dressing.
- *Dry-to-dry* dressings are used on wounds with no exudate or very serous exudates, but do require mechanical debridement of necrotic tissue and debris. Place dry sterile cotton gauze sponges in contact with the wound bed. An absorbent secondary layer is not necessary with this method.

Nonadherent Dressings

- Use non-adherent dressings in the management of newly formed granulation tissue, where minimal disruption of the wound bed is desirable. They are commonly used following the methods previously described for adherent dressing techniques or for surgically created wounds not amenable to primary closure. These dressings serve to keep wounds moist and to promote epithelialization.
- *Semiocclusive nonadherent* dressings are composed of man-made materials such as polyester films (Telfa pads) or gauze sponges with a layer of a petrolatum-based product (Adaptic, Johnson & Johnson).

- *Occlusive non-adherent dressings* (e.g., Ulcer Dressing, Johnson & Johnson) do not allow for absorption of wound exudate, and therefore are used in non-exudative wounds. Occlusive dressings also prevent gaseous exchange. These dressings are left in place for longer periods of time, often 2 to 4 days. Disadvantages of occlusive dressings include difficulty in accessing wound progress due to their nontransparent nature as well as delaying wound contracture.
- *Occlusive dressings* speed re-epithelialization of partial-thickness defects. Constituents of occlusive dressings include polyethylene, polyurethane, hydrocolloids, and hydrogels.

Wound Medications

- Wound management continues to advance as increasing knowledge of cellular and chemical mediators within the wound environment are more clearly defined. The trend toward the use of natural and synthetic growth factors is increasing. In addition, products used for dressing wounds with additional wound surface interaction and enhancement of healing are available.

▼ ***Key Point*** Sugar can be used in open wounds. Granulated sugar draws macrophages into the wound thereby decreasing the need for surgical debridement; facilitating the formation of a protein layer thereby providing additional surface layer protection; creating a hyperosmotic environment which is bactericidal; providing a local nutritional source for the wound; decreasing edema; and promoting granulation and epithelialization.

- Application of a thin layer of sugar at each bandage change is not painful to the patient and easily accomplished at little expense.
- Honey has also proven successful in the management of open wounds. Principles of its use are similar to those of sugar.
- Maltodextrin N. F. is a polysaccharide soluble powder, which also exhibits many of the same properties of sugar.
- Silver sulfadiazine (Silvadene cream) serves to penetrate into the wound and is effective against gram-negative and gram-positive bacteria and enhances epithelialization. There is some concern about cytotoxicity to fibroblasts and an inhibition to lymphocytes and polymorphonuclear cells.
- Triple antibiotic ointment is a broad-spectrum treatment, which may promote epithelialization due to the zinc component. It has little efficacy for treatment of pseudomonads. Its use may be greater for prevention of infection rather than treatment.
- Gentamicin sulfate is used to inhibit the growth of *Pseudomonas*, *Proteus*, and *E. coli* organisms.
- Nitrofurazone is a broad-spectrum antibacterial in a polyethylene base, which promotes removal of body fluid from the wound to dilute the thicker exudates resulting in easier transfer into the bandage. Some delay in epithelialization may be expected.
- Acemannan acts as a synthetic growth factor, which enhances wound healing through its effects on macrophages and cytokines.
- Bovine collagen has been used to stimulate fibroblast ingrowth and deposition of collagen. When placed in the wound it creates scaffolding for the patient's own fibroblasts and collagen. It is most effective during the late inflammatory and early reparative phases of healing.
- Tripeptide-copper complex acts as an attractant for cells such as macrophages, monocytes, and mast cells. The result is increased wound debridement, release of additional cytokines, and increased collagen synthesis.
- Enzymatic debriding agents (Granulex, Elase, Preparation H) function to chemically debride wounds through the effects of trypsin, deoxyribonuclease, and fibrinolysin and to increase angiogenesis, epithelialization and collagen synthesis.
- Ointments may leave residual material in or on the wound surface. Water-soluble creams leave a decreased amount of foreign material at the wound surface and are preferred.

Secondary Layer

- The secondary layer of the bandage functions as the absorptive constituent, drawing fluid away from the wound and then acting as a reservoir for wound exudate or the absorbed lavage solution.
- This layer is often composed of cotton pads or layers of rolled cotton or cast padding.

Tertiary Layer

- The tertiary layer functions to hold the other layers of the bandage in place and is a layer of rolled gauze covered with adhesive tape or self-adherent tape (e.g., Vetwrap, 3M). The more porous the layer, the more rapid the evaporation of fluids or drying of the deeper layers. Porosity may also allow for translocation of bacteria across the bandage.
- Wounds over areas of increased motion or on limbs with concurrent orthopedic injuries may require splints incorporated into the tertiary layers for support or immobilization. Increased motion will delay wound healing.
- When bandaging thoracic or abdominal wounds, bandages should be snug but not restrictive of normal respiration.

Tie-Over Bandage

- If the area of the wound is not amenable to standard bandaging techniques (e.g., over the shoulder, hip, or axilla), a tie-over bandage may be used to

secure the primary and secondary layers to the wound bed.

- To make a tie-over bandage, place six to eight "eyelet" sutures around the wound (Fig. 56-1). Place primary and secondary bandage layers over the wound, then lace umbilical tape through the sutures to hold the layers of the bandage in place (Figs. 56-2 and 56-3).

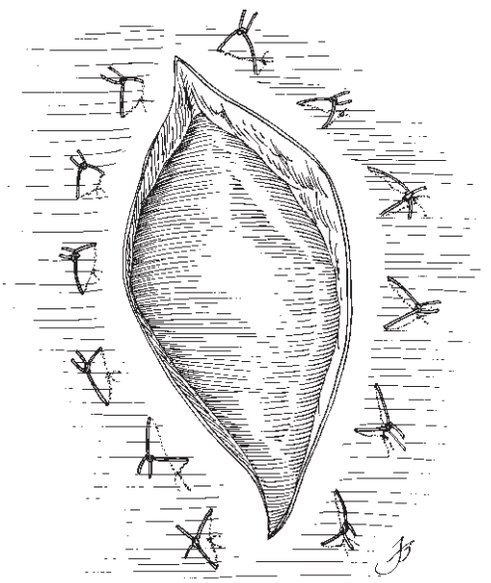

Figure 56-1. Place eyelets for a tie-over dressing around the wound using large suture material (e.g., 2-0 or 0 monofilament polypropylene).

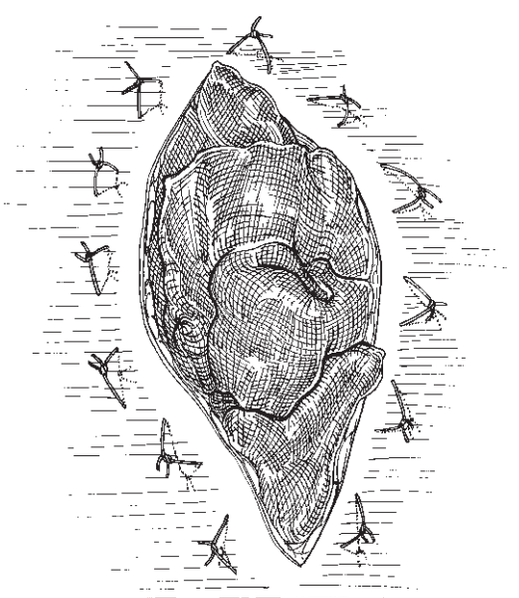

Figure 56-2. Place appropriate primary and secondary bandage layers over the wound.

- In cases where additional skin is recruited with the use of Velcro skin stretchers, the cable portion of the stretcher device can be used in a similar manner as a tie-over bandage.

Antibiotics

- Antibiotic therapy, whether applied topically or given systemically as a prophylactic measure, is controversial. If an established local infection exists, topical therapy is often all that is necessary.

▼ ***Key Point*** Control of infection is most effective through good open wound management, especially copious lavage and frequent bandage changes.

- Whenever possible, select antibiotics based on culture and sensitivity results. Use a broad-spectrum antibiotic while awaiting culture and sensitivity results.
- Use a combination of intravenous beta-lactam (e.g., cephalosporin) and aminoglycoside (e.g., gentamicin) antibiotics if septicemia is suspected.

DAILY WOUND MANAGEMENT

Frequency of Bandage Changes

- The timing of bandage changes is influenced by the need for debridement, the amount of exudate from the wound bed, and manageability of the patient.

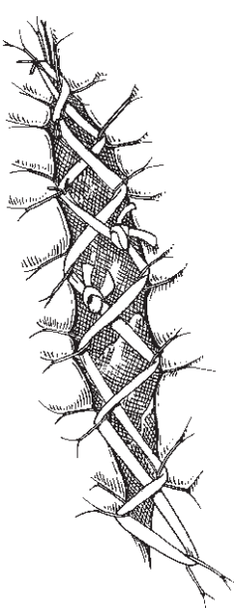

Figure 56-3. Lace sterile gauze or umbilical tape over the layers.

- Early in wound management, change bandages on a daily or twice-daily schedule. Wounds with healthy granulation tissue may be inspected and rebandaged every other or every few days.
- The volume of wound exudate or nature of the exudate in the bandage is often the guide to frequency of bandage changes. If wound drainage increases, consider more frequent bandage changes, and consider changing the primary layer.

Analgesia

- Animals with extensive wounds often require analgesics or, if discomfort is more severe, anesthetics to permit patient comfort at the time of bandage changes. This is particularly true with adherent dressings. Once granulation tissue begins to form, sedation/analgesia can be tapered or discontinued completely. Daily pain management may be provided through the use of nonsteroidal anti-inflammatory drugs (NSAIDs), narcotic injections, or a fentanyl patch (see Chapter 6).

Debridement

- During the early management of wounds, intermittent surgical debridement is the best means of removing necrotic tissue and debris.
- Surgical debridement is complemented by mechanical debridement through regular bandage changes.

Lavage

- Daily wound lavage aids in dislodgement of bacteria, removal of debris, dilution of exudates, and promotion of drainage.
- Whirlpool baths may benefit animals with extensive truncal wounds. If such treatments are instituted, monitor closely for signs of wound infection.

Bacterial Cultures

- With daily bandage changes and wound inspections the nature of the wound bed and exudate may be monitored. If during these inspections a change in the wound is noted and infection is suspected, submit wound swab samples of debrided tissue or punch biopsy samples of granulation tissue for culture and sensitivity.

Rebandaging

- As wound healing progresses to healthy granulation tissue, change the type of dressing from adherent to non-adherent and decrease the frequency of bandage changes.

▼ ***Key Point*** In cases of infection or deterioration of the wound, consider changing from a non-adherent to an adherent dressing.

WOUND CLOSURE

Closure and resolution of open wounds may be accomplished non-surgically by natural second intention healing or surgically by delayed primary closure or secondary closure. Surgical closures will decrease the labor-intensive component of open wound management and is often recommended when possible. Surgical methods of closure are described in Chapter 55. Skin grafts and skin flaps are described in Chapter 57. Consider surgical closure of open wounds once healthy granulation tissue is apparent.

Second Intention Healing

Second intention healing is the body's natural method of wound closure, and healing is the result of progressive formation of granulation tissue followed by wound contraction and epithelialization. Epithelialization often coincides with granulation tissue. In most cases this tissue provides adequate blood supply with little risk of infection. Additional closure is accomplished through wound contracture.

Advantages

- Additional surgery may be avoided.
- May be less expensive than other closure options.
- In wounds with no tension at the skin edges, the wound is covered with full-thickness, normal-appearing skin if contraction is complete.

Disadvantages

- Anatomic dysfunction and disfigurement from excessive contraction and scar tissue formation. If a joint is involved, decreased range of motion may result.
- With incomplete wound contraction, the epithelium may not cover the remaining defect.
- If the wound defect is large, the epithelium covering the defect is often fragile, easily disrupted, and has a poor aesthetic appearance.

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Chapter 57

Selected Skin Graft and Reconstructive Techniques

Stephen J. Birchard / Daniel D. Smeak

Large skin wounds can occur (1) from trauma directly to the skin or to its blood supply; (2) secondary to necrotizing skin diseases (see Chapter 49); and (3) after removal of large skin, subcutaneous, or body wall neoplasms. Most open wounds eventually heal by the formation of granulation tissue, wound contraction, and epithelialization. Skin flaps or grafts are indicated when wound healing is either not progressing or will take a very long time for completion. Full-thickness skin is necessary to prevent mechanical problems caused by repeated trauma (e.g., in the dorsum of the leg or paw). Skin reconstruction is also necessary if the open wound is so large it will cause significant patient morbidity or wound contracture is likely to cause a significant problem (e.g., the wound is over a joint and the scar limits full extension and weight-bearing). Skin flaps are usually preferred over skin grafts because they are simpler to perform and have a higher success rate. However, if a skin flap is not feasible due to lack of adjacent skin (such as the distal limb), consider a skin graft.

Consider several factors before performing skin flaps or skin grafts, such as viability of adjacent tissue, systemic illness that may affect wound healing, function of the affected area of the body, tolerance of the wound by the animal, feasibility of long-term bandaging of the affected area, desired cosmetic result, and cost to the owner. Thoroughly discuss these factors with the owner prior to performing any of these procedures.

This chapter describes practical methods of reconstructing skin using skin flaps and grafts. More complicated methods of skin grafting that require specialized skill or equipment, such as using a dermatome for split-thickness skin grafts, microvascular flap transfer, or tube grafts, are not discussed in this chapter. Primary closure of skin wounds is reviewed in Chapter 55, and open wound management in Chapter 56.

SURGICAL ANATOMY

Skin

The skin is composed of the epidermis and dermis.

- Structures that compose the skin adnexa, hair follicles, sweat glands, and sebaceous glands are located in the dermis.
- Besides adnexa, the dermis is composed of fibroblasts, collagen fibers, and various other structures, such as blood vessels, nerves, tissue cells, and fluid.

Subcutaneous Tissue

The subcutaneous tissue is mainly composed of loose connective tissue, including elastic fibers, fat, blood vessels, and nerves.

Cutaneous Muscles

- Thin, superficial muscles, collectively called the panniculus muscle, lie within the subcutis or hypodermis (the most superficial aspect of the subcutaneous layer) in certain body regions in both dogs and cats. Examples are the platysma muscle in the neck and the cutaneus trunci muscle in the trunk.
- Preservation of these muscles during undermining and flap creation is a very important principle in skin reconstruction.

Blood Supply to the Skin

- Deep or subdermal plexus
- This plexus is the major source of blood supply to the skin and of most importance to the surgeon.

▼ ***Key Point*** When creating skin flaps in dogs and cats, preserve the deep vascular plexus.

- In regions where cutaneous musculature is present, this vascular network is present on the superficial and deep layers of the muscle. Dissection beneath this thin muscle layer is critical to flap survival.
- Direct cutaneous arteries are present in several areas of the body. They arise from deep vessels that course superficially and run parallel to the skin. These direct cutaneous arteries communicate with the deep vascular plexus.

- Middle and superficial plexuses complete the layers of vascular network to the skin.

SKIN FLAPS

Skin flaps are a means of reconstructing open wounds by rotating, transposing, or advancing adjacent or regional skin to allow wound closure. Blood vessels supplying these flaps are maintained. Therefore, skin flaps do not rely on a bed of granulation tissue in the defect for their early blood supply and nutrition. Skin flaps can be classified according to their blood supply, such as *random subdermal flaps* versus *axial pattern flaps*, or according to their location with respect to the recipient bed, such as *local flaps* versus *distant flaps*.

Random Subdermal Flaps

Random subdermal skin flaps are those constructed without regard to the presence of a direct cutaneous artery. Viability of these skin flaps is dependent on the availability of local subdermal blood vessels supplied in the flap base, so they rely on a wide skin attachment to insure adequate blood supply. Random subdermal skin flaps can be further classified as *advancement flaps, rotation flaps,* and *transposition flaps,* depending on how the flap is moved to the defect; *single pedicle* and *bipedicle flaps,* depending on how the flap is attached to the body; and *direct distant flaps,* moving an extremity wound to a distant region of redundant host skin for flap coverage.

- Advancement refers to how the flap is moved to the wound. These are usually rectangular flaps. Simple advancement flaps are undermined and pulled (horizontally or vertically) directly to the wound (Fig. 57-1).
- A transposition flap is a tongue-shaped flap, usually constructed immediately adjacent to the wound. It is rotated (clockwise or counterclockwise) to cover the wound (Fig. 57-2).
- A rotation flap is a semicircular flap that pivots into an adjacent recipient bed. Single or paired flaps can be employed to close triangular defects (Fig. 57-3); no secondary defect is created with this flap.
- Direct distant flaps include thoracic or abdominal single pedicle or bipedicle flaps that can be used as a method for transferring skin to the distal extremities.
  - Single pedicle: Attached to the body only at one end (Fig. 57-4*A*, *C*). The pedicle provides the vascular attachment to the flap.
  - Bipedicle: Attached to the body at both ends (Fig. 57-4*B*).
  - These flaps are transferred from a distance to the recipient defect. The lesion is advanced to the flap rather than the flap being transferred to the lesion as in construction of advancement flaps.

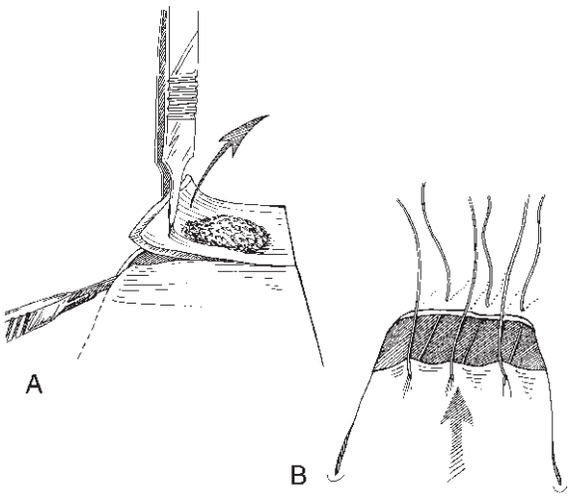

Figure 57-1. Simple advancement flap. Make the initial incisions *(A)*, then deeply undermine the flap and advance to the defect *(B)*.

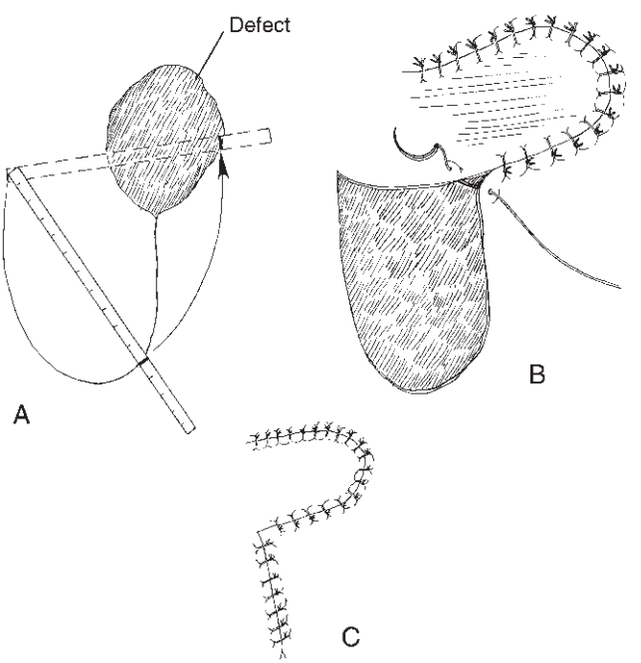

Figure 57-2. Transposition flap. After measuring the length of flap needed (*A*), make the incisions and rotate the flap to the defect (*B*). Suture the flap first and then close the remaining defect (*C*).

  - Forelimb defects are more often reconstructed using this technique than are rear limb defects.

Indications

Advancement, Rotation, and Transposition Flaps

- For large skin wounds that are located in areas with adjacent loose, redundant skin (e.g., neck, flank, dorsal trunk) that allows formation and closure of defects remaining after flap transfer without tension.

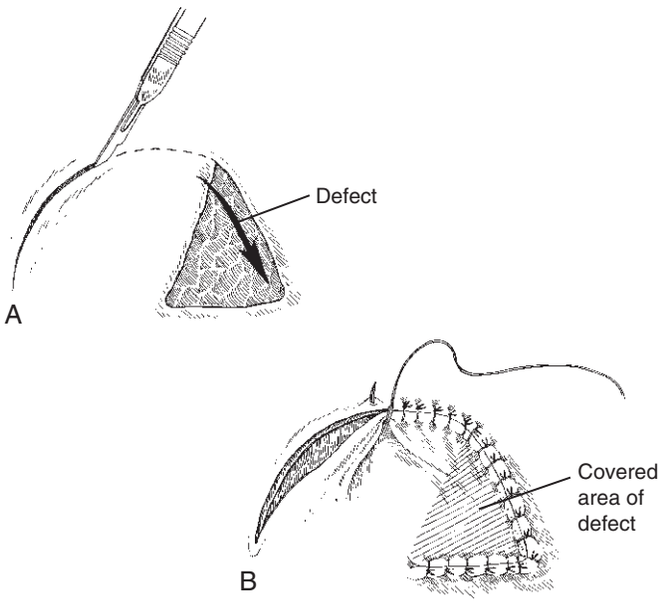

Figure 57-3. Create a curved incision in a stepwise fashion to close a triangular wound.

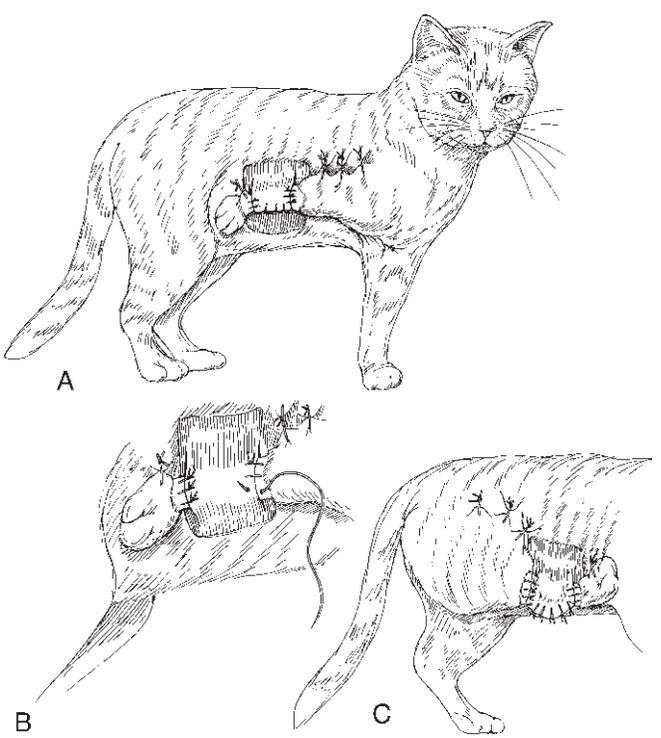

Figure 57-4. Direct distant flap. Make the skin flap using the lateral thoracic or abdominal skin. Suture the flap to the limb defect. This flap can have a single *(A)* or double *(B)* pedicle. Secure the limb to the lateral body wall with skin sutures placed between the leg and the body wall *(C)*. Place a padded bandage around the body to help stabilize the elevated limb.

- As a general rule, do not consider these flaps for wounds distal to the stifle, elbow, or tail head, since there is often not enough skin to close the donor site without excessive tension.

Direct Distant Pedicle Flaps

- For large wounds of the distal extremities in which local skin is not available or would be closed under excessive tension.
- These flaps are usually made from skin over the lateral thoracic or abdominal wall. The leg is attached to the side of the animal's body for a period of time while healing of the pedicle to the extremity wound progresses. The pedicle is then removed from the thorax or abdomen and the leg returned to its normal position.
- These flaps are very successful, but patient tolerance is variable.

Preoperative Considerations

- Carefully plan the surgical procedure. Review vascular anatomy of the region. The size, location, shape, and condition of the wound dictate the type of flap.
- Check the health, looseness, and pliability of the skin adjacent to the lesion or wound to determine feasibility of the intended skin flap.
- Consider administration of prophylactic antibiotics, given intravenously at induction of anesthesia, if significant contamination of the surgical site is possible.
- Prepare the recipient bed preoperatively to ensure that the area is free of infection, foreign material, and necrotic tissue.
- Direct distant flap technique requires two surgical procedures to complete. The owner is made fully aware of the costs involved, the postoperative management, and the problems related to the prolonged immobilization of the leg. Hair direction and cosmetic problems are more common with distant techniques than with local flap techniques.

▼ ***Key Point*** Consider the mobility of the extremity that contains the defect when determining the location and type of direct distant flap. Make sure the leg opposite the host limb is able to accept the extra weight-bearing load. Evaluate the size and temperament of the patient. Smaller animals with calm dispositions seem to tolerate this technique best.

Surgical Procedure

Objectives

- To provide full-thickness reconstruction of a large skin wound.
- To avoid tension along the suture line.
- To create flaps that maintain viability and provide satisfactory cosmesis.

Equipment

- Standard surgical pack and suture.
- Measuring device to plan length and width of flaps.
- Sterile marking pen to draw incisions (optional). Sterile methylene blue and a cotton-tipped applicator can be as effective as a marker.
- A piece of sterile double-knit cloth or section of paper drape can be used as a pattern for designing flaps intraoperatively.
- Penrose ($^1/_4$–$^1/_2$ inch) or closed suction drains (e.g., Jackson-Pratt drain).

Technique

Advancement or Transposition Flaps

1. Carefully position the patient to free up any available skin in the region and to reduce tension while the flap is being sutured.
2. Aseptically prepare a liberal amount of skin in the region of the proposed flap and donor sites.
3. Remove epithelialized portions of the granulation bed by sharp dissection (usually present at the edges of the granulation bed). Undermine attachments of skin at the margin of the granulation bed to free up the bordering skin.
4. Gently manipulate the skin margins surrounding the defect to ascertain the availability of adjacent local skin.
5. Optimally, the donor area has enough skin available to elevate a flap without leaving a secondary defect that cannot be closed primarily.
6. If possible, avoid choosing a donor area that may be subject to excessive motion or tension.
7. Choose the type of flap depending on the availability of skin, shape, and location of the defect and size of the area to be covered.
8. It is better to create two adjacent short flaps rather than one long flap, which have a greater risk of necrosis from inadequate blood supply.
9. Try to design the flap so that the base is slightly wider than the tip to avoid inadvertently devascularizing the flap.
10. Design the flap to fill the defect without tension.
11. Create the flap by sharply incising along the preplanned donor skin margins.
12. Use stay sutures or fine skin hooks when elevating the flap to avoid causing excessive damage.

▼ ***Key Point*** The depth of flap undermining is very important to preserve the deep vascular plexus under the panniculus muscle group. Be especially careful when undermining in the region of the base of the flap to avoid interrupting critical direct cutaneous vessel branches.

13. Transfer the skin flap to the defect (see Figs. 57-1 and 57-2).
14. Consider placing a drain in large dead space areas (under flaps and donor areas) if the condition of the tissues warrants it. If a Penrose drain is used, exit the drain in a ventral-dependent area of the wound away from the primary suture line.
15. Meticulously close subcutaneous tissues with fine (3-0 to 4-0), simple interrupted, absorbable suture material to evenly distribute skin tension.
16. Use fine (4-0) monofilament non-absorbable suture material placed in a simple interrupted pattern to close the skin. Skin staples may also be used. Simple interrupted sutures allow for individual control of suture tension. If fluid accumulation develops in the dead space, simple removal of one or two skin sutures in a gravity-dependent area often allows adequate drainage.

Technique

Direct Distant Flap (Single or Double Pedicle)

1. Aseptically prepare the entire limb and lateral thoracic wall for a forelimb defect or abdominal wall for a rear limb defect. When preparing a bipedicle flap, meticulously clip and clean the medial portion of the paw or limb that will be in contact with the skin of the trunk.
2. Position the affected limb in the most comfortable angle possible to locate the donor area (see Fig. 57-4).
3. Attempt to construct the flap so that any movement of the limb will pull the flap onto the defect rather than away from it.
4. Create a bipedicle flap if the defect is large or nearly circumferential (Fig. 57-4*B*), or a single pedicle flap if the defect is less than 180 degrees circumferential (Fig. 57-4*A, C*), using the principles described previously in the section on advancement flap technique.
5. After creating the pedicle flap, a skin defect remains on the trunk that must be closed. Use advancement or rotation flaps to close this defect.
6. Place the limb through the bipedicle flap or adjacent to the single pedicle flap.
7. Carefully prepare the host wound site for flap transfer. Remove any islands of epithelial tissue in the host wound bed; be sure there is no evidence of necrotic tissue or foreign material in the wound. Excise the margin of the wound to create a clean square skin edge, if necessary.
8. Suture as much of the flap to the defect margins as possible.
9. Drains may be placed to drain fluids that may accumulate under the flap or limb.
10. Use large (2-0 to 0) monofilament non-absorbable suture material to tack the skin of the limb to the thoracic wall skin in several areas to help immobilize the limb.

▼ ***Key Point*** Complete immobilization of the limb is mandatory for at least 14 to 18 days to ensure adequate vascularization of the flap from the wound bed.

11. Design a bandage for immobilization that will remain in place for the full 2 to 2.5 weeks but will still allow the flap area to be monitored and separately rebandaged.
12. If the flap appears healthy, sharply incise the pedicles from the donor area. Suture the remaining free skin margins to the defect to complete the transfer. If in doubt about the flap vascularization, delay the flap transfer. Incise half the length of the pedicle, close the incisions, and complete the flap transfer in 3 to 5 days.

Axial Pattern Flaps

Axial pattern flaps are those skin flaps that are developed using a major direct cutaneous artery as the primary blood supply. Considerably more flexibility in the length and mobility of these flaps is possible compared with random skin flaps. Since only the axial vessel is necessary for nourishment of these skin flaps, they can be made with or without skin attachment to the flap (island axial pattern flaps). These long vascular pedicles allow transfer of skin to more remote areas of the body because of the direct cutaneous artery allowing adequate perfusion of a large area of tissue. Consequently, axial pattern flaps usually allow reconstruction of a defect in a one-step procedure.

Axial pattern flaps can be based on many direct cutaneous arteries, such as the caudal superficial epigastric, the cervical cutaneous branch of the omocervical, the thoracodorsal, the deep circumflex iliac, and the genicular branch of the saphenous artery. More recently, an axial pattern flap based on the lateral thoracic artery holds promise for elbow and proximal forelimb wounds. Caudal auricular and the superficial temporal axial pattern flaps are used for maxillofacial and cervical wounds. The caudal superficial epigastric and thoracodorsal axial pattern flaps are commonly selected for large defects of the proximal thigh, perineum, and flank and thoracic, axilla, and proximal forelimb wounds, respectively. The thoracodorsal axial vessels are less robust than the caudal superficial epigastric vessels; hence, these flaps have higher risk of flap necrosis. Only these two flap techniques are described here. However, other axial pattern flaps as listed previously can be created using similar principles and are described in veterinary surgical textbooks (see Pavletic, 1998).

Indications

- Similar to those for random subdermal flaps except that axial pattern flaps are used when the skin defect is very large or when the donor skin needs to be transferred over a longer distance to the recipient site.
- A major direct cutaneous artery and vein must be in the region of the skin defect for this technique to be indicated.

Preoperative Considerations

- Same as those for random subdermal flaps, plus the following:
  - Carefully plan the design of the flap to include the direct cutaneous vasculature.
  - Consider how the resultant defect of the donor area will be closed.
  - Be sure the skin and the direct cutaneous artery that will be used for the flap are viable.

Surgical Procedure

Objectives

- Same as those for random skin flaps, plus:
  - Preserve viability of the direct cutaneous artery by avoiding excessive surgical trauma to the tissue.
  - Prevent undue tension on the vascular pedicle especially if flap rotation approaches 180 degrees.

Equipment

- Same as that for random skin flaps.

Technique

Caudal Superficial Epigastric Axial Pattern (CSE) Flap

1. Use preparation and tissue handling principles as described for advancement or rotation flaps.
2. Be particularly careful when positioning the patient so that the vascular pedicle will not become distorted before planning the incisions.
3. Incise the skin as shown in Figure 57-5.
4. The entire mammary chain up to the cranial thoracic gland can be included in this flap.
5. Deeply undermine the flap to the level of the abdominal fascia.
6. Dissect very carefully around the origin of the direct cutaneous vessel to avoid inadvertent damage to this vessel, which is vital to the survival of the flap.
7. Avoid creating a kink or excess tension in the base of the flap, which could obstruct blood flow.
8. Drain dead space if needed with a passive (Penrose) or closed suction (Jackson-Pratt) drain.
9. Suture the flap to the defect, as described for the other flap techniques.

Thoracodorsal Axial Pattern Flap

1. Use the same principles as described for the CSE flap.
2. The thoracodorsal vessel originates at the caudal shoulder depression, at a level parallel to the dorsal border of the acromion. Maintain this landmark as

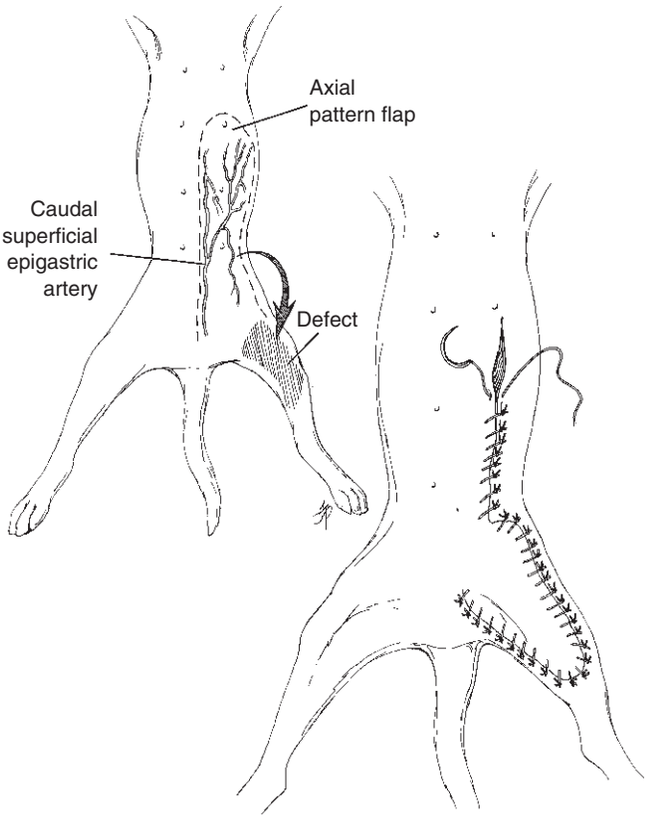

Figure 57-5. Example of an axial pattern flap. This flap is based on a direct cutaneous artery—the caudal superficial epigastric artery. Design the flap around this artery and deeply undermine the skin and mammary tissue. Rotate the flap and suture to the defect.

the flap is planned and undermined to preserve the vascular pedicle.

3. Make incisions to create the flap as shown in Figure 57-6. Direct the cranial incision along the spine of the scapula. Create the caudal incision parallel to the cranial incision. This incision line is made behind the caudal shoulder depression equal to the distance between the scapular spine and the caudal shoulder depression. The flap margins can be extended safely up to the level of the dorsal midline.
4. Elevate the flap just below the level of the cutaneous trunci muscle, beginning at the end of the flap. Be careful to avoid interrupting the thoracodorsal vasculature, which is often hidden from view in the deeper subcutaneous fat.
5. Pivot the flap into the host bed. Use a bridging incision between the host and donor beds if necessary. Alternately, tube the flap base to traverse the skin interposed between the two areas.
6. Prepare the host wound bed as explained for the direct distant flap technique.
7. Avoid kinking or excess tension at the base of the flap, which could obstruct blood flow from the axial vasculature.
8. Use the drainage and closure directions as for the CSE axial pattern flap.

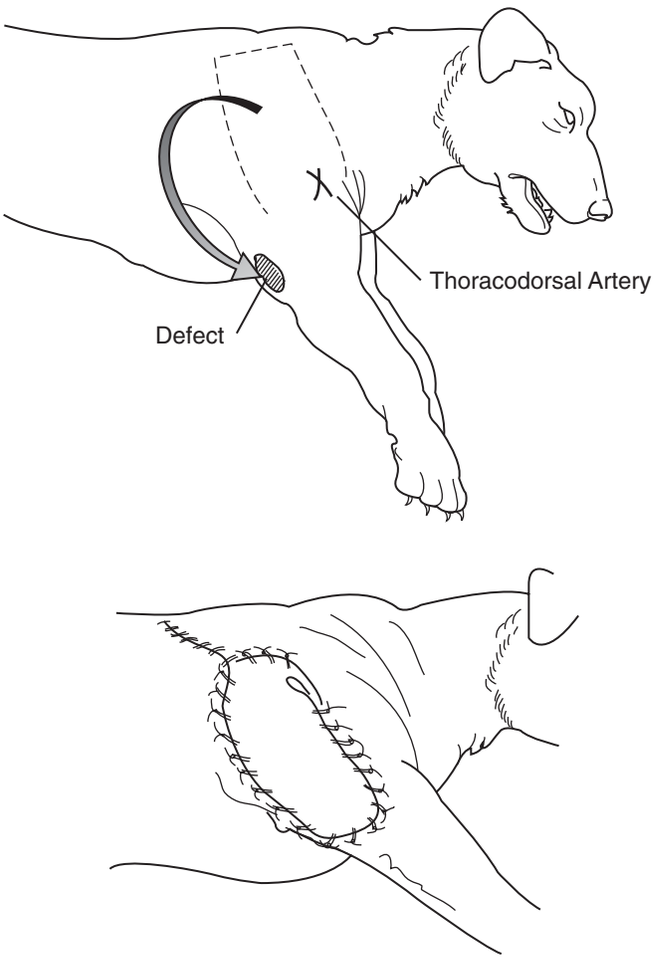

Figure 57-6. Thoracodorsal axial pattern flap reconstruction of a proximal brachial wound. Incisions are created as described in the text. Undermine the flap in a dorsal to ventral direction to the level of the origin of the thoracodorsal pedicle (caudal shoulder depression). Rotate the flap into the wound and suture the flap to the defect edges.

Postoperative Care and Complications

All Flap Types

- Restrict exercise until suture removal.
- If necessary, apply an Elizabethan collar as the patient is recovered from anesthesia and leave on the animal until the flaps are completely healed.
- Change wound dressings as necessary.
- Immobilize the limb for at least 14 days for direct distant flap techniques.
- Major complications resulting from skin flaps include local problems, such as partial or total ischemia of the flap, infection, seroma, and dehiscence of the flap or donor suture line.
- Carefully pad the elbow if the thoracodorsal (TD) flap extends over this area to avoid pressure necrosis over the olecranon.
- Dehiscence of donor site incisions is usually due to excessive skin tension. If dehiscence occurs, allow these areas to heal by second intention. Excise

ischemic areas of flaps when these areas are clearly demarcated. Let the wounds heal by second intention, or reconstruct the skin wound after all wound surfaces are lined with healthy granulation tissue.

FREE SKIN GRAFTS

Free skin grafts involve complete removal of skin from one area of the body and implantation to another. These grafts are completely separated from their blood supply, so they are solely dependent on the wound bed for viability in the early stages of graft healing. For the first 3 to 4 days after grafting, the skin graft obtains its nutrition from the wound bed by diffusion, a process called plasmatic imbibition. During this process, the graft acts like a sponge, soaking up fluid and oxygen from the granulation tissue of the wound. Imbibition is a very delicate process that is easily disrupted by excessive movement of the wound, seroma formation, and infection. During this initial phase of healing, the graft usually looks its worst, appearing congested and sometimes purple. After a few days, this appearance dramatically improves if the graft "takes."

After the first 3 to 4 days, viability of the graft depends on the growth of capillaries from the wound bed into the graft (i.e., inosculation). These invading capillary buds are very fragile structures and are easily damaged by trauma (such as licking of the graft), excessive shear motion, and infection. Once this blood supply becomes well established, viability of the graft is maintained.

Skin grafts vary in their final cosmetic result. The best cosmesis is obtained from a full-thickness skin graft, because there is growth of hair over the area. However, full-thickness grafts are the most difficult to establish because they are thicker than split-thickness grafts. This greater thickness makes the initial process of imbibition and inosculation more difficult, resulting in a higher incidence of graft failure. Some authors recommend harvesting skin from areas where the skin is thin, such as the cranio-ventral aspect of the lateral thorax. Thin skin grafts are preferred because they are more readily incorporated into the granulation tissue.

Pinch (or Punch) Skin Grafts

When rapid epithelization of a wound is needed, pinch grafts can be effective. Pinch skin grafting is performed by simply harvesting small (2–3 mm) sections of full-thickness skin and placing them into the wound granulation bed. They are not difficult to perform and are highly successful. However, the major disadvantage of pinch grafts is the final cosmetic result. Uniform full-thickness skin does not form over the wound with pinch grafts; therefore, very little hair grows over the area.

Preoperative Considerations

- Determine the desired result of the graft. If a high degree of success and rapid epithelial coverage of the wound are desired, consider pinch grafts. If complete regrowth of hair and excellent cosmesis are necessary, employ a different skin graft method, such as mesh graft. If the recipient site is over a joint or area that is frequently traumatized, the more durable full-thickness grafts may be needed and pinch grafts may not be satisfactory.

▼ ***Key Point*** Maximize the chances of graft "take" by properly preparing the wound bed before grafting.

Use standard techniques of wound debridement, lavage, and bandaging (see Chapter 56) for several days prior to grafting to establish a healthy bed of granulation tissue. Postpone the graft procedure if any evidence of infection is present.

Surgical Technique

Objectives

- To establish epithelial coverage of an open wound.
- To atraumatically harvest small plugs of skin from an area of healthy redundant skin.
- To implant these plugs of skin into an area of healthy granulation tissue for rapid epithelial coverage.

Equipment

- Same as for skin flaps, plus:
- Several #15 scalpel blades
- Skin biopsy punch (optional), size 4 and 5 mm.

Technique

1. Aseptically prepare the wound bed and the harvest site.
2. Gently pick up the skin with thumb forceps or stay suture and excise a 1-mm piece of skin, using the #15 scalpel blade. Be careful not to include subcutaneous tissue with the skin pinch.
3. Alternatively, harvest a punch graft using a 5-mm skin biopsy punch. Place the punch at the same angle as the hair follicle during harvesting.
4. Trim any subcutaneous tissue found deep to the dermis of the graft plug.
5. Place the skin pinch or punch in a saline-moistened surgical sponge.
6. Make a "vest pocket" stab incision in the granulation tissue with a #15 scalpel blade (Fig. 57-7).
7. Slide the skin pinch into the incision in the granulation tissue (Fig. 57-7). Be sure the epithelial side of the pinch is facing out.
8. Repeat this process as many times as necessary to have skin pinches (punches) covering the wound at about 1 to 2 cm apart.
9. If using a skin punch, use a 4-mm punch to make the hole in the granulation tissue. The slightly

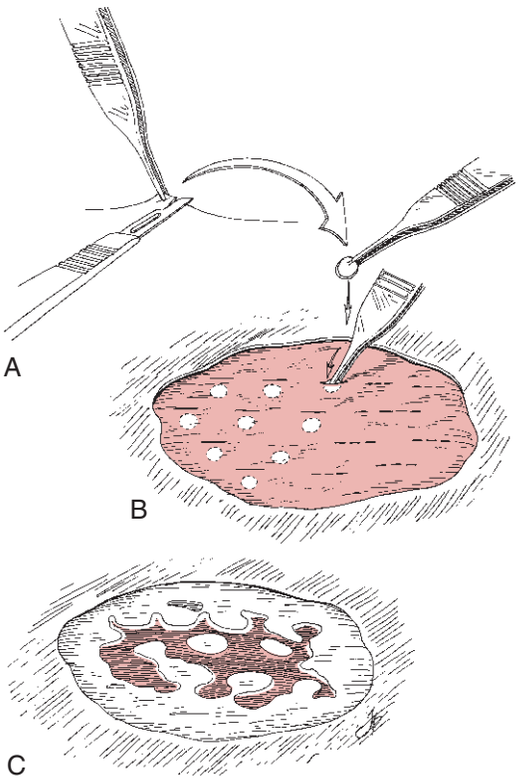

Figure 57-7. Pinch skin graft. *(A),* Obtain small pinches of skin using a scalpel. *(B),* Make small "vest-pocket" incisions in the granulation bed, and slide skin pinches into these incisions with the epidermal side facing out. Pinches can be approximately 1 to 2 cm apart. *(C),* Wound will be filled in by epidermal growth from the pinch grafts.

smaller hole compared to the skin punch will allow a snug fit of the graft in the granulation tissue.

10. Place a non-adherent dressing over the wound. The primary layer of the dressing can be petrolatum-impregnated gauze or Telfa pad with a thin layer of triple antibiotic ointment (Bacitracin-Neomycin-Polymyxin, Pharmaderm).
11. Let the donor sites heal by second intention, or close them with simple interrupted sutures of 4-0 nylon.

Postoperative Care and Complications

- Restrict exercise to leash walking only.
- Change the wound dressing every day for the first 5 to 7 days, then every 2 to 3 days if wound healing is progressing normally.
- Keep the wound dressed until it is completely covered with epithelium.
- If necessary, place an Elizabethan collar on the animal to prevent damage to the bandage or the wound.
- Potential complications include dislodgement of the pinch grafts due to self-trauma or excessive motion and poor cosmetic result due to scarcity of hair formation.

Mesh Skin Grafts

Mesh skin grafts are usually full-thickness skin grafts that are harvested, stripped of subcutaneous tissue, and "meshed" by making multiple scalpel cuts in them. The purposes of making holes in the graft are to increase coverage of the wound by "expanding" the graft and to allow escape of fluid from underneath the graft. Mesh grafts provide better cosmesis than pinch grafts. The healed wound has some hair coverage, although it may not be as much as on the surrounding skin, depending on how much the mesh is expanded.

Mesh grafts are fairly simple to perform and require no special equipment. Results are generally good when the tissues are in good condition and the techniques are performed appropriately.

Preoperative Considerations

- These are the same as those for pinch grafts.
- Consider giving a prophylactic systemic antibiotic (beginning preoperatively) to help prevent infection of the graft.
- Do not perform the procedure if any evidence of infection is present in either the donor or recipient sites.

Surgical Procedure

Objectives

- To establish epithelial and some full-thickness skin coverage of the wound.
- To atraumatically harvest the donor skin from an area of redundant skin.
- To meticulously prepare the graft for implantation by removing all subcutaneous fat and creating a mesh by making multiple small holes in the skin.

Equipment

- Same as for pinch grafts, plus:
  - A sterile board (plastic, wood, or cardboard) for stretching out and preparing the graft
  - #11 scalpel blade

Technique

1. Aseptically prepare the donor and recipient sites.
2. Estimate the size of the wound by measuring or cutting out a template using sterile drape material.
3. Sharply excise the donor skin from an area of thin and redundant skin (e.g., cranial ventral thorax and lateral flank area).
4. Avoid excising the subcutaneous tissue.
5. Note the direction of hair growth in the harvested skin.

6. Place multiple stay sutures at the edge of the harvested skin.
7. Place the skin on a sterile board (epidermal side down), and stretch it out using the stay sutures (Fig. 57-8) or 25-gauge needles.
8. Carefully dissect all remaining subcutaneous fat from the skin using sharp dissection (Fig. 57-8*A*). When this has been done correctly, exposed hair follicles create a stippled appearance on the dermal surface.
9. Lavage the skin frequently with sterile saline.
10. Make multiple full-thickness holes, approximately $\frac{1}{2}$ cm in length and $\frac{1}{2}$ cm to 1 cm apart (Fig. 57-8*B*).
11. Place the mesh graft on the wound, dermal side down.
12. Position the graft so that the hair growth will be in the same direction as that of the adjacent hair.
13. Suture the graft to the surrounding skin (Fig. 57-8*C*).
14. Suture the graft under slight tension so that the mesh expands and the granulation tissue can be seen through the graft (Fig. 57-8*C*).
15. Place additional tacking sutures from the center of the graft to the granulation bed to prevent movement of the graft and prevent separation of the graft from the wound bed.
16. Cover the wound with a nonadherent dressing (see the description under pinch grafts). Change the dressing as needed to prevent desiccation of the primary layer and adherence to the graft.

▼ ***Key Point*** When changing the contact dressing, be very careful to prevent separation of the graft from the underlying granulation tissue.

Postoperative Care and Complications

- Same as for pinch grafts, plus:
  - Prevent desiccation of the graft by applying small amounts of triple antibiotic ointment or sterile petrolatum on the contact layer of the bandage.
  - Immobilize the limb if grafting over a joint (e.g., elbow, carpus, stifle, hock) to prevent excessive movement of the graft.
  - The major complication is failure of the graft to heal due to infection, excessive motion, or lack of adherence of the graft to the underlying granulation tissue.

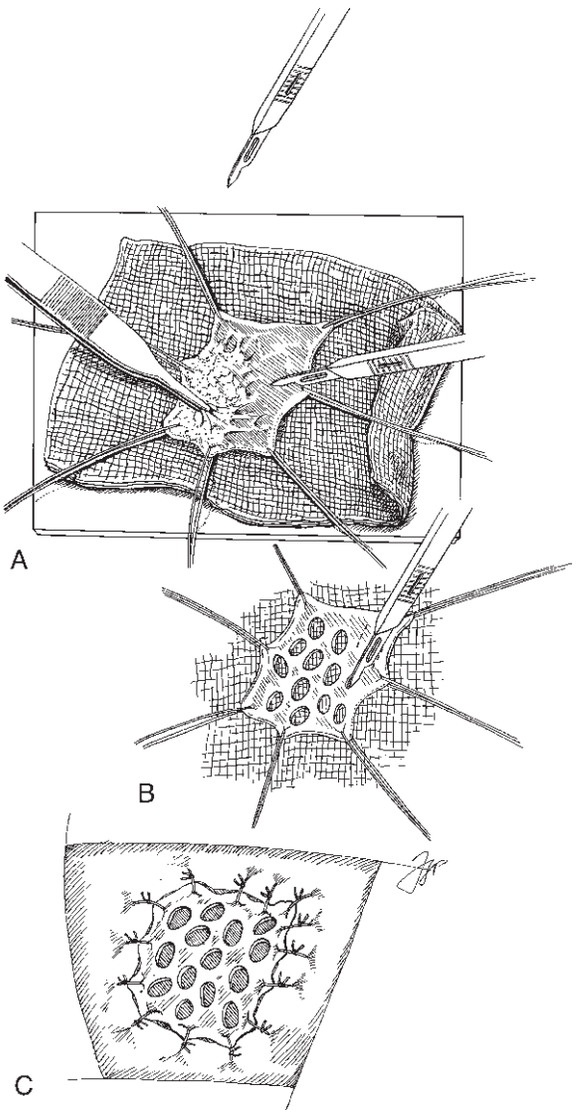

Figure 57-8. Mesh skin graft. Harvest skin and stretch it out on a sterile board using stay sutures and meticulously remove all subcutaneous fat *(A)*. Make multiple slits in the graft using a scalpel *(B)*. Suture the graft, with the epidermal side facing out, to the granulation bed *(C)*.

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Chapter 58

Diseases of the Pinna

Lynette K. Cole

The pinna is a mobile structure designed to localize and collect sound waves and transmit them to the tympanic membrane. The pinna has vastly different breed conformations in the dog, while in the cat; there is very little breed variation. The auricular cartilage expands to form the pinna, with the skin of the concave portion of the pinna tightly adherent to this cartilage. The cartilage of the pinna becomes funnel shaped at the opening of the external ear canal.

The pinna is a region of the body prone to numerous skin diseases. In most cases, the pinnal lesions are associated with lesions on other body areas. There are a few diseases where lesions are limited to the pinna (Table 58-1).

The work-up for all animals with pinnal disease should include a complete history, general physical examination, and dermatologic examination. Next, an otoscopic examination is performed, as well as microscopic examinations of skin scrapings for mites and fungi, cytology for bacteria and yeast, and mineral oil swabs for mites (*Otodectes cynotis* and *Demodex* spp.). A bacterial culture is indicated if rod bacteria are seen cytologically. Further testing may be needed such as a complete blood count, serum biochemical profile, urinalysis, allergy testing, food elimination trial, and skin biopsy for histopathology of the ear pinna (see Chapter 59 for diagnosis and treatment of otitis externa).

▼ ***Key Point*** In some cases, the definitive diagnosis of the pinnal disease is made based on the histopathological results from the pinnal biopsy.

The biopsy technique of the ear pinna can be difficult. For lesions on the margin of the pinna, a wedge biopsy is preferred, while for central lesions, a small punch biopsy, size 3.5 to 4 mm, is used to obtain samples. For additional information on the skin biopsy technique, please refer to Chapter 37).

INFECTIOUS DISEASES

Dermatophytosis (also see Chapter 42)

Clinical Signs

- The pinna is often affected in dogs and cats with dermatophytosis.
- In addition to the pinna, lesions may occur anywhere on the body.
- The lesions are quite variable and commonly include erythema, papules, pustules, alopecia, and crusts.

Diagnosis

- Tentative diagnosis: Wood's lamp examination, microscopic examination of the hair (potassium hydroxide [KOH] preparation, chlorphenolac), and histopathology.
- Definitive diagnosis: positive dermatophyte test medium (DTM) culture.

Treatment

- For localized lesions on the ear pinna only, topical therapy, such as miconazole (Conofite Lotion, Schering-Plough Animal Health) or clotrimazole (Clotrimazole Solution, Vet Solutions), may be effective.
- In generalized conditions where the pinna is not the only affected body site, topical rinses with lime sulfur (LymDyp, DVM Pharmaceuticals) along with systemic therapy (ketoconazole [generics; Nizoral, Janssen] or itraconazole [Sporanox, Janssen]) are necessary for resolution.
- Inform owners that this is a zoonotic disease.

Malassezia Dermatitis (also see Chapter 41)

Clinical Signs

- *Malassezia pachydermatis* may cause a pruritic dermatitis and otitis in the dog; cats are less frequently affected.
- In addition, the concave and convex portion of the pinna may be affected.
- Lesions include erythema, alopecia, scale, crusts, hyperpigmentation, and lichenification.

Diagnosis

- Obtain samples for cytology by skin scrapes, acetate tape preparations, swabs, and impression smears.
- The yeast organisms are identified microscopically.

Table 58-1. DERMATOSES OF THE PINNA

Affected Site(s)	Disease	Clinical Lesions Found on Pinna
Pinna only		
	Canine eosinophilic pinnal folliculitis	Erythema, papules, crusts
	Ear margin seborrhea	Scale, fissures
	Fly bite dermatitis	Ulcers, crusts, erythema, alopecia
	Proliferative thrombovascular necrosis of the ear pinnae	Ulcers, scale, hyperpigmentation
Pinna and other body areas		
	Actinic keratoses	Erythema, hyperkeratosis, crusts, hyperpigmented plaques
	Arteriovenous fistula	Edema
	Atopic dermatitis	Erythema
	Canine demodicosis	Erythema, papules, scale, alopecia, crusts
	Canine sarcoptic mange	Erythema, papules, crusts, scale, alopecia, excoriations
	Contact dermatitis	Erythema, macules, papules, erosions, ulcers
	Cutaneous adverse food reaction	Erythema
	Dermatomyositis	Alopecia, erythema, scale, crusts, ulcers, scars
	Dermatophytosis	Erythema, alopecia, papules, pustules, crusts
	Discoid lupus erythematosus	Alopecia, crusts, ulcers
	Feline demodicosis	Erythema, papules, scale, alopecia, crusts
	Feline sarcoptic mange	Erythema, papules, crusts, scale, alopecia, excoriations
	Frostbite	Ulcers, necrosis
	Hereditary lupoid dermatosis of German short-haired pointers	Scale, crusts
	Juvenile cellulitis	Papules, pustules, crusts
	Malassezia pachydermatis	Erythema, alopecia, scale, crusts, hyperpigmentation lichenification
	Melanoderma and alopecia in Yorkshire terriers	Alopecia, hyperpigmentation
	Pattern baldness	Alopecia, hyperpigmentation
	Pemphigus erythematosus	Erythema, scale, papules, pustules, alopecia, crusts
	Pemphigus foliaceus	Erythema, scale, papules, pustules, alopecia, crusts
	Psoriasiform-lichenoid dermatosis of springer spaniels	Erythema, hyperpigmentation, plaques, papules
	Sebaceous adenitis	Papules, alopecia, scale, follicular casts
	Systemic lupus erythematosus	Alopecia, crusts, ulcers
	Vasculitis	Erythema, alopecia, ulcers, crusts, necrosis
	Zinc-responsive dermatosis	Erythema, scale, crust, hyperkeratotic plaques

Treatment

- Topical therapy (miconazole, ketoconazole, chlorhexidine) in the form of lotions, sprays, leave-on conditioners, shampoos, or medicated pads
- Systemic therapy: oral ketoconazole ([generics; Nizoral, Janssen] or itraconazole [Sporanox, Janssen])
- Identification of the underlying dermatologic condition, such as allergic or endocrine diseases, that triggered the secondary infection.

PARASITIC DISEASES

Sarcoptic Mange (also see Chapter 44)

Clinical Signs

- Canine scabies (sarcoptic mange) is caused by the mite *Sarcoptes scabiei* var. *canis*, while feline scabies (notoedric mange) is caused by *Notoedres cati*.
- Both diseases cause intense pruritus and are contagious to other animals and humans.
- The lesions frequently start at the edge of the pinna.
- In dogs, the lesions may then spread to the ventral portions of the abdomen, chest, elbows, and legs.
- In cats, the lesions rapidly spread to the face, eyelids, and neck.
- The lesions consist of erythematous papules, thick crusts, scales, alopecia, and excoriations.

Diagnosis

- Perform superficial skin scrapings in animals suspected of sarcoptic mange.
- The mites may be extremely difficult to find; therefore, a negative skin scraping does not eliminate scabies as the cause of the lesions and pruritus.

▼ ***Key Point*** Pinnal pedal scratch reflex (vigorously rubbing the tip of one ear flap on the base of the ear with a response of a scratching movement of

the ipsilateral hind leg) for the diagnosis of sarcoptic mange in the dog was found to have a sensitivity and specificity of 81.8% and 93.8%, respectively.

- In the absence of identification of the mites, make the diagnosis of scabies based on response to therapy.

Treatment

- In multiple-pet households, treat all other in-contact animals.
- Conventional therapy consists of weekly lime sulfur dips (LymDyp, DVM Pharmaceuticals) for 6 to 8 weeks.
- Selamectin (Revolution, Pfizer Animal Health) is a novel, semi-synthetic avermectin approved for treatment of canine sarcoptic mange.
- Extra-label treatments (see below) for sarcoptic mange have also been used successfully, including amitraz dips (Mitaban, Pfizer Animal Health), ivermectin (Ivomec 1% injection for cattle and swine, Merial) (this form and dosage of ivermectin should not be given to collies, Shetland sheepdogs, Old English sheepdogs, other herding dogs, or their crosses), and milbemycin oxime (Interceptor Flavor Tabs, Novartis) (low incidence of side effects in collies).

Canine Demodectic Mange (also see Chapter 43)

Clinical signs

- Demodectic mange in the dog is caused by *Demodex canis*.
- Both the localized and generalized form may affect the ear pinna, in addition to other areas of the body.
- Lesions of demodicosis in dogs consist of erythema, scale, alopecia, papules, pustules, crusts, and secondary bacterial infections.

Diagnosis

- Make the diagnosis by identifying multiple demodectic mange mites on deep skin scrapings.

Treatment

- The majority of localized demodicosis cases will resolve without treatment; however, topical benzoyl peroxide (Pyoben Gel, Virbac; OxyDex Gel, DVM Pharmaceuticals) may be used on the alopecic areas.
- In cases of generalized demodicosis, the FDA-approved treatment is bi-weekly dips with amitraz (Mitaban, Pfizer Animal Health).
- Extra-label daily high dose ivermectin (Ivomec 1% injection for cattle and swine, Merial) or milbemycin oxime (Interceptor Flavor Tabs, Novartis) is effective in the treatment of generalized demodicosis. As stated previously, this form and dosage of ivermectin should not be given to collies, Shetland sheepdogs, Old English sheepdogs, other herding dogs, or their crosses.

Feline Demodectic Mange (also see Chapter 43)

Clinical Signs

- Demodectic mange in the cat is caused by two mites, *Demodex cati* and *Demodex gatoi*.
- *D. cati* is a rare disease.
- The localized form affects the head and neck while the generalized form affects the head, neck, trunk, and limbs
- Lesions consist of erythema, papules, alopecia, scales, and crusts.
- Generalized demodicosis is usually associated with an underlying disease (diabetes mellitus, feline leukemia virus infection, feline immunosuppressive virus infection).
- Mites have been isolated from skin scrapings of the external ear canal.
- Lesions of *D. gatoi* consist of alopecia, scale, and crusts of the head, neck, and elbows or non-inflammatory alopecia of the ventral abdomen.
- *D. gatoi* is contagious to other cats.

Diagnosis

- Diagnosis is based on identification of the mites on skin scrapings, deep scrapings for *D. cati*, and superficial scrapings for *D. gatoi*.

Treatment

- Treatment consists of weekly lime sulfur dips (LymDyp, DVM Pharmaceuticals).
- For *D. gatoi*, treat all in-contact cats.

Stable Fly Dermatitis (Fly Bite Dermatitis)

Clinical Signs

- Stable flies (*Stomoxys calcitrans*) are the most frequent cause of fly bite dermatitis.
- The rasping mouthparts shred the skin while they feed, which is highly irritating to the dog.
- The flies usually attack the tips of the ears or the folded edge of the ear.
- The flies produce small ulcers, which then may ooze blood and result in hemorrhagic crusts.
- The affected area may also be alopecic and erythematous.
- Ulceration, fibrosis, and scarring with deformation of the pinna may result if the condition is chronic.
- The lesions may become recurrent due to head shaking or scratching by the dog.

Diagnosis

- Diagnosis is based on clinical signs and a history of exposure to stable flies.

Treatment

- House the dog indoors and apply a fly repellent containing a pyrethrin or permethrin.
- Control the flies. Since the stable fly lays eggs in decaying hay and manure, manure clean up and environmental insecticides are indicated.

ALLERGIC DISEASES

Atopic Dermatitis and Cutaneous Adverse Food Reaction (also see Chapters 46 and 47)

Clinical Signs

- Hypersensitivity disorders such as atopic dermatitis and cutaneous adverse food reaction may involve pruritus of the pinna in addition to other areas of the body.
- In a small number of dogs, the ears may be the only affected sites.
- Lesions are characterized by erythema of the concave, convex, or both surfaces of the pinna and may occur in the presence or absence of otitis externa.

Diagnosis

- Diagnosis of atopy is based on history, clinical signs, and the exclusion of other diseases causing pruritus.

Treatment

- Treatment of atopic dermatitis includes allergen avoidance, antihistamines, fatty acids, glucocorticoids, cyclosporine (Atopica, Novartis), treatment of secondary bacterial and yeast infections, and allergen-specific immunotherapy.
- Diagnosis of cutaneous adverse food reaction is based on response to a food elimination trial consisting of a novel protein and carbohydrate source or hydrolyzed protein diet.

Contact Dermatitis

Clinical Signs

- Contact dermatitis is a rare dermatosis in small animals.
- Affected areas include sparsely haired areas of the body, such as the concave surface of the pinna, external ear canal, axillae, and inguinal region.
- It may occur due to topical application of medications or as a result of systemically administered medications.
- Pinnal lesions are usually caused by otic preparations. Some commonly implicated ingredients include neomycin and propylene glycol.
- Erythema, papules, and macules are seen initially, and with continued exposure, erosions and ulcerations may develop.

▼ ***Key Point*** Suspect contact dermatitis when a case of otitis fails to respond or worsens after appropriate topical medication is administered.

- A drug reaction to a systemically administered medication may present with lesions on the pinna as well as other parts of the body.

Treatment

- Discontinue the medication.
- Glucocorticoids may be needed for the inflammation.
- Pentoxifylline (10 mg/kg q12h) has been used for the prevention of clinical symptoms of allergic contact dermatitis in dogs with a confirmed allergy to plants of the *Commelinceae* family (spreading day flower, doveweed, wandering Jew).

IMMUNE-MEDIATED DISEASES

Pemphigus Foliaceus and Pemphigus Erythematosus (also see Chapter 48)

Clinical Signs

- Pemphigus is an autoimmune vesicular to pustular dermatitis.
- Pemphigus foliaceus is the most common autoimmune disease reported in the dog and cat.
- Lesions include papules, pustules, erythema, scale, alopecia, and crusts.
- In the dog, the lesions are most commonly found on the face, nasal planum, ear pinnae, and footpads, while the ear pinnae and face are commonly affected in the cat.
- Pemphigus erythematous is thought to be a benign form of pemphigus foliaceus and may represent a crossover between pemphigus and lupus erythematosus.
- Lesions are common on the face and pinnae and consist of erythema, scale, pustules, papules, alopecia, and crusts.
- The nasal planum may be depigmented.

Diagnosis

- Diagnosis is based on histopathology of skin biopsies.

Treatment

- Treatment for pemphigus foliaceus includes systemic glucocorticoids usually combined with other immunosuppressive medications.
- Pemphigus erythematosus may respond to less aggressive medications such as tetracycline and niacinamide, topical glucocorticoids, or topical tacrolimus (Protopic ointment, Fujusawa).

Systemic Lupus Erythematosus

(also see Chapter 48)

Clinical Signs

- Systemic lupus erythematosus is an autoimmune disease that affects multiple organ systems.
- Cutaneous lesions include alopecia, crusts, ulceration, and depigmentation.
- Skin lesions may be multifocal or generalized and frequently involve the face, ears, and distal limbs.

Diagnosis

- Diagnosis is based on clinicopathologic abnormalities, cutaneous histopathology, and a positive antinuclear antibody test.

Treatment

- Treat with immunosuppressive drugs. Base treatment upon specific organ involvement.

Discoid Lupus Erythematosus

(also see Chapter 48)

Clinical Signs

- Discoid lupus erythematosus usually presents as nasal ulceration and depigmentation.
- Rarely, the ear pinna, scrotum, and limbs may be alopecic with crusts and ulcers.

Diagnosis

- Diagnosis is based on cutaneous histopathology, lack of systemic signs of illness, and negative or normal diagnostic tests.

Treatment

- Treatments may include one or more of the following: topical steroids, oral steroids, sunscreen, tetracycline and niacinamide, tacrolimus (Protopic ointment, Fujusawa), and vitamin E.

Vasculitis

Clinical Signs

- Cutaneous vasculitis is uncommon in the dog and rare in the cat.
- It may be characterized by erythema, alopecia, ulcers, crusts, and necrosis involving the extremities and ear pinnae, which may be idiopathic, immune-mediated, drug induced, or associated with a concurrent infectious or neoplastic disease.

Diagnosis

- The diagnosis is made based on histopathology results.
- Perform other diagnostic tests to look for an underlying cause of the vasculitis.

Treatment

- Treat by removing the inciting cause, controlling the underlying disease, glucocorticoids, pentoxifylline (generics; Trental, Aventis Pharmaceuticals), sulfone (Dapsone, Jacobus Pharmaceutical Co., Inc.) and sulfasalazine (Azulfidine, Pharmacia & Upjohn).

Proliferative Thrombovascular Necrosis

Clinical Signs

- Proliferative thrombovascular necrosis is an uncommon disease in dogs.
- The etiology is unknown and there are no breed, sex, or age predilections.
- The lesions begin at the apical margin of the ears and spread along the concave surface.
- An ulcer may be located in the center of the lesions.
- A scaly, thickened, hyperpigmented zone surrounds the ulcer.
- Prominent vessels can be seen coursing the margins of the lesions.
- Older lesions undergo necrosis and eventually deform the ear pinna.

Diagnosis

- The diagnosis is based on history, physical examination, and histopathology.
- The histopathology reveals arteriolar proliferation, sclerosis, hyalin degeneration, and thrombosis.

Treatment

- The disease is slowly progressive. Treat with partial pinnectomy.
- However, there have been anecdotal reports of treatment with pentoxifylline (generics; Trental, Aventis Pharmaceuticals) or the combination of tetracycline and niacinamide.

ENVIRONMENTAL DISEASES

Frostbite

Clinical Signs

- Frostbite is due to prolonged exposure to freezing temperatures or contact with frozen metal objects.
- Frostbite may affect the tips of the ears, digits, scrotum, and tail tip.
- These areas are poorly insulated by the hair and the blood vessels are not protected.
- Frozen skin appears pale and is cool to the touch.
- In severe cases, the skin ulcerates, becomes necrotic, and sloughs.

Diagnosis

- Base the diagnosis on history and physical examination.

Treatment

- Handle frozen tissues gently and thaw by the application of warm water.
- In severe cases, amputation of the affected part may be necessary.
- Delay surgery until a distinction between viable and necrotic tissue can be made.

Actinic Keratoses

Clinical Signs

- Actinic (solar) keratoses are caused by excessive exposure to ultraviolet light.
- The lesions occur on lightly pigmented animals or on areas of the body that have sparse hair coverage (ear pinnae, face, abdomen).
- Actinic keratoses of the pinna occur rarely in dogs and occasionally in white-eared cats in sunny areas of the world.
- The lesions may be single or multiple.
- Acute lesions consist of poorly defined areas of erythema, hyperkeratosis, and crusting, while chronic lesions are indurated, crusted, hyperpigmented plaques.

Diagnosis

- Base the diagnosis on history, physical examination, and histopathology.

Treatment

- Treatment for early lesions is reduction of ultraviolet exposure.
- Actinic keratoses are premalignant lesions capable of becoming squamous cell carcinomas. Surgery (pinnectomy, cryosurgery, laser surgery) is the treatment of choice for advanced actinic keratoses or neoplastic lesions.

Arteriovenous Fistula

Clinical Signs

- An arteriovenous fistula is a direct communication between an artery and vein that bypasses the capillary circulation.
- They are rarely reported in dogs and cats.
- They may be congenital or acquired, with acquired being the more common of the two.
  - Acquired arteriovenous fistulas may result from penetrating wounds, blunt trauma, infection, neoplasia, and surgical procedures and mainly affect the paws, neck, temporal region, pinna, legs, flank, and tongue.
- Affected areas are edematous and painful.
- Superficial blood vessels proximal to the fistula may be distinct and tortuous.
- The fistula is characterized by pulsating vessels, palpable thrills, and continuous murmurs.

Diagnosis

- Base diagnosis on history, physical examination, and demonstration of the fistula by contrast radiography.

Treatment

- Treatment includes removal of the fistula or amputation of the affected part.

Neoplastic Disease (also see Chapter 28)

Clinical Signs

- Ears are common sites for skin tumors.
- Neoplasms that affect the ear pinnae include squamous cell carcinoma, histiocytomas, mast cell tumors, basal cell tumor, sebaceous adenomas, hemangiomas, hemangiosarcomas, epitheliotropic lymphoma, and fibrosarcomas.
- Refer to Chapter 28 for a complete discussion of cutaneous neoplasia.

HEREDITARY DISEASES

Pattern Baldness

Clinical Signs

- One form of pattern baldness affects the pinna of male and rarely female Dachshunds.
- Hair loss from the pinna occurs at 6 to 9 months of age and slowly progresses to complete pinnal alopecia.
- As the alopecia progresses, the skin hyperpigments.
- Complete baldness may occur by 8 to 9 years of age.

Diagnosis

- Base the diagnosis of pattern baldness on history, physical examination, and histopathology.
- Histologically, there is a decrease in size (miniaturization) of the hair follicles with normal adnexal structures.

Treatment

- Studies evaluating melatonin (5 mg PO q24h and constant-release implants, 1–3 implants containing 12 mg each, SC) as a treatment for pattern baldness have shown it to be effective for hair regrowth.
  - Hair regrowth is apparent in 1.5 months after initiation of therapy, with maximum growth in 3 to 4 months.

Psoriasiform-Lichenoid Dermatosis of English Springer Spaniels

Clinical Signs

- Psoriasiform-lichenoid dermatosis of English Springer spaniels is a rare disease.

- Asymptomatic, symmetric, erythematous, lichenoid plaques and papules are noted on the concave portion of the pinna, in the external ear canal, and in the inguinal region.
- The lesions become hyperkeratotic, and spread to involve the face, ventral trunk, and perineal region.

Diagnosis

- Base diagnosis on history, physical examination, and histopathology.

Treatment

- Four cases treated with cephalexin showed excellent response with complete resolution of the lesions. No other treatment to date has been found effective.

Melanoderma and Alopecia in Yorkshire Terriers

Clinical Signs

- Melanoderma and alopecia in Yorkshire terriers is presumed to be a genetic dermatosis.
- Lesions consist of symmetric alopecia and hyperpigmentation over the bridge of the nose, pinnae, tail, and feet.
- The syndrome usually begins at 6 months to 3 years of age.

Diagnosis

- Base diagnosis on history, physical examination, and histopathology

Treatment

- Mild lesions may resolve spontaneously.
- Most dogs are affected for life.

Hereditary Lupoid Dermatosis of German Shorthaired Pointers

Clinical Signs

- Hereditary lupoid dermatosis of German shorthaired pointers is an uncommon disease.
- Lesions are first seen at 6 months of age and consist of scaling and crusting on the face, ears, and back and then become generalized.
- The hocks and scrotum may be severely affected.

Diagnosis

- Diagnosis is made based on history, physical examination, and histopathology.

Treatment

- Dogs respond poorly to treatment.
- Treatments that have been tried include antiseborrheic shampoos, glucocorticoids, fatty acid supplementation, and retinoids.

Dermatomyositis

Clinical Signs

- Dermatomyositis is a hereditary disease seen most commonly in collies and Shetland sheepdogs. Other breeds have been reported.
- Lesions begin before 6 months of age and consist of alopecia, erythema, scaling, and mild crusting.
- Ulcerations and scarring may be seen in severely affected dogs.
- Lesions are found on the face, tips of ears, carpal and tarsal regions, digits, and tail tip.
- The myositis occurs after the skin lesions are recognized and correlate with the severity of the skin disease.

Diagnosis

- Base diagnosis on history, physical examination, and histopathology of the skin and muscle.

Treatment

- Treatments include sun avoidance, vitamin E, pentoxifylline (generics; Trental, Aventis Pharmaceuticals), fatty acid supplementations, and glucocorticoids.

MISCELLANEOUS DERMATOSES

Zinc-Responsive Dermatosis

Clinical Signs

- In dogs, two syndromes of zinc-responsive dermatosis have been recognized.
  - In Syndrome I, young adult Siberian huskies, Alaskan malamutes, and bull terriers develop erythematous, crusty, scaly lesions affecting the mouth, chin, periocular region, and ears.
  - Syndrome II occurs in rapidly growing puppies fed zinc-deficient diets, high-calcium or high-cereal diets that have high levels of phytate and thus poor zinc absorption, or diets oversupplemented with vitamins and minerals.
- Hyperkeratotic plaques occur over areas of repeated trauma.

Diagnosis

- Base diagnosis on history, physical examination, and histopathology.

Treatment

- Zinc supplementation is necessary for treatment of Syndrome I. Supplementation is life long.
- Treatment for Syndrome II involves changing to an appropriate diet.

Juvenile Cellulitis

Clinical Signs

- Juvenile cellulitis is an uncommon disease that usually affects puppies 6 to 14 weeks of age.
- The etiology is unknown.
- Predisposed breeds include golden retrievers, dachshunds, and pointers.
- Lesions mainly affect the eyelids, pinna, periocular, and muzzle region.
- Initially, the affected areas are swollen. Papules and pustules develop, which then fistulate, drain, and crust.
- They may have concurrent otitis externa.
- Systemic signs of fever, depression, and inappetence are usually present.
- There is severe submandibular lymphadenopathy.

Diagnosis

- Base diagnosis on history, physical examination, and histopathology.

Treatment

- Treatment consists of high doses of oral glucocorticoids.

Ear Margin Seborrhea (also see Chapter 50)

Clinical Signs

- Ear margin seborrhea is a keratinization disorder and is a common condition in the dachshund.
- Cocker spaniels and springer spaniels may be affected.
- Ear margin seborrhea is characterized by numerous small, greasy plugs and scale adhering to the skin and hairs of the medial and lateral margins of the pinna.
- The disease is frequently asymptomatic. In chronic cases, fissuring may occur which is painful.

Diagnosis

- Base diagnosis on history, physical examination, and histopathology. Histopathologically there is marked surface and follicular orthokeratotic or parakeratotic hyperkeratosis.

Treatment

- Remove the accumulated debris using sulfur-salicylic or benzoyl peroxide shampoos.

Canine Eosinophilic Pinnal Folliculitis

Clinical Signs

- Canine sterile eosinophilic pinnal folliculitis is an uncommon, non-seasonal, bilaterally symmetric dermatosis in dogs. The etiology is unknown.
- Lesions consist of erythematous papules and crusts on the concave surface of the pinna.

Diagnosis

- Base diagnosis on history, physical examination, cytology, C/S, and histopathology.
- Cytologic examination of a papule reveals numerous eosinophils, cultures are negative, and histology reveals an eosinophilic folliculitis and furunculosis.

Treatment

- The disease is responsive to topical or oral glucocorticoids but may recur.

Sebaceous Adenitis

Clinical Signs

- Sebaceous adenitis is an uncommon dermatosis of the dog and rare in the cat.
- Many breeds may be affected; however, there are breed predilections for standard poodles, Akitas, Vizslas, and Samoyeds.
- Lesions are commonly found on the face, pinnae, head, and dorsal trunk.
- Lesions consist of papules, alopecia, scales, and follicular casts.

Diagnosis

- Diagnosis is made based on history, physical examination, and histopathology.

Treatment

- Treatment includes topical antiseborrheic shampoos, emollient rinses, fatty acid supplementation, glucocorticoids, cyclosporine (Atopica, Novartis), vitamin A, and retinoids.

SUPPLEMENTAL READING

Matousek JL. Diseases of the ear pinna. Vet Clin Small Anim 34: 511, 2004.

Chapter 59

Otitis Externa

James O. Noxon

The external ear canal consists of skin overlying cartilage, which provides the structural support to keep the canal open. The auricular cartilage is the framework for the pinnae and vertical aspect of the ear canal, and the annular cartilage supports the horizontal component of the external ear canal. The cartilage is covered by skin, which contains sebaceous sweat glands, apocrine (ceruminous) glands, and hair follicles. Otitis externa is defined as inflammation of the skin and adnexal structures of the ear canal. This condition is one of the most common and frustrating problems encountered in small animal practice.

▼ ***Key Point*** Otitis externa is often a clinical manifestation of a generalized dermatologic condition.

The cause of otitis externa in a patient is usually multifactorial especially when chronic and requires a systematic diagnostic and therapeutic plan for resolution and to prevent recurrence.

ETIOLOGY AND PATHOGENESIS

Primary Factors

- Primary factors are those conditions or disorders that *initiate* the inflammatory process within the ear canal.
- Examples include parasites *(Otodectes cynotis);* allergies (food, atopic dermatitis, contact); foreign bodies (grass awns, foxtails); keratinization disorders (seborrhea); and, less frequently, trauma, autoimmune disease (pemphigus), sebaceous adenitis, zinc-responsive dermatoses, and endocrinopathies (hypothyroidism)
- Primary factors may initially induce disease outside the external ear canal. Otitis externa may be an extension of a pinnal disorder (see Chapter 58), otitis media, or otitis interna (see Chapter 61).

▼ ***Key Point*** Identification and management of the primary factors is the key to long-term control of otitis externa.

Predisposing Factors

- Predisposing factors facilitate the inflammation by *promoting* an environment conducive to survival of perpetuating factors.
- Examples include conformation of the ear canal (long canal with a deep vertical component), moisture in the canal (dogs that swim, residual cleaning agents in the ear canal), hair in the ears (e.g., in poodles and terriers), breed predisposition (e.g., Chinese Shar-Pei, stenotic canals), immunodeficiency syndromes, endocrine imbalances, iatrogenic ear trauma (e.g., unnecessary hair removal and cleaning with cotton-tipped applicators), and obstructive disease (e.g., cancer, polyps, and hyperplasia).

▼ ***Key Point*** Predisposing factors do not initiate otitis externa.

Perpetuating Factors

- Perpetuating factors *sustain and aggravate* the inflammatory process.
- Mechanisms include occlusion of the canal, which prevents drying or proper application of medication; secretion of irritating factors; alterations in pH of the canal; and formation of a focus of infection (otitis media).
- Examples include bacterial infections *(Staphylococcus intermedius, Proteus mirabilis, Pseudomonas aeruginosa,* and *Escherichia coli),* and yeast infection *(Malassezia pachydermatis).* Otitis media serves as a source of infectious agents, and chronic hyperplastic changes of the ear canal may obstruct the canal.

▼ ***Key Point*** Medication may also act as a perpetuating factor (or a primary factor) of otitis externa, by causing secondary contact irritation or allergy (e.g., neomycin and topical anesthetics), or by leaving residue in the canal (e.g., oil-based preparation).

CLINICAL SIGNS

Signs Directly Related to Ear Involvement

- Head shaking
- Scratching and rubbing of the ears
- Discharge from the ears
- Pain around the ears or head (manifested as crying or whining)
- Malodor
- "Hotspots" around the periauricular skin (cheek, behind the ear)
- Behavioral changes: pets may become irritable and aggressive toward family members as a result of ear pain.
- Licking of ears by *other* pets in the household may indicate malodor and an inflammatory process.
- The pet's loss of hearing, although difficult to document, is a common owner's complaint.

Signs Reflecting an Underlying (Predisposing) Dermatologic Disorder

- Face rubbing, sneezing, foot licking, anal scooting, and generalized scratching suggest underlying allergic disease.
- Severe pruritus may incriminate parasitic (scabies, *Notoedres* mange) or allergic (flea allergy dermatitis) causes.
- Scaling and crusting may indicate seborrheic disease, sebaceous adenitis, or pemphigus foliaceus as a primary disease.
- Recurrent bacterial dermatitis may suggest an allergy, an endocrine imbalance, or immunologic insufficiency.
- Accompanying alopecia may reflect an underlying endocrine imbalance or ectoparasitic infestation.
- Bilaterally symmetrical alopecia with easily epilated hair is a feature of endocrine disease.
- Focal alopecia or alopecia characterized by broken or fragmented hairs may indicate trauma (pruritus) or infectious (bacterial, fungal) disease.

Signs of Associated Otitis Media and Otitis Interna

Typically, the most common clinical sign of otitis media is chronic and recurrent otitis externa. Neurologic signs are more specific for otitis media (sympathetic and facial neuropathy) and otitis interna (peripheral vestibular syndrome) but are not always present in dogs with middle or inner ear disease. Refer to Chapter 61.

DIAGNOSIS

Use diagnostic procedures to identify primary factors (initiating factors), predisposing factors, and perpetuating factors. All etiologic factors must be considered for successful long-term management of the patient.

History

- Use the history to detect evidence of allergies (seasonality), parasites (possible exposure), and environmental factors of concern.
- Determine the frequency of ear problems and the response to previous treatment, which may give important clues about the pathologic processes.

Physical Examination

- Physical evaluation includes palpation of the external ear canals for pain or evidence of calcification of the external canals (firm or hard on palpation), smelling of the ears, and careful examination of the skin over the entire body for evidence of systemic disease.
- Examine the skin surrounding the opening of the ear canal and the ear pinna
- Examine for vestibular and cranial nerve abnormalities that could indicate otitis media and otitis interna (see Chapter 61).

Otoscopic Examination

- For equipment, a standard otoscope with a diagnostic or operating head is generally adequate; however, a video otoscope is strongly recommended for enhanced imaging and its specialty applications.
- Evaluate for the size of the ear canals; the presence of parasites, exudate, hair, or foreign material; the color of the epithelium; the presence of ulcers or masses; and the appearance and integrity of the tympanic membrane (see Chapter 1).
- Sedation of the animal may be necessary.
  - Topical anesthesia with 1% to 2% lidocaine HCl, 0.5% proparacaine, or other similar agents may be sufficient.
  - General anesthesia is indicated for removal of most foreign objects; for biopsy, and for thorough evaluation of the horizontal ear canal.
- Avoid trauma to the ear canal by advancing the otoscope cone only while directly visualizing the canal.

Otoscopic Abnormalities

- **Erythema:** reddened epithelium
- **Exudation:** dark, dry, granular exudate is generally found with ear mite infection; moist, yellow, odoriferous exudate is generally a sign of bacterial infection; brown, waxy exudate is generally consistent with yeast infection and overgrowth; and yellow, waxy-to-dry scale may be found with keratinization disorders. Cytology of otic exudates is always indicated to confirm these clinical clues.
- **Hyperplasia** (lichenification, hyperpigmentation) is a sign associated with chronicity. Surgical management

may be necessary in patients with severe hyperplasia (occlusion) that is unresponsive to therapy.
- **Ulcers** suggest more severe disease and indicate a need for aggressive treatment—seen especially with *Pseudomonas* and yeast infections.

Cytology

- Cytology often provides an indication for the best initial treatment plan and is essential in the assessment of secondary bacterial and yeast infections.
- Use a cotton-tipped applicator to swab the external canal, if possible at the outer end of the horizontal ear canal. Remove and gently roll the applicator onto a clean glass slide.
- Heat fix and stain the slide with a modified Wright-Giemsa preparation (Diff-Quik; American Scientific Products). Examine a separate slide after adding mineral oil (and without heat fixing or staining) to look for external parasites.
- Examine for parasites, cellular components, and infectious agents (bacteria, yeast, fungi). Notice whether infectious agents are present within inflammatory cells or free in the exudate and whether the infectious agents are present as a single population or part of a mixed population.

▼ ***Key Point*** Cytology is a rapid, inexpensive diagnostic procedure that is indicated in all cases of otitis externa. It should be repeated at every recheck examination and the results used to modify and adjust therapy. Document the extent (or severity) of bacteria and/or yeast for comparisons at follow-up visits.

Culture and Susceptibility Testing

- Bacterial culture of the external ear canal is recommended when:
  - Cytologic examination of exudate from the external ear canal shows a uniform population of gram-negative bacteria (or rod-shaped bacteria if Diff Quick is the stain used).
  - Ulcers are present in the external ear canal and bacteria are present on cytologic examination of exudate.
  - A bacterial infection continues to be present (as demonstrated by cytologic examination of smears from the ear canal) despite appropriate empiric antimicrobial treatment.
- Otitis media should also be suspected in animals with chronic (recurrent or persistent) otitis externa even when the tympanic membrane is intact. Bacterial culture of the middle ear (by myringotomy if the tympanic membrane is intact) may be indicated if the tympanic membrane appears at all abnormal (see Chapter 61).

Biopsy

- Biopsy is indicated when abnormal growths are detected.
- Biopsy instruments designed for endoscopic procedures are useful to collect a small tissue sample from the ear canal.
- Excisional biopsy of lesions is preferred whenever possible.

Diagnostic Imaging

- Radiography is occasionally indicated (especially in severe or chronic otitis) to evaluate the patency of the ear canal, to aid in detecting the presence of otitis media and otitis interna, and to determine the extent of involvement of surrounding structures.
- Computerized tomography (CT scans) and magnetic resonance imaging (MRI) are more sensitive diagnostic tests to evaluate the patency of the ear canal (and involvement of the middle ear).
- All imaging techniques are more valuable in evaluating the middle and inner ear than the external ear canal, where their main benefit would be to determine if the ear canals are patent and the extent of any calcification of the canal (considered a poor prognostic indicator if extensive).

Other Tests

- Miscellaneous diagnostic tests are helpful to identify predisposing and primary factors. See respective chapters for details on these tests. Tests frequently recommended include hematology, serum biochemistry profiles, urinalysis, thyroid function tests, adrenal function tests, intradermal allergy tests, serum (in vitro) allergy tests, skin scrapings, fungal cultures, and dietary trials.

TREATMENT

The initial treatment of otitis externa is directed toward control of the active inflammatory process, because this aspect of the disease is of immediate concern to the client and patient. After the perpetuating factors are controlled, treatment is directed toward removing the underlying predisposing factors and managing the primary etiologic factor.

Successful long-term management of otitis externa requires identification and treatment of perpetuating factors, predisposing factors, and primary etiologic factors.

Principles of Medical Treatment

- Most commercial ear preparations contain multiple therapeutic agents. Select otic preparations carefully for the desired active agents (Table 59-1). Do not use products with agents that are not specifically indicated

Table 59-1. ACTIVE INGREDIENTS COMMONLY PRESENT IN OTIC PREPARATIONS

Ceruminolytic/softening agents
- Hexamethyltetracosane
- Docusate sodium (dioctyl sodium sulfosuccinate, DSS)
- Squalane

Keratolytic
- Carbamide peroxide
- Benzoic acid
- Salicylic acid
- Sulfur
- Resorcinol

Antifungal
- Nystatin
- Thiabendazole
- Miconazole
- Clotrimazole
- Cuprimyxin
- Silver sulfadiazine

Antibacterial
- Bacitracin
- Chloramphenicol
- Colistin
- Enrofloxin
- Gentamicin
- Neomycin B sulfate
- Polymyxin B
- Penicillin G
- Silver sulfadiazine
- Sulfacetamide
- Sulfur

Anti-inflammatory

Glucocorticoids
- Hydrocortisone
- Prednisolone
- Isoflupredone acetate
- Triamcinolone acetonide
- Dexamethasone
- Fluocinolone acetonide

Dimethyl sulfoxide

Antiparasitic
- Pyrethrins
- Thiabendazole
- Carbaryl
- Rotenone

Topical Anesthetic
- Tetracaine
- Lidocaine

in the ear being treated (i.e., do not use a product with antibiotics if there is not a bacterial infection).

▼ ***Key Point*** Do not apply cleansing agents, parasiticides, ceruminolytic/keratolytic agents, disinfectants, ototoxic antimicrobials, or oil-based medications into the ear canal of animals in which the tympanic membrane is ruptured.

- Choose the delivery vehicle for medication carefully.
  - Lotions and solutions are more easily applied deep in the external canal.
  - Oil-based medications are useful to treat dry, scaly lesions, such as those of seborrhea sicca. These products penetrate into the skin well, but their penetration deep into the canal is often limited by hair or debris.
  - Creams, pastes, and powders are difficult to apply deep in the external ear canal and may leave a residue. These formulations are rarely indicated in the treatment of otitis externa in dogs and cats.
- Apply topical otic medications liberally to ensure delivery of adequate amounts of medication to the deeper aspects of the canal. An average size dog (around 20 kg) would require 0.5 to 1.0 ml of medication in the ear canal to penetrate to the level of the tympanic membrane.
- Gently massage the external canal for 15 to 30 seconds to help to deliver medications deep into the horizontal canal.

Cleaning the External Canal

▼ ***Key Point*** The initial objective of medical management of otitis externa is to clean and dry the external canal. This process makes the environment less favorable for sustained microbiologic growth and reduces the inflammatory process in most patients.

Cleaning Techniques

- There are several techniques useful to clean ears. In order of increasing effectiveness, they include: hand cleaning by infusion and massage, the use of commercial ear flushing equipment, deep ear flushing, and spot flushing and suction through the otoscope.
- Hand cleaning is generally the easiest and fastest method to clean ears. It is the technique used for rapid cleaning in the hospital and may be taught to pet owners to be done at home (Table 59-2).
- A commercial ear-cleaning unit (AuriFlush, Schering-Plough) is useful and moderately effective for cleaning ears. Limitations include poor cleaning deep in the horizontal canal and loud noise for the patient, which will result in low tolerance by unsedated patients.
- Deep flushing of the ear canal is done under general anesthesia with a pediatric gastric tube, which has dual ports, one for flushing sterile saline and one for constant suction. This is a highly effective technique to clean deep in the ear canal.
- The most thorough ear cleaning can be accomplished using a catheter (Figure 59-1) passed through a hand-held or video otoscope (Table 59-3).

Cleaning Procedures

- Deep flushing and thorough cleansing of the ear canal requires the patient to be placed under a general anesthetic.

Table 59-2. EAR-CLEANSING TECHNIQUE

Several commercial ear cleansing solutions are suitable for this procedure (see Table 59-4). Isotonic (0.9% saline) is recommended for ear cleansing if the integrity of the tympanic membrane is unknown.

1. Supplies needed include ear cleansing solution, clean cotton balls, and cotton-tipped applicators.
2. Fill the entire ear canal with the desired cleansing solution.
   a. Do not force the solution into the ear canal under pressure.
   b. Fill the entire canal, so that the solution is overflowing from the external ear canal.
3. Place a clean, dry cotton ball into the opening of the external ear canal.
4. Gently massage the external canal using an upward, circular motion in an attempt to pull cleansing solution up from the canal into the cotton ball.
5. Replace the cotton ball periodically to absorb the solution and to remove exudate.
6. Repeat the process as many times as needed to ensure cleansing of the canal. The amount of exudate removed during the massaging process should decrease with each rinsing.
7. Remove any excess fluid (not removed by the cotton balls) by using a dry cotton ball without adding cleanser. Cotton-tipped applicators may be used to dry visible portions of the ear. They should *not* be used to clean deep in the vertical or horizontal external ear canal, as this is likely to cause trauma and lead to impaction of debris and exudates deeper into the ear canal.
8. Infuse a drying solution into the ear canal if necessary. Wipe out excess.

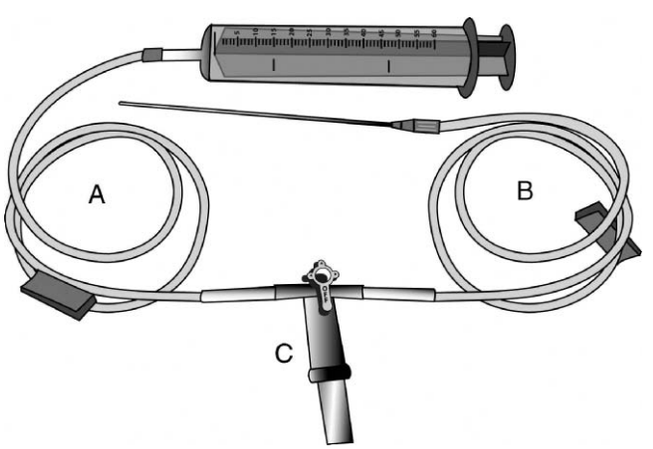

Figure 59-1. Catheter setup for deep ear flushing. *(A),* Intravenous extension set from syringe, *(B),* Intravenous extension set from stopcock to catheter, *(C),* suction attachment to stopcock.

- Several commercially available irrigating solutions are effective for routine cleansing of the external ear canal (Table 59-4).
- Use warm 0.9% saline to flush the ear canal when the integrity of the tympanic membrane is unknown.
- Use an ear loop carefully to remove impacted debris and wax. General anesthesia is strongly recommended.
- Owners of pets with chronic otitis externa, especially ceruminous otitis externa, should be taught the proper ear-cleansing technique that facilitates long-term management of their pet's condition.
- Ceruminolytic agents may be applied in cases of severe, exudative otitis to facilitate removal of the wax; they are most effective when applied to the external canal for 15 minutes before flushing. Ceruminolytic agents act primarily as softening agents and are contraindicated when the tympanic membrane is not intact. One product, (Cerumene, Vetoquinol) has been shown to be safe when it was experimentally deposited and left in the middle ear. If the integrity of the tympanic membrane is not known and ear cleaners are used, a final rinse with sterile saline may remove excess cleaning agents that could be ototoxic if left in the ear.

Table 59-3. DEEP EAR CLEANING TECHNIQUE

1. Supplies needed include a 3-way stopcock, a 60 cc syringe, two intravenous extension sets, a 14-gauge (hand-held otoscope) or 16-gauge (video otoscope) Teflon coated intravenous catheter, and a suction unit with adjustable suction intensity.
2. Suction is attached to one port of the stopcock, the 60 cc syringe with sterile saline is attached via an extension set to the second port, and the catheter is attached to the third port via another extension set.
3. The catheter is passed through the hand-held or video endoscope and the flushing is done by an assistant as the operator guides the catheter to "trouble spots."
4. Suction is used both to clean saline from the field of view and to remove particulate matter.
5. The process is repeated as necessary to thoroughly clean the ear.
6. A dual adaptor (Y-piece) is useful for the video otoscope, to allow constant saline infusion through one port with directed suction through the other port.

▼ ***Key Point*** If inflammation is severe or hyperplasia of the ear canal is moderate to severe, then glucocorticoid therapy is necessary before adequate cleaning can be achieved.

Drying the External Canal

- Several commercial drying solutions are available (see Table 59-4). Active ingredients include acetic acid, sulfur, boric acid, alcohol, benzoic acid, and Burow's solution.
- Infusion of solutions containing alcohol can result in severe discomfort (stinging sensation) to the patient and are avoided when the external ear canal is ulcerated.

Topical Medications

Topical Anti-inflammatory Agents

▼ ***Key Point*** Glucocorticoids applied to the external canal are significantly absorbed and may affect the hypothalamic-pituitary-adrenal axis.

Table 59-4. COMMERCIAL PREPARATIONS USEFUL IN CLEANING AND DRYING THE EXTERNAL EAR CANAL*

Category	Product	Active Ingredients
Cleansing/Flushing Solutions	Oti-Clens (SmithKline)	Propylene glycol Malic acid Benzoic acid
	Epi-Otic (Allerderm)	Lactic acid Salicylic acid Propylene glycol Docusate sodium Chitosanide
	Panotic (Pfizer)	Diazolidinyl urea methylparaben dioctyl sodium sulfosuccinate octoxynol sodium lauryl sulfate, propylene glycol
	OtiCalm Cleansing Solution (DVM Pharmaceuticals)	Propylene glycol Salicylic acid Malic acid Eucalyptus oil
	Zymox Ear Cleanser (Pet King Brands, Inc.)	Glycerin Propylene glycol Benzyl alcohol Zinc gluconate
	Dermapet Malacetic Otic (DermaPet)	Boric acid Acetic acid
	Otifoam Ear Cleanser (DVM Pharmaceuticals)	Cocamidopropyl betaine Salicylic acid Eucalyptus oil
Drying Solutions	ClearX Drying Solution (DVM Pharmaceuticals)	Acetic acid Sulfur Hydrocortisone acetate
	Bur-OticHC Ear Treatment (Virbac)	Burow's solution Acetic acid Propylene glycol
	Panodry (Solvay)	Boric acid Isopropyl alcohol

*Commercial otic cleansers may include both cleansing and drying agents. Products listed are examples—many other effective medications are commercially available.

- Topical glucocorticoids are indicated in most cases of otitis externa to reduce inflammation and swelling, to alleviate pain, and to help minimize fibrosis.
- Otic glucocorticoid administration may interfere with diagnostic procedures, such as intradermal skin tests, adrenal function tests, thyroid function tests, and routine hematologic and biochemical tests (e.g., serum alkaline phosphatase activity); therefore, perform these tests prior to treating with topical glucocorticoids if possible.
- Use the least potent glucocorticoid necessary to accomplish the desired effect.
- Most otic glucocorticoid preparations also contain antiparasitic and/or antimicrobial agents.

Topical Antibacterial Agents

- Base choice on cytologic findings or culture and susceptibility results.
- Medications with antibacterial properties include aminoglycosides, polymyxin B sulfate, chloramphenicol, chlorhexidine, enrofloxacin, iodophors, propylene glycol, and silver sulfadiazine.
- Tris-EDTA alone or added to antimicrobials increases the sensitivity of resistant *Pseudomonas* spp. to several antibiotics.
- Several antibacterial agents, such as ticarcillin (see under "Pseudomonas Infection"), are available in formulations for injection and may be formulated as topical preparations for specific problems.
- Other antibiotic preparations, available as otic or ophthalmic preparations for humans, may be applied to the external ear canal. Examples include colistin sulfate (Coly-mycin Otic, Parke-Davis) and tobramycin (Tobrex Ophthalmic Solution, Alcon).

Topical Antifungal Agents

- Clotrimazole (Lotrimin, Schering) is effective against *Malassezia* spp. yeast.
- Miconazole lotion (Conofite, Pitman-Moore) may be used in the external canal to control yeast or fungal infections (contains alcohol and may be irritating).

- Chlorhexidine
- Povidone-iodine
- Cuprimyxin cream
- Silver sulfadiazine cream (1% Silvadene, Marion) may be diluted with sterile saline or water (1 part cream to 9 parts saline or water) and infused into the ear twice daily as effective treatment against *Malassezia pachydermatis*.

Topical Antiparasitic Agents

- Preparations containing pyrethrins, carbaryl, thiabendazole, milbemycin oxime (MilbeMite, MilbeMite Otic solution, Novartis), ivermectin (Acarexx, Idexx Pharm), and rotenone are effective against ear mites.
- Apply these preparations to the external ear canal regularly (every day or every other day) for 3 weeks or as directed.
- Apply a topical parasiticide (i.e., preparations used for adult fleas) to the skin over the remainder of the animal once weekly during the treatment period.

Acidifiers

- Acidifiers, such as acetic acid and benzoic acid, are somewhat helpful in controlling yeast and bacterial infections.
- Vinegar and water, mixed in a 1:2 ratio, appears to be a safe and effective acidifying agent in the external ear canal of dogs and cats.

Systemic Therapy

Glucocorticoid Therapy

- Systemic glucocorticoids may help alleviate the pain and inflammation of otitis externa.
- Administer a short-acting glucocorticoid (e.g., prednisone [1.1 mg/kg PO q24h]) for 5 to 7 days.
- In a patient with inflammation and hyperplasia of the ear canal and painful ears, use of a short-acting glucocorticoid will help reduce the inflammation and the pain and will facilitate thorough evaluation and cleansing of the ear canal. Administer the glucocorticoid as described previously, and perform the otic examination 24 to 48 hours later.
- Longer term glucocorticoid therapy may be necessary in patients with poorly controlled allergic otitis. Topical glucocorticoids are preferred to systemic.

Antimicrobial Therapy

- Systemic antimicrobial therapy is indicated in a patient with bacterial otitis externa when the tympanic membrane is ruptured (see Chapter 61), the epithelium of the canal is ulcerated, or inflammatory cells containing bacteria are found during cytologic examination.
- Systemic antifungal therapy (see Chapter 20) is rarely necessary but is indicated in patients with severe recurrent yeast infections, in patients that are difficult to medicate topically, or in patients with otitis externa that is caused by a systemic mycotic agent (e.g., *Cryptococcus* spp.). Ketoconazole is effective against *Malassezia pachydermatis* infection in dogs, while itraconazole (5 mg/kg PO q24h) is recommended for use in cats.

Antiparasitic Therapy

- Selamectin (Revolution, Pfizer), milbemycin oxime (MilbeMite, Novartis), and ivermectin (Acarexx, Idexx) are effective topical agents for the treatment of ear mites in dogs and cats.
- Ivermectin (0.3 mg/kg PO) is reported to be effective against ear mite infections in dogs and cats. Treatment may be necessary weekly for 3 to 4 doses to eliminate infection. Do not administer this to collies and collie-mix breed dogs or to heartworm-infected animals because treatment of these breeds or in these circumstances may result in profound adverse reactions. The use of ivermectin in this manner is off-label use; thus, obtain prior owner consent in writing.
- In the case of ear mite infestations, treat all pets in contact with the affected pet with the selected miticidal therapy.

Surgical Management

- Surgical management of otitis externa is indicated to correct conformational defects that predispose an animal to inflammatory disease and to improve ventilation and drainage in affected ears (see Chapter 60).

Treatment of Specific Otic Conditions

All of the following conditions are considered perpetuating factors. Successful long-term management also requires identification and treatment of the primary etiologic factors.

Malassezia Infection

- Instill topical antifungals, such as 1% clotrimazole, once or twice daily (see Table 59-1).
- Give oral ketoconazole (dogs: 5 mg/kg, PO, q12h for 7 days, then q24h) when owners are unable to administer topical medications or when the ears have severe hyperplastic changes that reduce penetration of topical preparations.
- Topical or oral glucocorticoids will help reduce inflammation and edema.
- Some cleansers, such as Epi-Otic (Virbac) and DermaPet Ear Cleanser (DermaPet) have been shown to have some efficacy against yeast infections.
- Acidification of the ear canal with commercial products, such as Advanced pHormula Ear Cleanser

(EVSCO Pharmaceuticals) or with white vinegar and water in a 1:2 ratio will reduce yeast populations.

Pseudomonas Infection

- *Pseudomonas* infections generally cause ulcers and severe pain in the ears and are accompanied by a mucoid to purulent exudate.
- Suspected *Pseudomonas* infections (i.e., if rods are seen on cytology) should be cultured to obtain a sensitivity pattern to allow for the best antibacterial treatment.
- Topical agents with some efficacy include tobramycin, gentamicin, enrofloxacin, silver sulfadiazine, and polymixin B sulfates.
- The effectiveness of topically-applied fluoroquinolones, aminoglycosides, and some other antibiotics may be enhanced by co-treating with Tris-EDTA buffered solution (TRIZ-EDTA, DermaPet; T8 Solution, DVM Pharmaceuticals).
- Ticarcillin may be applied as a 3% solution (Ticar, GlaxoSmithKline) twice daily. Dilute the 3.1 gm vial for injection with 100 ml of sterile water for injection, draw up in 1.0 ml aliquots with an additional 0.5 ml of air added to each syringe, cap each syringe, then freeze. The content of one syringe is applied to each ear, after thawing to room temperature, twice daily for 25 to 30 days. Reevaluate cytology or a bacterial culture after completion of therapy.
- Systemic antibacterial therapy is indicated when otitis media is suspected or when owners are unable to treat ears topically. The fluoroquinolone antibiotics, especially marbofloxacin (Zenequin, Pfizer), are the most likely systemic antibiotics to be effective.
- Give prednisone (1.1 mg/kg, PO, q24h for 5–10 days) to reduce pain and inflammation.

Hyperplastic Changes

- Hyperplastic changes are seen clinically as lichenification and proliferative changes within the external canal and on the pinnae. They are perpetuating factors.
- Manage bacterial and yeast infections with appropriate medications. Orally administered or parenteral medications may be necessary due to the obstructive nature of hyperplastic changes.
- Give prednisone (1.1–2.2 mg/kg, q24h for 14 days) then reevaluate the ears:
  - If there has been no reduction in the degree of hyperplasia, surgery (e.g., total ear canal ablation) is indicated as the best therapeutic option (see Chapter 60).
  - If there has been a partial reduction of the hyperplasia, continued prednisone therapy (either at the same dose or at a reduced q48hr dose) may be necessary.
  - Perform cytology to monitor the type and extent of secondary infection.
- Apply a topical glucocorticoid, such as fluocinolone acetonide (Synotic Otic Solution, Fort Dodge) once or twice daily to each ear canal. Instill medication as deeply into the canal as possible.

PREVENTION

- Use behavioral modification directed toward decreasing activities that predispose the animal to otitis, such as swimming and running through the woods and fields.
- Use regular medical care to decrease the recurrence of otitis externa in predisposed patients.
- Thoroughly clean and dry ears after swimming. Infuse a topical medication containing an astringent, such as boric acid or Burow's solution, into the ears of patients who swim to help keep the ears dry and make the local environment less favorable for bacterial and yeast infections.
- Regularly clean ears of pets with seborrheic disorders.

▼ ***Key Point*** Remove hair only when indicated by the patient's history. Hair clipping or plucking is not recommended as part of routine ear care in most animals because the irritation associated with these procedures may predispose them to otitis externa.

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Chapter 60

Surgery of the External Ear Canal and Pinna

Daniel D. Smeak

External ear canal surgery is performed to provide exposure and drainage for the vertical and horizontal ear canal or to remove irreversibly infected tissue or neoplasia. Procedures for the external ear canal include lateral ear canal resection, vertical ear canal ablation, and total ear canal ablation. Drainage of auricular hematoma is the most common surgical procedure of the pinna; this is discussed later in this chapter.

Success of ear surgery relies on the following:

- An accurate diagnosis
- An appreciation of the severity and extent of the disease
- Correct choice and technical execution of the procedure
- Appropriate postoperative medical treatment of the local disease and any underlying primary skin disorder (see Chapter 59)

▼ ***Key Point*** As a general rule, surgical intervention is considered when appropriate medical treatment for otitis externa fails, or when medical treatment is not expected to be successful.

As ear disease progresses, more extensive surgery is often required to relieve clinical signs. Risk of complications, however, also increases as the surgery becomes more extensive.

GENERAL SURGICAL INDICATIONS

- For ear disease that fails to respond to appropriate medical treatment
- For relapse of clinical signs after initial response to medical therapy
- For extensive irreversible changes of cartilage and/or epithelium
- For certain predisposing factors causing the ear condition (congenital or acquired malformation, stenosis or atresia of the ear canal, or neoplasia)

▼ ***Key Point*** External ear surgery rarely is indicated in the cat except for traumatic or neoplastic conditions. Inflammatory polyps extending into the external ear canal from the tympanic cavity usually do not require external ear surgery for removal. See middle ear surgery (see Chapter 62) for further information.

ANATOMY

A clear understanding of ear anatomy and related structures is critical to uncomplicated ear surgery. The surgeon must identify and preserve several key structures, especially during horizontal canal dissection.

External Ear Canal

- The normal external ear canal (Figs. 60-1 and 60-2) is a 5- to 10-cm–long pliable cartilaginous tube lined by glandular epithelium, extending from the base of the pinna to the tympanic membrane.

Vertical Ear Canal

- From the external opening (aditus), the vertical canal (auricular cartilage) runs ventrally and slightly rostrally, before bending toward the skull to form the shorter horizontal canal.

Horizontal Ear Canal

- The horizontal canal consists of a circular (annular) cartilage extending from the ligamentous attachment to the auricular cartilage medially to the short osseous ear canal (projection of the petrous temporal bone). The canal ends at the tympanic membrane.

Important Local Structures

Salivary Glands (Fig. 60-2*B*)

- The V-shaped parotid salivary gland overlays the ventrolateral aspect of the vertical ear canal and extends ventral to the distal aspect of the horizontal ear canal.

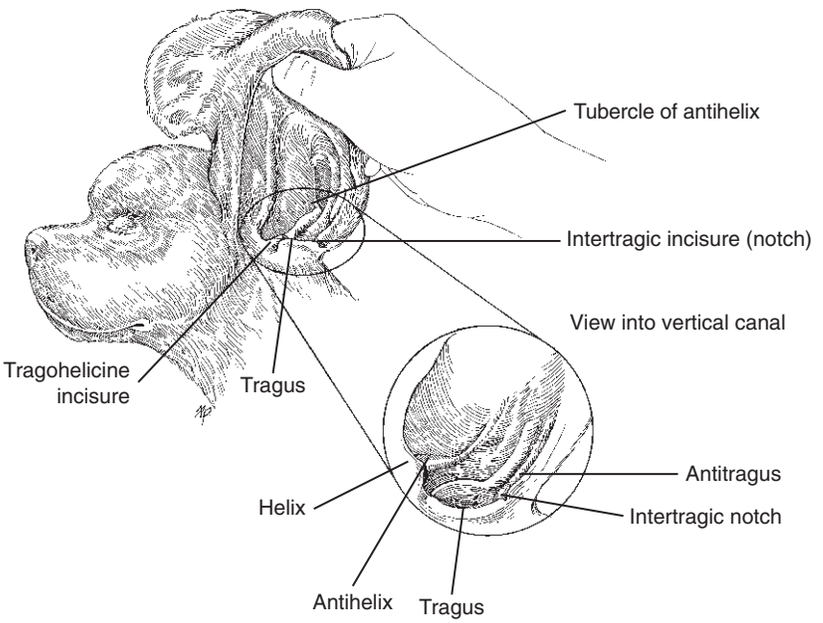

Figure 60-1. Anatomy of the external aditus of the ear.

Blood Vessels (Fig. 60-2*B*)

- Blood supply to the ear is via the great auricular artery, arising from the external carotid artery located medial to the parotid gland and ventral to the osseous bulla.
- Small branches of the great auricular and maxillary arteries run dorsally, parallel to the long axis of the pinna, and medial to the pinna cartilage.

Nerves (Fig. 60-2*B*)

- The facial nerve arises from the stylomastoid foramen located just caudodorsal to the osseous ear canal.
- The nerve is closely associated with the caudal aspect of the horizontal ear canal shortly after it exits the foramen, and courses directly under the horizontal ear canal.
- Terminal branches of the facial and auriculotemporal branch of the mandibular portion of the trigeminal nerve are located just rostral to the ear canal.

PREOPERATIVE CONSIDERATIONS

An accurate preoperative diagnosis along with determination of the extent and severity of disease is important when choosing the surgical procedure. Attempt to identify and control any systemic skin condition before surgery. Changes in the ear canal that usually represent *irreversible* disease include neoplasia, thickening and calcification of cartilage, and firm hyperplastic or proliferative epithelium. Determine if middle ear disease is present concurrently since exploration and drainage of the middle ear is recommended in addition to surgical treatment of the external ear disease (see Chapter 62).

The ear canal is difficult to prepare aseptically, and contamination is inevitable during surgery; so antibiotics should be given during the procedure. Administer a broad-spectrum, bactericidal, intravenous (IV) antibiotic (optimally based on preoperative culture and susceptibility) before and during surgery so that adequate levels are maintained in tissues during dissection.

Ear Palpation

Carefully palpate the ear canal and surrounding structures and determine the degree of pain elicited and if there is evidence of end-stage disease.

- Sharp pain elicited on deep palpation of the external ear canal usually indicates concurrent middle ear infection.
- Palpation of severely thickened and firm ear canal tissue indicates that irreversible changes have occurred.

Dermatologic Examination

Most chronic bilateral ear conditions in dogs are manifestations of a generalized skin condition. Failure to identify and control the primary skin condition may cause failure of the surgical procedure since the disease will likely progress in any remaining ear tissue after surgery.

- Perform a complete dermatologic examination and obtain appropriate tests to determine whether primary systemic skin disease (e.g., hypothyroidism, atopy) is present.

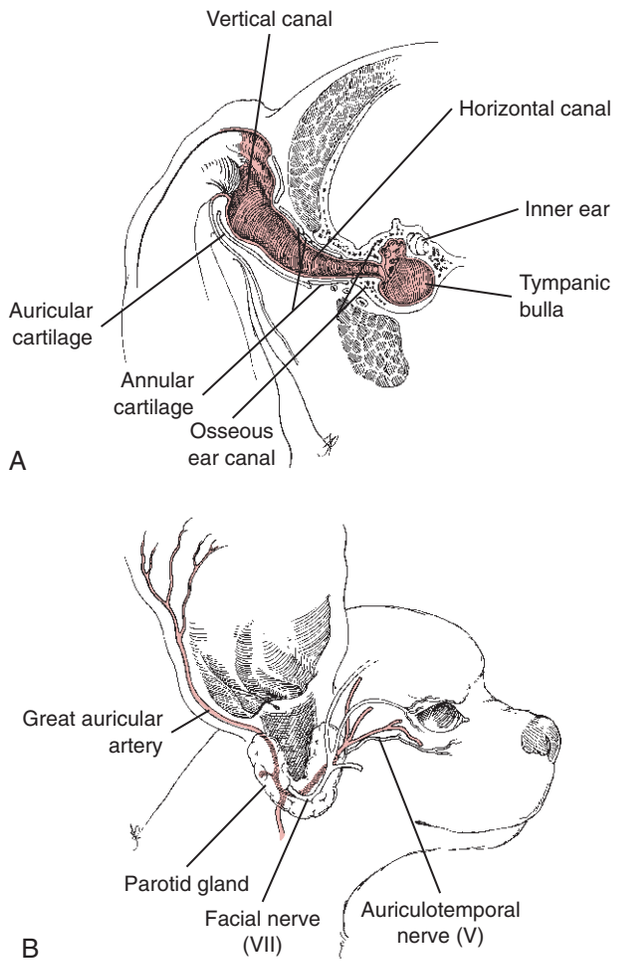

Figure 60-2. Important anatomic structures of the external ear canal. *A*, Transverse section of the head showing ear canal regions and middle ear and inner ear structures. *B*, Location of branches of the external carotid artery in relation to the ear canal and middle ear, and important neural structures in the external ear canal region.

Neurologic Examination

- Perform a neurologic examination, especially in chronic cases of otitis externa, to evaluate for facial nerve involvement (e.g., hemifacial spasm and slow or absent palpebral reflex) and involvement of inner ear structures (e.g., nystagmus and circling).
- Evaluate the patient's ability to hear and alert the owner to any problems before contemplating bilateral ear canal ablation.

Radiographic Examination

Perform any imaging tests before otoscopic examination because irrigation fluid entering the bulla through a damaged tympanic membrane could be misinterpreted as middle ear disease.

- Ventrodorsal skull radiograph is the view of choice to evaluate horizontal canal diameter and to help determine whether the walls of the canal have undergone irreversible calcification.

▼ ***Key Point*** Evaluate for middle ear involvement (Chapter 61) before deciding on the surgical procedure.

- Open-mouth radiography of the bulla is the view of choice to evaluate for middle ear involvement (see Chapter 4).

▼ ***Key Point*** Lack of osseous changes on bulla radiographs does not rule out otitis media.

- Bulla osteitis takes months to form after deep-seated infection. Changes are often very subtle, and evaluation of fluid density within the bulla on plain radiographs also is not an accurate method of diagnosis.
- Computed tomography (CAT scan) is a more sensitive imaging modality to detect subtle changes in the tympanic bulla and cavity.

Otoscopic Examination

- Perform a thorough ear cleansing after obtaining the appropriate diagnostic specimens for culture and susceptibility, cytology, and biopsy (see Chapter 59).
- Otoscopic examination is the most important diagnostic modality to evaluate the severity and extent of disease and tympanic membrane rupture.

▼ ***Key Point*** Otoscopic examination usually requires general anesthesia to completely assess the entire ear canal and tympanum.

Staging of Neoplastic Disease

- Perform regional lymph node aspiration, cytology, biopsy, and thoracic radiography if neoplasia is suspected in the underlying ear disease.

LATERAL EAR CANAL RESECTION—ZEPPS MODIFICATION (LECR)

Surgical Procedure

Objectives

- To expose the medial portion of the vertical canal and horizontal ear canal. Exposure enhances medical treatment of otitis externa and changes local ear conditions favoring drainage. Ventilation of the area improves the local environment by decreasing moisture, humidity, and temperature in the ear canal.
- To resect the lateral portion of the vertical ear canal to remove tumors or to relieve congenital or acquired non-proliferative vertical canal stenosis that is restricting ear drainage and interfering with medical treatment.

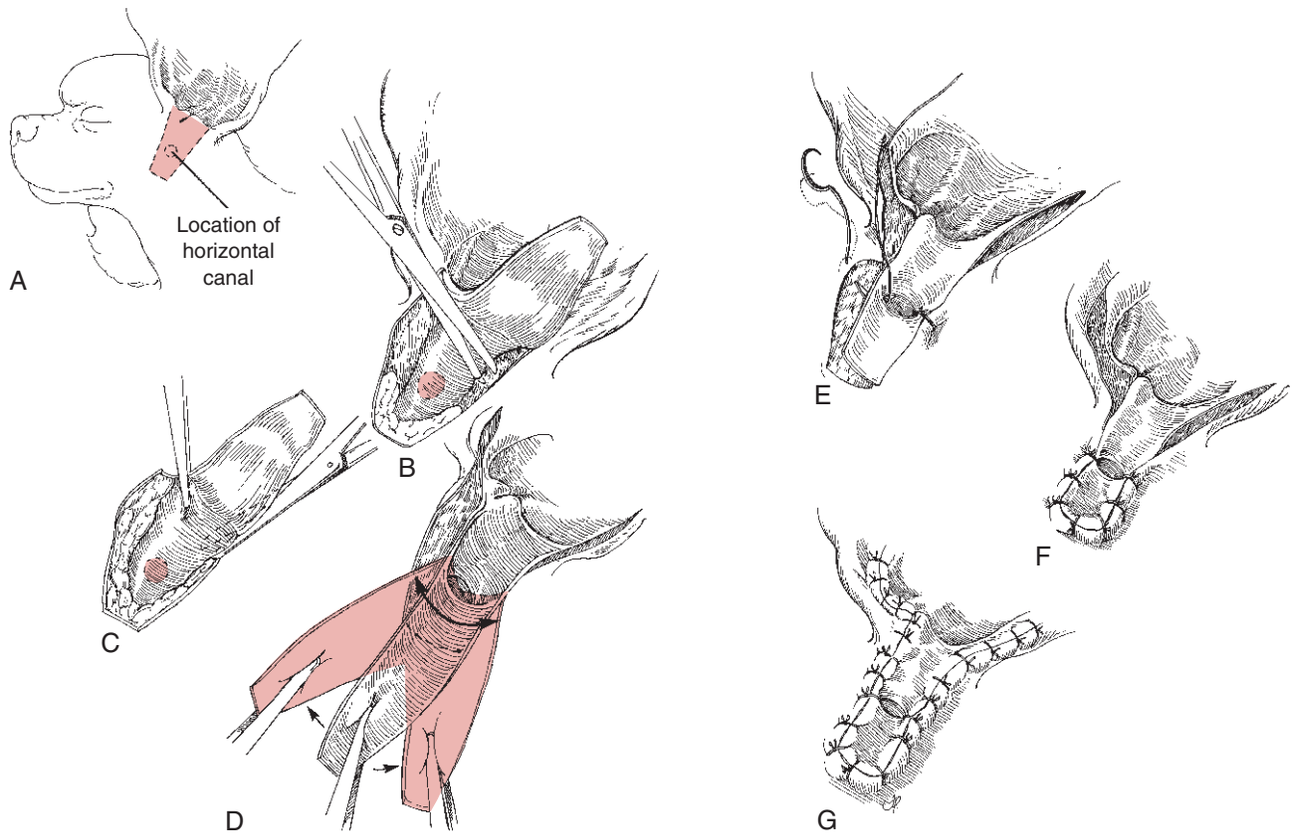

Figure 60-3. Lateral ear canal resection technique. *A,* Two skin incisions are extended parallel to each other from the intertragic notch and tragohelicine notch, tapering down to a distance of 1.5 to 2 cm between the incisions, about 1.5 to 2.5 cm (depending on the size of the animal) ventral to the horizontal ear canal. A transverse incision joins the two vertical incisions. Undermine the skin flap dorsally up to the margin of the aditus. *B,* Incise through the subcutaneous tissue to the level of the vertical ear cartilage. Expose the entire lateral aspect of the vertical ear canal by blunt and sharp dissection of the subcutaneous tissue in a rostral and caudal direction and parotid gland ventrally. *C,* Place an Allis tissue forceps on the tragus, and apply dorsal traction so that the vertical ear canal can be seen from the dorsal aspect of the head. With serrated scissors, make two incisions through the vertical ear canal on the rostrolateral and caudolateral margins while maintaining dorsal traction. Extend the rostral and caudal incisions ventrally in an alternating fashion until the floor of the horizontal canal is reached. The vertical canal essentially is divided into lateral and medial halves. *D,* Extend incisions medially toward the head until the horizontal canal is fully exposed after the lateral wall is reflected ventrally. The base of the lateral wall flap should approximate the width of the horizontal canal. More cartilage can be removed from the remaining ear canal as necessary to fully expose the remaining vertical canal. Manipulate the flap rostrally and caudally until the horizontal canal is held open as wide as possible. *E,* Remove the skin flap and all but the proximal portion of the lateral wall. The 1.5- to 2-cm cartilage (drain board) flap remaining is modified to lie flat and fit the skin defect ventral to the horizontal ear canal. *F,* Begin closure by placing simple interrupted 3-0 to 4-0 monofilament nonabsorbable sutures from the caudal and rostral margins of the most proximal aspect of the drain board to the skin. Throughout closure, place sutures through ear canal epithelium and cartilage first and then to skin to aid in skin coverage of cartilage. *G,* Appose the remaining portion of the flap to the skin with simple interrupted sutures so that the flap is flat against the head. Place additional sutures so that the skin and ear canal epithelium edges are apposed but not crushed.

▼ ***Key Point*** Do not perform LECR if the horizontal or vertical ear canal is hyperplastic and lined with proliferative tissue. In one study, LECR failed in 85% of Cocker spaniels, most likely due to their propensity to develop early hyperplastic disease. Likewise, LECR is contraindicated if medically uncontrolled primary skin disease (e.g., seborrhea) is present because progressive ear disease would be expected in the remaining section of the ear canal.

▼ ***Key Point*** Assess whether there is evidence of concurrent otitis media in the patient; if so, surgical drainage of the middle ear is recommended along with LECR. Left untreated, clinical signs of otitis externa will persist due to persistent otic discharge originating from the middle ear.

Equipment

- Standard general surgical pack and suture
- Heavy serrated straight Mayo scissors

Technique (Fig. 60-3)

1. Place the animal in lateral recumbency with the head positioned, aseptically prepared, and draped so that

the ear region, including the pinna, is exposed and all anatomic relationships are identifiable.
2. Use forceps to determine vertical canal depth and position of the horizontal canal.
3. Incise the lateral portion of the vertical ear canal and reflect ventrally.
4. Preserve the proximal portion of the lateral canal flap for a "drain board."
5. Begin closure at the base of the flap; then appose the distal flap to the skin. Appose the remaining ear epithelium and skin so that no cartilage is exposed.

Postoperative Care and Complications

- Administer appropriate analgesics after surgery (see Chapter 6).
- Continue systemic antibiotics until the incisions are healed and the ear discharge has stopped.
- Continue appropriate topical medical treatment and ear cleansing (see Chapter 59) until no signs of ear infection are present.
- Place an Elizabethan collar to prevent self-inflicted trauma to the wound until suture removal.
- Bandages are rarely necessary unless violent head shaking is noticed in the early postoperative period.
- If wound dehiscence occurs, let it heal by secondary intention closure.
- Remove sutures in 14 days.
- Continue treatment of primary skin disorders as required.

Prognosis

- Prognosis for control of ear disease is good provided that
  - Surgery is performed correctly and for the right indication.
  - No middle ear disease is present.
  - Postoperative medical management of otitis externa is appropriate.
- Up to 35% of LECRs fail because the aforementioned considerations are not met.

VERTICAL EAR CANAL ABLATION (VECA)

This technique combines some of the advantages of the LECR (maintenance of horizontal canal drainage) and total ear canal ablation (removal of chronically infected vertical canal tissue). VECA is a less complicated procedure than total ear canal ablation (TECA); however, surgical treatment of concurrent chronic middle ear disease must be made through a separate ventral bulla approach (see Chapter 62).

▼ ***Key Point*** VECA is contraindicated if irreversible hyperplastic thickening or neoplasia is present in the horizontal canal.

If chronic hyperplastic tissue is present in the vertical canal, it usually extends into the horizontal canal. Therefore this procedure is not commonly indicated, but VECA may be an alternative method for those patients requiring LECR. As with LECR, hearing is preserved, but more diseased ear canal tissue is removed, reducing the need for extensive ear cleaning except at the opening of the horizontal ear canal. Some clinicians believe that VECA may be performed in dogs with end-stage inflammatory ear disease. Owners need to be aware that clinical signs may improve, but continued ear cleaning and antimicrobial therapy may be necessary long after surgery.

Surgical Procedure

Objectives

- To remove the vertical ear canal and preserve the horizontal canal.
- To provide drainage for the horizontal canal.

Equipment

- Same as that for LECR.

Technique (Fig. 60-4)

1. Patient positioning, skin preparation, and vertical ear canal exposure are the same as those described for LECR.
2. Isolate the entire vertical ear canal and resect lateral to the annular cartilage.
3. Incise the remaining section of the ear canal to create a dorsal and ventral flap.
4. Appose the skin to ear epithelium without tension.
5. The closure forms a T shape.

Postoperative Care and Complications

- Similar to those of lateral ear canal resection.
- This procedure affects ear carriage; LECR rarely does.

Prognosis

Prognosis is good provided the procedure is performed for the correct indications. In a large retrospective study of 75 dogs undergoing VECA, 72 were asymptomatic within 12 weeks postoperatively.

TOTAL EAR CANAL ABLATION (TECA)

Total ear canal ablation is a salvage procedure that involves removal of the entire vertical and horizontal ear canal cartilage and epithelium. If severe horizontal canal disease is present, only TECA is successful in eliminating the associated clinical signs.

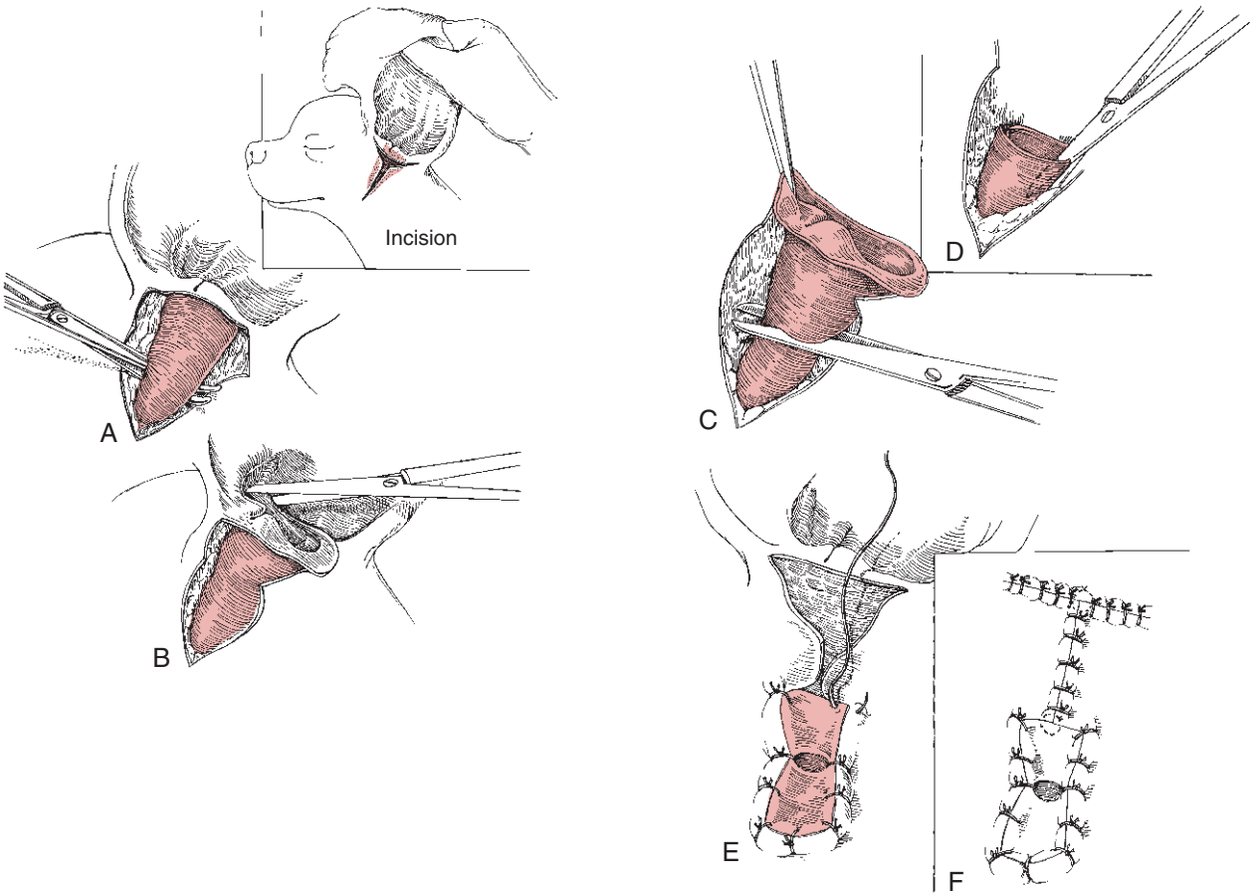

Figure 60-4. Vertical ear canal ablation technique. Begin with T-shaped skin incision over the ear canal. *A,* Continue blunt dissection medially until the entire vertical canal is isolated and freed up. Dissect just underneath the cartilage to avoid damaging vascular supply to the pinna. *B,* Cut the auricular cartilage with heavy straight Mayo scissors, removing all affected tissue on the dorsal aspect of the medial vertical canal and pinna. This step allows complete mobilization of the vertical canal, which remains attached only at its proximal aspect. *C,* Remove the vertical canal approximately 1 to 2 cm distal to the annular cartilage junction. *D,* Incise remaining vertical canal rostrally and caudally, if necessary, to fully expose the horizontal ear canal. *E,* Suture the ventral flap to the skin in a fashion similar to that in lateral ear resection. *F,* Suture the dorsal flap to appose the cut edges of the canal and skin with simple interrupted 3-0 to 4-0 monofilament nonabsorbable material. Remaining skin is apposed to form a T-shaped closure.

▼ ***Key Point*** Neglected chronic otitis externa results in extensive chronic inflammatory changes in periannular tissue. These greatly increase the risk of iatrogenic complications associated with difficult ear canal dissection.

Preoperative Considerations

TECA is most often performed in dogs to treat end-stage otitis externa or global ear disease unresponsive to medical therapy. In cats, about half are performed to treat neoplastic disease such as ceruminous gland adenocarcinoma.

- Severe ear trauma that cannot be managed adequately with reconstruction.
- Congenital or acquired deformity affecting the horizontal ear canal.
- Irreversible hyperplastic and proliferative ear disease or neoplasia extending into the horizontal canal.
- Persistent otitis externa after LECR or VECA. If signs stem from middle ear infection, drainage of the middle ear is all that may be required, provided the horizontal ear canal is not affected irreversibly.

▼ ***Key Point*** TECA alone is contraindicated when middle ear infection is present because it eliminates a major drainage exit for the tympanic cavity. The auditory tube cannot be relied on to drain thickened exudates within the middle ear. In these common instances, TECA can be performed successfully if a means of tympanic bulla drainage also is provided.

- TECA is an aggressive surgical procedure, and appropriate analgesia must be provided. Application of a

fentanyl patch (Duragesic, Janssen, Titusville, New Jersey) 12 hours before the procedure ensures that serum levels of the analgesic will be at therapeutic levels *before* the procedure. Local nerve blocks or constant local anesthetic infusion devices can be used successfully through the early postoperative period. Supplemental systemic narcotics are also commonly used to treat breakthrough pain postoperatively (see Chapter 6).

Surgical Procedure

Objectives

- To remove the entire external ear canal without trauma to the facial nerve.
- To provide access to the tympanic bulla to observe and treat infection or other disease.

Equipment

- Standard general surgical pack and suture
- Gelpi or Weitlaner self-retaining retractors
- Senn retractors
- Heavy serrated Mayo scissors
- Suction apparatus and Frazier suction tip
- Electrocoagulation unit and sterile electrode
- Lempert and Cleveland bone rongeurs
- Straight Simon and Daubenspeck curettes
- $\frac{1}{4}$-inch Penrose drains (surgeon preference)

Technique (Fig. 60-5)

1. Use the same positioning, skin preparation, and draping as for LECR.
2. Lavage the ear canal repeatedly with iodinated antiseptic solution to remove as much debris and contamination as possible.
3. Administer appropriate prophylactic IV antibiotics (preferably based on culture and susceptibility results) and maintain appropriate blood levels during the surgery. Fluoroquinolone and ampicillin + sulbactam (Unisyn) are appropriate antibiotics if no culture is available. Continue antibiotic administration until intraoperative culture results are available; revise the regimen if necessary.
4. Make a T-shaped skin incision to expose the ear canal.
5. Reflect loose connective tissue from the vertical ear canal.
6. Isolate the vertical and horizontal canal by blunt and sharp dissection. Maintain dissection immediately adjacent to the ear canal cartilage. Occasionally, the facial nerve is found embedded in the annular cartilage.
7. Careful dissection along the caudal aspect of the proximal horizontal ear canal isolates the origin of the nerve.
8. Carefully dissect the nerve out along its course adjacent to the horizontal canal.
9. In some patients with chronic proliferative otitis externa, a greenish-brown epithelial pouch forms between the tympanic bulla and the annular cartilage. This epithelium extends lateral and ventral to the tympanic bulla. Removal of this tissue is critical to the success of the surgery because chronic fistulation occurs if it is not removed fully. Use hemostatic forceps to grasp the edges of the pouch and, with traction, bluntly dissect the pouch out without injuring major local vessels and nerves.
10. Sharply amputate the annular cartilage from the petrous temporal bone, excise the ear canal, and submit it for biopsy.
11. Carefully remove the secretory epithelial lining of the short osseous external auditory canal by curettage. Submit this lining for culture and susceptibility.
12. Examine the middle ear for exudates and chronic thickened epithelium.
13. Routinely remove the ventral and lateral aspect of the bulla with rongeurs (see Chapter 62).
14. Remove all epithelium and debris in the tympanic cavity with irrigation and curettage.
15. Avoid inner ear structures on the craniodorsal aspect of the tympanic cavity during curettage.
16. If massive contamination has occurred during surgery, or signs of periauricular inflammation are present after the ear canal is removed, place a Penrose drain within the dead space remaining where the ear canal was removed, exiting ventral to the T-shaped incision. Place a percutaneous suture through the dorsal end of the Penrose tube to prevent premature dislodgement.
17. Place subcutaneous and skin sutures to form a T-shaped wound.

Postoperative Care

- Examine the wound for evidence of fluid accumulation or ensuing infection.
- If a Penrose drain is used, rebandage daily until drainage ceases.
- Place an Elizabethan collar to prevent self-inflicted trauma to the wound until suture removal.
- If acute postoperative infection occurs, open the wound for drainage. Flush and bandage the open wound daily.
- Administer systemic antibiotics based on susceptibility testing for a minimum of 3 to 4 weeks, if otitis media is present (see Chapter 61).
- If facial nerve injury has occurred, place eye lubricants (e.g., Hypotears, Cibavision) in the affected eye q6h, especially if the dog has decreased tear production or has an exophthalmic conformation.
- Remove skin sutures in 14 days.
- Remove Penrose tubes when drainage has decreased significantly. Generally, this is in 2 to 3 days.

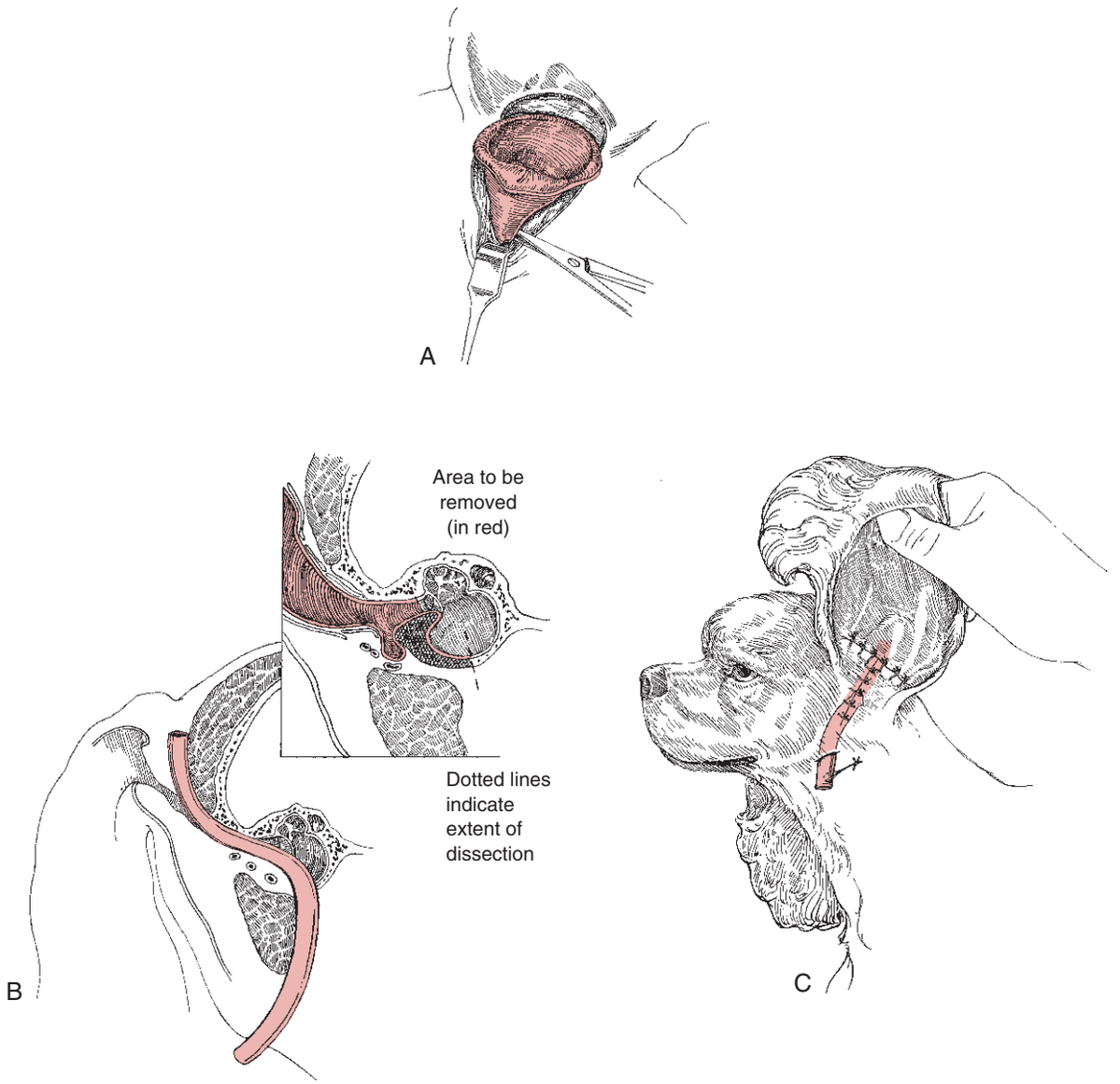

Figure 60-5. Total ear canal ablation technique. Make a horizontal incision parallel and just below the upper edge of the tragus between the tragohelicine and intertragic notches (also see Fig. 60-4*B* inset). Make a vertical incision perpendicular from the midpoint of the horizontal incision to a point just ventral to the horizontal canal, forming a T-shaped incision. The two triangular skin flaps are undermined and retracted, exposing the lateral aspect of the ear canal. After hemostasis is achieved, bluntly dissect the proximal aspect of the vertical canal free from the surrounding tissues, avoiding the auricular vessels located medial to the canal *(A)*. Use heavy serrated Mayo scissors to cut the medial aspect of the proximal vertical ear canal connecting the ends of the original horizontal incision. Retention of as much of the normal medial vertical canal as possible encourages ear support in cats and dogs with erect ears (see Fig. 60-4*B*). The parotid gland is retracted ventrally. By a combination of blunt and sharp dissection, isolate the horizontal canal to the level of the tympanic bulla. While maintaining meticulous hemostasis, dissection continues as close to the cartilage as possible, carefully exposing and retracting the facial nerve away from the line of dissection. Excise the ear canal and remove epithelium from osseous ear canal. *B,* Transverse section of head shows common location of epithelial pouch between annular cartilage and petrous temporal bone. All epithelium must be removed to avoid chronic fistulation after surgery. If otitis media is present, an aggressive lateral bulla osteotomy is performed to expose the bulla for curettage and to improve ventral drainage. Crosshatching indicates area of resection of the lateral and ventral osseous bulla. Be sure all exudate and abnormal tissue are moved from the tympanic cavity. A Penrose drain is shown exiting ventral to the skin incision. *C,* Completed ear ablation showing placement of drain and skin closure.

- Patients with established severe otitis media may require extensive postoperative wound management.
- If the surgical wound is left open, irrigate it once or twice daily with 25 ml of lukewarm (1:100) diluted povidone-iodine (Betadine) solution and saline (or TRIS-EDTA if *Pseudomonas* sp. is isolated) for 5 to 10 days.
- Administer nonsteroidal anti-inflammatory drugs for 5 to 7 days after surgery to reduce post-surgical pain and inflammation (see Chapter 6).

Complications

▼ ***Key Point*** Owner education is critical before attempting TECA because the following serious and long-standing complications are possible:

- Acute pharyngeal edema and upper airway obstruction.
- Acute postoperative wound infection (up to 40% of patients).
- Facial nerve damage (usually temporary; but permanent paralysis occurs in <10% of patients).
- Transient hypoglossal nerve dysfunction (rare and usually temporary).
- Chronic fistulation from unresolved middle ear infection or retained ear canal epithelium may occur up to 1 to 2 years after surgery (<10% of patients). Perform middle ear exploration and complete removal of epithelial remnants, and administer systemic antibiotic therapy for 4 to 6 weeks.
- If inner ear signs are present before surgery, their exacerbation is common after surgery. Neurologic signs usually improve over time if otitis media is controlled, but minor signs usually persist indefinitely.
- Horner's syndrome (rare and usually temporary) if middle ear surgery also is performed, especially in cats.
- Pinna necrosis from damage to the vasculature during dissection is rarely seen. It usually occurs at the proximal aspect of the caudal pinna margin. Debride the necrotic area and let it heal by secondary intention closure.
- Dogs undergoing bilateral TECA generally hear about as well as they did before surgery.
- Like VECA, this procedure affects ear carriage.

Prognosis

Long-term follow-up for dogs undergoing TECA shows improvement in clinical signs in up to 90% of patients and shows the same or worse in 10%. Poor results usually are caused by persistent infection from unresolved middle ear infection or retained infected epithelial tissue. A total of 25 of 26 owners of dogs undergoing TECA with long-term follow-up indicated satisfaction with the procedure and improvement in their dogs' demeanor.

AURICULAR HEMATOMA

Auricular or aural hematoma is an accumulation of blood within the cartilage of the pinna, usually caused by violent head shaking or scratching. The blood collection usually is confined to the concave surface of the pinna. This injury is seen most often in pendulous-eared dogs but occasionally is seen in erect-eared dogs and, less frequently, in cats.

▼ ***Key Point*** Auricular hematomas occur secondary to inflammatory conditions of the pinna or external ear canal, such as foreign bodies, atopy, food allergy, bacterial infection, yeast infection, and ear mites. Identify the underlying cause of the irritation, if possible, to avoid further injury and recurrence. Recent findings do not support an autoimmune pathogenesis but suggest that an early immunologic event may cause early cartilage erosion. Weakened cartilage is more readily damaged, leading to hematoma formation from minor trauma.

Anatomy

The major blood supply to the pinna is derived from branches of the external carotid artery and internal maxillary vein. The great auricular arteries and veins arborize and course longitudinally along the long axis on the convex side of the pinna. Mattress pattern sutures placed through the ear are oriented parallel to these vessels to avoid interrupting the blood supply to the pinna.

Preoperative Considerations

- The first objective for management of auricular hematoma is to identify the source of the ear irritation.
- Perform a thorough otoscopic examination to identify abnormalities within the ear canal.
- Obtain a complete history and perform a dermatologic examination, particularly when no obvious cause of the irritation is uncovered during otoscopic examination.
- Rule out the diagnosis of atopy or other systemic manifestation of skin disease.

▼ ***Key Point*** Drain auricular hematomas as soon as possible because delay often leads to enlargement and extension throughout the pinna. With time, fibrous organization of the hematomas eventually leads to a permanently thickened, cauliflower-like ear.

- If the cosmetic appearance of the pinna is of secondary importance to the owner, the incision and drainage technique is the most consistently successful. I prefer this technique for more chronic

hematomas because it allows for thorough debridement of organized clots.
- A more cosmetic and less time-consuming technique is the drainage-only procedure. Use this technique only in hematomas with fluid consistency (acute cases) and, preferably, those located toward the distal aspect of the pinna. Owners must understand that recurrence develops more often with drainage only compared with incision and suture.
- Simple aspiration alone is not the best option because of a high rate of hematoma recurrence.
- A CO_2 laser has been used successfully to create multiple small incisions into the hematoma for drainage and to allow for evacuation of blood, similar to the punch technique.

Surgical Procedure

Objectives

- To treat the source of irritation.
- To drain the hematoma.
- To maintain apposition of cartilage surfaces for an adequate time to prevent recurrence.

Equipment

- Standard general instrument pack
- Penrose drain, $^1/_4$ inch (if drain-only technique is planned)
- Skin biopsy punch (3.5 or 5 mm) for alternative punch technique

Technique

Incision, Drainage, and Bandage

1. Clip both sides of the pinna and prepare the ear for aseptic surgery. Place sterile 4 × 4 sponges in the ear canal to soak up blood from the hematoma.
2. Incise the hematoma with a #10 blade in a linear fashion on the concave side no closer than 1 cm from the margin of the pinna.
3. Make this incision along the long axis of the pinna extending the length of the hematoma. Removal of a strip of skin to widen the incision and permit drainage is not usually necessary.
4. Explore the hematoma and remove any fibrin tags or blood clots.
5. Place 1-cm–wide mattress sutures (3-0 or 4-0 monofilament nonabsorbable material) parallel to and no closer than 0.5 cm from the incision.
6. Hold the incised edges of the skin 2 to 3 mm apart when placing the first row of sutures. Sutures need not penetrate both skin surfaces because this creates another source of irritation and entry way for contamination.
7. Pass the needle carefully from the concave surface of the pinna, catching both cartilage planes.
8. Place the remaining mattress sutures in a staggered fashion 1 cm apart until the entire dead space area is obliterated.
9. Tie sutures with just enough tension to appose cartilage surfaces. Do not crush skin.

Alternative Technique Using Biopsy Punch and Suture (Fig. 60-6)

1. For acute hematomas, this technique creates a cosmetic result with minimal recurrence problems.
2. Prepare pinna for surgery as described for incision and drainage technique.
3. Punch staggered holes over hematoma on concave pinna surface. Avoid creating holes any closer than 1 cm from the ear margin.
4. Tack skin adjacent to punch holes to underlying cartilage.
5. Bandaging after the first postoperative day usually is not necessary.

Drainage Only

1. Aseptically prepare the skin on the concave surface of the pinna only. It is not necessary to clip the convex, haired surface (unless the patient is long-haired) because this creates more inflammation, which could lead to continual head shaking or scratching. Place 4 × 4 sponges in the ear canal to soak up blood from the hematoma.
2. Make a small (0.5–1-cm) incision extending into the hematoma at its most proximal and distal extent on the pinna.
3. Remove all fluid and fibrin tags with mosquito hemostats and digital expression.
4. Place a drain ($^1/_4$-inch Penrose or sterilized IV extension tubing) through the dead space and exiting both stab wounds.
5. Suture the drain to the skin near the stab incisions with a loose nonabsorbable suture.

Postoperative Care and Complications

- After treatment of the hematoma by the incision method, bandage the affected ear over the top of the head in pendulous-eared dogs. Bandage erect ears in an upright position.
- Leave the ear canal exposed in each method to permit cleansing and medication as needed.
- Leave the bandages on for at least 10 days and change as needed.
- Remove sutures in 3 weeks (incision or punch method).
- If aspiration of the hematoma is elected, remove reaccumulating fluid daily with a 20-gauge needle, and a tapering anti-inflammatory dose of prednisone is given for 7 to 14 days to reduce head shaking from otic irritation.

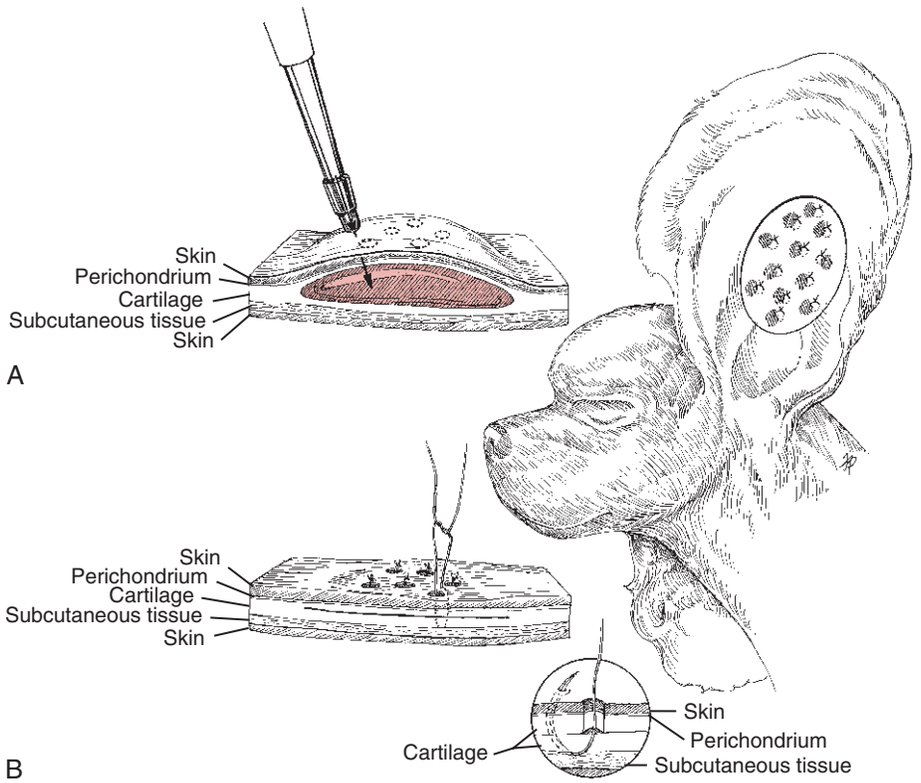

Figure 60-6. Concave surface of the pinna. Shaded area indicates hematoma location. Create staggered (3.5- or 5-mm) punch biopsies approximately 1 to 1.5 cm apart over the hematoma. Use 4-0 filament nonabsorbable sutures to tack through each punch into underlying cartilage to adjacent skin edge for dead space obliteration.

- No bandages are used after the first day for the drainage-only method or punch method unless the patient continues violent or persistent head shaking.
- Use an Elizabethan collar to reduce the incidence of self-trauma in all cases.
- Leave drains in place for 3 weeks.
- Instruct the owners to watch for signs of infection and to milk out any fluid (drain technique only) that may accumulate within the hematoma during this time.
- Instruct the owners about the proper treatment of the primary source of the ear irritation.
- The appearance of the ear after surgery is related to the drainage technique and to the chronicity of the hematoma. Inadequate drainage or continued inflammation results in a permanently thickened pinna.
- Make no guarantees to the owners regarding the final cosmetic appearance of the ear and the impossibility of recurrence, because these are often unpredictable.
- Reevaluate the patient weekly after drainage to determine the response to primary treatment and any problem related to wound management.

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Chapter

61 Otitis Media and Otitis Interna

Lynette K. Cole

Otitis media: *Otitis media* is defined as inflammation of the middle ear and is an important perpetuating cause of recurrent otitis externa.

- Otitis media occurs as a direct extension from an existing otitis externa through a ruptured tympanic membrane.

▼ ***Key Point*** The presence of an intact tympanic membrane does not rule out otitis media since the defect in the membrane may have healed.

- In a recent study, 72.5% of the ears in dogs with otitis media diagnosed by a myringotomy had an intact tympanic membrane.
- Less common routes include extension through the eustachian tube or hematogenous dissemination.

Otitis interna: *Otitis interna* is defined as inflammation of the inner ear structures, which include the cochlea, vestibule, and semicircular canal. Otitis interna usually occurs as a direct extension from an existing otitis media.

ETIOLOGY

- *Bacteria:* The most common etiology of otitis media is a bacterial infection. The two most common bacterial isolates are *Staphylococcus intermedius* and *Pseudomonas* spp.
- *Yeast* may be a significant pathogen, and in one study was the sole isolate in 23.7% of the middle ears of dogs with otitis media.
- *Congenital palatine defects* (secondary cleft palate) have been associated with radiographic signs of middle ear disease.
- *Primary secretory otitis media* has been reported in the Cavalier King Charles spaniel. Clinical signs include moderate to severe pain in the head or cervical region; neurologic signs such as ataxia, facial paralysis, nystagmus, head tilt, or seizure; otic pruritus; otitis externa; and fatigue. In most cases in the study, a bulging but intact tympanic membrane was observed. A highly viscous mucous plug was removed with ear forceps or a suction catheter. Removal of the mucous plug and flushing the middle ear had to be repeated up to five times for resolution.
- *Neoplasia* and *polyps* can cause otitis media. Tumors present in both the ear canal and tympanic bulla can be malignant. Inflammatory polyps are common in the cat, whereas they are relatively uncommon in the dog.
- *Otoliths* (mineral opacities) of the middle ear have been reported in three dogs; however, their significance is unknown, since only one dog had clinical signs of vestibular disease.
- *Cholesteatomas* are abnormal growths of the epithelium within the middle ear consisting of keratinizing stratified squamous epithelium, inflammatory cells, and ceruminous debris. These may occur congenitally or secondary to chronic otitis media and require surgical removal.
- Other causes of otitis media include trauma and foreign bodies.
- Otitis media may lead to otitis interna.
- Otitis media is uncommon in cats.

CLINICAL SIGNS

Otitis Media

▼ ***Key Point*** Recurrent otitis externa may be the only clinical sign associated with otitis media.

- Signs of recurrent otitis externa include discharge from the external ear canal, pawing or rubbing of the affected ear, head shaking, and pain.
- Specific clinical signs indicative of otitis media are facial nerve paralysis and Horner's syndrome. Injury to the facial nerve, as it courses near the middle ear, produces clinical signs such as drooping of or inability to move the ear or lip, drooling of saliva, or decreased/absent palpebral reflex. Horner's syndrome is due to injury to the sympathetic nerve fibers, which course near the middle ear, and is characterized by ptosis, miosis, enophthalmus, and protrusion of the nictitating membrane.

- Keratoconjunctivitis sicca (KCS) may occur if the parasympathetic nerves that innervate the tear gland are injured. The parasympathetic nerve fibers course with the facial nerve. Tear production can be evaluated with the Schirmer tear test.

▼ ***Key Point*** Otitis media is uncommon in dogs with acute otitis externa; however, it is quite common in dogs with chronic, recurrent otitis externa, with an incidence of 50% to 88.9%.

Otitis Interna

- Signs of otitis interna are those typically associated with peripheral vestibular syndrome and include a head tilt, circling, falling, or rolling toward the affected side; horizontal or rotary nystagmus with the fast phase away from the affected side; and asymmetric ataxia with strength preserved (Table 61-1).

DIAGNOSIS

History

- Obtain a thorough history in order to establish the age of onset, duration of clinical signs, and the extent of the involvement of the skin (such as pruritus), to be able to identify the primary underlying dermatologic disease. See Chapter 59 for details on the primary underlying diseases causing otitis externa.
- Identify past treatment protocols and response to therapy to help guide decisions for future treatments.

Physical Examination

- Perform a *dermatologic examination* to identify an underlying disease, such as parasitic disease, allergic disease, keratinization disorder, endocrine disease, or autoimmune disease.
- Perform a thorough *physical examination* and include the lymph nodes, oral cavity, and nasopharyngeal region.
- Perform a *neurologic examination* to evaluate for signs of facial nerve paralysis or Horner's syndrome, which would be consistent with otitis media, as well as nystagmus and vestibular disease, which would support otitis interna.

▼ ***Key Point*** Peripheral vestibular signs, which occur in otitis interna, must be differentiated from central vestibular signs, which occur with diseases of the brain stem.

▼ ***Key Point*** The absence of neurologic signs does not rule out the possibility of otitis media and otitis interna.

- Perform an *otoscopic examination* to evaluate the external ear canal and tympanic membrane. The examination is performed with a hand-held otoscope or video otoscope (see under Video Otoscopy, following). Palpate the external ear canals to determine if there is any calcification indicating chronic disease.

▼ ***Key Point*** In cases of chronic otitis externa, an otoscopic examination on initial presentation may not be possible, due to ulcerations, hyperplasia, or stenosis. Two to three weeks of topical and systemic glucocorticoids are often necessary in order to be able to perform an otoscopic examination.

- In addition, an otic examination may not be possible without sedation or general anesthesia, due to pain.
- The normal tympanic membrane is translucent and concave. Suspect otitis media if the tympanic membrane is ruptured, bulging, opaque, or cloudy.

Table 61-1. VESTIBULAR SIGNS ASSOCIATED WITH INNER EAR VS. BRAIN STEM LOCATIONS

Sign	Inner Ear	Brain Stem
Head tilt	Present	Present
Circling	Present	Present
Falling, rolling	Present	Present
Positional strabismus	Present	Present
Nystagmus	Usually spontaneous and type (horizontal, rotary) does not vary with head position	Usually not spontaneous but found with changes in head position; type (horizontal, rotary, vertical) varies with head position
Conscious proprioception	Normal	Delayed or absent
Horner's syndrome	May be present	Usually absent
Gait changes	Mild to severe ataxia	Ataxia and weakness
Postural reactions (e.g., hopping, hemiwalking, wheelbarrowing)	Normal if examined slowly	Weak or absent
Cerebellar signs (hypermetria, head intention tremors)	Absent	May be present

Video Otoscopy

- Perform video otoscopy using an otoendoscope, camera, light source, and monitor.
- The vertical and horizontal ear canal and tympanic membrane are brightly illuminated and magnified, allowing better evaluation of these structures than with the hand-held otoscope.
- While the patient is sedated or anesthetized, utilizing the opening on the otoendoscope, the ears can be flushed; foreign objects, debris, or parasites may be retrieved with the grasping forceps; biopsies can be obtained with biopsy forceps; and myringotomy may be performed with a catheter.
- With an attachable dual-port adapter, suction and saline may be used simultaneously to completely clean the ear. See Deep Otic Flush and Myringotomy later in this chapter for further details.

Cytology and Bacterial Culture and Susceptibility Testing (C/S)

Cytology and C/S are diagnostic tests used to aid in the choice of systemic and topical antimicrobial agents. Cytology is a rapid and inexpensive procedure indicated in all cases of otitis (also see Chapter 59). It is the best method for detection of yeast organisms.

- After collecting the sample, roll the swab onto a glass slide, heat fix, and stain with a modified Wright's stain (Diff-Quik) or gram stain. Under scanning power (100×), locate keratinocytes or inflammatory cells. Once those are found, apply immersion oil to the slide and examine under oil immersion power (1000×). Count and record the number and type of bacteria, yeast, and inflammatory cells.
- Obtain samples for cytology and C/S from the horizontal ear canal prior to a deep otic flush.
- After the deep flush, obtain samples directly from the middle ear cavity if the tympanic membrane is ruptured, or via a myringtomy if the tympanic membrane is abnormal (bulging, discolored, opaque). See below for specifics on the deep otic flush and myringotomy procedure.

Radiography

- Radiography is indicated in suspected cases of otitis media to evaluate the soft tissue structures of the external ear along with the bony structures of the middle ear. Radiography is also used as a prognostic indicator for the success of medical management of otitis media. With significant radiographic changes, such as sclerosis or osteolysis, surgical intervention may be required for resolution. Animals must be anesthetized to allow for proper positioning for the procedure.
- The most commonly utilized radiographic projections of conventional radiography of the bulla include the dorsoventral, right and left lateral obliques, and rostroventral-caudodorsal open mouth.

Computed Tomography Scan

- Computed tomography (CT) allows cross-sectional imaging of the external, middle, and internal parts of the ear. The overall accuracy of CT and conventional radiography for the diagnosis of otitis media are similar; however, CT is a more sensitive indicator of otitis media. CT can be used to better define changes in bony structures, while magnetic resonance imaging (MRI) is superior to CT for detecting soft tissue changes. MRI is also helpful in investigation into the pathology of the inner ear.

▼ ***Key Point*** For conventional radiography and CT, the absence of evidence of otitis media does not rule out the disease.

Positive Contrast Canalography

- Positive contrast canalography evaluates the patency of the tympanic membrane by infusing positive contrast medium (iohexol) into the ear canals of anesthetized dogs. Pre- and post-bullae radiographs are performed.
- This procedure may aid in the identification of tympanic membrane rupture; however, lack of contrast medium in the tympanic bulla does not rule out a ruptured tympanic membrane.

Pneumotoscopy

- The purpose of pneumotoscopy is to assess the mobility of the tympanic membrane (compliance) and to determine the presence or absence of fluid in the middle ear.
- Pneumotoscopy is performed using a hand-held otoscope and a pneumatic bulb. In order to perform this procedure, the animal may need to be sedated or under general anesthesia.

Technique

- Attach the pneumatic bulb to the side of the otoscope.
- Insert the otoscopic cone into the horizontal ear canal and make a seal with the cone and the ear canal.
- Identify the tympanic membrane. Air is gently "puffed" with the bulb while observing for motion of the tympanic membrane.
- A noncompliant tympanic membrane may occur if there is a tear in the membrane or fluid in the middle ear. One must be able to identify the tympanic membrane in order to perform the procedure.
- A noncompliant tympanic membrane is suggestive of otitis media; however, a compliant tympanic membrane does not rule it out.

Ultrasonography

- An ultrasonographic technique has been described to differentiate between gas and fluid in the bulla of dog cadavers. Studies to determine the usefulness of this technique in the clinical situation have not been performed as yet.

Biopsy

- Biopsy any mass found in the vertical ear canal, horizontal ear canal, and middle ear. Submit the biopsy specimens in formalin for histopathologic evaluation.

TREATMENT

▼ ***Key Point*** The goals of treatment are to clean the external and middle ear; remove infected, inflammatory, or foreign debris; and allow drainage of the middle ear.

Deep Otic Flush and Myringotomy

Deep Otic Flush

- Perform under general anesthesia.
- Soak the ear canal for 10 minutes with a ceruminolytic ear cleaner, then flush using warm saline: first with a bulb syringe, then using an 8-French polypropylene urinary catheter attached to a 12-ml syringe passed through an otoscopic cone.
- Other flushing options include a red rubber feeding tube, water-propulsion dental device, or the Auriflush system (Shering-Plough Animal Health).
- Once the exudate and debris are removed from the ear canal, evaluate the tympanic membrane with an otoscope or video otoscope.
- If the tympanic membrane is not intact, perform cytology and bacterial C/S from the middle ear cavity using the hand-held otoscope or the video otoscope. Using a hand-held otoscope, insert a sterile otoscopic cone into the horizontal ear canal and a pass sterile swab (Calgiswab, Hardwood Products Company LLC) into the middle ear cavity. Use the first swab for C/S. Pass a second swab into the middle ear cavity for cytologic analysis.
- If the video otoscope is used, place an open-end $3^1/_2$-Fr tomcat catheter attached to a 12-ml syringe through the port of the otoendoscope. Flush 1 ml of warm sterile saline into the middle ear cavity and aspirate back for culture.

▼ ***Key Point*** Some ceruminolytic agents may be ototoxic. If the tympanic membrane is not intact, remove the ear cleaner by repeatedly flushing the middle ear with warm saline after collection of samples.

Myringotomy

- If the tympanic membrane is intact, appears abnormal, and otitis media is suspected, perform a myringotomy to obtain samples for cytology and bacterial C/S and to flush the middle ear cavity.
- Using a hand-held otoscope, insert a sterile otoscopic cone into the horizontal ear canal, and identify the tympanic membrane. Use a sterile Calgiswab to make an incision into the caudoventral quadrant of the tympanic membrane. Submit the swab used for the myringotomy incision for bacterial C/S. Insert a second swab into the original incision and submit the sample obtained for cytologic analysis.
- If the video otoscope is used to perform the myringotomy, place an open-end, sterile $3^1/_2$-Fr tomcat catheter through the port of the otoendoscope. Use the tomcat catheter to make the incision, and flush 1 ml of warm sterile saline into the middle ear cavity for culture.
- A spinal needle may also be used to make the myringotomy incision.
- After the myringotomy procedure, flush the middle ear with warm sterile saline until all of the exudate is removed from the middle ear.
- The normal tympanum has been shown experimentally to heal in 21 to 35 days.

▼ ***Key Point*** Possible complications of a deep otic flush and myringotomy are Horner's syndrome, facial nerve paralysis, vestibular disturbances, and deafness. Although the occurrence of these complications is uncommon to rare when the procedures are performed with care, owners should understand these complications and sign a consent form prior to the procedure. These complications occur more commonly in the cat than in the dog.

Systemic and Topical Antimicrobial/Antifungal Agents

Systemic

- Once the ear has been cleaned and flushed, begin systemic and topical antimicrobial/antifungal treatment based on cytologic results from the external and middle ear.
- The most common coccoid bacteria isolated from the middle ear of dogs with otitis media is *S. intermedius;* appropriate antibiotic choices include cephalexin, 22 mg/kg PO q12h (generics), and amoxicillin and clavulanate, 13.75 to 22 mg/kg PO q12h (Clavamox, Pfizer Animal Health).
- The most common rod bacteria is *Pseudomonas aeruginosa.* A fluoroquinolone such as enrofloxacin, 5 to 20 mg/kg PO q24h (canine only) (Baytril, Bayer

Animal Health), or marbofloxacin, 2.75 to 5.5 mg/kg q24h PO (Zeniquin, Pfizer Animal Health), would be appropriate. Once the C/S results are known, modification of the treatments may be needed.
- Certain systemic antibiotics (primarily aminoglycosides) are ototoxic and should be used cautiously.
- Use ketoconazole (generics; Nizoral, Janssen) or itraconazole (Sporanox, Janssen) at 5 mg/kg PO q24h for yeast otitis media.
- Administer antibiotics and/or antifungal agents until the infection resolves, clinically, cytologically, and on bacterial C/S, and then for an additional 2 to 4 weeks, or until resistance to the antibiotic is found on subsequent bacterial C/S.

Topical

▼ ***Key Point*** With topical medications, one is able to achieve concentrations in the ear 100 to 1000 times higher than if the drug were given systemically. An antibiotic that is resistant on bacterial C/S may thus be efficacious when administered topically.

- Numerous otic medications are available (e.g., neomycin sulfate, polymyxin B sulfate, and hydrocortisone [Neo-Poly-W/HC Otic Solution, generics], enrofloxacin and silver sulfadiazine [Baytril Otic, Bayer Animal Health], gentamicin sulfate and betamethasone valerate [generics; Gentocin Otic Solution, Schering-Plough Animal Health]; thiabendazole, dexamethasone, and neomycin sulfate solution [Tresaderm, Merial]).
- However, none of these otic medications is labeled for use with a non-intact tympanic membrane. Do not use otic preparations in an ointment base with a non-intact tympanic membrane.
- In addition, ophthalmic solutions (e.g., tobramycin [Tobramycin Ophthalmic Solution 0.3%, generics]), as well as extra-label solutions (e.g., silver sulfadiazine [Silvadene Cream 1%, Monarch Laboratories], enrofloxacin [Baytril Antibacterial Injectable Solution 2.27%, Bayer Animal Health]), are also used topically for otitis, but again, their ototoxic potential has not been established.

▼ ***Key Point*** Always warn the owner of the possibility of neurologic signs of ototoxicity while administering topical medications when the tympanic membrane is not intact.

- Use enough topical medication to fill the ear canal, and repeat the application q12h.
- Topical otic and/or systemic treatment in animals with chronic otitis may need to be continued for weeks to many months to achieve complete resolution of the infection, especially in animals with chronic otitis.

Systemic and Topical Glucocorticoids

- Anti-inflammatory doses (1 mg/kg PO q24h, then taper) of oral glucocorticoids (e.g., prednisone [generics]) reduce hyperplasia and stenosis of the ear canal to facilitate therapy.
- Topical glucocorticoids may be used solely or in combination with oral glucocortocoids to reduce hyperplasia and stenosis of the ear canal.
- Glucocorticoids are available in topical combination products, with antibacterial and antifungal agents, or in combination with acetic acid (ClearX Ear Drying Solution, DVM Pharmaceuticals), acetic acid and Burow's solution (Bur-Otic-HC, Virbac), Burow's solution (CortAstrin, Vedco), and dimethyl sulfoxide (DMSO) (Synotic Otic Solution, Fort Dodge).

Topical Cleaning and Drying Agents

- These are used to aid in keeping the external ear clean by removing exudate. Most products contain an acid to dry the ear. Some examples include lactic acid and salicylic acid (Epi-Otic, Virbac); salicylic acid, benzoic acid, and malic acid (OtiCalm Cleansing Solution, DVM Pharmaceuticals); alcohol, salicylic acid, lactic acid, and benzoic acid (OtiRinse Cleansing/Drying Ear Solution, DVM Pharmaceuticals); and olefin and citric acid (Advanced pHormula Ear Cleanser, EVSCO).

Prevention of Recurrent Otitis Externa

- Prevention of recurrence of otitis is dependent on diagnosing and controlling the primary underlying disease.
- While the primary disease is being diagnosed or if the primary disease has been diagnosed but has not controlled the recurrence of the otitis, maintenance ear cleaning (i.e., ear cleaning and drying agents) and topical therapy (i.e., glucocorticoids) may be helpful in preventing a recurrence.

Surgical Management

- Consider surgical intervention in unresponsive or recurrent cases of otitis media (see Chapter 62).
- Perform surgery if middle ear polyps, neoplasia, foreign bodies, or osteomyelitis of the tympanic bulla is present.
- The surgical technique depends on the specific condition.

Other Treatments

- Treat exposure keratitis due to facial nerve paralysis or KCS with artificial tears, lubricating eyedrops, or topical cyclosporine (Optimmune, Schering–Plough Animal Health).

PATIENT MONITORING

- Reevaluate the animal every 2 weeks until the infection has resolved.
- Perform otoscopic examination with a hand-held otoscope or video otoscope.
- Perform otic cytology at each reevaluation to monitor the response to therapy. If there is no response or the infection has worsened, obtain samples for a bacterial C/S.
- Monitor healing of the tympanic membrane.
- Repeat ear flushing under general anesthesia may be required to keep the ear canal clean of otic exudate.

Neurologic Signs

- Horner's syndrome and facial nerve paralysis/paresis may persist even when infection has resolved.

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Chapter 62

Surgery for Otitis Media and Otitis Interna

Harry W. Boothe

Selection of a surgical procedure to treat otitis media and otitis interna is based on duration of clinical signs, response to previous treatment, status of the external ear canal, and the surgeon's familiarity with related anatomy and technique. Surgical options for treating otitis media and otitis interna include myringotomy (see Chapter 61), lateral bulla osteotomy, and ventral bulla osteotomy. Nasopharyngeal polyps are most appropriately excised using a bulla osteotomy in combination with other excision techniques. Potential complications of bulla osteotomy surgery include facial nerve injury, Horner's syndrome (ptosis, miosis, enophthalmos, nictitating membrane protrusion), and vestibular signs. See Chapter 61 for diagnosis and medical treatment of otitis media and otitis interna.

ANATOMY

- The tympanic membrane slopes downward, forward, and inward—toward the middle ear cavity. The membrane is composed of a larger, more peripherally located pars tensa and a smaller, triangular-shaped pars flaccida.
- The air-filled tympanic cavity constitutes the major portion of the middle ear and is connected to the nasopharynx by the auditory (eustachian) tube.
- Structures located within the dorsal aspect of the tympanic cavity include the three auditory ossicles, associated muscles and ligaments, and tympanic nerve.

▼ ***Key Point*** The feline tympanic cavity is divided into a larger ventromedial and a smaller dorsolateral compartment by a nearly complete thin bony septum.

- Surgically important structures near the tympanic bulla are the facial nerve (ventrolaterally), the carotid artery (medially), and the hypoglossal nerve (ventrally).

LATERAL BULLA OSTEOTOMY

Preoperative Considerations

- Thoroughly examine the external ear canal.
- Evaluate the radiographic appearance of the tympanic bulla and the microbiologic status of the middle ear before lateral bulla osteotomy. Computed tomography, or CAT scan, (see Chapter 4) is particularly helpful in assessing disorders of the tympanic bulla.
- Lateral bulla osteotomy is simplest when performed in conjunction with a total ear canal ablation. If the external ear canal is normal or only mildly affected by infection, bulla osteotomy can be performed via a lateral (without ear canal ablation) or ventral approach. The ventral approach is preferred by most surgeons.
- Assess the integrity of the facial nerve preoperatively.

Surgical Procedure

Objectives

- Provide access to the tympanic cavity to obtain samples for diagnosis.
- Provide drainage and access to the middle ear cavity for therapeutic intervention (e.g., flush, curettage, and resection of abnormal tissue).

Equipment

- Standard general surgery pack and suture
- Periosteal elevator, Steinmann pin, hand chuck, and rongeurs
- Warm saline solution and tubing for flushing the tympanic cavity

Technique for Lateral Bulla Osteotomy without Total Ear Canal Ablation

1. Position the patient in lateral recumbency, and prepare the lateral aspect of the head and neck.
2. Incise the skin over the vertical ear canal to a point ventral to the horizontal ear canal (Fig. 62-1).

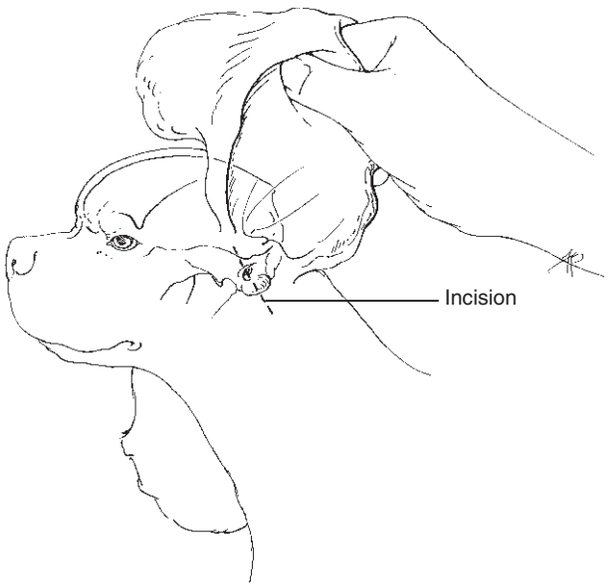

Figure 62-1. Skin incision for performing a lateral bulla osteotomy without total ear canal ablation.

3. Bluntly dissect between the parotid salivary gland and the ventral aspect of the horizontal ear canal to reveal the facial nerve.
4. Retract the facial nerve ventrocaudally near its exit from the stylomastoid foramen.
5. Elevate the soft tissue overlying the lateral aspect of the osseous bulla using a periosteal elevator.
6. Enter the tympanic cavity ventral to the horizontal ear canal with the Steinmann pin and hand chuck.
7. Enlarge the osteotomy site ventrally with rongeurs.
8. Obtain microbiologic samples, and flush the middle ear cavity using warm saline solution. If curettage is performed, avoid traumatizing the inner ear structures on the dorsomedial aspect of the bulla.
9. Place and secure a drain tube (e.g., Penrose drain) into the tympanic cavity by suturing it to the adjacent soft tissue with fine absorbable suture material.
10. Routinely close the subcutaneous tissue (simple interrupted, absorbable suture) and the skin (simple interrupted, nonabsorbable suture).
11. Position the drain tube so that it exits the skin adjacent to the primary incision.

Technique for Lateral Bulla Osteotomy with Total Ear Canal Ablation

1. Position the patient in lateral recumbency, and prepare the lateral aspect of the head and neck, including the external ear canal.
2. Incise the skin over the vertical ear canal, and perform a total ear canal ablation (see Chapter 60).
3. Reflect the soft tissue from the lateral aspect of the tympanic bulla, insert the rongeur tips into the external auditory meatus, and remove the ventral aspect of the bony auditory meatus.
4. Extend the osteotomy site as far ventrally into the middle ear cavity as possible. Obtain samples of tissue and fluid for culture and sensitivity. Flush the cavity with warm saline solution.
5. Use a bone curette to carefully remove epithelium and debris from the bulla. Avoid curretting the dorsal aspect of the bulla to prevent injury to structures of the inner ear.
6. Place a drain tube to exit the ventral aspect of the bulla osteotomy site and skin adjacent to the primary incision.

Postoperative Care and Complications

Short-Term

- Prevent self-inflicted trauma to the drain tube by using an Elizabethan collar or similar device.
- Facial nerve damage, manifested by inability to close the eye and by drooping of the upper lip on the ipsilateral side, may be observed.

▼ ***Key Point*** Administer eye lubricant (artificial tears) to animals with facial nerve damage to prevent corneal ulceration.

- Remove the drain tube when drainage has decreased significantly, generally within 3 to 4 days.
- Continue an appropriate systemic antibiotic for at least 3 weeks.

Long-Term

▼ ***Key Point*** Incomplete removal of secretory epithelium from the tympanic bulla can result in recurrent deep tissue infections. Clinical signs include pain on opening the mouth and on palpation of the area over the tympanic bulla, and nonspecific signs such as anorexia, lethargy, and fever.

Prognosis

- Response to bulla osteotomy tends to be incomplete in long-standing cases of otitis media and otitis interna.
- Immediate response following bulla osteotomy indicates a more favorable prognosis.

VENTRAL BULLA OSTEOTOMY

Preoperative Considerations

- See Preoperative Considerations under Lateral Bulla Osteotomy.
- Radiographically assess the density of the tympanic bulla to assist in the initial osteotomy procedure.

Surgical Procedure

Objectives

- See Objectives under Lateral Bulla Osteotomy.
- To establish ventral drainage of the middle ear cavity.

Equipment

- See Equipment for Lateral Bulla Osteotomy without Total Ear Canal Ablation.

Technique

1. Position the patient in dorsal recumbency with the neck slightly hyperextended over a pad or rolled towel, and prepare the ventral cervical region from the mid-mandibular area to the wings of the atlas.
2. Incise the skin just off the midline between the level of the angular process of the mandible and the wings of the atlas (Fig. 62-2).
3. Bluntly dissect between the digastricus muscle and the hyoglossal and styloglossal muscles. The hypoglossal nerve on the lateral aspect of the hyoglossal muscle helps verify the proper dissection plane.
4. Carefully retract the adjacent musculature to reveal the rounded tympanic bulla between the more angular jugular process of the skull (caudal) and the angular process of the mandible (rostrolateral).
5. Reflect the thin jugulohyoideus muscle that covers the osseous bulla in the dog.
6. Accurately locate the bulla before proceeding with the osteotomy. Carefully penetrate the ventral aspect of the tympanic bulla with a Steinmann pin in a hand chuck, and enlarge the osteotomy site using rongeurs (Fig. 62-3). In cats, remove the septum to fully expose the tympanic cavity.
7. Carefully remove abnormal tissue and fluid from the tympanic bulla. Obtain samples of tissue and fluid for histopathology and culture. Avoid trauma to the inner ear structures and auditory ossicles. Do not curette the dorsal aspect of the bulla.
8. Flush the middle ear cavity with warm saline solution, and place a drain to exit the ventral cervical skin through a separate skin incision.
9. Routinely close the subcutaneous tissue (simple interrupted, absorbable suture) and the skin (simple interrupted, nonabsorbable suture).

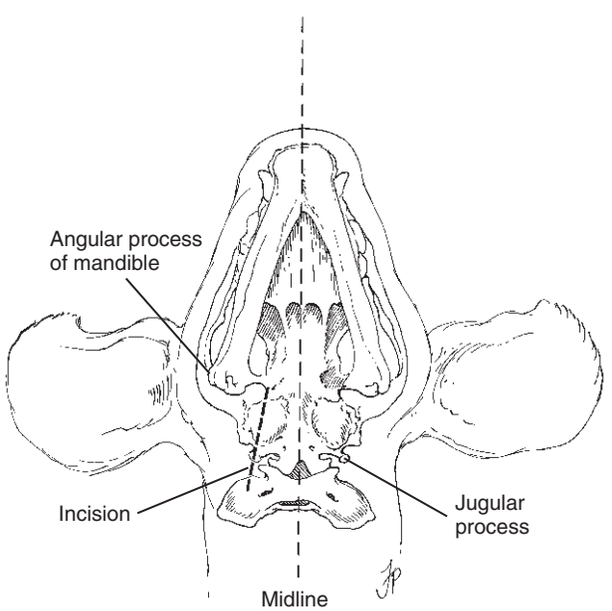

Figure 62-2. Skin incision for ventral bulla osteotomy.

Postoperative Care and Complications

- See Postoperative Care and Complications under Lateral Bulla Osteotomy.

SURGICAL MANAGEMENT OF NASOPHARYNGEAL POLYPS

Preoperative Considerations

- Carefully inspect the nasopharynx by rostrally displacing the soft palate to assess the size of the nasopharyngeal mass.
- Radiographically assess the tympanic bulla to determine the potential involvement of the middle ear cavity. Computed tomography is helpful in identifying changes in the affected tympanic bulla.
- See Chapter 161 for additional information on nasopharyngeal polyps.

Surgical Procedure

Objectives

- Excision of the mass using both an oral approach and a ventral bulla osteotomy.

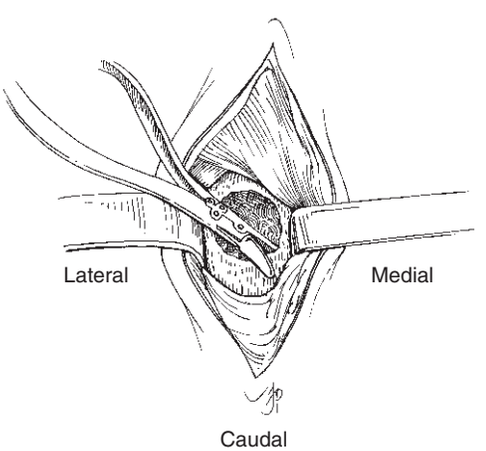

Figure 62-3. Use bone rongeurs to enlarge the opening in the ventral tympanic bulla.

- Removal of the mass from the nasopharynx or ear canal using a simple traction technique, while carefully excising polypoid tissue from the tympanic cavity via a ventral bulla osteotomy.

Equipment

- See Equipment for Lateral Bulla Osteotomy without Total Ear Canal Ablation.

Technique

1. Position the cat in dorsal recumbency and prepare the ventral cervical region from the mid-mandibular area to the wings of the atlas. Perform the procedure with the cat's mouth held open.
2. Displace the soft palate rostrally using a soft tissue retractor or stay suture to provide adequate exposure of the mass.
3. Apply traction to the mass to remove the pharyngeal component of the polyp.
4. Perform a ventral bulla osteotomy, as previously described, and excise tissue proliferations within the tympanic cavity using careful curettage. Perform a bilateral bulla osteotomy if it is unclear which middle ear is involved.
5. Examine the ipsilateral ear canal, and excise any polypoid tissue.

Postoperative Care and Complications

Short-Term

- Temporary Horner's syndrome of 1 to 2 weeks' duration is common following curettage of the middle ear cavity.
- See short-term complications following lateral bulla osteotomy.

Long-Term

- Recurrence of the polyp is possible, although less likely, following both excision by traction and ventral bulla osteotomy than following excision by traction alone.
- Disruption of the otic ossicles from trauma to the dorsal aspect of the tympanic cavity results in hearing loss.

Prognosis

- The long-term prognosis following removal of nasopharyngeal polyps using both the traction excision and ventral bulla osteotomy techniques is good. Recurrence is uncommon.

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Chapter 63

Disorders of the Claw

Ralf S. Mueller

INTRODUCTION

Onychology (the study of nails) is an area of veterinary dermatology that has only recently become the focus of more detailed study. In the past decade, several studies have shed light on the etiology, diagnosis, and treatment of claw disease in the dog. Some relevant terms are explained in Table 63-1. A thorough diagnostic approach is essential, as treatment is successful only when the cause of the disease is known. In this chapter, a review of claw anatomy is followed by the diagnostic approach to claw disease, and finally a discussion of the treatment options for the most common disorders affecting the claw is presented.

ANATOMY

- The anatomy of the claw is shown in Figure 63-1. The superficial layers of the epidermis are modified to form the claw horn. The claw is curved and consists of a sole (the most distal portion), two laterally compressed walls (forming the axial and abaxial surfaces of the claw), and a central dorsal ridge. This ridge is thicker than the walls and sole, which maintains the pointed appearance of the claw. The coronary border (vallum) of the claw fits into the space under the ungual crest, a crescent-shaped dorsal process of the distal third phalanx. Most of the claw is formed from the coronary band, which is surrounded and hidden by the claw fold.
- The claw fold is a fold of skin at the proximal border of the claw that is continuous with the horn of the claw. Dorsally, it is a modification of haired skin. The periosteum of the distal phalanx is continuous with the dermis of the claw; these two tissues occupy the space between the bone of the distal phalanx and the claw itself.
- The corium or dermis underneath the claw epidermis and horn is often referred to as the quick. This tissue is highly vascularized, which is readily demonstrated by hemorrhage after excessive trimming of the claws.
- Any inflammation of the dermis, which is present between these two rigid structures, leads to swelling and explains why pronounced pain occurs rapidly with any disease of the canine claw matrix.
- The keratogenous zone (the basal cell layer and lower spinous cell layers) at the very proximal end of the claw is the proliferative claw matrix thought to be actively involved in producing the claw plate. Damage to the claw matrix typically results in malformation of the plate.
- The normal canine claw epithelium lacks a granular layer. The epithelium produces keratinocytes that flatten, cornify, and fuse to form the claw horn. The claw wall is curved, laterally converging and enclosing the sole distally.

Table 63-1. Definition of Terms Used to Describe Claw Disease

Paronychia	Inflammation involving the folds of tissue surrounding the claw
Onychodystrophy	Malformation of the claw
Onychomadesis	Separation of the claw from its bed
Onychomalacia	Softening of the claw
Onychomycosis	Fungal disease of the claw
Onychorrhexis	Brittleness, spontaneous splitting, or breaking of the claws
Onychoschizia	Separation of the claw from its bed
Onychia	Inflammation of the claw or claw bed, resulting in loss of the claw
Onychogryposis	Abnormal hypertrophy and curving of the claws
Onycholysis	Complete loss of the claws

ETIOLOGY

- *Trauma* is the most common cause of claw disease, particularly if only a single claw or a single paw is affected. Animals typically present with lameness and pain, particularly if the claw plate is loose.
- *Neoplasia* is a common cause of claw disease affecting single digits. A variety of tumors such as melanoma, mast cell tumors, keratoacanthoma, inverted papil-

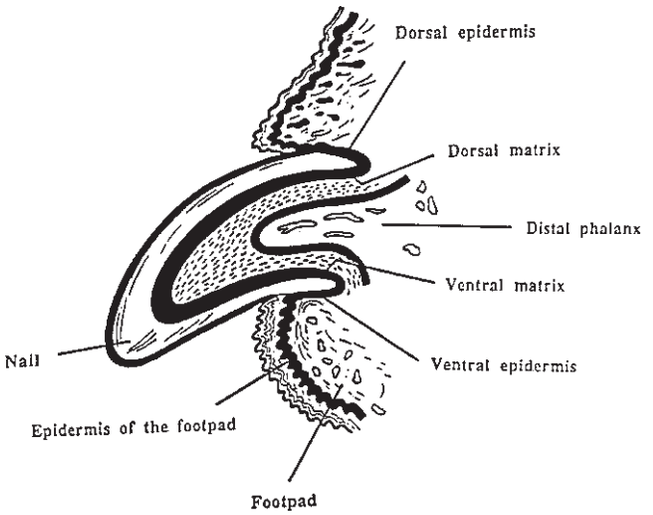

Figure 63-1. Schematic anatomy of the canine claw. (From Mueller RS, Sterner-Kock A, Stannard AA: Microanatomy of the canine claw. Vet Derm 4:5, 1993, with permission.)

loma, lymphosarcoma, fibrosarcoma, osteosarcoma, and others have been reported to affect the canine claw and claw bed. However, squamous cell carcinoma is the most common neoplasm of the distal digit and seems to be particularly frequent in large-breed dogs with black hair coats. Squamous cell carcinoma often invades the bone of the distal phalanx.

- *Systemic disease* is likely if multiple digits on several paws are affected. Consider drug reactions, immune-mediated diseases such as lupus erythematosus or the pemphigus complex, or allergies such as food adverse reactions. Involvement of dew claws with other claws also is indicative of systemic disease. Paronychia or inflammation of the claw fold is most commonly caused by infection with bacteria and/or yeast organisms. However, immune-mediated diseases such as pemphigus foliaceus and pemphigus vulgaris may also cause paronychia.
  - Immune-mediated diseases such as lupus erythematosus, pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, drug eruption, and cold agglutinin disease have all been reported to cause claw disorders. In the majority of cases other cutaneous or non-cutaneous signs will provide clinical clues for the diagnosis. See Chapter 48 for discussion of the clinical signs, diagnosis, and treatment of immune-mediated diseases.
- *Bacterial infection* is commonly seen secondary to an underlying disease such as trauma, hyperadrenocorticism, hypothyroidism, pemphigus foliceus, or systemic lupus erythematosus.
- *Onychorrhexis* (brittle claws) may be due to chronic infection in some dogs. In old dogs, it may involve all claws including the dew claws and is most likely a degenerative change. Onychorrhexis can also be seen in dogs with nutritional deficiencies.
- *Idiopathic onychomadesis* or *lupoid onychodystrophy* is the most common cause of symmetrical claw disease in my experience. The condition is characterized by histopathology resembling lupus erythematosus typically with no other abnormal clinicopathological findings. The disease has an acute onset with loss of one or several claw plates, followed rapidly in the ensuing weeks with shedding of most or all other claw plates. The pathogenesis has not been completely elucidated, but allergic, infectious, or immune-mediated diseases may all be able to cause this disease. Thus, the lupoid reaction histopathologically and onychomadesis clinically may be a reaction pattern of the claw rather than an individual disease. Perform an extensive diagnostic work-up for allergies and infections before an immune-mediated pathogenesis is assumed.
- *Onychomycosis*, although a common disease in human medicine and thus familiar to most owners, is a rare cause of claw disease in small animals. Transient contamination of distal extremities with fungal organisms is possible and may result in positive fungal cultures. Biopsies or cytology should confirm the disease and document invasion of the tissue.
- *Demodex* infection of the claw has been reported in some dogs.

CLINICAL SIGNS

- Pain and resultant lameness is a very common sign of a claw disorder.
- Onychomadesis or claw shedding is another common clinical sign in patients with claw disease. The dermis of the claw is situated between the claw horn itself and the bone of the distal digit; there is no subcutis present in this structure. Thus, inflammation of the claw matrix and/or the dermis and the associated swelling between the bone and horn quickly leads to pain and onychomadesis. This can be seen with trauma, infection, immune-mediated diseases, and most other causes of claw disorders affecting single or multiple digits.

DIAGNOSIS

History

- As many diseases of the canine claw present very similarly, the history is essential in providing clinical clues to the underlying disease. Age of onset and breed may be helpful. The American cocker spaniel is predisposed to keratinization defects that may affect the claws. German shepherd dogs are predisposed to onychomadesis of unclear etiology associ-

ated with abnormal mineral composition. Young dogs tend to be affected more by contagious disease, whereas neoplastic diseases are more commonly seen in old dogs.

- An acute onset may be seen with trauma or immune-mediated disease. A slow progression is to be expected with dermatophytosis or keratinization defects. Commonly, trauma affects only single claws or is restricted to one foot, while multiple paws are affected more often by systemic disease. Other systemic signs such as polyuria and polydipsia or recurrent lameness point to a systemic disease such as lupus erythematosus. Investigate the possibility of other animals in the household or humans in contact having skin disease. Pay special attention to fungal infections such as athlete's foot in the owner, which may serve as a source of infection for the dog.

Physical Examination

- Perform a thorough overall physical examination to look for evidence of generalized diseases.
- Carefully examine the claws. Twisted, curled, or malformed claws are usually due to disturbed growth of the claw horn frequently associated with a damaged claw matrix, trauma, or congenital defects. This malformation can lead to shedding of the claw.

Diagnostic Tests

Cytology

- Many patients with claw disease have inflammation of the tissue surrounding the claw. In these animals, material (pus, debris, keratinaceous material) may be squeezed out and applied to a glass slide with a small, soft paint brush. Alternatively, use a swab to remove material deep inside the claw fold and roll it onto a slide. Impression smears may be useful, if the skin adjacent to the claw fold is abnormal.
- If the claws and claw folds are dry, moisten swabs with saline prior to sampling the claw fold. Alternatively, in patients with changes of the claw horn, use a #10 scalpel blade and scrape material from the most proximal portion of avulsed or affected claws. Apply the material to the slides and use the staining techniques and methods of microscopic evaluation of specimens discussed in Chapter 37.
- *Interpretation* of results of cytology may be difficult at times. The presence of bacteria alone is not diagnostic of bacterial infection. However, if bacteria are present in large numbers, suspect infection and initiate trial therapy with antibiotics. Numerous yeast organisms or inflammatory cells with intracellular bacteria confirm clinically relevant infection and the need for appropriate therapy. If these bacterial or yeast infections are secondary to trauma, treatment with antimicrobial agents alone may be successful without a relapse of the claw disease. However, if another disease is responsible for the infection, identify and treat to prevent recurrence of claw disease.

Bacterial Culture

- Bacterial culture is not performed routinely, since most bacterial infections (due to cocci) of the claw respond well to empirical therapy.
- Indications for a bacterial culture and sensitivity are (1) bacterial infections not responding to appropriate antimicrobial therapy and (2) infections where a significant number of rod-shaped organisms have been identified on cytology. Obtain material for bacterial cultures as for cytological specimens. Prior clipping of the claw may decrease the risk of contamination. Interpret results of culture in light of cytology results.

Fungal Culture

- If the history and clinical examination indicate a possible fungal infection or spores/hyphae are identified on cytology or histopathology, perform a fungal culture to confirm the diagnosis and to allow determination of the fungal species involved. Different fungal organisms have different zoonotic potential.
- Obtain scales from the claw fold and/or proximal part of avulsed or intact claws and hair from the area directly adjacent to the claw fold for culture agars. Use Sabouraud's agar and dermatophyte test medium. Apply shaved thin slices of the claw to the culture medium to improve the probability of fungal growth. Cleaning of the claw and surrounding skin with alcohol may reduce bacterial contamination.
- Transient contamination of claws with *Trichophyton* spp. and *Microsporum gypseum* is possible. Identify organisms not only on culture, but also directly on hairs, in hair follicles, or in claw material cytologically and/or histopathologically to confirm the diagnosis.

Skin Scrapings

- Deep skin scrapings for *Demodex canis* may be useful since they may cause claw disease in some dogs. After gently clipping the skin adjacent to an affected claw, perform scrapings with a #15 scalpel blade until capillary bleeding is observed. Typically, heavy sedation or general anesthesia is required to achieve proper skin scrapings in dogs with claw disease.
- An alternative to the scraping may be a trichogram, where numerous hairs adjacent to the claw fold are plucked and examined under the microscope. If mites are identified, the diagnosis is confirmed. If no mites are present, perform a skin scraping.

Biopsy

▼ ***Key Point*** Claw biopsy is the diagnostic tool of choice for neoplastic disease, but may also confirm immune-mediated diseases such as the various

forms of pemphigus and bullous pemphigoid and may give important clues to diseases such as drug reactions.

- Claw biopsy may identify fungal or bacterial organisms in the tissue, thus complementing culture results. Histopathologic features similar to lupus erythematosus such as interface onychia, basal cell vacuolization, a band-like or perivascular to diffuse lymphocytic and plasmacytic infiltrate, and pigmentary incontinence are not always associated with immune-mediated diseases but can be found in other disorders as well. These "lupoid" changes may be a reaction pattern of canine claw epithelium rather than a diagnostic change.

Biopsy Technique

- To obtain appropriate specimens of claw matrix, surgically remove the distal phalanx (see Chapter 114) to allow the pathologist to evaluate the changes most thoroughly. However, amputation of the digit is often met with owner resistance.
- Recently, a biopsy technique was developed that allows evaluation of the claw matrix while avoiding onychectomy. To minimize postsurgical discomfort, take specimens from claws bearing no or little weight. If dew claws are not present or not affected, obtain samples from P2 and/or P5 of one hind paw.
- Place the animal under general anesthesia, and clip the affected paw. Apply a tourniquet to reduce hemorrhage during the procedure.
- Obtain the biopsy specimen by rotating a biopsy punch slowly in one direction deep into the tissue, initially cutting medially through the horn of the claw and then through the bone of the distal phalanx and laterally through normal skin on the lateral aspect of the claw fold (Figs. 63-2 and 63-3). Cut the base of the sample with iris scissors or scalpel blades.
- Place the specimen in 10% buffered formalin. Close the incision with two monofilament nonabsorbable sutures. Bandage the paw for 2 to 3 days postoperatively. Analgesic therapy may be used postoperatively for the first 8 to 10 hours. Remove the sutures after 2 weeks.

Blood Tests

- Blood samples have been reported to be rarely useful in patients with exclusive claw disease. However, complete blood counts, serum biochemistry, and urinalysis may be helpful in individual patients (particularly in older pets). They are essential when systemic diseases such as lupus erythematosus are suspected. Antinuclear antibody titers or determination of cold agglutinins may also be useful in individual patients.

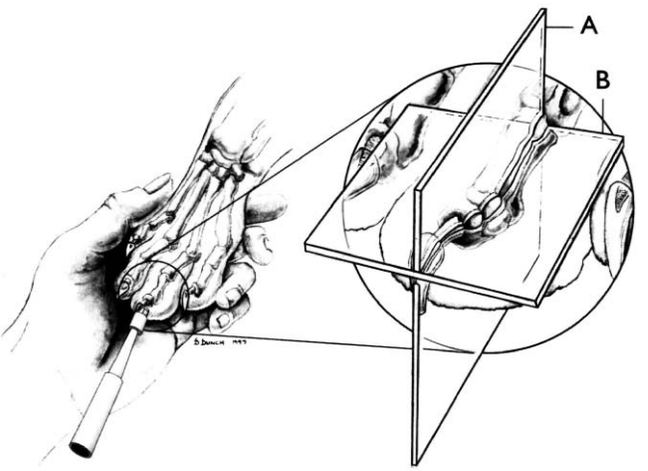

Figure 63-2. Positioning of the biopsy punch for onychobiopsy. Place the punch horizontally such that the direction of the cutting edge is perpendicular to planes A and B. The medial edge of the punch needs to cut through the lateral edge of the claw. (From Mueller RS, Olivry T: Onychobiopsy without onychectomy: description of a new biopsy technique for canine claws. Vet Derm 10:55, 1999, with permission.)

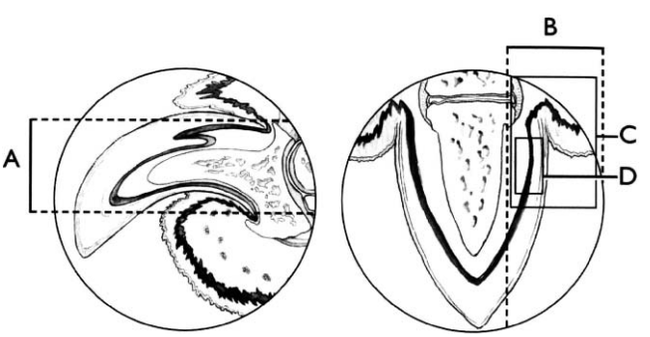

Figure 63-3. Localization of the excised biopsy specimen. Areas A and B depict the incision direction of the punch throughout the procedure, and area C delineates the area evaluated histopathologically. (From Mueller RS, Olivry T: Onychobiopsy without onychectomy: description of a new biopsy technique for canine claws. Vet Derm 10:55, 1999, with permission.)

Radiography

- Radiographs can identify lysis of bone, soft tissue swelling, and periosteal elevation and thus may be helpful in diagnosing secondary osteomyelitis and invasive neoplastic lesions in dogs with severe pain and swelling of the affected digit.

TREATMENT

General Therapy of the Claw

- To decrease pressure and associated pain, keep the claws very short so that the foot pads absorb most of

the weight. Distorted or brittle claws also benefit greatly from frequent clipping. In addition, clipped claws are less likely to catch on material. However, take care not to cause significant hemorrhage by clipping beyond the cornified part of the claw.

- Remove the claw plate if it is partially separated from the claw bed and causes constant pain or discomfort. Sedation or even general anesthesia may be necessary. Removal will typically diminish clinical signs of discomfort quickly. Apply antimicrobial ointments and a bandage for 1 to 3 days to minimize pain and bleeding. The prognosis for regrowth is good as long as the claw matrix is not significantly damaged.
- Topical antimicrobial solutions such as chlorhexidine at 0.05% to 0.1% (or available in 1–2% concentration in some products such as Malaseb [DVM Pharmaceuticals], Resichlor [Virbac]) may be beneficial with bacterial or fungal paronychia and can be used as a spray or shampoo daily to weekly.
- When an underlying etiology cannot be identified or treated successfully, and multiple claws are affected, amputation of all affected distal digits can be performed. However, long-term lameness may be seen following exercise.

Therapy for Bacterial Infection

- Perform antibacterial soaks or shampoos two to three times daily. Alternatively use 2% mupirocin ointment twice daily. Apply the ointment before walking or feeding the dog or before play time to prevent foot licking for the first 10 minutes after application. However, any topical therapy of the feet is cumbersome and often not tolerated easily by the patient, and systemic therapy may be preferred.
- If cytology has revealed an infection with cocci, cephalexin (20–30 mg/kg PO q12h), enrofloxacin (for dogs, 5–10 mg/kg PO q24h), or clavulanic acid/amoxycillin combination (12.5–25 mg/kg PO q8h) are all reasonable choices. If rod-shaped organisms predominate on cytology, perform culture and sensitivity to determine the choice of antibiotics. Continue treatment for 3 to 8 weeks depending on the underlying disease and the severity of the infection. If radiographs have indicated the presence of bacterial osteomyelitis, long-term systemic antibiotic therapy will be necessary (see Chapter 120).
- Consider amputation of the distal phalanx in conjunction with antibiotic therapy to avoid the risk of treatment failure and financial obligation associated with long-term antimicrobial therapy.

Therapy for Fungal Infection

- Onychomycosis is a refractory or recurrent disease that needs to be treated aggressively. Administer antifungal agents for extended time periods. Clinical improvement is an indicator of effective therapy, but continue treatment for several months beyond a negative fungal culture in conjunction with clinical remission.
- Griseofulvin at 50 mg/kg PO daily has been used successfully. Administer with a fatty meal to maximize absorption. Griseofulvin is teratogenic; do not give to breeding bitches.
- Other options include ketoconazole at 10 mg/kg PO q12h or itraconazole at 10 mg/kg PO q12h. Both of these drugs are occasionally hepatotoxic and may lead to vomiting and nausea, although these side effects are much more common with ketoconazole than with itraconazole.
- Terbinafine (25–30 mg/kg q24h) may also be used for onychomycosis in dogs. Pulse therapy may be useful with itraconazole or terbinafine; the drugs are given at their normal dose every other week.
- Consider amputation of the distal phalanx for clients with financial constraints. If the disease recurs after discontinuing extended therapy, onychectomy is recommended. Another reported alternative is long-term, low-dose daily therapy with systemic antifungal agents.

Therapy for Neoplasia

▼ ***Key Point*** In all patients with neoplasia of the claw, amputation of the digit is the therapy of choice.

Obtain lymph node aspirates or biopsies and radiographs to evaluate the extent of tumor invasion and the possibility of metastases. If the local lymph nodes show evidence of neoplastic cells, consider excision of the affected lymph node and limb amputation, or adjunctive therapy, depending on tumor type (see Chapter 115).

Idiopathic Onychomadesis (Lupoid Onychodystrophy)

- I have had reasonable success with a combination of tetracycline and niacinamide at 250 to 500 mg/animal PO q8h. If a good response is seen within 8 to 12 weeks, treatment may be changed to doxycycline hydrochloride or preferably doxycycline monohydrate at 5 to 10 mg/kg PO once daily. Many patients will stay in remission with this once-daily therapy, which is less cumbersome than administration of tetracycline/niacinamide and thus preferred by many owners.
- In a recent study, some patients also responded to pentoxifylline at 200 to 800 mg/dog PO once daily. However, the condition in some dogs may wax and wane, and spontaneous remission has been seen.
- Supplementation with essential fatty acids (omega-6 and omega-3 fatty acids (DermCaps, DVM Pharmaceuticals) or vitamin E (at 400 IU twice daily) has been reported to be very effective. However, in my

experience, response to supplements has been less reliable.

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Section

6 Digestive System

Susan E. Johnson

Chapter

64 Dentistry and Diseases of the Oropharynx

Sandra Manfra Marretta

Dental disease and diseases of the oropharynx are common in dogs and cats. These diseases can be divided into categories including oral surgical disease, periodontal disease, endodontic disease, orthodontic disease, stomatitis/gingivitis, neoplastic disease, and salivary gland disease. Neoplastic disease of the maxilla and mandible is discussed in Chapter 99.

ORAL SURGICAL DISEASE

The two major categories of oral surgical (non-neoplastic) disease are:

- Diseases requiring dental extraction
- Oronasal fistulas and palatal defects that can be surgically corrected

Anatomy

Proper performance of dental extractions requires a thorough knowledge of dental formulas, dental root structure, and pericoronal and periradicular anatomy.

▼ ***Key Point*** Determine the number of roots in any tooth to be extracted to ensure that all roots are removed during extraction.

- Deciduous and permanent dental formulas for dogs and cats are listed in Table 64-1.
- The dentition, including root structure, of dogs and cats is illustrated in Figures 64-1 and 64-2, respectively. Tooth roots for both species are listed in Table 64-2.
- Basic anatomic structures of the teeth and related areas are illustrated in Figure 64-3 and defined in Table 64-3.

Diseases Requiring Dental Extraction

Etiology

Dental diseases in which extraction is a treatment option include retained deciduous and supernumerary teeth, malocclusion teeth, advanced periodontal disease, fractured teeth, gross decay/erosions, diseased teeth in the fracture site of the mandible or maxilla, periapical abscess, impacted and deformed teeth, and teeth causing ophthalmic problems.

Clinical Signs

Common historical findings and signs of dental disease include changes in eating habits, halitosis, pawing at the mouth, abnormal salivation, oral hypersensitivity, facial swelling, oral hemorrhage, sneezing, nasal discharge, ophthalmic changes, and abnormal behavior.

Diagnosis and Indications for Extraction

The decision to perform dental extraction depends not only on the dental disease present but also on the

Table 64-1. DECIDUOUS AND PERMANENT DENTAL FORMULAS FOR DOGS AND CATS

Deciduous Dentition
Dog: 2(I3/3 C1/1 P3/3) = 28
Cat: 2(I3/3 C1/1 P3/2) = 26

Permanent Dentition
Dog: 2(I3/3 C1/1 P4/4 M2/3) = 42
Cat: 2(I3/3 C1/1 P3/2 M1/1) = 30
C, canine; I, incisor; M, molar; P, premolar.

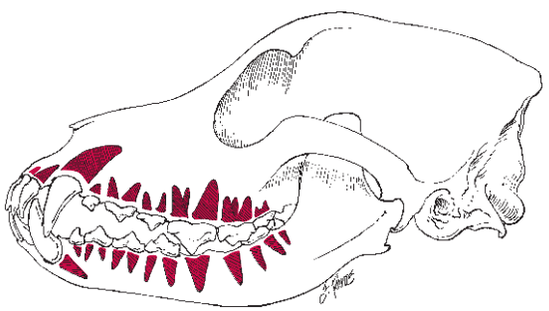

Figure 64-1. Dental root structure in the dog.

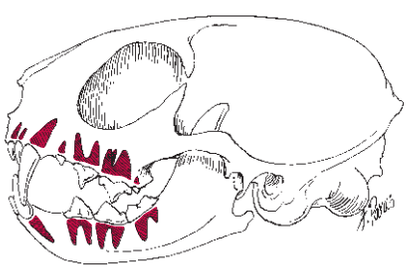

Figure 64-2. Dental root structure in the cat.

client's ability and desire to pursue alternatives to extraction, such as periodontal, endodontic, and orthodontic therapy.

▼ ***Key Point*** If a client is unwilling to pursue alternatives for treatment of a painful tooth, then the tooth should be extracted.

Overly Retained Deciduous and Supernumerary Teeth

Deciduous teeth are considered overly retained if they are firmly attached following the initial stage of eruption of the permanent tooth. Failure to extract deciduous teeth during this initial stage may result in malocclusion of the permanent teeth. Retained deciduous teeth and supernumerary teeth can be diagnosed as extra teeth present in the dental arcade. Deciduous teeth may be differentiated from supernumerary permanent teeth by their smaller crown size grossly and smaller root structure radiographically.

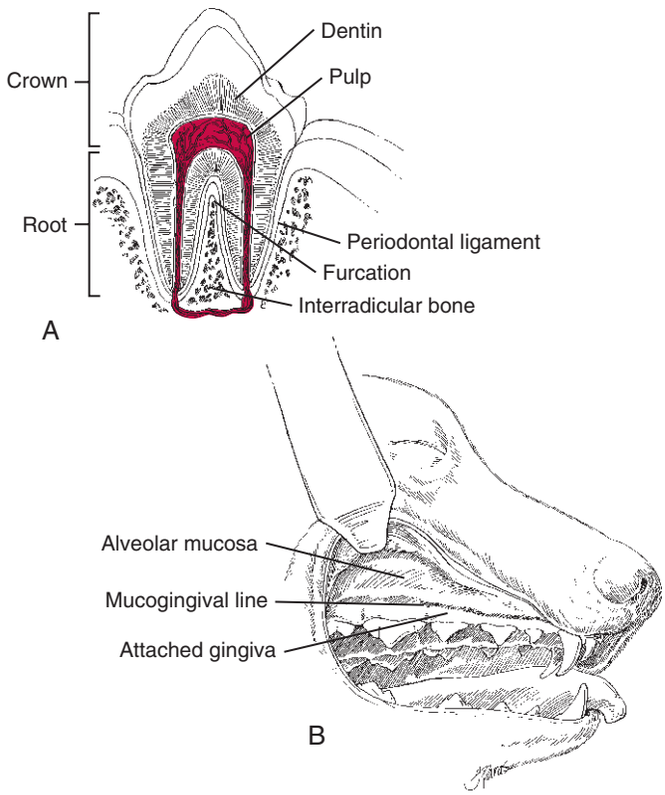

Figure 64-3. *A,* Anatomy of the tooth. *B,* Gingival anatomy.

Table 64-2. TOOTH ROOTS IN DOGS AND CATS

Type of Tooth	No. of Roots
In Dogs	
Incisor	1
Canine	1
Maxillary (upper) cheek teeth:	
1st (1st P)	1
2nd and 3rd (2nd and 3rd P)	2
4th–6th (4th P; 1st and 2nd M)	3
Mandibular (lower) cheek teeth:	
1st and last (1st P; 3rd M)	1
2nd–6th (2nd–4th P; 1st and 2nd M)	2
In Cats	
Incisor	1
Canine	1
Maxillary (upper) cheek teeth:	
1st (2nd P)	1
3rd (4th P)	3
All others	2
Mandibular (lower) cheek teeth:	
All	2

M, molar; P, premolar.

Table 64-3. BASIC ANATOMIC STRUCTURES OF THE DENTITION

Crown:	Portion of the tooth located in the oral cavity. It is covered by enamel.
Root:	Portion of the tooth that lies within the alveolar bone. It is covered by cementum.
Furcation:	The space between the roots of a multirooted tooth.
Periodontal ligament:	Ligament that attaches the root of the tooth to the alveolar bone.
Interradicular bone:	Bone located between the roots.
Buccal bone:	Bone located on the buccal, or cheek, side of the tooth root.
Attached gingiva:	Keratinized gingiva firmly attached to the underlying alveolar bone.
Alveolar mucosa:	Mucosa that is loosely attached to the underlying bone.
Mucogingival line:	Anatomic landmark that separates the attached gingiva from the alveolar mucosa.

Maloccluded Teeth

Extraction may be required for maloccluded teeth that cause traumatic soft tissue occlusion or interfere with proper closing of the mouth. Orthodontic therapy is a viable alternative in these cases.

Advanced Periodontal Disease

Extremely mobile teeth caused by severe periodontal disease should be extracted. Other indications for extraction of teeth affected by periodontal disease include periodontal pockets extending to the apex of the tooth, pockets that reach the nasal cavity or maxillary sinus, and periapical abscess (discussed later).

Fractured Teeth

Extract fractured teeth with exposed pulp tissue if endodontic therapy is not an option. To diagnose pulpal exposure, place a dental explorer over the suspected exposure site. If the explorer penetrates into the tooth, the pulp is exposed.

Gross Decay/Dental Erosion

Gross decay, characterized by soft areas of demineralized enamel or dentin, is rare in dogs and cats. Dental erosive lesions or odontoclastic resorptive lesions are very common in cats.

- In dogs, gross decay, which usually occurs on the occlusal or biting surface of the maxillary first molar, and less frequently on the distal cusp of the mandibular first molar, can be identified with a dental explorer placed into the soft carious lesion. Penetration of the explorer into the soft demineralized enamel/dentin confirms gross decay. Radiographs of the affected tooth will show the extent of the lesion.
- Odontoclastic resorptive lesions are very common in cats. These defects are referred to as feline odontoclastic resorptive lesions (FORLs).
- FORLs often are extensive and painful and usually are covered by granulation tissue. Removal of the granulation tissue reveals the underlying erosive lesion.
  - Determine the extent of the resorptive lesion in the region of the cementoenamel junction and crown of the tooth with a dental explorer.
  - Radiographs are imperative to determine the severity of root resorption, because minor resorptive lesions in the crown may be associated with major root resorptive lesions.
- Treat dental caries and odontoclastic root resorptive lesions that extend into the pulp with extraction. Minor lesions can be restored with various dental restorative materials.

Diseased Teeth in a Mandible or Maxilla Fracture Site

Extract teeth in a fracture site that are severely affected with periodontal disease or that have fractured roots. If the fracture line in the jaw is located along the periodontal ligament and communicates with the apex of the tooth, extraction may also be necessary; however, temporary retention of the teeth that are not severely affected with periodontal disease may assist in anatomic reduction of the fracture site. Careful gross assessment and radiographic examination of the fracture site can determine if an extraction is necessary.

Periapical Inflammation

In small animals, a periapical inflammatory reaction (inflammation around the apex of a tooth) usually is secondary to periodontal or endodontic disease and is often characterized by acute, severely painful swelling in the area of the affected tooth. Periapical inflammation may be associated with a tooth that appears grossly normal. Concussive trauma without overt trauma to the tooth surface can cause pulpal necrosis with a secondary periapical inflammatory reaction.

- Carefully examine teeth in the area of acute facial swelling for deep periodontal pockets with a periodontal probe and for pulpal exposure with a dental explorer.
- Periapical lysis will be present around the apex of the affected root. Radiographs can confirm the diagnosis.
- Extraction of the affected tooth is recommended.

Impacted Teeth

Impacted (unerupted) teeth may cause nasal discharge, orthodontic problems, and bone loss.

- Dentigerous cysts may occur and can cause expansion of bone with subsequent facial asymmetry, extreme

displacement of teeth, severe root resorption of adjacent teeth, and bone loss.
  - Dentigerous cysts may give rise to ameloblastomas.
- Radiography can diagnose impacted teeth. Perform extraction if they are causing problems and when associated with a dentigerous cyst. Remove the entire cyst lining to prevent recurrence of the cyst and submit cyst lining for histopathology to confirm diagnosis.

Deformed Teeth

Diagnose deformed teeth based on gross and radiographic appearance. Usually they result from trauma or fever that occurred during tooth development. Abnormalities in development of teeth occur rarely and include dens-in-dente and gemination of teeth, which results when a single tooth bud attempts to divide into two teeth. Dens-in-dente results when there is invagination of enamel and dentin into the pulp space often resulting in secondary endodontic disease.

- Diagnose minor dental deformities such as enamel hypoplasia based on the observation of symmetric defects and staining of enamel combined with a history of illness during tooth development. No treatment is required in most cases.
- Extract severely deformed teeth that are causing pain.
- Gemination of the teeth usually requires no treatment. When a tooth has this developmental defect and extraction is necessary, perform dental radiography before extraction to determine the location of abnormal roots.

Ophthalmic Manifestations of Dental Disease

Tooth roots of the maxillary fourth premolar and first and second molars in dogs are in close proximity to the orbital floor and globe. Periodontal and endodontic disease of these teeth can result in ophthalmic signs, including orbital, periorbital, conjunctival, nasolacrimal, and neuro-ophthalmologic abnormalities.

- When signs of ophthalmic disease are suggestive of a primary dental disorder, do a complete oral examination under general anesthesia or sedation.
- Examine the maxillary teeth for fractures or deep periodontal pockets.
- Take dental radiographs of the maxillary teeth to check for periapical lysis.
- Extract teeth that are causing secondary ophthalmic disease.

Preoperative Considerations

- Before performing dental extractions, perform a thorough physical examination, standard laboratory tests including a complete blood count (CBC), serum biochemistry, and urinalysis.
- Perform appropriate radiographic procedures, based on the animal's clinical signs, physical examination findings, and age.
- Correct any underlying metabolic abnormalities such as dehydration, azotemia, electrolyte imbalances, hyperglycemia, and hypoglycemia.

Surgical Procedure

There are three basic types of extractions: simple, multirooted, and complicated surgical. An alternative to routine extraction techniques, feline crown amputation with intentional root retention can be utilized in feline teeth with advanced odontoclastic resorptive lesions following proper screening.

Equipment

- See Tables 64-4, 64-5, and 64-6.

Simple Extraction

Simple extraction refers to the extraction of a small single-rooted tooth such as an incisor.

Technique

1. Place an appropriate-size dental elevator in the periodontal ligament to sever the attachments of the gingiva around the tooth.
2. Advance the elevator apically (toward the apex or tip of the root) between the alveolar bone and root.
3. Rotate the elevator and hold for 15-second intervals to tear the periodontal ligament (Fig. 64-4*A*).

Table 64-4. DENTAL EQUIPMENT APPLICATIONS

Equipment	Applications
Portable electric dental drill with low-speed hand piece and prophy angle (Vetroson Millennium Motor Pack, Henry Schein, Inc.; Port Washington, NY)	Sectioning teeth, removal of alveolar bone, polishing teeth
Mobile delivery system with high-speed handpiece, low-speed handpiece, water and air syringe (Vet-Base, Henry Schein, Inc.)	Sectioning teeth, removal of alveolar bone, polishing teeth, cavity and crown preparations
Piezoelectric scaler, electric or air driven (Spartan USA, Inc.; Fenton, MO)	Permits rapid, easy removal of dental calculus
Dental radiography unit (AFP Imaging, Elmsford, NY)	Permits rapid, easy exposure of dental radiographs

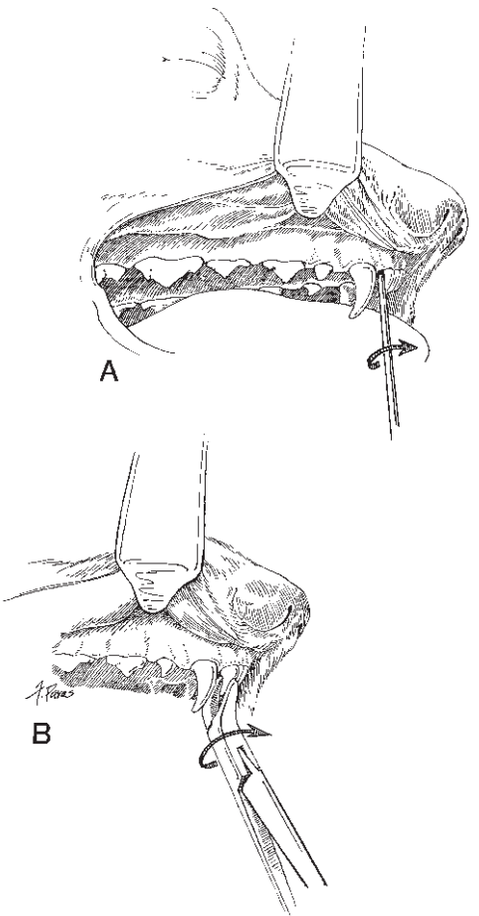

Figure 64-4. *A,* Dental elevator in periodontal ligament space is rotated 90 degrees. Tooth is rotated with extraction forceps.

4. Advance the elevator again apically, rotate it 90 degrees, and hold for 15 seconds.
5. When the tooth is loose, place an appropriate-size dental extraction forcep on the crown near the gingival margin and rotate and remove the tooth from the alveolus (Fig. 64-4*B*).
6. Examine the tooth to confirm that the root has been removed completely.

Multirooted Extraction

Multirooted teeth such as premolars and molars are more difficult to extract than incisors. Often only one root is affected and the other root(s) are firmly attached to the alveolar bone. Furthermore, most roots are embedded in the alveolar bone at divergent angles, making removal of the intact tooth difficult.

▼ ***Key Point*** Sectioning of a multirooted tooth into two or three sections converts the procedure into multiple simple extractions. A high-speed handpiece or a low-speed electric handpiece with adequate irrigation can be used for sectioning teeth.

Technique

1. Locate the furcation with a dental elevator.
2. Place a tapered fissure bur (#701 in small animals and #702 in larger animals) at the furcation and direct it through the crown (Fig. 64-5*A*).
3. Advance the elevator apically between two roots.
4. Gently rotate the elevator and hold for 15 seconds to gently force the roots apart (Fig. 64-5*B*).
5. Advance the elevator further apically, rotate it 90 degrees, and hold for 15 seconds.

Table 64-5. DENTAL INSTRUMENTATION

Instrumentation*	Applications
Oral Surgery	
Dental elevator	Tears periodontal ligament during extraction
Dental luxators	Has a thinner, sharper blade than traditional elevators
Extraction forceps	Completes breakdown of periodontal ligament and removal of tooth from alveolus during extraction
Root tip pick	Removal of small-breed deciduous teeth or broken root tips
Bone curette	Debridement of alveolus following extraction
Periosteal elevator	Elevation of mucoperiosteum during oronasal fistula repair and palatal surgery
Periodontic	
Periodontal probe/explorer	Measurement of depth of periodontal pocket (probe); detection of pulpal exposures and carious lesions (explorer)
Hand scalers	Subgingival scaling
Curette (Columbia #13/14)	Removal of accretions on the root surface and removal of granulation tissue from the pocket wall
Prophylaxis paste	Polishing teeth following scaling
Endodontic	
Endodontic files (Hedstrom/K-Files)	Debridement of necrotic pulpal tissue from canal
Root canal plugger	Compression of gutta percha into the apex
Light-Speed and SimpliFil System†	

*Available from Henry Schein, Inc.; Port Washington, NY and from Cislak Manufacturing Inc, Niles, IL.
†Available from Light Speed Endodontics, San Antonio, TX.

Table 64-6. DENTAL MATERIALS

Material	Applications
Composite resins (Prodigy, sdsKerr, Orange, CA)	Aesthetic restorations following endodontic therapy or cavity preparation
Glass ionomers (Vitrebond, 3M EPSE, St. Paul, MN)	Restoration of feline external root resorptive lesions
Endodontic sealers (AH Plus, Dentsply, Konstanz, Germany)	Endodontic filling material
Mineral trioxide aggregate (ProRoot MTA, Dentsply Tulsa Dental, Tulsa, OK)	Stimulates closure of an apex and reparative dentin formation following spulpotomies
Gutta percha (Successfil, Hygenic)	Fills the pulp canal following debridement during root canal therapy

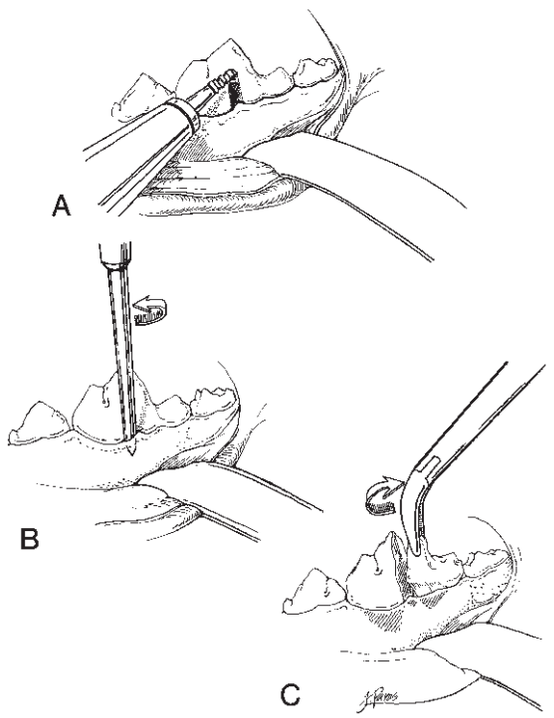

Figure 64-5. *A,* Tooth is sectioned with a tapered fissure bur. *B,* Elevator is rotated 90 degrees. *C,* Extraction forceps is used to extract each root separately.

6. Place a dental extraction forceps on each crown segment and rotate to extract each root independently (Fig. 64-5*C*).

Complicated Surgical Extraction

This procedure involves the removal of teeth with large roots, such as the canine teeth in dogs, or large multirooted teeth, such as the maxillary fourth premolars and the mandibular first molars.

Technique

1. Reflect a mucoperiosteal flap to expose buccal alveolar bone overlying the root (Fig. 64-6*A*).
2. Remove the buccal alveolar bone overlying the root with a large round bur (Fig. 64-6*B*).
3. If the tooth is multirooted, section it with a #702 bur.
4. Elevate and extract the tooth.

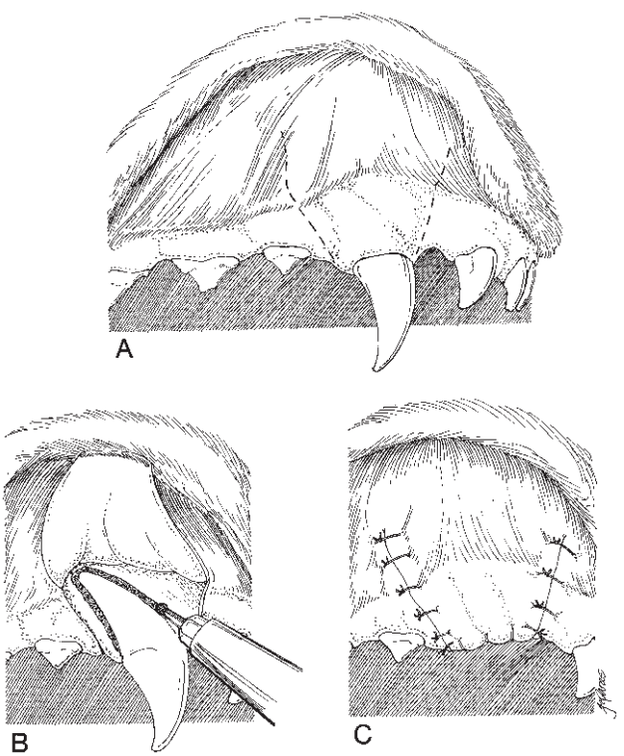

Figure 64-6. *A,* Proposed mucoperiosteal flap incision site for extraction of a maxillary canine tooth. *B,* Buccal alveolar bone is removed. *C,* Mucoperiosteal flap is replaced and sutured.

5. Perform an alveoloplasty to remove the rough edges of the alveolus, using a large, round bur.
6. Curette and flush the alveolus.
7. Incise the deepest layer of the flap, the periosteal layer, over the entire width of the apical aspect of the flap to prevent tension on the flap closure.
8. Replace and suture the mucoperiosteal flap to the adjacent mucosa and gingiva with a simple interrupted pattern (Fig. 64-6*C*).

Crown Amputation with Intentional Root Retention (DuPont Technique)

This procedure involves the removal of the crown with intentional retention of the roots in appropriately screened feline teeth with severe odontoclastic resorptive lesions.

Technique

1. Reflect a small flap to expose the marginal alveolar bone of affected tooth (Fig. 64-7A).
2. Retract the gingival and protect it with the end of a small flat feline periosteal elevator while the crown is amputated with a #3 round bur on a high-speed handpiece at or slightly apical to the level of the alveolar crest (Fig. 64-7B).
3. Check the crown amputation with a dental explorer and remove any residual crown or sharp bony projection with the bur (Fig. 64-7C).
4. Flush the site with sterile saline, replace the flap, and close with simple interrupted absorbable sutures (Fig 64-7D).

Postoperative Care and Complications

- Offer a soft diet for 3 to 10 days, depending on the number and complexity of dental extractions.
- Administer a broad-spectrum antibiotic (e.g., amoxicillin clavulanate) for 3 to 7 days when infection is present.

Hemorrhage

Hemorrhage is a common complication of dental extractions and usually is minor and can be easily controlled with a gauze sponge and digital pressure. Control persistent alveolar hemorrhage by suturing the gingiva over the alveolus, thereby permitting clot formation.

Broken Root Tips

Broken root tips are common when inappropriate dental extraction techniques are used. Various types of dental pathology such as odontoclastic resorptive lesions, dental caries, and ankylosis of the root to the alveolar bone may predispose to broken root tips.

▼ ***Key Point*** Always remove any tooth roots that break during extraction.

- Differentiate broken root tips from surrounding alveolar bone by the following features:
  - The tooth is whiter than the surrounding off-white bone.
  - The tooth is harder than the surrounding bone, as detected by a dental explorer.
  - The hard tissues of the tooth do not bleed.
  - Remove root tips with a root tip pick or obliterate with an appropriate-size round bur (Fig. 64-8). Removal with a root tip pick is preferred because obliteration of roots with a bur may cause damage to underlying structures.

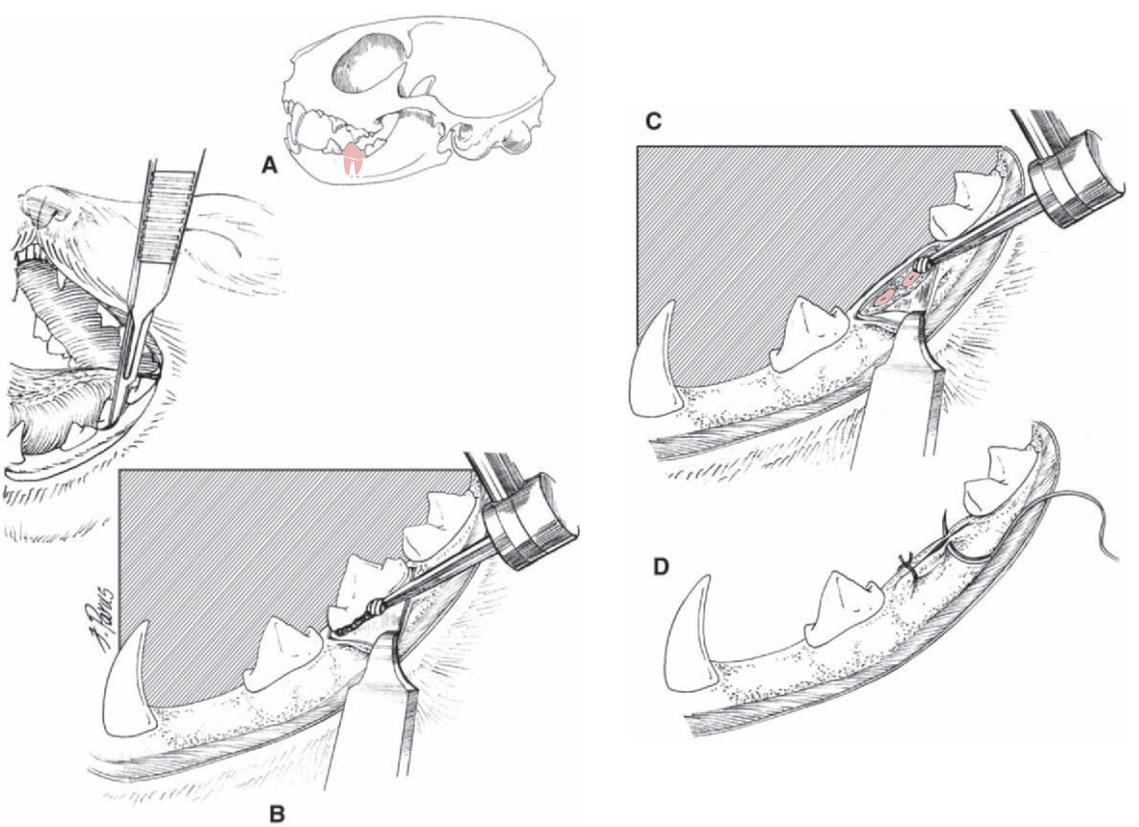

Figure 64-7.

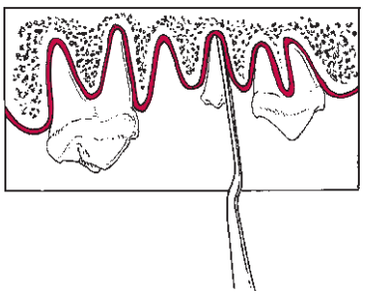

Figure 64-8. Elevation of root tip with root tip pick.

Damage to Permanent Teeth

▼ ***Key Point*** Permanent teeth may be damaged during the extraction of deciduous teeth.

Careful extraction of deciduous teeth can help minimize this complication. However, extraction of deciduous teeth before complete formation of the permanent crowns (especially at 8–12 weeks of age) can result in enamel hypocalcification, enamel hypoplasia, crown deformity, and eruption failure.

Misplaced Tooth or Root Tip

A tooth or root tip infrequently may be misplaced in the nasal cavity or mandibular canal during an extraction. Advanced periodontal disease in combination with aggressive extraction techniques can force a tooth or root tip into the nasal cavity or mandibular canal.

- Enlarge the defect in the floor of the extraction site to remove a misplaced tooth or root tip.

Iatrogenic Fractures

Severe periodontal disease, inappropriate extraction techniques, and metabolic bone disease in geriatric animals may be predisposing factors in iatrogenic mandibular fractures.

- Careful elevation of the tooth, digital support of the mandible during extraction, and a rotational movement with the dental extractor can help prevent iatrogenic mandibular fractures.

Osteomyelitis and Bony Sequestra

Osteomyelitis following extraction of teeth may be caused by retained tooth roots, exposed alveolar bone, and osseous necrosis. A bone sequestrum may develop when a segment of alveolar bone is fractured off during a dental extraction and left in the extraction site.

- Treat osteomyelitis and bony sequestra by removing retained tooth roots and bony sequestra and by curettage of necrotic bone to the level of healthy, bleeding bone and closing extraction site with a mucoperiosteal flap.

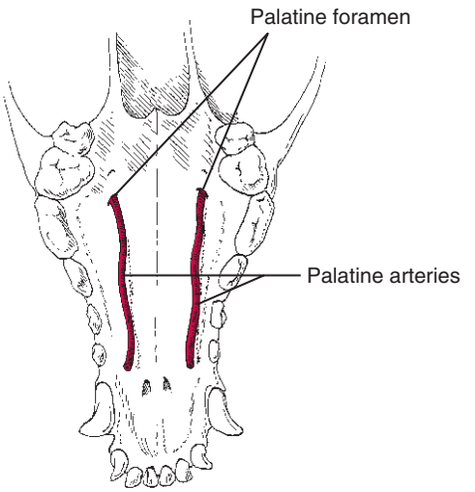

Figure 64-9. Palatine arteries.

Ophthalmic Complications of Dental Extractions

Inappropriate techniques during extraction of the maxillary fourth premolar and the first and second molars in dogs may result in severe ophthalmic complications caused by penetration of the elevator into the orbit or globe, causing orbital cellulitis, orbital abscess, or endophthalmitis.

- Prevent ophthalmic complications of dental extractions by using a finger stop near the tip of the elevator during extraction of the maxillary fourth premolar and the first and second molars to prevent deep penetration of the elevator into orbital tissues or the globe.

Oronasal Fistulas and Palatal Defects

Oronasal fistulas are abnormal communications between the oral and nasal cavity. Palatal defects may occur anywhere in the palate and result in a communication between the oral and nasal cavities.

Anatomy

▼ ***Key Point*** Oronasal fistulas are associated most frequently with defects in the area of the maxillary canine tooth.

The surgical anatomy varies with the location of the defect. The mucoperiosteal flap used in the repair of oronasal fistulas extends from the margins of the defect across the mucogingival line (the anatomic landmark separating the attached gingiva from the alveolar mucosa). Surgical techniques used to repair defects in the hard palate often require preservation of the palatine arteries, which arise approximately 1 cm palatal to the maxillary fourth premolar and course rostrally along the hard palate (Fig. 64-9).

Etiology

Palatal defects may be congenital or acquired.

Congenital Defects

Congenital palatal defects occur primarily in brachiocephalic breeds, miniature schnauzers, cocker spaniels, beagles, and cats. Congenital abnormalities of the primary palate (incisive bone) are referred to as a hare lip. These defects may occur concomitantly or independent of secondary palate (hard and soft palate) abnormalities.

Acquired Defects

- Acquired palatal defects are most frequently caused by a deep maxillary periodontal pocket that has progressed toward the apex of the tooth, resulting in lysis of the thin layer of bone that separates the palatal aspect of the root of the maxillary tooth and the nasal cavity.
- Acquired palatal defects that have etiologies other than dental disease usually are located in the hard palate and may be caused by various types of trauma including dog bites, blunt head trauma, electrical shock, gunshot wounds, foreign body penetration, and pressure necrosis. They also may occur as a complication of maxillectomy for oral neoplasia.

Clinical Signs

- Clinical signs associated with oronasal fistulas and palatal defects include unilateral or bilateral mucopurulent and occasionally hemorrhagic nasal discharge.
- Animals often are presented because of recurrent episodes of sneezing, especially after eating.

Diagnosis

- Identify defects in the hard palate by an oral examination.
- Perform a thorough periodontal examination to identify oronasal and oroantral fistulas secondary to periodontal disease. This requires tranquilization or general anesthesia.
- Insert a periodontal probe into the suspected periodontal pocket, which often is located on the palatal aspect of the maxillary canine tooth but may be located anywhere along the periodontal ligament of the maxillary cheek teeth.
- If the probe penetrates easily into the nasal cavity the presence of an oronasal fistula is confirmed.

Preoperative Considerations

▼ ***Key Point*** Tube- or bottle-feed animals with congenital hard palatal defects until they are 3 to 4 months of age to decrease the incidence of inhalation pneumonia.

- Perform surgery when the animal is 3 to 4 months of age following thoracic radiography to check for pneumonia.
- Give animals with severe, purulent rhinitis or pneumonia antibiotics before surgery.

Surgical Procedure

Two techniques used frequently for the repair of oronasal fistulas are the single-layer and the double-layer mucoperiosteal flap. The overlapping flap technique is used frequently for the repair of hard palatal defects.

Objectives

- Maintain blood supply to the tissue.
- Provide a tension-free closure of the defect.

Equipment

- Standard general surgical instruments and suture
- Periosteal elevator

Single-Layer Mucoperiosteal Flap

Technique

1. Place the animal in lateral recumbency.
2. Remove the epithelial margin of the fistula with a #15 scalpel blade.
3. Make two divergent incisions in the mucosa, beginning at the mesial and distal aspects of the fistula and extending across the mucogingival line (Fig. 64-10*A*).
4. Using a periosteal elevator, gently raise the flap (Fig. 64-10*B*).
5. Reflect the flap apically and incise the deepest layer of the flap (the periosteal layer) the entire width of the flap at its most dorsal aspect (Fig. 64-10*C*).
6. If necessary, remove excess buccal bony plate and sharp edges of bone with a rongeur or dental bur to permit tensionless apposition of tissues (Fig. 64-10*D*).
7. Before closure, remove all debris and granulomatous tissue with a bone curette, and irrigate the surgical site with sterile saline.
8. Suture the flap to the palatal and gingival mucosa with 3-0 or 4-0 poliglecaprone (Monocryl) in a simple interrupted pattern (Fig. 64-10*E*).

Double-Layer Mucoperiosteal Flap

- Use to repair large chronic or recurrent oronasal fistulas.

Technique

1. Remove the mesial, distal, and buccal epithelial margins of the fistula with a #15 blade. Do not remove the palatal epithelial margin.
2. Elevate an elliptical palatal mucoperiosteal flap with a periosteal elevator, preserving the lateral attachment of the base of the flap (Fig. 64-11*A*).

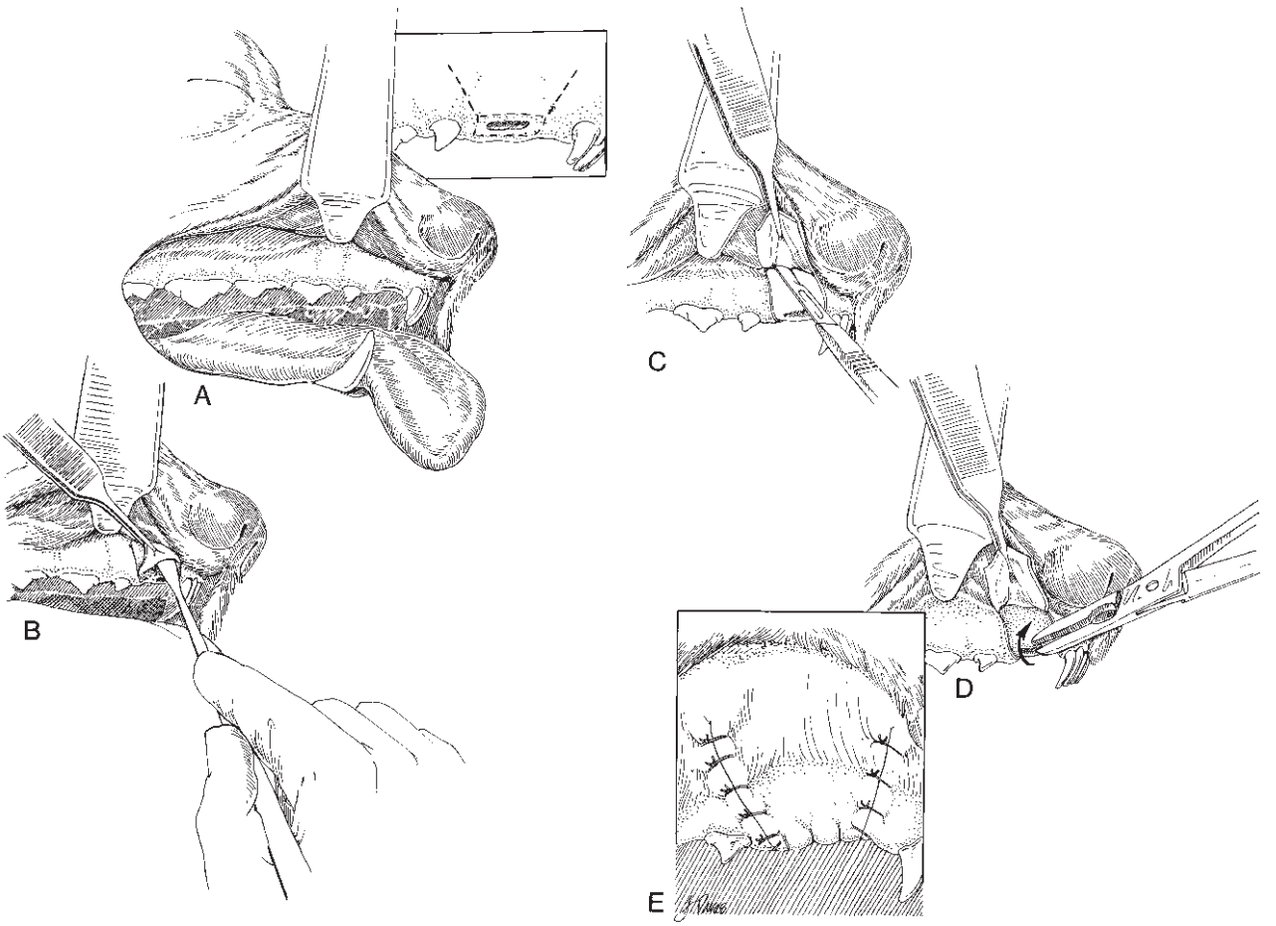

Figure 64-10. *A,* Proposed incision sites in mucosa for oronasal fistula repair. *B,* Elevation of mucoperiosteal flap. *C,* Incision of periosteal layer of flap. *D,* Removal of rough edges of buccal alveolar bone with rongeurs or round bur. *E,* Mucoperiosteal flap is replaced and sutured.

3. Fold over and suture the flap to the periosteum of the edge of the defect with 3-0 or 4-0 poliglecaprone (Monocryl) in a simple interrupted pattern (Fig. 64-11*B*).
4. Elevate a buccal mucoperiosteal flap from the lateral aspect of the oronasal fistula (see Fig. 64-10*C*).
5. Advance the buccal mucoperiosteal flap palatally to cover the inverted flap and the denuded palatine bone (Fig. 64-11*C*).
6. Suture the flap to the palatal and gingival mucosa with 3-0 or 4-0 poliglecaprone (Monocryl) in a simple interrupted pattern (Fig. 64-11*D*).

Overlapping Flap Technique

- Use for repair of hard palatal defects, especially on the midline.

Technique

1. Make an incision the length of the palatal defect in the palatal mucosa just palatal to the maxillary dental arcade. The rostral and caudal aspects of these incisions are connected to the rostral and caudal aspects of the hard palatal defect (Fig. 64-12*A*).
2. Incise the opposite side of the palatal defect along the entire length of the defect and gently elevate with a periosteal elevator to create a recipient site for the mucoperiosteal flap. Carefully elevate the mucoperiosteal flap with a periosteal elevator, preserving the palatine artery (see Fig. 64-9) that arises approximately 1 cm palatal to the upper fourth premolar (Fig. 64-12*B*).
3. Hinge the mucoperiosteal flap at the end of the palatal defect and place beneath the mucosa on the other side of the defect.
4. Preplace 3-0 PDS (polydioxanone) sutures in an interrupted vest-over-pants suture pattern through the recipient site and the flap.
5. Tie the sutures from caudal to rostral to complete the procedure (Fig. 64-12*C*).
6. Make an incision along the edges of the soft palatal defect and close in two layers by apposing nasal

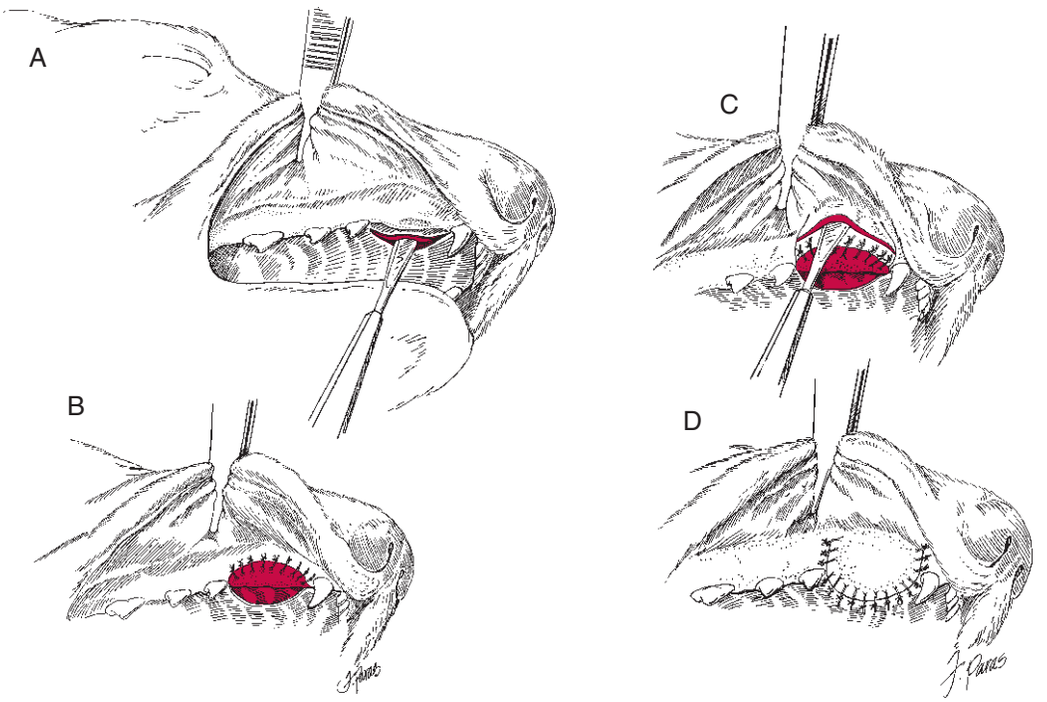

Figure 64-11. *A,* Periosteal elevation of palatal flap. *B,* Palatal flap is sutured to debrided edges of defect. *C,* Buccal mucoperiosteal flap is elevated and advanced palatally. *D,* Flap is sutured to palatal and gingival mucosa.

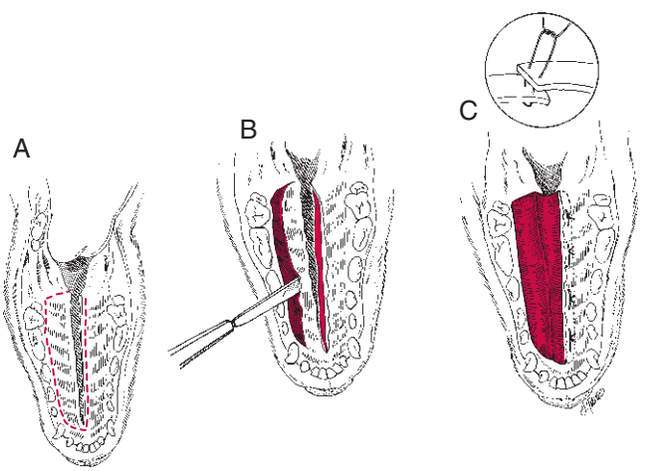

Figure 64-12. *A,* Palatal incisions to create flaps for overlapping flap technique. *B,* Periosteal elevation of flap. *C,* The larger flap is placed beneath the smaller flap and the flaps are sutured together.

mucosa to nasal mucosa with the knots in the nasopharynx and oral mucosa to oral mucosa with the knots in the oral cavity.

Postoperative Care and Complications

- Feed a soft diet (gruel or liquid) for 2 to 3 weeks. For animals requiring complicated repair, consider using esophagostomy or gastrostomy tube feeding (see Chapter 3). Place Elizabethan collars on patients that paw at the oral cavity.
- In 3 weeks, reexamine the patient to assess the integrity of the repair.
  - If the repair is intact, gradually return to a normal diet over the next 2 to 3 weeks.
  - If the repair was unsuccessful, schedule a second operation in approximately 4 weeks.

PERIODONTAL DISEASE

▼ ***Key Point*** Periodontal disease is the most common cause of oral infection and tooth loss in dogs.

- Periodontal disease occurs in two forms: gingivitis and periodontitis. Gingivitis is a reversible inflammation of the gingiva. Periodontitis involves deeper inflammation with loss of tooth support and permanent damage.
- The purpose of periodontal therapy is to prevent gingivitis from progressing to periodontitis and to delay the progression of periodontitis once it is established.

Anatomy

The periodontal tissues are composed of the gingiva, cementum, periodontal ligament, and alveolar bone. An accurate estimate of the amount of support that has been lost around a tooth depends on the appropriate

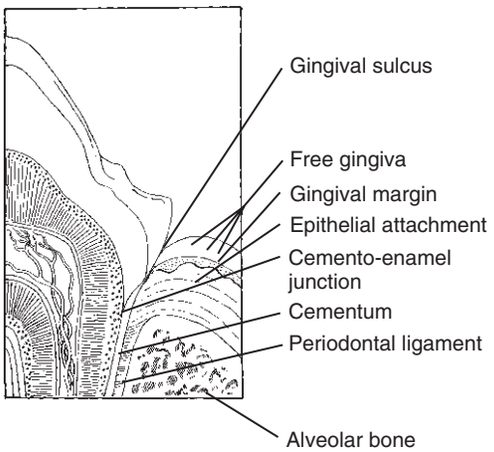

Figure 64-13. Normal periodontal anatomy.

use of a periodontal probe and the recognition of a few anatomic landmarks.

- Locate the cemento-enamel junction that separates the anatomic crown from the anatomic root, 1 to 2 mm below the normal gingival margin (Fig. 64-13).
- The free gingival margin, an important anatomic landmark when assessing periodontal disease, is the highest point of gingival tissue that lies on the tooth. In normal tissues, the free gingival margin is just above the CEJ (see Fig. 64-13).
  - When gingival recession is present, the free gingival margin is below the CEJ.
  - In cases of gingival hyperplasia, it is >2 mm above the CEJ.
- Measure and record the depth of the pocket in millimeters. Also note the relationship of the free gingival margin to the CEJ. These values will adequately assess the level of attachment and thereby dictate the appropriate therapy.

Etiology

- Periodontal disease is initiated by an accumulation of large amounts of bacteria at the junction of the tooth and the gingiva. Prolonged retention of these bacteria results in a change of the predominant flora from gram-positive aerobic coccoid bacteria to more motile gram-negative anaerobic rod-shaped bacteria.
- Tissue destruction occurs secondary to inflammation, resulting in a loss of periodontal support. Over a period of time (usually years), the presence of plaque, calculus, and gingivitis results in loss of periodontal support.

Clinical Signs

- Common signs include mobile teeth, periodontal and periapical inflammation, facial swelling, periodontal pockets, nasal discharge, and oronasal fistulas.
- Severe gingival sulcus hemorrhage, pathologic mandibular fractures, intranasal tooth migration, painful contact buccal mucosal ulcers, osteomyelitis, and ophthalmic manifestations of periodontal disease develop infrequently.

Diagnosis

The diagnosis of periodontal disease is based on a thorough oral and periodontal examination and dental radiography.

Gingivitis

- Animals with gingivitis have swollen gingival margins that bleed after the application of light pressure. Serous or purulent exudate may be produced from the gingival sulcus. Halitosis commonly is present.
- Examination with a periodontal probe demonstrates no attachment loss and there is no radiographic evidence of bone loss around the teeth.

Periodontitis

- Hyperplasia and gingival recession are seen, as well as severe gingival inflammation with various amounts of calculus and debris.
- Periodontal probing reveals periodontal pockets that can progress to tooth loss if untreated.
- Dental radiographs can identify bone loss, which most frequently is horizontal or parallel to the cemento-enamel junction (CEJ), which separates the crown from the root. The bone loss may also be vertical or parallel to the long axis of the root.

Preoperative Considerations

- Prior to treatment, a thorough physical examination and clinical laboratory testing are recommended to rule out concurrent disease.
- In severe cases, administer perioperative broad-spectrum antibiotics (amoxicillin clavulanate). Initiate antibiotic therapy before the dental procedure so that adequate blood levels are present during the dental procedure.

Surgical Procedures

Several procedures are used to treat periodontal disease. These include scaling, root planing, subgingival curettage, polishing, gingivectomy, and open-flap curettage.

Dental Scaling

Dental scaling can be divided into two main categories: supragingival and subgingival.

Supragingival Scaling

This involves the removal of calculus located above the gingival margin. It is most easily performed with a power scaler.

Technique

1. A universal tip is most appropriate for use in small animals.
2. Place the side of the tip below the edge of the calculus and gently lift to remove calculus.
3. Move the tip gently across the surface of the tooth with a paint brush–type movement.
4. Continuously move the tip across the dentition during scaling; never hold it on one tooth continuously for more than 10 to 15 seconds.
5. Spray copiously with water to prevent overheating of the tooth and to wash away dislodged calculus.

Subgingival Scaling

Following supragingival scaling, perform subgingival scaling, root planing, and curettage with a power scaler designed for subgingival scaling, hand scalers, and curettes.

Technique

1. Use a power scaler such as a piezoelectric scaler subgingivally with a light touch, copious water spray, and constant motion to remove the major portion of subgingival calculus. Alternatively, hand scalers may be used.
2. With a hand instrument such as the Columbia 13/14 curette, complete the root cleaning. Place the curette at the bottom of the pocket, then engage the root with the edge of the curette and pull the curette coronally along the surface of the root (Fig. 64-14).
3. Continue subgingival scaling and root planing (scaling of the root) until the root is smooth and clean.
4. Following removal of subgingival calculus, record areas of pathologic deepening (>3 mm) on a dental chart.
5. Perform subgingival curettage by gently scraping the soft tissue lining of the pocket with a sharp curette until all epithelial and granulation tissue is removed.

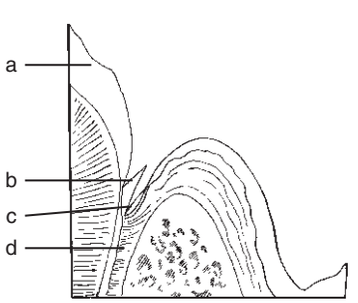

Figure 64-14. Cross section of curette placed beneath calculus for subgingival scaling: (a) enamel, (b) calculus, (c) curette in cross section, (d) periodontal ligament.

Polishing Technique

1. Place a prophylaxis angle on a slow-speed handpiece. Fill the cup with medium-grit prophylaxis paste.
2. Rotate the cup over the entire exposed surface of the teeth, smoothing the surface of the enamel.
3. Rinse the teeth with forced air and water spray to remove any residual debris.

Gingivectomy

Gingivectomy is the resection of unsupported gingival tissue. This technique is used to eliminate periodontal pockets greater than 5 mm deep that are caused by horizontal bone loss. Gingivectomy is also used to remove hyperplastic gingival tissue and for harvesting gingival biopsies.

▼ ***Key Point*** Do not perform gingivectomy unless sufficient attached gingiva (>3 mm) can be retained following the procedure, because removal of tissue below this point may result in dehiscence of the gingiva.

Technique

1. With a periodontal probe, mark the depth of the periodontal pocket on the gingiva opposite the affected tooth (Fig. 64-15*A*).

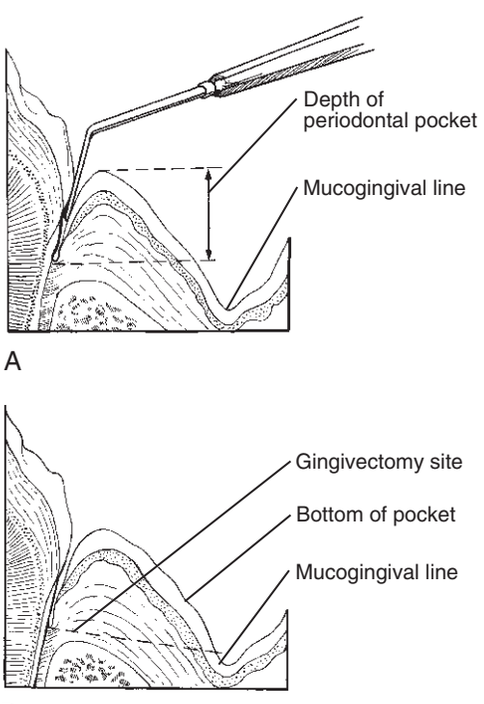

Figure 64-15. *A*, Periodontal probe measures pocket depth. *B*, Proposed gingivectomy site.

2. Make a beveled incision in the gingiva, slightly apical to the pocket mark, to create a natural gingival contour to the gingiva following the gingivectomy (Fig. 64-15*B*). The incision can be made with a gingivectomy knife, scalpel blade, or electrosurgery tip. If electrosurgery is used, surgical cutting modes are recommended.
3. Following removal of excessive hyperplastic tissue and pocket elimination, scale and polish the exposed tooth surface.

Open-Flap Curettage

This technique is used to treat periodontal pockets that extend beneath the level of the alveolar crest. Open-flap curettage permits access to intrabony defects without loss of attached gingiva.

Technique

1. Make an incision with a #11 or #15 scalpel blade 1 to 2 mm from the tooth and directed toward the alveolar crest (Fig. 64-16*A*).
2. Make a scalloped incision on the buccal and lingual or palatal surfaces of the affected tooth, dipping interproximally (between the teeth) to preserve most of the gingival tissue.
3. Elevate the mucoperiosteal flaps 3 to 5 mm from the edge of the incision, using a sharp periosteal elevator (Fig. 64-16*B*).
4. Remove the collar of gingival tissue around the tooth with curettes.
5. Perform scaling and root planing on the exposed tooth surface.
6. Polish the tooth and liberally irrigate the area with sterile saline.
7. Reposition the flaps and hold in place with 4-0 chromic catgut sutures in a simple interrupted pattern, placed interdentally (Fig. 64-16*C*).

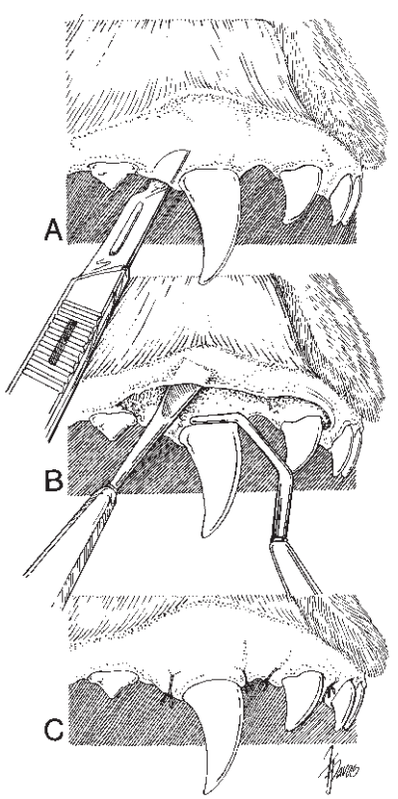

Figure 64-16. *A,* Open-flap curettage is initiated with an incision directed toward the alveolar crest. *B,* Mucoperiosteal flaps are elevated 3–5 mm to permit open curettage. *C,* The flaps are repositioned with 4-0 chromic sutures.

Postoperative Care and Complications

- To retard the recurrence of plaque and calculus accumulation, instruct the owner to irrigate the animal's mouth with a 0.2% chlorhexidine solution (CET chlorhexidine solution; Virbac, Fort Worth, TX) for 2 weeks. Additionally, recommend daily toothbrushing with CET toothpaste (Virbac, Fort Worth, TX).
- If significant stomatitis (discussed later in this chapter) or abscess secondary to periodontal disease occurs, give broad-spectrum antibiotics such as amoxicillin clavulanate (Clavamox, Pfizer, 14 mg/kg PO q12h).
- Reevaluate the animal in 2 weeks. Annual or semiannual scaling is recommended.
- Complications are minimal when procedures are properly performed.

▼ ***Key Point*** Prolonged application of an ultrasonic tip to a tooth without adequate water spraying can result in pulpal necrosis.

- Failure to remove subgingival calculus adequately can result in progressive periodontal disease.
- Inadequate irrigation of the gingival sulcus following therapy can result in entrapment of debris subgingivally and subsequent periodontal abscess.

ENDODONTIC DISEASE

Endodontic disease refers to disease of the pulp (the inner aspect of the tooth). It occurs frequently in small animals and may cause significant pain. Pulp cap, pulpotomy, apexogenesis, apexification, and nonsurgical and surgical endodontic therapy can result in the resolution of endodontic disease and retention of a functional, painless tooth.

Anatomy

Surgical anatomy varies with each tooth. The endodontic system is divided into two parts: the pulp chamber and the pulp canal.

- The endodontic system generally follows the external anatomic contours of the tooth, including its root structure.
- The size of the endodontic system also varies with the age of the patient. Young animals have immature teeth with open apices. As the tooth develops, the apex is formed and, as the tooth matures, the dentinal layer thickens, resulting in a thinner endodontic system.

Etiology

- The most common cause of endodontic disease in small animals is a fractured tooth with pulpal exposure.
- Less common causes include rapid dental attrition (tooth wear), deep odontoclastic resorptive lesions in cats, deep dental caries, severe periodontal disease with secondary endodontic disease, and dental trauma with secondary internal pulpal hemorrhage or damage to the apical vessels.

Clinical Signs

Pulpal exposure can result in the progressive development of the following conditions:

- Bacterial pulpitis
- Pulp necrosis
- Periapical granuloma
- Periapical inflammation
- Acute alveolar periodontitis
- Osteomyelitis
- Sepsis

The time required for this progression varies from months to years. When a tooth is fractured and the pulp is exposed, the pulp will bleed.

▼ ***Key Point*** Pulpal exposure is extremely painful, and animals with a fractured tooth with pulpal exposure may hypersalivate, may be reluctant to eat, and may exhibit other abnormal behaviors.

Over a period of several months, the pulp becomes necrotic and the animal no longer has signs of pain until an inflammatory reaction occurs around the apex of the tooth, at which time the pain recurs.

Diagnosis

The diagnosis is based on a thorough oral examination and dental radiography.

Physical Examination

- Differentiate teeth suspected of being diseased secondary to fractures from worn teeth. Worn teeth, or dental attrition, rarely result in pulpal exposure.
  - A dental explorer will penetrate into the pulp canal when the pulp is exposed.
  - When dental attrition is the cause of a shortened crown, the explorer will not penetrate the tooth but will be stopped by the reparative dentin, or "brown spot," that fills in the area of receded pulp.
- Evaluate the color of the tooth. A discolored tooth (red, purple, or gray) may be diseased.
- Percussion of a tooth with endodontic disease may be painful because of periapical inflammation.
- Soft tissue fistulas may occur secondary to endodontic disease. Usually they are located apical to the mucogingival line. When probed, they will be found to originate from the apex of an endodontically diseased tooth.
- Severe maxillary or mandibular swelling may be present with endodontic disease when the disease process has progressed to severe periapical inflammation and/or osteomyelitis.

Radiography

Perform dental radiography to delineate the endodontic system and confirm endodontic disease. Radiography reveals the stage of apical development.

- Chronic endodontically diseased teeth have an area of periapical lysis around one or more roots.
- When soft tissue fistulas are present, radiopaque material such as a gutta percha point may be placed into the fistula before radiography to confirm that the fistula arises from the apex of the affected tooth.

Preoperative Considerations

- Examine the teeth for concurrent periodontal disease with a periodontal probe.

▼ ***Key Point*** Teeth with combined periodontal and endodontic lesions have a poorer prognosis than teeth with only endodontic lesions.

Surgical Procedures

Numerous endodontic procedures are available (Table 64-7). The type selected depends on the status of the endodontic system and the following factors:

- Vital pulp versus non-vital pulp
- Mature versus immature tooth
- Closed versus opened apex
- Exposure time

Partial Coronal Pulpectomy (Pulpotomy) with Direct Pulp Capping

This procedure is used when the pulp of a vital tooth is exposed during a dental procedure or when the pulp of an immature tooth has been recently exposed.

Table 64-7. ENDODONTIC PROCEDURES RECOMMENDED FOR COMMON ENDODONTIC PROBLEMS PROCEDURE INDICATION

Pulp cap	Vital tooth with iatrogenic pulpal exposure
Pulpotomy and apexogenesis	Vital immature tooth with open apex and traumatic pulpal exposure <5 days
Apexification	Immature nonvital tooth with open apex
Nonsurgical root canal	Nonvital mature tooth with closed apex
	Vital mature tooth with prolonged pulpal exposure
Surgical root canal	Nonvital mature tooth with apical lysis
	Unsuccessful nonsurgical root canal

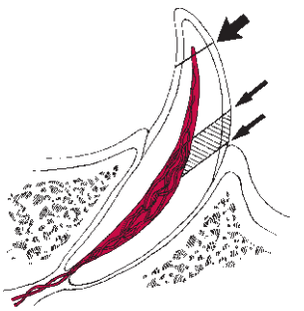

Figure 64-17. *Large arrow* points to fracture site; *small arrows* show straight access site to apex.

Technique

1. Flush the tooth with 0.2% cholorhexidine solution.
2. Remove approximately 6 to 8 mm of the most coronal aspect of the pulp with a diamond pear-shaped bur.
3. Flush the remaining pulp with sterile saline.
4. Control pulpal hemorrhage with the blunt end of point points moistened with saline.
5. Apply a layer of mineral trioxide aggregate (ProRoot, Dentsply Tulsa Dental, Tulsa, OK) to the exposed pulp with a sterile amalgam carrier.
6. Apply an intermediate layer of flowable glass-ionomer (Vitrebond, 3M EPSE, St. Paul, MN).
7. Apply a final layer of compactible composite material (Prodigy, sdsKerr, Orange, CA).

Apexogenesis

This endodontic procedure allows the root to continue to grow. Apexogenesis is useful in cases in which apical development and closure are not complete and the pulp is not irreversibly compromised. Maintenance of vitality of an immature tooth is desirable so that the tooth will continue to develop, resulting in a thicker dentinal layer and a formed apex.

Technique

Remove the involved or injured portion of the pulp and treat as described for pulpotomy.

Apexification

This procedure is used in the treatment of immature teeth in which there is an absence of vital tissue. Teeth in which early pulp death has occurred have large open apices, making root canal filling by non-surgical techniques difficult. Apexification permits closure of the apex by cementum formation, which is stimulated by the application of mineral trioxide aggregate.

Technique

1. Remove the necrotic contents of the immature root canal just short of the radiographic apex with endodontic files. During debridement, do not disrupt the root-forming tissues beyond the apex.
2. Irrigate the canal with 2.5% sodium hypochlorite solution and then rinse with sterile saline.
3. Carefully dry the canal with pre-measured paper points to prevent penetration beyond the apex, which can result in additional hemorrhage.
4. Apply mineral trioxide aggregate into the apical aspect of the root canal with a sterile carrier, and condense gently with a sterile plugger.
5. Mix calcium hydroxide powder and sterile saline to a thick consistency and fill remainder of canal.
6. Restore the access site with a temporary filling material and take a dental x-ray.
7. In 4 weeks remove the temporary filling and the calcium hydroxide and complete treatment by performing a non-surgical root canal procedure.

Non-surgical (Conventional) Root Canal

This procedure is used to treat non-vital mature teeth with closed apices and vital mature teeth with pulpal exposure of greater than 8 hours.

▼ ***Key Point*** Non-surgical root canal therapy is preferable to partial coronal pulpectomy (pulpotomy) with direct pulp capping in mature teeth because of a higher success rate associated with non-surgical root canal therapy. Non-surgical root canal therapy is preferable to surgical treatment in most cases of endodontic disease because of its relative ease and speed of completion, non-invasive nature, and relative decreased cost.

Technique

1. Using a #1 or #2 round bur, obtain access to the pulp at a point that will permit straight delivery of the files to the apex of the tooth (Fig. 64-17).
2. Enlarge the access site with orifice shapers.
3. Begin debridement of the canal with a #15 file inserted to the apex of the tooth. Use a rubber stop to mark the length of the file, and insert all subsequent files to that depth.

4. Introduce progressively larger files into the canal. Flush the canal with 2.5% sodium hypochlorite solution before changing files.
5. Debridement is complete when white dentinal shavings are present on the file and there is no further bleeding from the canal. An alternative technique to hand filing canals is an engine-driven rotary file system (Light Speed Endodontics, San Antonio, TX).
6. Flush canal with sterile saline.
7. Dry the canal with paper points.
8. Apply a sealer (AH Plus, Dentsply, Konstanz, Germany) into the canal with a paper point or endodontic file rotated in a counter-clockwise direction.
9. Obturate (fill) the root canal with gutta percha.
   a. Gutta percha may be applied using a vertical condensation using hot gutta percha. In this technique small amounts of hot gutta percha (Successfil, Hygenic) are placed on the end of a sterile file and rotated counterclockwise into the canal and then vertically condensed with a plugger. This process is repeated until the canal is adequately filled.
   b. An alternative technique for preparing and filling canals is the Light Speed and SimpliFil technique (Light Speed Endodontics, San Antonio, TX) in which a 5 mm gutta percha plug is placed in the apex followed by a solitary gutta percha master cone.
10. Remove any excess gutta percha and sealer from the access site.
11. Apply a restorative material such as a compactible composite (Prodigy, sdsKerr, Orange, CA) to the access site to complete the procedure.

Surgical (Non-conventional) Endodontic Therapy

This is the treatment of endodontic problems with an approach through oral soft tissue and bone rather than through the crown of the tooth. In a non-surgical root canal procedure, the pulp canal is accessed by the crown only.

Indications for surgical endodontic therapy include

- Apical root resorption
- Incomplete root development
- Complications during conventional root canal therapy (broken files)
- Recurrent apical abscessation following non-surgical root canal therapy (recurrent swelling over the apex of the tooth root or periapical draining fistulous tracts)
- Size, length, or curvature of the canal that makes instrumentation impossible

Technique

1. Perform a conventional root canal procedure before surgical endodontic therapy. Do not flush or fill the canal, if the apex is open, until the periapical tissues around the apex are packed off with cotton pellets.
2. An apical approach for most teeth is through a mucoperiosteal incision just apical to the mucogingival line. However, access to the apex of the mandibular canine is most easily gained through a cutaneous incision overlying the ventral border of the mandible.
3. Access to the apex is achieved by removing the alveolar bone overlying the apex with a #4 or #6 round bur.
4. Perform apical curettage to remove necrotic and fibrotic granulation tissue surrounding the periapical region.
5. Perform an apicoectomy (amputation of the apex of the tooth) using a #701 bur. The exposed face of the cut root tip is beveled at a 45° angle to increase exposure of the canal access site.
6. Flush the periapical region with sterile saline solution.
7. Pack the periapical region with #0 cotton pellets or a hemostatic agent to control hemorrhage.
8. Create an undercut in the root canal of the apex with a #33 inverted cone bur.
9. Place at least a 4-mm layer of mineral trioxide aggregate (ProRootMTA, Dentsply Tulsa Dental, Tulsa, OK) in the apical end of the canal, using a retrograde carrier, and condense the MTA with a small plugger.
10. Before closure, remove all cotton pellets and flush the periapical region with sterile saline solution.
11. Reposition the mucoperiosteal flap and suture with 3-0 chromic catgut in a simple interrupted pattern. Procedures involving the mandibular canine teeth are closed with non-absorbable suture material in the skin.

Postoperative Care and Complications

- Immediately following endodontic therapy, take a radiograph to document and assess the procedure.
- Administer a broad-spectrum antibiotic, such as amoxicillin clavulanate, for 1 week.
- Reexamine and radiograph the treated tooth 6 months postoperatively, and then annually, to evaluate the success of the endodontic therapy.

Intraoperative Complications

Intraoperative complications usually are associated with improper use of instrumentation or inappropriate technique. Examples are:

- Broken endodontic files lodged in the root canal
- Perforation of the root canal or pulpal floor

Postoperative Complications

Postoperative complications usually are associated with improper technique, inadequate apical seal, or inadequate follow-up.

- Vital endodontic procedures such as partial coronal pulpectomy (pulpotomy) with direct pulp capping and apexogenesis require oral and radiographic reevaluations 3 to 6 months postoperatively and then annually. If there are persistent signs such as periapical swelling, periapical fistulas, painful tooth percussion, and progressive radiographic periapical lysis in teeth previously treated with vital endodontic techniques, repeat treatment with non-vital techniques.
- Non-vital techniques include apexification and nonsurgical and surgical root canal therapy.
  - Perform surgical root canal therapy on teeth unsuccessfully treated with apexification and nonsurgical root canal techniques.
  - If there is persistent endodontic pathology following surgical root canal therapy, retreatment or extraction is recommended.

ORTHODONTIC DISEASE

Orthodontic disease refers to malocclusions. Veterinary orthodontics involves the movement and repositioning of teeth to a more normal position.

▼ ***Key Point*** Veterinary orthodontic therapy is indicated to alleviate traumatic malocclusions that result in pain or in an inability to function or eat; it should not be used to correct cosmetic or genetic dental alignment defects.

Etiology

The majority of malocclusions are genetic in origin. Previous trauma or an eruption pattern discrepancy resulting from retained deciduous teeth may also result in a malocclusion of the permanent dentition.

Clinical Signs

Clinical signs depend on the severity of the malocclusion.

- Animals with pronounced prognathic occlusion (mandibular teeth are rostral to their normal position in relation to the maxillary dentition) may be presented because of difficulty in prehending food. This condition is not severe enough to cause nutritional problems.
- Animals with brachygnathic occlusion (maxillary teeth are rostral to their normal position in relation to the mandibular dentition) may be presented because of drooling, but this is usually not severe.
- The majority of dental malocclusions are cosmetic and cause no clinically significant problems. However, animals with lingually displaced mandibular canines may have painful palatal defects caused by traumatic occlusion.
- A dental malocclusion in which one tooth traumatically occludes against another tooth can result in dental attrition of the affected teeth.

Diagnosis

The diagnosis is based on a thorough oral examination. Assess the following factors:

- Incisor relationship: The maxillary incisors should overlap the labial surface of the mandibular incisors.
- Canine tooth relationship: The lower canines should be centered between and not touching either the maxillary canine or the maxillary lateral incisor.
- Mandibular fourth premolar: The large cusp of the lower fourth premolar should be centered between the upper third and fourth premolar.
- Interdigitation of other premolars: The cusp tips of the maxillary premolars should interdigitate with the cusp tips of the mandibular premolars.
- Premolar horizontal alignment: The space between the maxillary and mandibular premolars should have good horizontal alignment.
- Head symmetry: The midlines of the maxillary and mandibular dental arches are centered over each other, and these must also be in alignment with the midplane of the head.

Deviations from these criteria for normal occlusion result in malocclusions of varying severities.

Orthodontic Principles

Tipping is the most common type of corrective movement used in veterinary orthodontics. A single force is applied to the crown of a tooth, resulting in a tipping action. During orthodontic movement, alveolar bone is *resorbed* (osteoclastic activity) on the side of the tooth with less tension on the periodontal ligament. Conversely, alveolar bone is *deposited* (osteoblastic activity) on the side of the tooth with more tension on the periodontal ligament.

Preoperative Considerations

Prior to correction of orthodontic defects, attempt to determine the etiology of the problem. Correction of genetically induced, cosmetic orthodontic defects is contraindicated. Attempt to correct orthodontic defects resulting in a traumatic occlusion. The timing of orthodontic movement is important.

▼ ***Key Point*** Delay orthodontic movement until the animal is 1 to 2 years of age unless simple, quick interceptive movements of the tooth can be achieved.

Surgical Procedures

▼ ***Key Point*** Extraction of overly retained deciduous teeth can prevent malocclusions of the permanent dentition.

Extraction of overly retained deciduous teeth is referred to as *interceptive orthodontics*. Extract a deciduous tooth that is still firmly attached when the permanent tooth starts to erupt to allow the permanent tooth to erupt in its normal position. Perform extraction carefully to avoid disruption of the permanent tooth.

Correction of Lingually Displaced Mandibular Canines

A technique that can be easily applied in one visit is the intraorally fabricated acrylic inclined plane.

Technique

1. Clean and polish the teeth with pumice.
2. Fabricate an inclined plane with a self-curing composite material (Pro-temp 3 Garant, 3MESPE, St. Paul, MN) until the splint is approximately 1 cm thick.
3. When the composite material becomes hard, create the appropriate inclined plane with an acrylic bur, so that when the lingually displaced mandibular canine hits the side of the inclined plane it will be deflected labially and mesially into a normal position. The incline path for the affected tooth should be formed so that the sloping angle is approximately 60° toward its target site.
4. Add additional composite to create a band around the canine teeth to provide retention for the splint.

Postoperative Care and Complications

- Instruct the client to:
  - Restrict the animal's chewing activities and to feed a soft diet.
  - Observe the orthodontic device daily, making sure that it is not displaced or causing excessive soft tissue trauma.
  - Gently clean the device daily with a stream of water from a curved-tip syringe.
  - Leave the orthodontic appliance in place until the appropriate movement has been achieved. This usually takes about 6 weeks.
- Complications usually are caused by inappropriate techniques or inadequate postoperative care.
  - Misapplication of orthodontic forces can result in resorbed roots, devitalized teeth (necrotic pulp), avulsed teeth, periodontal pockets, gingivitis, and failure to achieve the desired orthodontic movement.

STOMATITIS/GINGIVITIS

Stomatitis/gingivitis is a common clinical problem. Always attempt to identify a specific underlying cause, because this can determine the therapeutic approach and prognosis. When a specific cause cannot be identified or specific therapy is not available, treatment is symptomatic and supportive. Chronic relapsing stomatitis can be particularly frustrating to manage.

Etiology

Causes of stomatitis/gingivitis are listed in Table 64-8. Many systemic diseases that cause stomatitis/gingivitis are discussed in detail elsewhere in this book, including viral upper respiratory infections of cats (see Chapter 11), feline leukemia virus (FeLV) (see Chapter 8), feline immunodeficiency virus (FIV) (see Chapter 9), renal failure (see Chapter 77), autoimmune diseases such as systemic lupus erythematosus (SLE) (see Chapter 24) and pemphigus (see Chapter 48), and eosinophilic granuloma complex (see Chapter 53).

Periodontal Disease

Periodontal disease is a common predisposing cause of stomatitis/gingivitis in dogs and cats (see previous discussion).

▼ ***Key Point*** In any animal with stomatitis/gingivitis, perform a complete periodontal examination and dental prophylaxis, including tooth extractions if necessary, to eliminate periodontal disease as a contributing factor.

Physical Injury

Foreign bodies (plant awns, sticks, bones), oral trauma, and thermal, electrical, and radiation burns can cause stomatitis/gingivitis. A history of exposure combined with the oral examination may be diagnostic.

- Plant awn stomatitis (bur tongue, vegetative stomatitis) occurs in outdoor dogs that groom burs from their coat or eat horse feces containing burs. The awns become embedded in the tongue and gingiva, causing glossitis, gingivitis, and gingival hyperplasia.
  - On oral examination, close inspection will reveal tiny plant spicules embedded in tissue, and plant material may be seen on biopsy.

Chemical Injury

Strong alkalis (lye solutions) and acids, petroleum distillates, and phenols can damage the oral cavity. In many cases, the specific agent is not identified and the diagnosis is based on circumstantial evidence. Concurrent esophageal and gastrointestinal mucosal injury supports the diagnosis of ingestion of a caustic substance.

Nocardia Infection

Nocardia spp. have been associated with severe halitosis, gingivitis, and oral ulcerations in dogs. In severe cases,

Table 64-8. DIAGNOSIS AND TREATMENT OF STOMATITIS

Disorders	Diagnosis	Treatment*
Periodontal Disease	Oral exam, dental radiography	Dental prophylaxis, antibiotics
Physical Injury		
Foreign bodies (e.g., plant awns, for plant sticks, bones, fiberglass); trauma; thermal, electrical, radiation burns	Exposure history, oral exam, tissue biopsy for microscopic agents	Remove foreign bodies; awns, scrape with dry 4 inch × 4 inch sponge or scalpel blade Debride necrotic tissue
Chemical Injury		
Strong alkalis (lye solutions); acids; petroleum distillates; phenol	Exposure history, oral exam (lesions may extend into esophagus and GI tract)	Immediate therapy; rinse mouth with water Alkaline chemicals: flush with vinegar solution or citrus juice Acid chemicals: flush with bicarbonate solution
Drug- or Toxin-Induced		
Drug reaction; toxic epidermal necrolysis; heavy metal poisoning (thallium); *Dieffenbachia* (house plant) ingestion	Exposure history	Symptomatic therapy only
Infection		
Feline herpesvirus/calicivirus	History, physical exam (naso-ocular discharges, fever)	Symptomatic therapy only
Ulcerative necrotizing stomatitis	Oral exam, bacterial culture, impression smears for spirochetes	Treat with antibiotics for at least 3 wk
Candidiasis	Oral exam, fungal culture	Ketoconazole (Nizoral) 5 to 10 mg/kg PO q12h Nystatin 2% in Orabase applied topically
Nocardiosis	Oral exam, bacterial culture	Sulfadiazine, 80 mg/kg PO q8h
Bartonella	Bartonella titer	Azithromycin, 5–10 mg/kg PO q24h for 5 days
Immunodeficiency or Immunosuppression		
Feline leukemia virus (FeLV)	FeLV antigen test	Symptomatic therapy only
Feline immunodeficiency virus (FIV)	FIV antibody test	Same as above
Metabolic Disorders		
Renal failure	Creatinine, BUN, urinalysis	Correct or control underlying disorder
Diabetes mellitus	Blood and urine glucose	Same as above
Hypothyroidism	T_4, TSH stimulation tests	Same as above
Autoimmune Disorders		
Systemic LE; pemphigus complex; bullous pemphigoid	Physical exam (other mucocutaneous areas affected); biopsy (including IFA test); ANA and LE tests	Immunosuppressant therapy (e.g., glucocorticoids, azathioprine, cyclophosphamide, gold salts)
Neutropenia		
Cyclic neutropenia; agranulocytosis; leukemia	CBC, bone marrow aspiration	Symptomatic therapy only
Nutritional Deficiencies†		
Niacin deficiency (black tongue)	Diet history	Vitamin supplementation
Idiopathic		
Feline plasma cell stomatitis	Biopsy, total serum protein; protein electrophoresis; dental radiography	Symptomatic therapy including antibiotics and dental prophylaxis initially; other therapies include prednisolone, megestrol aetate, gold therapy and low-dose azathioprine: results are inconsistent Dental extractions in refractory cases
Eosinophilic granuloma	Physical exam (may have other dermatologic involvement); biopsy	Cats: methylprednisolone acetate (Depo-Medrol), 20 mg/cat SC q2wk for at least 30 days; alternate therapy for refractory cases includes megestrol acetate, surgery, cryosurgery, CO_2 laser, radiation therapy, levamisole, gold salts; correct underlying problem (flea control, hypoallergenic diet, hyposensitization) Dogs: Prednisolone, 0.5 to 1.0 mg/kg PO q12h for 7 days; then taper dose over 2 to 3 wk
Underlying Oral Neoplasia		
	Physical exam (enlarged regional lymph node with metastases); biopsy and needle aspirate of lesion and lymph nodes; thoracic and skull radiography	Treat underlying neoplasia (see text)

*Symptomatic therapy appropriate for all causes of stomatitis may include systemic, oral antibiotics, especially for severe gingivitis or necrotic oral ulcerations, such as amoxicillin (10 to 20 mg/kg q12h), metronidazole (25 mg/kg q12h), clindamycin (10 mg/kg q12h), and tetracycline (20 mg/kg q8h); oral rinses with 0.1% to 0.2% chlorhexidine or 1% hydrogen peroxide, three to four times daily; dental prophylaxis as needed; and soft food (canned or gruel).

†Rare in clinical practice.

ANA, antinuclear antibody; BUN, blood urea nitrogen; CBC, complete blood count; GI, gastrointestinal; IFA, indirect fluorescent antibody; LE, lupus erythematosus; T_4, thyroxine; TSH, thyroid-stimulating hormone.

necrosis and pseudomembranes are present. Lesions are most severe in periodontal areas. Rarely, mandibular lymph nodes and adjacent skin may be involved.

Oral Candidiasis

This uncommon cause of stomatitis is characterized by white plaques or pseudomembranes on the oral mucosa. Conditions that may predispose to candidal stomatitis include immunosuppression (including chemotherapy), systemic diseases, and long-term antibiotic therapy.

Necrotizing Ulcerative Stomatitis

This form of stomatitis is characterized by gingivitis, oral ulcerations, tissue necrosis, severe halitosis, and pain on eating. Numerous bacteria have been incriminated as contributing to this disorder, including spirochetes and fusiform bacilli.

Immunosuppression

Immunosuppression secondary to FeLV and FIV infection is an important predisposing cause of chronic stomatitis/gingivitis in cats.

▼ ***Key Point*** Always test for FeLV and FIV in cats with chronic stomatitis/gingivitis.

Uremia

Uremia is a common cause of stomatitis and oral ulcerations. Urease-containing bacteria metabolize urea to ammonia, which is irritating to the oral mucosa. Dehydration and drying of the oral mucous membranes may contribute to the problem. In uremic animals, the rostral portion of the tongue may slough, possibly owing to uremic vasculitis and thrombosis.

Plasma Cell Stomatitis

Plasma cell stomatitis in cats is a disease of unknown etiology characterized by proliferative, often symmetric, hyperemic friable lesions at the glossopalatine arches or angles of the mouth, also called *fauces*. The condition is also called *faucitis*.

- Concurrent pharyngitis is common.
- Ulcerative gingivitis may occur. This condition is extremely painful and can cause difficulty on eating.
- Some cats have concurrent plasma cell pododermatitis.
- An association with chronic calicivirus infection has been found in some cases and supported by experimental and epidemiologic evidence.
- On biopsy, lesions are characterized by plasma cells infiltrated with lesser numbers of lymphocytes, neutrophils, and histiocytes.
- Hyperglobulinemia, characterized as a polyclonal gammopathy, is often present and probably indicates chronic immune stimulation. An immune-mediated basis for the disease is suspected.

▼ ***Key Point*** Underlying dental disease, including periodontal and/or odontoclastic resorptive lesions, may occur concurrently.

- Perform dental radiography to identify odontoclastic resorptive lesions, bone loss secondary to periodontal disease, broken teeth, and retained roots. Cases with severe inflammation around the teeth often respond well to extraction of the teeth.
- FeLV, FIV, and *Bartonella* infection may be contributing factors; however, most cases are FeLV, FIV, and *Bartonella* negative. Calicivirus infection has been identified in many cats by virus isolation.
- The disease is often refractory to medical treatment, and relapse is common after treatment is discontinued.
- Treatment of inflamed mucosa with a CO_2 laser may be beneficial.

Feline Eosinophilic Granuloma Complex

This disorder is an important cause of oral lesions in cats.

- Any of three forms (indolent ulcer, collagenolytic [linear] granuloma, and eosinophilic plaque) may occur in the oral cavity. The indolent ulcer involving the upper lips is most common.
- Differentiate lesions from squamous cell carcinoma.
- Oral lesions may coexist with dermatologic involvement. The disorder may be a hypersensitivity reaction associated with underlying atopy, food allergy, or flea bite hypersensitivity. Diagnosis and treatment are discussed in Chapter 45.

Canine Oral Eosinophilic Granuloma

This disorder occurs in all breeds of dogs, but especially in young Siberian huskies.

- The cause is unknown but a hypersensitivity reaction to an as yet unidentified antigen is suspected, based on the dramatic response that occurs with corticosteroid therapy. Spontaneous regression also may occur. Hereditary factors may play a role.
- Lesions are characterized by proliferative tissue with superficial ulcerations that occur primarily on the lateral and ventral surfaces of the tongue. Soft palate involvement may also occur.
- Peripheral eosinophilia is common. Histologically, the lesion appears identical to collagenolytic (linear) granuloma in cats. Degenerating collagen is surrounded by granulomatous inflammation with an eosinophilic component.

- Differentiate lesions from neoplasia (especially mast cell tumor), mycotic infections, and foreign body reaction.

Clinical Signs

Clinical signs of stomatitis/gingivitis include hypersalivation, drooling, halitosis, oral bleeding, reluctance to eat dry food, dysphagia, anorexia, and weight loss.

▼ ***Key Point*** Chronic stomatitis/gingivitis can be extremely painful and can cause behavioral changes such as reclusive behavior, dropping food while eating, and running away from the food dish because of pain on eating.

Diagnosis

Base the overall strategy for diagnosis of stomatitis/gingivitis without an obvious underlying cause (e.g., foreign body) on the following measures:

- Rule out underlying systemic disorders with appropriate laboratory testing.
- Pursue specific diagnostics such as dental evaluation and oral biopsies and cultures.
- Perform dental prophylaxis (as needed) and initiate symptomatic therapy while awaiting test results (see Table 64-8).

History

- Obtain a complete history, with special emphasis on potential exposure to foreign bodies, chemicals, drugs, and toxins.
- Look for signs suggesting underlying systemic disease (see Table 64-8).

Physical and Oral Examinations

- Perform a general physical examination. In particular, evaluate for concurrent dermatologic lesions, especially at mucocutaneous junctions (e.g., nail beds, anus, vulva, prepuce) that suggest an underlying autoimmune disorder.
- Oculonasal discharges and fever in a cat supports the diagnosis of an underlying viral upper respiratory infection (see Chapter 11).
- Perform a complete oral examination, including periodontal evaluation, to identify and characterize the nature and extent of the lesions. This usually requires sedation or general anesthesia. A specific diagnosis can sometimes be made on oral examination (e.g., foreign body, periodontal disease).

Laboratory Evaluation

- Perform routine laboratory tests including a CBC, biochemical profile, and urinalysis to identify underlying systemic diseases such as renal failure (see Chapter 77) and diabetes mellitus (see Chapter 34).
- If general anesthesia is required for complete oral examination, obtain results of laboratory tests before anesthesia.
- Perform ancillary tests as suggested by specific historical and physical examination findings, such as FeLV, FIV, and *Bartonella* tests in cats with chronic stomatitis/gingivitis; fine-needle aspiration of enlarged mandibular lymph nodes for suspected neoplasia; and antinuclear antibody (ANA) and lupus erythematosus (LE) tests for suspected SLE.
- Bacterial and fungal cultures of the oral cavity can be performed on scrapings, swabs, or pieces of tissue. Unfortunately, cultures are not usually helpful, owing to the large number of potentially pathogenic organisms present as normal flora. Exceptions include isolation of *Candida* and *Nocardia* organisms.
- If bacterial cultures yield a large growth of a single organism, antibiotic therapy based on sensitivity patterns may be warranted.
- Specialized laboratories can use virus isolation techniques to detect calicivirus infection, but the clinical significance of a positive result in cats with chronic stomatitis is poorly understood.

Radiography

- In animals with periodontal disease, radiograph involved areas to identify periodontal defects, retained root tips, and odontoclastic root resorptive lesions, as discussed elsewhere in this chapter.
- Skull radiographs may show lysis of bone secondary to neoplastic disease.

Biopsy and Histopathologic Evaluation

Tissue biopsy is essential when evaluating chronic stomatitis, especially when proliferative lesions are present. Histopathology is useful to characterize the cellular response, identify specific causes, and differentiate neoplastic from non-neoplastic lesions.

- If autoimmune disease is suspected, evaluate oral and skin biopsies as described in Chapter 37.
- Cytology can be performed on impression smears of exudates or biopsied tissue and may be useful to diagnose underlying neoplasia (e.g., melanoma) and infection (e.g., *Nocardia* and *Candida* spp.).

Treatment

Treatment is based on the initiating cause. Whenever possible, institute specific therapy, such as removal of foreign bodies, immunosuppressive therapy for autoimmune diseases, corticosteroids for eosinophilic granuloma complex, sulfadiazine for nocardiosis, and ketoconazole for candidiasis (see Table 64-8). Symptomatic treatment of stomatitis usually is warranted, regardless of whether specific therapy is available.

- Because periodontal disease may be the underlying cause of stomatitis or, at the very least, an important contributing factor, perform thorough dental prophylaxis in all animals.
- Apply a 0.1% to 0.2% chlorhexidine solution topically at the gingival margin once a day to retard plaque formation and provide local antibacterial activity.
- Cleanse the oral cavity in animals with stomatitis with cotton-wrapped applicators soaked in saline or an oral rinse such as 0.1% to 0.2% chlorhexidine solution three to four times daily.
- Administer systemic antibiotics such as amoxicillin, metronidazole, clindamycin, amoxicillin clavulanate, and tetracycline to control secondary bacterial infections, particularly in cases of severe gingivitis or oral ulcerations (see Table 64-8).
- Initiate fluid therapy (see Chapter 5) and tube feeding (nasogastric, esophagostomy, or gastrostomy tube) as needed in animals with severe stomatitis/gingivitis that refuse food and water.
- Consider extraction of the teeth (at least of the premolars and molars) in animals with severe stomatitis/gingivitis that is refractory to medical management and for which extensive diagnostic tests do not reveal an underlying cause.
- Cats with plasma cell stomatitis/gingivitis/pharyngitis, in particular, may have an excellent response following extraction of all teeth or all teeth except the canine teeth when the inflammation is limited to areas around the teeth. Cats with severe pharyngeal or glossopalatine arch inflammation should be given a more guarded prognosis and may require continued medical management with antibiotics and corticosteroids or CO_2 laser treatment.

▼ ***Key Point*** Advise owners of animals with chronic non-responsive stomatitis/gingivitis that long-term therapy may be necessary to control the problem.

- Reexamine animals with chronic stomatitis/gingivitis 2 weeks after initial therapy, and then every 1 to 3 months to assess and reevaluate response to treatment.
- In animals with chronic non-responsive stomatitis/gingivitis treated with tooth extraction, thoroughly examine the oral cavity 1 month postoperatively to assess proper gingival healing. Take radiographs of regional areas of gingival hyperemia to reveal retained roots. Extraction of these roots permits normal gingival healing.

TONSILLITIS

Tonsillitis is seen occasionally in dogs and less frequently in cats.

▼ ***Key Point*** Tonsillitis usually occurs secondary to other diseases associated with chronic irritation or contamination of the pharynx.

Etiology

Disorders that predispose to tonsillitis (and pharyngitis) include chronic vomiting or regurgitation, chronic productive cough, and chronic contamination of the nasopharynx (e.g., severe periodontal disease, cleft palate, nasal disease with discharge). Primary tonsillitis is rare but may occur in young, small-breed dogs.

- The spectrum of bacteria cultured from dogs with pharyngitis/tonsillitis is similar to that cultured from the pharynx of healthy dogs, including *Escherichia coli,* and *Streptococcus, Staphylococcus, Pasteurella, Proteus, Pseudomonas,* and *Diplococcus* organisms.
- Group A *Streptococcus pyogenes,* the cause of "strep throat" in humans, does not cause signs of pharyngitis/tonsillitis in dogs and cats, and the prevalence of infection appears to be low. Dogs and cats can acquire a transient infection from close contact with infected humans; thus, they may serve as a reservoir for human reinfection. When recurrent group A *S. pyogenes* infection in humans in the household is a problem, treatment of pets as well as humans is warranted to prevent reinfection. In dogs and cats, effective antibiotics include penicillin, erythromycin, and chloramphenicol.

Clinical Signs

- Signs of tonsillitis include retching, cough, fever, anorexia, and lethargy.
- When tonsillitis is secondary to other disorders, signs of the primary disease overshadow those of the tonsillitis.

Diagnosis

- Base the diagnosis of tonsillitis on the gross appearance of the tonsils, which may be swollen and bright red with small hemorrhages or punctate white foci (abscesses). Concurrent pharyngitis is common.
- Attempt to identify important predisposing disorders (see Etiology) with a complete history, physical examination, and appropriate laboratory tests.
- Perform bacterial cultures in cases of primary tonsillitis refractory to routine antibiotic therapy.
- Differentiate chronic enlargement of the tonsils from underlying neoplasia (e.g., lymphoma, squamous cell carcinoma), which can be diagnosed by tonsillar biopsy.

Treatment

Secondary tonsillitis is usually resolved with identification and treatment of the predisposing disorder. When a predisposing disorder cannot be identified, adminis-

ter a course of broad-spectrum antibiotics such as ampicillin or amoxicillin (10–20 mg/kg PO q8–12h) for 2 weeks. Tonsillectomy rarely is necessary.

TONSILLAR NEOPLASIA

Etiology

Squamous cell carcinoma and lymphoma are the most common tumors of the tonsil.

Clinical Signs

- Retching and coughing may occur owing to pharyngeal irritation by the mass.
- A cervical mass may be present as a result of metastasis to regional lymph nodes.

▼ ***Key Point*** Carefully examine the tonsils in all dogs with a cranial cervical mass.

Diagnosis

- Diagnosis is based on oral examination and biopsy (tonsillectomy) findings. The tonsils appear enlarged and inflamed, and may have an obvious irregular mass.
- Perform partial or complete tonsillectomy to obtain tissue for histopathology.

Technique

Tonsillectomy (Biopsy)

1. Place the animal in ventral recumbency. Place an oral speculum.
2. Grasp the tonsil with an Allis tissue forceps.
3. Cut the base of the tonsil with a CO_2 laser and remove the tonsil.
4. Control any residual hemorrhage with the CO_2 laser.
5. Submit the tissue for histopathology.

Treatment

- For the management of tonsillar lymphoma, see Chapter 27.
- In animals with tonsillar squamous cell carcinoma, combination chemotherapy (doxorubicin and cisplatin) and radiation therapy have been reported to give the best results.

Prognosis

The prognosis is poor.

SALIVARY GLAND DISEASES

Diseases of the salivary glands that may be encountered include

- Mucoceles
- Fistulas
- Sialoadenitis
- Neoplasia

Anatomy

There are four pairs of major salivary glands in the dog and cat: parotid, mandibular, sublingual, and zygomatic (Fig. 64-18).

- The *parotid salivary gland* is located at the base of the auricular cartilage. The parotid duct is formed by two or three short radicles and passes lateral to the masseter muscle. It enters the oral cavity opposite the maxillary fourth premolar.
- The *mandibular salivary gland* is located at the junction of the maxillary and linguofacial veins. It is covered by a dense capsule. The mandibular duct leaves the medial surface of the gland and courses between the masseter muscle and mandible laterally and the digastricus muscle medially and then passes over the digastricus muscle and between the styloglossus muscle medially and the mylohyoides muscle laterally. The mandibular duct enters the mouth on a papilla lateral to the rostral end of the frenulum.
- The *sublingual salivary glands* consist of a caudal portion (monostomatic) located at the rostral pole of the mandibular gland and a rostral portion (polystomatic) that lies directly below the oral mucosa lateral to the tongue. The sublingual salivary duct originates at the caudal portion of the gland and accompanies the mandibular duct to a common or separate opening on the papilla at the rostral end of the frenulum.
- The *zygomatic salivary glands* are located ventral to the zygomatic arch. The major zygomatic duct opens about 1 cm caudal to the parotid papilla on a ridge of mucosa.

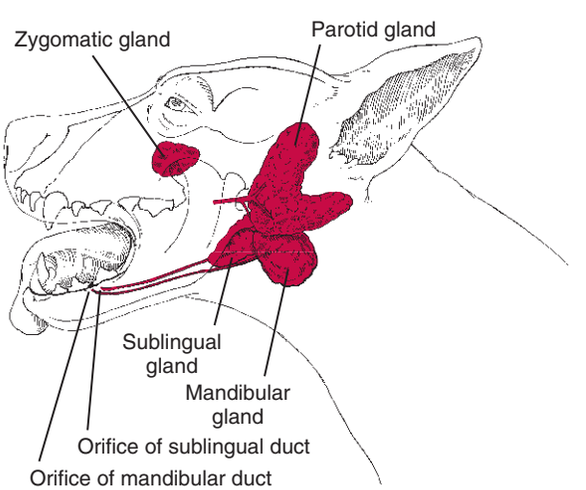

Figure 64-18. Salivary glands in the dog.

Etiology

Mucoceles

Salivary mucoceles, or sialoceles, result from damage to the duct or gland, with subsequent leakage of saliva into the tissues. Salivary mucoceles are lined with granulation tissue rather than epithelium. The sublingual and mandibular salivary glands are most commonly involved. The sites for mucoceles include cervical mucoceles, sublingual mucoceles (ranulas), and, less commonly, mucoceles of the pharyngeal and orbital region.

Fistulas

Salivary gland fistulas occur infrequently in small animals, and they are usually the result of trauma to the parotid salivary gland or duct.

Sialoadenitis

Sialoadenitis (an inflammatory reaction in the salivary glands) occurs infrequently in small animals. The zygomatic salivary gland is most commonly involved.

Sialadenosis

Poorly characterized syndrome of mandibular salivary gland enlargement, associated with hypersalivation, retching, gulping, regurgitation, and vomiting in dogs. Cytologic and histologic evaluations of the salivary glands are unremarkable. Removal of the salivary glands does not result in improvement, suggesting that signs are not related to the physical effect of salivary gland enlargement. Response to oral phenobarbital is rapid and dramatic. Altered parasympathetic or sympathetic innervation or an unusual form of limbic epilepsy has been proposed.

Neoplasia

Tumors of the salivary glands (e.g., adenocarcinoma) are rare. The parotid and submandibular salivary glands are most susceptible to tumor formation.

Clinical Signs

Clinical signs depend on the salivary gland affected and the type of disease present.

Mucoceles

Clinical signs depend on the location of the mucocele.

- Animals with cervical mucoceles usually are presented because of a soft, fluctuant non-painful mass in the cervical area.
- Animals with a ranula often are presented because of abnormal tongue movements, reluctance to eat, dysphagia, and blood-tinged saliva.
- Animals with a pharyngeal mucocele usually are presented because of difficulty breathing or swallowing.
- Animals with zygomatic mucoceles usually have exophthalmos, divergent strabismus, and a fluctuant non-painful swelling in the orbital area.

Fistulas

- Clinical signs include a small skin opening in an area overlying a salivary gland that drains serous fluid. The amount of drainage increases when the animal is eating.

Sialoadenitis

- Zygomatic sialoadenitis—exophthalmos, tearing, divergent strabismus, reluctance to eat, extreme pain on opening the mouth, inflammation of the oral mucosa near the papilla, and mucopurulent discharge from the duct
- Parotid sialoadenitis—a painful, warm, firm parotid salivary gland with mucopurulent discharge from the duct

Sialadenosis

- Clinical signs include hypersalivation, retching and gulping (especially after mild excitement), lip smacking, drooling, reduced food consumption, weight loss, regurgitation, and vomiting. Signs are usually chronic (2- to 18-month duration).

Neoplasia

- Most dogs and cats with salivary gland tumors are usually presented because of an asymptomatic non-painful palpable mass in the region of a salivary gland.
- Associated clinical signs from enlargement, impingement on adjacent structures, and local infiltration can occur.

Diagnosis

The diagnosis of salivary gland disease is based on history, clinical signs, clinical pathologic findings, radiography, and histopathology.

- The diagnosis of mucoceles usually is based on palpation and aspiration of a clear or blood-tinged, viscid, mucinous fluid that is consistent with saliva.

▼ ***Key Point*** Perform aspiration of mucoceles under aseptic conditions to prevent infection of a mucocele.

- Sialography also can be used; however, it is somewhat difficult to perform and is usually not necessary.
- Base the diagnosis of sialoadenitis on clinical signs, an elevated white blood cell count, and histopathology.
- Histopathology is necessary to diagnose salivary gland neoplasia. Thoracic radiography can evaluate for metastatic disease.

- With sialadenosis, the mandibular salivary glands are firm and enlarged to almost twice normal size. Exophthalmos is less common and may occur due to enlargement of zygomatic salivary glands. Dogs are sensitive to external palpation of the throat, which elicits signs of retching and gulping, but not pain.
- Sialadenosis is a diagnosis of exclusion when other causes of salivary gland enlargement, hypersalivation, retching, gulping, regurgitation, and vomiting have been ruled out and a dramatic response to oral phenobarbital is noted within 24 to 36 hours. Long-term therapy (phenobarbital or potassium bromide) is usually required, although in some dogs, anticonvulsant medication can be tapered and discontinued after 6 months.

Preoperative Considerations

- Prior to salivary gland surgery, perform a thorough physical examination and appropriate laboratory tests and radiographic procedures, based on the animal's clinical signs, physical examination findings, and age.
- Diagnosis of the type of salivary disease is necessary before surgical intervention.

▼ ***Key Point*** Surgery is not recommended for animals with sialoadenitis. Treat with systemic antibiotics, drainage of the abscess, and application of warm compresses.

Surgical Procedure

Several surgical procedures have been described in the treatment of salivary gland diseases, including

- Excision of the mandibular and sublingual salivary glands
- Marsupialization of ranulas
- Drainage and excision of the zygomatic salivary gland
- Management of pharyngeal mucoceles

Excision of the Mandibular and Sublingual Salivary Glands (Fig. 64-19)

Technique

1. Determine the affected side by placing the animal in dorsal recumbency. The mucocele will gravitate to the affected side.
2. Place the animal in dorsolateral recumbency and routinely prepare the surgical site.
3. Make a skin incision from the junction of the maxillary and linguofacial veins to the angle of the mandible.
4. Locate the mandibular salivary gland and make an incision in the capsule.
5. Bluntly dissect the mandibular salivary gland from the capsule, ligating and severing the arteries and veins that enter the dorsomedial aspect of the gland.

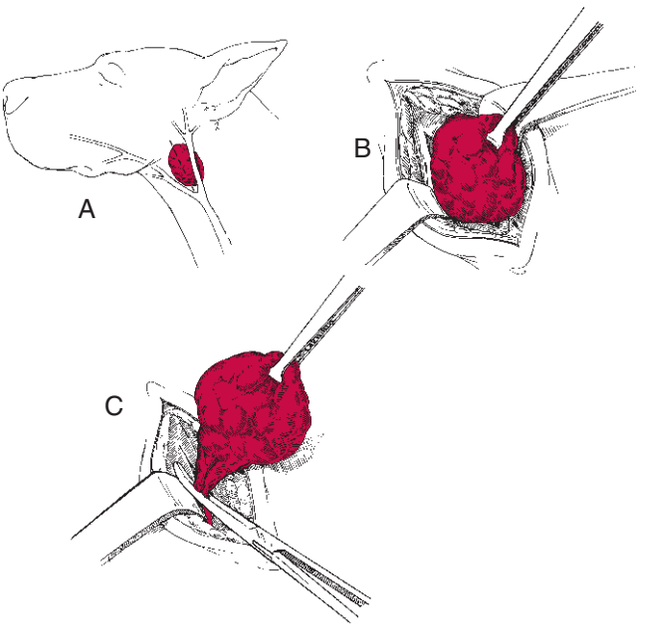

Figure 64-19. Surgical excision of the mandibular and sublingual salivary glands. See text for details.

6. Continue dissecting the sublingual gland rostrally between the masseter and digastricus muscles.
7. Clamp and ligate the glands and ducts as far rostrally as possible with a monofilament non-absorbable suture or a hemoclip. Transect the duct and remove the tissue.
8. Using a simple interrupted pattern, close the dead space with a few sutures in the capsule and deep tissue.

▼ ***Key Point*** To prevent the formation of seroma and provide drainage of the mucocele, place a Penrose drain from the site of the excised gland to the most ventral aspect of the mucocele.

9. Close the skin routinely.

Marsupialization (Surgical Management of Ranula)

Technique

1. Place the animal in lateral recumbency and routinely prepare the surgical site.
2. Incise the ranula longitudinally and remove the redundant portion of the mucosa.
3. Join the mucosal edges of the ranula to the adjacent oral mucosa with a few 4-0 absorbable, monofilament sutures.

If the ranula recurs, remove the mandibular-sublingual salivary gland complex.

Drainage of Zygomatic Salivary Gland (Treatment of Sialoadenitis)

Technique

1. Place the animal in lateral recumbency and swab the mucosa caudal to the maxillary second molar with dilute povidone-iodine (Betadine) solution.
2. Gently advance a small mosquito forceps through a small stab incision in the inflamed oral mucosa caudal to the last maxillary molar.
3. Use caution to prevent damage to the maxillary artery and nerve that course ventromedial to the orbit.

Surgical Excision of Zygomatic Salivary Gland (Treatment of Mucocele)

Technique

1. Place the animal in lateral recumbency and routinely prepare the surgical site.
2. Protect the animal's eyes from irritants with ophthalmic ointment.
3. Make an incision along the dorsal aspect of the zygomatic arch.
4. Reflect the periosteum of the zygomatic arch ventrally and retract the palpebral fascia dorsally.
5. Remove the dorsal aspect of the zygomatic arch, using rongeurs.
6. Retract the globe dorsally to expose the zygomatic salivary gland beneath the periorbital fat.
7. Retract the gland dorsally, ligate the vessels supplying the gland, and remove the gland.
8. Suture the palpebral fascia to the periosteum of the zygomatic arch, using absorbable sutures.
9. Close the subcutaneous tissues and skin routinely.

Management of Pharyngeal Mucoceles

- Treat by marsupialization or by excision of the entire mucocele.
- Remove the ipsilateral mandibular and sublingual salivary glands to prevent recurrence of the mucocele (see previous section in this chapter).

Postoperative Care and Complications

- Administer broad-spectrum antibiotics perioperatively.
- Feed a soft diet for 1 week postoperatively.

Complications

Complications vary according to the initial problem.

- *Salivary mucocele recurrence*—re-explore for residual salivary tissue. Ligation of the mandibular and sublingual salivary ducts with a non-absorbable suture during the initial surgery will aid in the localization of residual salivary tissue. Removal of residual tissue is curative.
- *Sialoadenitis*—clinical response is good if drainage is adequate and appropriate antibiotics, based on bacterial culture and sensitivity testing, are given.
- *Neoplasia*—recurrence is possible. Postoperative adjuvant chemotherapy and/or radiation therapy may be beneficial in animals with salivary gland adenocarcinomas.

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Chapter 65

Diseases of the Esophagus and Disorders of Swallowing

Susan E. Johnson / Robert G. Sherding

OVERVIEW

Etiology

Esophageal diseases in dogs and cats can be categorized as structural disorders (e.g., foreign body, stricture, and vascular ring anomaly) and motility disorders (e.g., oropharyngeal dysphagia, and megaesophagus). Motility disorders may be caused by primary neuromuscular disease of the esophagus or may be secondary to systemic neuromuscular disorders.

Clinical Signs

Clinical signs of esophageal disease include regurgitation, dysphagia, odynophagia (painful swallowing), ptyalism, and exaggerated swallowing. Weight loss, polyphagia, anorexia, cough, dyspnea, and fever also may be seen.

Regurgitation

Regurgitation is the passive expulsion of food or fluid from the esophagus and is influenced by mechanical events in the esophagus. The timing of regurgitation in relation to eating is determined by the location of esophageal dysfunction, degree of obstruction, and presence or absence of esophageal dilatation.

- Regurgitation immediately after eating is most likely with proximal esophageal lesions or esophageal obstruction.
- Regurgitation may be unassociated with eating when the esophagus is dilated, because this provides a reservoir for food and fluid.
- Selective retention of fluids over solid food is more likely with partial obstruction.

▼ ***Key Point*** Distinguish regurgitation, which is the passive expulsion of esophageal contents, from vomiting, which is the centrally mediated reflex expulsion of contents from the stomach and duodenum.

- In contrast to regurgitation, vomiting is preceded by hypersalivation, retching, and abdominal contractions.

Dysphagia, Odynophagia, Ptyalism, and Exaggerated Swallowing

These signs are most likely to occur with oropharyngeal and proximal esophageal disorders.

Weight Loss

Weight loss occurs secondary to inadequate food intake and is related to the severity of esophageal dysfunction.

Polyphagia

Polyphagia occurs when an animal is otherwise healthy but is unable to retain ingested food because of partial or complete esophageal obstruction (e.g., esophageal stricture).

Anorexia, Cough, Dyspnea, and Fever

These signs may be seen with complicating aspiration pneumonia, esophageal perforation, or bronchoesophageal fistula.

Diagnosis

The diagnosis of esophageal disease requires an accurate history, radiographic evaluation of the esophagus, and in many cases, esophagoscopy.

▼ ***Key Point*** Aspiration pneumonia is a frequent and serious complication of esophageal disease that must be identified and treated appropriately.

Signalment

The signalment may suggest certain breed predispositions for esophageal disease (Table 65-1). The age at onset is also important because regurgitation caused by a vascular ring anomaly or congenital idiopathic megaesophagus usually begins at the time of weaning.

Table 65-1. PROFILES FOR ESOPHAGEAL DISEASE BASED ON SIGNALMENT

Parameter	Clinical Association
Age	
Young	Vascular ring anomaly; idiopathic megaesophagus; foreign body
Mature	Esophageal neoplasia
Breed	
Abyssinian	Acquired myasthenia gravis
Akita	Acquired myasthenia gravis
Boston terrier	Vascular ring anomaly (PRAA)
Bouvier	Dysphagia due to hereditary muscular dystrophy (oropharyngeal dysphagia and megaesophagus)
Cocker spaniel	Cricopharyngeal achalasia
Collie	Familial canine dermatomyositis (oropharyngeal dysphagia and megaesophagus)
English bulldog	Vascular ring anomaly (esophageal compression by left subclavian artery and brachiocephalic artery)
	Esophageal deviation cranial to the heart (normal variant)
German shepherd	Idiopathic megaesophagus
	Vascular ring anomaly (PRAA)
	Acquired myasthenia gravis
	Giant axonal neuropathy
Golden retriever	Idiopathic megaesophagus
	Acquired myasthenia gravis
	Cricopharyngeal dysphagia
Great Dane	Idiopathic megaesophagus
	Vascular ring anomaly (PRAA)
Greyhound	Idiopathic megaesophagus
Irish setter	Idiopathic megaesophagus
	Vascular ring anomaly (PRAA)
Jack Russell terrier	Congenital myasthenia gravis
Labrador retriever	Idiopathic megaesophagus
	Hereditary myopathy (megaesophagus)
Miniature schnauzer	Idiopathic megaesophagus
Newfoundland	Idiopathic megaesophagus
	Acquired myasthenia gravis
Rottweiler	Spinal muscular atrophy (megaesophagus)
Shar-Pei	Idiopathic megaesophagus
	Hiatal hernia
	Esophageal deviation cranial to the heart (mild regurgitation)
Smooth fox terrier	Congenital myasthenia gravis
Springer spaniel	Cricopharyngeal achalasia
	Polymyopathy (megaesophagus)
	Congenital myasthenia gravis
Wire-haired fox terrier	Idiopathic megaesophagus
Terriers	Acquired myasthenia gravis
Siamese cat	Idiopathic megaesophagus

PRAA, persistent right aortic arch.

History

Obtain a complete history with emphasis on exposure to foreign bodies, chemicals, or drugs such as doxycycline in cats (esophageal stricture), recent anesthesia (reflux esophagitis, esophageal stricture), and systemic signs such as neurologic dysfunction or muscle weakness, atrophy, or pain (central nervous system [CNS] disease, generalized peripheral neuromuscular disorders). The onset and duration of clinical signs may provide important clues to the underlying disorder.

- When the onset of regurgitation is acute, consider an esophageal foreign body or caustic esophagitis.
- A long-standing history of regurgitation is consistent with disorders such as idiopathic megaesophagus, vascular ring anomaly, and esophageal neoplasia.
- Intermittent signs often are seen with hiatal hernia and secondary reflux esophagitis.
- If regurgitation and vomiting occur together, consider hiatal hernia, gastroesophageal intussusception, or reflux esophagitis secondary to disorders causing chronic vomiting.
- In the southern United States, consider *Spirocerca lupi*–associated granuloma and neoplasia of the esophagus.

Physical Examination

Perform a complete physical examination. Observe how the animal eats (using both dry and canned food) to detect abnormalities of prehension and swallowing (suggesting oropharyngeal dysphagia) and to confirm that regurgitation rather than vomiting is occurring.

- Palpate the cervical esophagus to detect masses and foreign bodies.
- Distention of the cervical esophagus may occur with mechanical obstruction or diffuse hypomotility, and it frequently can be induced in animals with megaesophagus by compressing the thorax while the nostrils are occluded.
- A mucopurulent nasal discharge, pulmonary crackles, and fever are indicative of aspiration pneumonia.
- A rigid stance, in conjunction with fever and depression, may indicate mediastinitis secondary to esophageal perforation.
- Weight loss and emaciation can be seen with severe, long-standing esophageal disease.
- Horner syndrome and non-compressible cranial thorax may indicate a mediastinal mass.
- Muscle weakness, atrophy, or pain may indicate a generalized muscle disorder.
- Neurologic deficits may indicate primary CNS disease and esophageal denervation.
- Enlargement of the mandibular salivary glands is indicative of sialadenosis (see Chapter 64).

Radiography

Radiography is the most important tool available for diagnosis of esophageal disease. Survey and contrast radiography provide adequate information to diagnose structural disorders. Esophageal motility disorders are best identified with fluoroscopy.

- Perform survey thoracic and cervical radiography to evaluate the entire esophagus. The esophagus is not normally visible unless it contains air, fluid, food, or

foreign material. Evaluate thoracic radiographs for complications of esophageal disease such as aspiration pneumonia and esophageal perforation.

- Many esophageal diseases can be diagnosed by a contrast esophagram using barium sulfate paste or an aqueous organic iodine (see Chapter 4).

▼ ***Key Point*** For contrast radiography of the esophagus when perforation is suspected, use a water-soluble, non-ionic iodinated contrast agent such as iohexol (Omnipaque, Amersham Health) instead of barium, because it is readily absorbed and less irritating to periesophageal tissues.

- Esophageal motility disorders, especially those causing oropharyngeal dysphagia, are best evaluated with image-intensified fluoroscopy and rapid-sequence filming. Availability of fluoroscopy is limited to universities and referral hospitals because of the cost of equipment.

Endoscopy

Endoscopic evaluation of the esophagus is a unique, noninvasive method for diagnosis of esophageal disorders. The gross appearance of the mucosa can be assessed and tissue can be obtained for biopsy, cytology, and culture. In addition, esophageal foreign body removal or dilatation of esophageal strictures with endoscopy can be therapeutic. Either rigid or flexible endoscopes can be used for esophagoscopy.

- The normal esophagus of the fasted animal is usually empty or contains a minimal amount of clear fluid or foam.
- Under anesthesia, the normal esophagus becomes flaccid and dilated, which makes the lumen appear large when distended by air insufflation.
- The canine esophagus has longitudinal folds throughout. The feline esophagus has less prominent longitudinal folds in the proximal two-thirds and a ring-like pattern of circular annular ridges in the distal one-third.
- Normal esophageal mucosa is smooth, glistening, and pale pink. Superficial submucosal vessels are more visible in the cat. Heavily pigmented dog breeds (e.g., chow chow, Shar-Pei) may have patchy pigmentation of the esophageal mucosa.
- The gastroesophageal sphincter is normally closed, forming a slit-like opening that is eccentrically located at the confluence of a rosette pattern of mucosal folds.

Esophageal Manometry

Manometry evaluates intraluminal esophageal pressures and is useful for evaluation of esophageal motility disorders. Unfortunately, this procedure is infrequently performed in veterinary patients because of lack of availability of equipment and lack of patient cooperation.

Treatment

Treatment of esophageal disease is discussed under each specific disorder. General management of esophageal disease involves fluid therapy as needed (see Chapter 5), management of complications such as secondary aspiration pneumonia (see Chapter 163), and in severe cases, nutritional support by tube gastrostomy (see Chapter 3).

OROPHARYNGEAL DYSPHAGIA

Oropharyngeal dysphagia is defined as difficulty in moving a bolus of food or water from the oral cavity to the cervical esophagus. This disorder can be subclassified as oral dysphagia or pharyngeal dysphagia based on the clinical findings (Table 65-2).

- Oral dysphagia involves difficulty with prehension or aboral transport of ingesta to the hypopharynx during bolus formation.
- Pharyngeal dysphagia is defined as interrupted transport of a bolus from the oropharynx through the cranial esophageal sphincter into the cervical esophagus. It includes disorders of the cranial esophageal sphincter (cricopharyngeus muscle) referred to as cricopharyngeal dysphagia. Cricopharyngeal dysphagia may consist of failure of the sphincter to open (cricopharyngeal achalasia) or lack of coordination between pharyngeal contraction and cranial esophageal sphincter relaxation during swallowing (cricopharyngeal asynchrony).

Etiology

Oropharyngeal dysphagia usually is caused by morphologic disease that interferes with normal prehension and swallowing (see Table 65-2). Functional oropharyngeal dysphagia is associated with neuromuscular disorders that affect the tongue, muscles of mastication, or cranial nerves involved in voluntary and involuntary swallowing.

Clinical Signs

- Oral dysphagia is characterized by abnormalities of prehension and mastication. Weight loss is not a problem because animals compensate for their deficits and maintain food intake. Secondary aspiration pneumonia is uncommon because pharyngeal function is unaffected.
- Pharyngeal dysphagia is characterized by repeated unsuccessful attempts to swallow, with gagging, retching, and spitting out of saliva-covered food. Aspiration pneumonia is a common and serious complication. Weight loss is also common.
- Regurgitation may be a prominent clinical sign since many of the systemic neuromuscular disorders that cause oropharyngeal dysfunction can also cause esophageal hypomotility (megaesophagus).

Table 65-2. DIAGNOSIS OF OROPHARYNGEAL DYSPHAGIA*

	Anatomic Association	Clinical Findings	Etiology	Diagnosis	Treatment
Oral Dysphagia					
			Morphologic Disorders		
(Abnormalities of prehension and mastication)	Teeth, tongue, hard palate, bony structures, and TMJ	Difficulty prehending food or lapping water Excessive chewing and chomping Exaggerated head movements when eating Submerging muzzle to drink Dropping food from mouth Pawing at face Excessive salivation No weight loss or aspiration pneumonia	Dental disease	Oral exam, radiography	See Chapter 64 for treatment of morphologic disorders.
			Oral foreign body	Oral exam, radiography	
			Oral neoplasia	Oral exam, radiography, biopsy	
			Severe stomatitis	Oral exam, biopsy	
			Cleft palate	Oral exam	
			Persistent frenulum	Oral exam	
			Skeletal disorders (e.g., TMJ, craniomandibular osteopathy)	Oral exam, skull radiography	
			Functional Disorders		
			CNS disease or peripheral neuropathy (cranial nerves V, VII, XII)	Oral exam (atrophy or deviation of tongue secondary to denervation), neurologic exam, EMG, nerve biopsy, CSF tap, CT scan (see Chapter 125)	See Chapters 126 and 129.
			Neuromuscular disease (e.g., myasthenia gravis, botulism)	Neurologic exam, EMG with repetitive nerve stimulation, Tensilon test, ARA titer (see Chapter 130)	See Chapter 130.
			Myopathy or myositis (e.g., masticatory myositis, immune polymyositis, hypothyroidism)	EMG, muscle biopsy, CK, AST, ANA, LE, T_4 and TSH assay (see Chapter 130)	See Chapter 130.
Pharyngeal Dysphagia					
			Morphologic Disorders		
(Abnormalities of bolus transport from the oropharynx through the cranial esophageal sphincter)	Pharyngeal constrictor muscles, soft palate, cranial esophageal sphincter	Normal food and water uptake but repeated unsuccessful attempts to swallow Spitting out saliva-covered food Eating with head and neck tucked ventrally	Inflammatory or neoplastic diseases of the pharynx, tonsils, or retropharyngeal lymph nodes	Oral exam, skull and pharyngeal radiography, biopsy of inflammatory or mass lesions, fine-needle aspiration of lymph nodes, endoscopy	See Chapter 64 for treatment of morphologic disorders.
			Retropharyngeal foreign body or abscess	Oral exam, pharyngeal radiography, fine-needle aspiration, endoscopy	
		Pharyngeal food retention and pharyngitis Gagging, retching Regurgitation Nasal discharge Cough, fever (pneumonia)	Soft palate disorders (e.g., cleft soft palate or iatrogenic shortening)	Oral exam	

Table continued on following page

Table 65-2. DIAGNOSIS OF OROPHARYNGEAL DYSPHAGIA*—cont'd

	Anatomic Association	Clinical Findings	Etiology	Diagnosis	Treatment
Pharyngeal Dysphagia (cont'd)					
			Functional Disorders		
			CNS disease or peripheral neuropathy (cranial nerves V, VII, IX, X)	Neurologic exam, EMG, nerve biopsy, CSF tap, CT scan (see Chapter 125)	See Chapters 126 and 129
		Weight loss	Myopathy or myositis (e.g., immune polymyositis, hypothyroidism)	EMG, muscle biopsy, CK, AST, ANA, LE, T_4 and TSH assay (see Chapter 130)	See Chapter 130
			Neuromuscular disease (e.g., myasthenia gravis, botulism)	Neurologic exam, EMG with repetitive nerve stimulation, Tensilon test, ARA titer (see Chapter 130)	See Chapter 130
			Congenital cricopharyngeal achalasia	Barium swallow with fluoroscopy, response to myotomy	Cricopharyngeal myotomy (see Chapter 66)
			Cricopharyngeal asynchrony†	Barium swallow with fluoroscopy	Cricopharyngeal myotomy is contraindicated
			Sialadenosis	Diagnosis of exclusion	Phenobarbitol (see Chapter 64)

*The type of dysphagia is first characterized as oral dysphagia versus pharyngeal dysphagia based on observing the animal eat (e.g., prehension of food and water, swallowing). Barium swallow with fluoroscopy is useful to characterize functional oropharyngeal dysphagia but is not indicated for evaluation of morphologic disorders.
†Lack of coordination between cranial esophageal sphincter opening and pharyngeal contraction.
ANA, antinuclear antibody; ARA, acetylcholine receptor antibody; AST, aspartate aminotransferase; CK, creatine kinase; CNS, central nervous system; CSF, cerebrospinal fluid; CT, computed tomography; EMG, electromyography; LE, lupus erythematosus; T_4, thyroxine; TMJ, temporomandibular joint; TSH, thyroid-stimulating hormone.

- When a neuromuscular disorder is the underlying cause of oropharyngeal dysphagia, generalized signs of muscle weakness, atrophy, and neurologic deficits are often present.

Diagnosis

The strategy for diagnosis of oropharyngeal dysphagia is as follows:

- Identify underlying morphologic disorders with a complete oropharyngeal and radiographic evaluation.
- Characterize functional dysphagia by the affected stage of swallowing.
- Pursue ancillary testing to identify underlying neuromuscular disorders that may be associated with functional dysphagia (see Table 65-2).

Signalment and History

The signalment may suggest certain breed predispositions for congenital neuromuscular disorders associated with oropharyngeal dysphagia (see Table 65-1). Obtain a complete history, including a description of eating and drinking. Evaluate for signs suggestive of aspiration pneumonia (cough, dyspnea, anorexia, depression) or a systemic neuromuscular disorder (weakness, muscle pain, gait abnormalities).

Physical Examination

Many of the morphologic diseases that cause dysphagia are detected initially by visual examination of the oropharynx. Tranquilization or general anesthesia may be required for a thorough oropharyngeal evaluation. A general physical and neurologic examination (see Chapter 125) are particularly important to identify focal and generalized neuromuscular abnormalities that may be associated with functional oropharyngeal dysphagia.

▼ ***Key Point*** Observation of the animal eating and drinking is an important extension of the physical examination to confirm that dysphagia is present and to characterize it as an oral or pharyngeal problem (see Table 65-2).

Radiography

- Perform survey radiographs of the skull and pharyngeal area to identify morphologic disorders such as a pharyngeal foreign body or retropharyngeal abscess that can cause oropharyngeal dysphagia.
- Perform thoracic radiographs to detect aspiration pneumonia and associated megaesophagus.
- A barium swallow with fluoroscopic examination is required for definitive characterization of functional swallowing abnormalities, and it is essential for the diagnosis of cricopharyngeal achalasia. Unfortunately, fluoroscopy is available only at large referral centers.

Ancillary Testing

Ancillary tests are frequently necessary to determine the cause of functional oropharyngeal dysphagia.

- Use a Tensilon response test (edrophonium chloride) (Tensilon, ICN Pharmaceuticals), acetylcholine receptor antibody titer, and electromyography (EMG) for myasthenia gravis (MG) (see Chapter 130).
- Use an EMG and muscle biopsy for polymyositis and polymyopathy (see Chapter 130).
- Use a cerebrospinal fluid (CSF) tap, computed tomography (CT) scan, or magnetic resonance imaging (MRI) for primary CNS diseases (see Chapter 125).

Treatment

- The treatment and prognosis for oropharyngeal dysphagia depend on the underlying disorder (see Table 65-2).
- Supportive care is especially important with pharyngeal dysphagia. Identify and treat aspiration pneumonia (see Chapter 163) and provide appropriate nutritional support, including a gastrostomy tube in severely emaciated animals (see Chapter 3).

ESOPHAGEAL HYPOMOTILITY (MEGAESOPHAGUS)

Esophageal hypomotility refers to a decrease in esophageal tone or peristalsis that may be segmental or diffuse. The term *megaesophagus* commonly is used when a diffuse, severe motility disorder results in a large, flaccid esophagus. In most cases, the primary disturbance is an abnormality of the body of the esophagus rather than a failure of the gastroesophageal sphincter to relax (achalasia), as occurs in humans. Clinical findings associated with megaesophagus reflect impaired esophageal transport with secondary complications such as weight loss and aspiration pneumonia.

Etiology

- Esophageal hypomotility disorders may be congenital or acquired. A familial predisposition for congenital idiopathic megaesophagus has been suggested for many breeds of dogs and Siamese cats (see Table 65-1).

▼ ***Key Point*** Breeding of animals with congenital megaesophagus is not recommended because of potential hereditability of the trait.

- Acquired megaesophagus may occur secondary to many disorders, especially diseases causing diffuse neuromuscular dysfunction (Table 65-3). However, in most dogs, a cause is not identified and the diagnosis is *idiopathic megaesophagus*.
- Megaesophagus is less likely to be idiopathic in cats. Esophagitis associated with hiatal hernia and gastroesophageal reflux is an important cause of feline esophageal hypomotility.
- The underlying pathophysiologic mechanism for idiopathic megaesophagus is unknown. Efferent neuromuscular pathways appear to be intact, and a defective afferent component of the neural reflex is suspected. Mechanisms may be similar for both congenital and acquired idiopathic megaesophagus.

Clinical Signs

- Regurgitation, which may or may not be related to eating, is the primary clinical sign of megaesophagus. In most cases, the more liquid the food, the less likely it is to be regurgitated. Weight loss and emaciation occur secondary to inadequate retention of food.
- Dyspnea, cough, and fever are indicative of secondary aspiration pneumonia, a common complication of megaesophagus.
- Cats with esophageal hypomotility typically present for either upper gastrointestinal signs (regurgitation, vomiting) or chronic or recurrent respiratory tract disease (acute or chronic cough, dyspnea, noisy breathing, nasal discharge) due to secondary aspiration pneumonia.
- In cases in which megaesophagus is associated with an underlying disorder (see Table 65-3), additional clinical signs may be detected, including the following:
  - Generalized muscle weakness with MG, polymyositis, polymyopathy, or hypoadrenocorticism
  - Neurologic deficits with CNS disease or polyneuropathy
  - Generalized muscle atrophy or pain with polymyositis
  - Obesity and alopecia with hypothyroidism
  - Oropharyngeal dysphagia with generalized neuromuscular dysfunction

Table 65-3. CAUSES OF ESOPHAGEAL HYPOMOTILITY (MEGAESOPHAGUS)

Idiopathic
Congenital
Acquired
Central and Peripheral Neuropathies
CNS (caudal brain stem) disorders (e.g., distemper, trauma, neoplasia)
Immune polyneuritis
Polyradiculoneuritis (coonhound paralysis)
Bilateral vagal nerve damage (e.g., surgery, trauma, neoplasia)
Giant axonal neuropathy
Hereditary spinal muscular atrophy
Dysautonomia
Ganglioradiculitis
Neuromuscular Junctionopathies
Myasthenia gravis (congenital or acquired)
Botulism
Tick paralysis
Anticholinesterase toxicity
Myopathy or Myositis
Polymyositis (e.g., SLE, idiopathic, infectious)
Muscular dystrophy
Hereditary myopathy
Familial canine dermatomyositis
Glycogen storage disease type II
Tiger snake envenomation
Miscellaneous
Hypothyroidism
Hypoadrenocorticism (typical and atypical forms)
Lead toxicity
Thallium toxicity
Acrylamide toxicity
Thymoma
Pituitary dwarfism
Esophagitis
Hiatal hernia
Esophageal fistula
Tetanus
Gastric dilatation volvulus
Dystrophin deficiency

CNS, central nervous system; SLE, systemic lupus erythematosus.

Diagnosis

Idiopathic megaesophagus is a diagnosis of exclusion. Strategies for diagnosis of megaesophagus should include the following:

- Confirmation of a persistently dilated esophagus
- Evaluation for underlying obstructive esophageal disease
- Evaluation for underlying causes of esophageal hypomotility (see Table 65-3)

Signalment and History

The signalment is important since idiopathic megaesophagus is a common disorder in young animals with regurgitation and certain breeds are predisposed (see Table 65-1).

- In young animals with congenital idiopathic megaesophagus, regurgitation is often noted at weaning when solid food is first introduced. Multiple animals in a litter may be affected.
- Historical findings that indicate the need for a more complete evaluation for predisposing causes include systemic lethargy or weakness, concurrent oropharyngeal dysphagia, and neurologic abnormalities.
- A history of chronic or recurrent respiratory infections (aspiration pneumonia) may overshadow the gastrointestinal signs when a subtle esophageal motility disorder is present.

Physical Examination

The physical examination is often unremarkable except for weight loss.

- Distention of the cervical esophagus can be accentuated by compressing the thorax while the nostrils are occluded.
- A mucopurulent nasal discharge, pulmonary crackles, and fever suggest secondary aspiration pneumonia.
- Perform a complete neurologic examination with emphasis on cranial nerves IX (glossopharyngeal) and X (vagus).
- Evaluate all skeletal muscles (especially temporal and limb muscles) for weakness, atrophy, or pain.
- Additional physical examination findings are determined by the underlying cause (see Table 65-3).

Radiography

- Survey thoracic radiography usually shows distention of the entire intrathoracic esophagus with gas, fluid, or food. If hypomotility is mild, radiographs may be unremarkable. Evaluate for evidence of aspiration pneumonia.
- A barium contrast esophagram is useful for confirming persistent dilatation of the esophagus and for identifying possible mechanical obstruction at the gastroesophageal junction.
- Esophageal motility disorders are best evaluated with barium swallow fluoroscopy, which provides a means of subjectively assessing the intensity and coordination of esophageal peristalsis and is the only modality that can detect subtle esophageal motility disorders.
- Most cats with esophageal hypomotility do not have overt megaesophagus on survey thoracic radiographs. A barium esophagram with fluoroscopy is required to identify esophageal hypomotility.

Routine Laboratory Tests

Perform a minimum database of tests, including the following:

- *Biochemical profile* to screen for changes associated with underlying systemic disorders that cause megaesophagus (e.g., hyponatremia and hyperkalemia in hypoadrenocorticism; hypercholesterolemia in hypothyroidism; and increased creatine kinase [CK] and aspartate aminotransferase [AST] levels in polymyositis)
- *Complete blood count* (CBC) to detect a neutrophilia and left shift consistent with aspiration pneumonia
- *Acetylcholine receptor antibody titer* to evaluate for acquired MG, even in the absence of generalized muscle weakness, because acquired focal MG may mimic idiopathic megaesophagus (see Chapter 130)

Ancillary Tests

Perform other tests as indicated by clinical and laboratory findings to identify underlying causes of megaesophagus.

- Adrenocorticotropic hormone (ACTH) stimulation test for hypoadrenocorticism
- Thyroid-stimulating hormone (TSH) assay and thyroxine level for hypothyroidism
- Antinuclear antibody (ANA) and lupus erythematosus (LE) tests for systemic LE
- Blood lead assay for lead poisoning
- Tensilon test for MG
- EMG for polymyopathy, polymyositis, polyneuropathy, and MG
- Muscle biopsy for polymyopathy and polymyositis
- CSF tap for CNS disease
- Transtracheal wash for cytology, and culture and sensitivity testing if aspiration pneumonia is suspected

Esophagoscopy

Esophagoscopy is not routinely indicated for evaluation of megaesophagus unless obstructive disease of the gastroesophageal sphincter or reflux esophagitis is suspected. With idiopathic megaesophagus, the esophagus appears flaccid and dilated throughout its entire length and contains variable amounts of froth, fluid, or food. The esophageal mucosa is usually normal.

Esophageal Manometry

This is an extremely useful diagnostic tool to detect and characterize esophageal motility disorders in humans, but it is not widely used in veterinary medicine because of the expense and the lack of patient cooperation.

Treatment

▼ ***Key Point*** Treatment of megaesophagus is primarily supportive and symptomatic, unless a reversible underlying disorder can be identified.

- Offer frequent small meals with the animal in an upright position. Maintain the upright position for 10 to 15 minutes after eating so that gravity can assist entry of food into the stomach. In most cases, the more liquid the diet, the easier it is for it to reach the stomach. However, different types of food should be given on a trial basis to identify those best tolerated.
- Place a gastrostomy tube for temporary nutritional support of animals with severe malnutrition (see Chapter 3).
- Give antibiotics for treatment of aspiration pneumonia based on results of culture and sensitivity testing (see Chapter 163). Caution the owner that recurrent pneumonia is a common problem and that early detection and treatment are essential for long-term success.
- Treat the underlying disorder whenever possible (see Table 65-3). Institute treatment for esophagitis (as discussed later in this chapter) when esophagitis is confirmed endoscopically or when esophageal hypomotility is associated with risk factors for reflux esophagitis (post-anesthesia, hiatal hernia).
- Smooth muscle prokinetic drugs such as metoclopramide (Reglan, Robins) or cisapride (Propulsid, Janssen) do not appear to be useful in the management of idiopathic megaesophagus in dogs, because the dog's esophagus consists entirely of skeletal muscle. These prokinetic agents (cisapride more so than metoclopramide) may be useful in cats with motility disorders involving the distal esophagus because of the smooth muscle composition of this segment of the feline esophagus.
- A therapeutic trial with the cholinergic drug bethanechol may be warranted, since it has been shown to increase the amplitude of esophageal contractions determined manometrically in some dogs with idiopathic megaesophagus. Potential systemic side effects of bethanechol include salivation, lacrimation, urination, and defecation.
- Surgical myotomy of the gastroesophageal sphincter is not recommended because "achalasia" of the sphincter is not usually present.

Prognosis

- Some animals with congenital idiopathic megaesophagus may improve in time with diligent supportive care.
- Idiopathic acquired megaesophagus is usually irreversible. The animal may do well for months to years if the owner is dedicated to performing appropriate feeding procedures and if pneumonia is detected and treated early.
- Aspiration pneumonia and euthanasia are the most common causes of death in animals with megaesophagus.

ESOPHAGEAL FOREIGN BODY

Esophageal foreign bodies are common. They usually lodge at narrowed areas of the esophagus including the thoracic inlet, base of the heart, or hiatus of the diaphragm. The extent of secondary esophageal damage depends on the type of object, its size and shape, and the duration of time in contact with the mucosa. Complications of esophageal foreign bodies include esophagitis, esophageal perforation and mediastinitis, aortic perforation, esophageal stricture, and bronchoesophageal fistula.

Etiology

The most commonly encountered esophageal foreign bodies are bones. Other objects include needles, fishhooks, string, toys, and in cats, vomited hairballs.

Clinical Signs

- Most dogs and cats with esophageal foreign bodies are presented for evaluation of acute onset of gagging, salivation, dysphagia, and regurgitation.
- If esophageal foreign bodies go undiagnosed initially, they may cause chronic regurgitation and dysphagia.

Diagnosis

Consider esophageal foreign body based on clinical signs, especially when ingestion of foreign body is observed by the owner.

Physical Examination

- The physical examination often is normal except for dysphagia, ptyalism, or gagging and retching.
- Cervical esophageal foreign bodies may be palpable.
- Findings of depression, anorexia, fever, cough, and dyspnea may suggest secondary aspiration pneumonia or esophageal perforation. Cervical swelling may be palpated with foreign body-induced perforation of the cervical esophagus.

Radiography

- Thoracic and cervical radiographs usually are diagnostic for metal or bone foreign bodies. Evaluate thoracic radiographs for aspiration pneumonia. Findings of pneumomediastinum, pneumothorax, and mediastinal or pleural effusion suggest esophageal perforation.
- Barium contrast esophageal radiography may be necessary to identify radiolucent objects. Use iohexol (Omnipaque, Amersham Health), a water-soluble, non-ionic iodinated contrast agent, rather than barium sulfate if perforation is a possibility (see Chapter 4).

Routine Laboratory Tests

A CBC, serum biochemical profile, and urinalysis may be indicated.

- Perform routine blood work before general anesthesia for foreign body removal, especially in older animals with possible concurrent systemic diseases (e.g., renal failure) that might warrant special anesthetic considerations.
- With secondary aspiration pneumonia or esophageal perforation, the CBC may indicate a neutrophilia and left shift.

Esophagoscopy

Esophagoscopy is indicated to confirm the diagnosis, remove the object, and assess secondary mucosal damage (see under "Technique for Foreign Body Removal").

Treatment

Esophageal foreign bodies should be considered an emergency situation. Do not delay foreign body removal, as the likelihood of complications increases with time. Institute fluid therapy as needed to correct secondary fluid and electrolyte imbalances before general anesthesia.

▼ ***Key Point*** Endoscopic removal of esophageal foreign bodies is usually successful and should be attempted before surgery.

Surgical exploration is preferred over endoscopy when retrieving penetrating esophageal foreign bodies located at the heart base because of the risk of lacerating the aorta or pulmonary vessels.

Technique for Foreign Body Removal

1. Perform esophagoscopy with the animal under general anesthesia.
2. Use a rigid or flexible endoscope with foreign body retrieval (grasping) instruments.
3. Grasp the object and attempt to dislodge it by gentle rotation. Perform all manipulations cautiously to prevent further mucosal damage or perforation.
4. If the object cannot be extracted orally without causing additional esophageal trauma, advance it into the stomach and remove it by gastrotomy. Gastrotomy is not required for bone foreign bodies, as they dissolve rapidly once reaching the stomach. In this situation, perform serial abdominal radiographs to confirm that the bone has dissolved and does not cause obstruction.
5. If a fishhook is embedded in the esophageal wall, use a rigid endoscope and pass rigid alligator forceps through the lumen of the endoscope to grasp the fishhook. Apply torque to the fishhook with the forceps to dislodge it from the wall. If the hook

cannot be dislodged, perform surgery to expose the esophagus so that the barbs can be cut off the hook. Retrieve the remainder of the hook endoscopically.
6. Once the object is removed, assess the mucosa for hemorrhage, erosions, lacerations, and perforations.
7. Following an uncomplicated foreign body retrieval, withhold oral food and water for 24 hours and give parenteral fluids and parenteral broad-spectrum antibiotics such as ampicillin (22 mg/kg q8h SC, IM, or IV) if mild esophagitis is detected. (See elsewhere in this chapter for diagnosis and management of complications of esophageal foreign bodies such as esophagitis, esophageal perforation, and esophageal stricture.)
8. If the foreign body cannot be removed endoscopically and cannot be advanced into the stomach, an esophagotomy is indicated (see Chapter 66).

Prognosis

The prognosis for recovery after endoscopic foreign body removal is excellent unless secondary complications occur. With perforation and mediastinitis, the prognosis is guarded.

ESOPHAGEAL PERFORATION

Perforation of the intrathoracic esophagus is more likely to be associated with significant morbidity than is perforation of the cervical esophagus.

Etiology

- Esophageal foreign bodies are the most common cause of esophageal perforation, especially objects with irregular or sharp edges, such as bones, and chronically lodged foreign bodies that cause secondary pressure necrosis.
- Iatrogenic perforation can occur during endoscopic removal for esophageal foreign bodies and during therapeutic dilatation of esophageal strictures. Perforation may also be a sequela of esophageal surgery or laser treatment.
- Penetrating injuries of the cervical esophagus can be caused by bite wounds and gunshot injuries.

Clinical Signs

- Anorexia, depression, odynophagia, fever, and a rigid stance are seen with esophageal perforation.
- Cough and dyspnea may occur when perforation of the thoracic esophagus leads to mediastinitis and pleuritis.

Diagnosis

Exposure to potential foreign bodies or trauma to the cervical esophagus may be determined from the history.

Physical Examination

Findings suggesting perforation include depression, fever, and pain. With cervical perforations, there may be cervical swelling, cellulitis, or a draining fistula.

Routine Laboratory Tests

CBC usually reveals neutrophilia and a left shift.

Radiography

- Thoracic radiography shows pneumomediastinum, pneumothorax, and mediastinal or pleural effusion.
- Perform a contrast esophagram using Omnipaque, a water-soluble, non-ionic iodinated contrast agent, to confirm perforation (see Chapter 4).

Esophagoscopy

Esophageal perforation may be detected by esophagoscopy as a deep laceration in the esophagus or a defect in the thoracic esophagus that bubbles bloody fluid.

▼ ***Key Point*** If perforation is present or occurs during endoscopy, life-threatening tension pneumothorax may require immediate thoracentesis and chest tube placement (see Chapter 3).

Treatment

- If a small tear occurs secondary to a sharp foreign body or during endoscopic manipulations, conservative medical management may be sufficient.
- Give broad-spectrum parenteral antibiotics, fluid therapy, and nothing per os for 5 to 7 days; monitor closely for clinical deterioration.
- Consider nutritional support by tube gastrostomy or parenteral alimentation (see Chapter 3).
- Repeat thoracic radiographs on a daily basis to monitor response to therapy and to detect evidence of mediastinitis and pleuritis.
- If perforation is accompanied by fever, and mediastinitis or pleuritis, surgical exploration for primary repair is indicated (see Chapter 66).

ESOPHAGITIS

Etiology

- *Foreign bodies* are a common cause of esophagitis (see "Esophageal Foreign Body"). This includes vomited hairballs that become lodged in the esophagus.
- *Chemical irritants* or caustic substances may cause esophagitis. Concurrent stomatitis and gastritis may occur.
- *Oral medications* (especially doxycycline tablets given to cats) can result in esophagitis and esophageal stricture secondary to prolonged esophageal retention and local tissue irritation (see later). Many other

oral medications, including nonsteroidal anti-inflammatory drugs and bisphosphonates, are reported to cause esophageal irritation in humans and have the potential to cause mucosal injury in dogs and cats.
- *Thermal injury* may occur with ingestion of food that has been heated to high temperature (e.g., in a microwave).
- *Gastroesophageal reflux* of gastric or duodenal contents is a common cause of esophagitis. Esophageal damage is attributed to mucosal contact with gastric acid, pepsin, bile acids, and trypsin. Predisposing factors that may contribute to reflux esophagitis include general anesthesia, use of a head-down tilt table for surgery, an indwelling nasogastric tube or pharyngostomy tube, hiatal hernia, chronic vomiting, and delayed gastric emptying.
- *Pythium insidiosum* as a cause of severe necrotizing pyogranulomatous esophagitis has been described in two dogs from the southern United States. Infection is believed to occur from the ingestion of zoospores in stagnant fresh water. Diagnosis is confirmed by demonstrating characteristic hyphae with Grocott's methenamine silver stain on an esophageal biopsy. Medical therapy of pythiosis is usually unsuccessful; however, the combination of itraconazole (10 mg/kg PO q24h) and terbinafine (5–10 mg/kg PO q24h) has been effective in some dogs with pythiosis (see Chapter 40).

Clinical Signs

- Signs of esophagitis are nonspecific for esophageal disease in general and include dysphagia, regurgitation, repeated swallowing, and excess salivation.
- Anorexia, depression, and fever suggest secondary aspiration pneumonia or perforation.
- Weight loss and dehydration may occur with chronic or severe esophagitis.
- With mild esophagitis, signs may be absent.

Diagnosis

Consider potential predisposing factors in the patient's history, such as recent general anesthesia or exposure to foreign bodies, doxycycline (cats), or caustic materials.

Physical Examination

Oral ulcerations or stomatitis may be present if caustic injury occurred. Weight loss and dehydration may be detected when esophagitis is severe.

Radiography

- Survey radiographs usually are unremarkable. Occasionally, small amounts of gas may be seen in the esophagus and mild to moderate focal esophageal dilatation may occur secondary to delayed motility.
- Contrast radiography is often normal. When esophagitis is severe, the mucosa may appear irregular. Segmental luminal narrowing can occur with involvement of the submucosa and tunica muscularis. This radiographic appearance can be difficult to distinguish from a fibrous stricture.

Endoscopy

Endoscopic evaluation of the esophageal mucosa is the most sensitive method for detecting esophagitis.

- Findings include mucosal erythema, hemorrhage, increased friability, erosions or ulcers, and in severe cases, pseudomembranes, indistensibility, and strictures.
- If gastroesophageal reflux is the cause of esophagitis, lesions are most severe in the distal esophagus, especially linear erythematous streaks and erosions, and the gastroesophageal junction may appear dilated.
- Reflux of gastric contents into the esophagus may be noted during endoscopy.

Treatment

Mild esophagitis frequently resolves without treatment and may not require additional therapy, especially when the cause (e.g., foreign body) can be easily resolved.

General Therapy

- Administer antibiotics (e.g., ampicillin, amoxicillin, or cephalosporins) routinely to prevent or control infection of the altered mucosa by oral bacteria.
- Maintain adequate nutrition in mild cases with frequent oral feeding of small portions of a nonabrasive, soft food. Place a gastrostomy tube in animals with severe esophagitis, prolonged anorexia, or inability to retain food.

Therapy for Reflux Esophagitis

See Chapter 67 (Table 67-3) for pharmacology, adverse effects, and prescribing information concerning each of the following medications.

- Give a promotility agent, such as metoclopramide (Reglan, Robins) (0.2–0.4 mg/kg PO or SC q8h) or cisapride (Propulsid, Janssen) (0.25–0.5 mg/kg PO q8–12h in dogs or 2.5–5.0 mg total dose per cat PO q8–12h), to decrease gastroesophageal reflux (by increasing gastroesophageal sphincter pressure) and promote gastric emptying.
- Decrease acidity of refluxed gastric juice by giving an H_2-receptor blocker such as famotidine (Pepcid, Merck) (0.5–1.0 mg/kg PO or IV q12–24h) or ranitidine (Zantac, GlaxoSmithKline) (2 mg/kg PO or IV q8–12h in dogs or 3.5 mg/kg PO q12h in cats). H_2-receptor blockers are preferable to antacids for control of acid secretion because of their potency and ease of administration.

- Consider a proton pump inhibitor, such as omeprazole (Prilosec, AstraZeneca) (0.75–1.0 mg/kg PO q12–24h), for treatment of severe reflux esophagitis in dogs and cats that is unresponsive to the previously described treatments. Use pantoprazole (Protonix, Wyeth-Ayerst) (0.7–1.0 mg/kg IV q24h) if an injectable proton pump inhibitor is required.
- Sucralfate suspension is beneficial in the treatment of reflux esophagitis. Sucralfate (Carafate, Axcan Scandipharm) (0.5–1.0 g total dose for dogs or 0.25 g total dose for cats PO q8–12h) is an aluminum salt that binds selectively to injured gastroesophageal mucosa and acts as an effective barrier against the damaging actions of acid, pepsin, and bile acids associated with reflux esophagitis.
- Prednisolone (0.5 mg/kg PO q12h) is frequently recommended (but has unproven effectiveness) for animals with severe circumferential esophagitis to prevent healing by fibrosis and stricture formation. Be sure to control any infection (e.g., aspiration pneumonia) before starting corticosteroid therapy.

Prognosis

The prognosis is good for mild to moderate esophagitis and guarded or poor for severe esophagitis, especially when accompanied by perforation. Strictures may occur secondary to severe esophagitis (see the next section).

ESOPHAGEAL STRICTURE

An intramural esophageal stricture results when severe esophagitis involving the submucosa and tunica muscularis heals by fibrosis. Multiple strictures can result from diffuse esophagitis.

ETIOLOGY

Esophageal stricture may occur secondary to severe esophagitis of any etiology (see the previous section).

- Reflux esophagitis associated with gastroesophageal reflux of gastric acid and enzymes during general anesthesia and esophageal foreign bodies are the most commonly recognized causes.
- Administration of oral doxycycline tablets to cats has been associated with esophagitis and esophageal stricture formation secondary to prolonged esophageal retention of the tablet and local tissue irritation. This complication can be prevented by following tablet administration with a 6-ml bolus of water, by placing a small amount of butter or Nutrical on the nose following dry tablet administration to stimulate licking, or by giving doxycycline as a suspension.
- Esophageal surgery may be complicated by healing with stricture formation.

Clinical Signs

- Clinical signs of regurgitation and dysphagia are attributable to esophageal obstruction.
- Regurgitation usually occurs immediately after eating. If the stricture is chronic, regurgitation may not be related to eating because esophageal distention cranial to the stricture acts as a food reservoir.
- A ravenous appetite is common because of inability to get food past the strictured area.

Diagnosis

Suspect esophageal stricture from the history. Progressive dysphagia for solid foods with preferential retention of liquids is common. Clinical signs from a stricture usually occur 3 to 14 days after the onset of esophageal injury and esophagitis.

Physical Examination

The physical examination is often unremarkable unless the stricture has been present for a long time, resulting in weight loss. Animals are often otherwise bright and alert.

Radiography

- Survey radiographs usually are normal unless the esophagus is distended with food or fluid proximal to the stricture. Evaluate for aspiration pneumonia.
- A contrast study of the esophagus using barium paste or barium mixed with food demonstrates the stricture (see Chapter 4). Contrast radiography is useful to assess the number, location, and length of strictures.

Endoscopy

Endoscopy can diagnose an esophageal stricture and, at the same time, allow treatment of the stricture by bougienage or balloon dilatation.

- At endoscopy, a stricture appears as a ring or ridge of white fibrous tissue that circumferentially narrows the esophageal lumen and fails to distend with insufflation. Multiple strictures are sometimes present, causing the tubular shape of the esophagus to be distorted and angulated. Esophagitis, erosions, and ulcers may also be observed.

Procedure

- If possible, pass the endoscope through the stricture to assess its length and to evaluate the esophagus distal to the strictured area.
- Perform a complete endoscopic examination of the esophagus and stomach to evaluate for severity of esophagitis and to identify potential underlying causes of esophagitis and stricture formation (e.g., foreign bodies and hiatal hernia/intussusception).
- If the endoscope cannot be passed through the stricture, contrast studies may be necessary (if not previ-

ously performed) for complete evaluation of number and length of strictures. Balloon dilatation of the stricture to 10 mm should allow subsequent passage of the endoscope.
- Mucosal biopsies of the strictured area may be warranted in some cases to rule out underlying neoplasia, especially when the stricture is associated with a mass effect or mucosal proliferations or fails to respond to therapy.

Complications

Gastric overdistention can be a significant complication of endoscopy in animals with esophageal stricture; thus, use insufflation sparingly. If the stricture precludes passage of the endoscope into the stomach, air introduced during insufflation will pass through the stricture and accumulate in the stomach, and it cannot be suctioned off through the endoscope.

Treatment

Esophageal strictures can be managed surgically or endoscopically. Surgery may be indicated if the stricture is too small to pass a dilator or if inadequate dilatation is achieved after multiple attempts (see Chapter 66). Mechanical dilatation of the stricture is performed under general anesthesia with endoscopic visualization.

▼ ***Key Point*** Conservative management of esophageal strictures with endoscopically guided balloon catheter dilatation or bougienage is preferable to surgery.

Bougienage

- A well-lubricated dilator, such as a bougie or tapered probe (or the endoscope itself), is passed through the stricture. Avoid excessive force because esophageal perforation is a life-threatening complication.
- Passage of progressively larger bougies results in stretching and dilatation of the stricture.
- The procedure is repeated at intervals of 4 to 7 days as needed to maintain clinical improvement.
- The total number of dilatations (3–10) is determined by the severity of the stricture and the clinical response.

Balloon Catheter Dilatation

This technique provides radial stretching of the stricture and is currently considered preferable to bougienage. Balloon catheters (Rigiflex dilator, Microvasive, Milford, MA) used in dogs and cats have 10-mm, 15-mm, and 20-mm diameters and a 8-cm length when inflated. These catheters can be passed through a 2.8-mm endoscopic biopsy channel, or they can be carefully passed adjacent to the endoscope using endoscopic or fluoroscopic guidance.

Procedure

With the patient under anesthesia and using endoscopic guidance, insert the catheter with deflated balloon into the lumen of the stricture and center the balloon in the stricture. Distend the balloon with distilled water (or contrast material for fluoroscopy) to the pressure recommended by the manufacturer (usually 45–50 psi). Use a pressure gauge to avoid overdistention and inadvertent balloon rupture. Distend the balloon for 1 to 2 minutes, and then deflate it to evaluate the size of the stricture and the extent of secondary mucosal hemorrhage. The procedure can be repeated immediately using the next larger balloon.

- Balloon dilatations are usually performed 2 to 5 times at intervals of 4 to 7 days. Refractory strictures may require more than five dilatation procedures initially. Some patients have recurrence of signs weeks to months after initial treatment, requiring periodic balloon dilatation to maintain a functional lumen.
- Give prednisolone, 0.5 mg/kg PO q12h for 10 to 14 days, to prevent further healing by fibrosis and stricture recurrence; taper the dosage over the remaining period of time that the stricture requires dilatation. An alternative consideration is to perform endoscopic-guided intralesional corticosteroid injections (triamcinolone, 10 mg/ml; 0.2 ml per injection site, given in four circumferential sites), at the time of balloon dilation.
- During the series of dilatation procedures and for at least 2 to 3 weeks after the final one, institute medical therapy as described for esophagitis.
- For refractory fibrotic strictures, endoscopically guided four-quadrant electrocautery or laser incisions through the fibrous stricture, followed by balloon dilation, have been recommended.
- An esophageal diameter of 1 cm is usually adequate for a cat or small dog to be maintained on canned food. Larger dogs may require an opening 1.5 to 2 cm in diameter.

ESOPHAGEAL DIVERTICULA

Etiology

- Esophageal diverticula are large pouch-like sacculations of the esophageal wall that may be congenital or acquired. They are rare in veterinary medicine. Diverticula most commonly affect the esophagus at the thoracic inlet or just cranial to the diaphragm.
- Acquired diverticula are classified as *pulsion* or *traction* diverticula. Pulsion diverticula are believed to occur because of increased intraluminal pressure secondary to obstruction or altered motility. They have been associated with foreign bodies, stricture, vascular ring anomalies, esophagitis, idiopathic megaesophagus, and hiatal hernia.

- Traction diverticula occur secondary to periesophageal inflammation that results in fibrosis and contraction, which pulls out the wall of the esophagus into a pouch.

Clinical Signs

- Large diverticula interfere with orderly movement of ingesta through the esophagus and cause clinical signs because they predispose to impaction with foreign bodies or food, which may lead to esophagitis and even perforation.
- Signs include regurgitation, distress after eating, anorexia, weight loss, intermittent thoracic or abdominal pain, and respiratory signs.
- Clinical signs may not occur with small diverticula.

Diagnosis

Radiography

- Thoracic radiography frequently reveals a gas- or food-filled mass in the area of the esophagus.
- A barium esophagram confirms that a pouch communicates with the esophageal lumen.

Endoscopy

- Esophagoscopy reveals a sac-like outpouching with variable esophagitis and accumulation of ingesta and fluid in the sac.
- Use caution to avoid perforation of diverticula.

Treatment

- Large diverticula require surgical resection (see Chapter 66).
- Small diverticula can be managed medically with upright feeding of frequent small meals of a soft-food diet.
- Identify predisposing causes and treat when possible.

ESOPHAGEAL FISTULA

Esophagotracheal, esophagobronchial, and *esophagopulmonary fistulas* are patent communications between the esophagus and the respective airways. They occur rarely in dogs and cats. Of these, esophagobronchial (bronchoesophageal) fistulas are most commonly described. Clinical signs are related to contamination of the airways with esophageal secretions and food.

Etiology

Esophageal fistulas may be congenital or acquired. Acquired fistulas are most likely and are usually associated with esophageal foreign bodies, especially bones. In most cases, a lodged esophageal foreign body is suspected to cause esophageal wall necrosis with subsequent development of a fistula. Other causes include trauma, malignancy, and severe infection.

- Most esophagobronchial fistulas occur in the caudal esophagus, probably due to the close anatomic proximity of the caudal esophagus and bronchi in this region.
- Esophagobronchial fistulas commonly are accompanied by an esophageal diverticulum.
- A traction diverticulum may develop secondary to periesophageal inflammation and fibrosis in the region of the fistula.
- A pulsion diverticulum may develop secondary to lodging of a foreign body.
- The diverticulum may occur first and predispose to lodging of a foreign body and subsequent fistula formation.

Clinical Signs

- Clinical signs are primarily associated with the respiratory tract. Coughing, especially after drinking liquids, is a common presenting sign. Anorexia, fever, dyspnea, and weight loss are attributed to aspiration pneumonia.
- Signs of esophageal disease such as regurgitation, gagging, and retching may be seen but are not consistently described.
- Contamination of the airways can lead to recurrent localized bacterial pneumonia, pulmonary abscesses, and pleuritis.

Diagnosis

Suspect an esophageal fistula when there is a history of chronic cough, recurrent localized pneumonia, and signs of esophageal disease.

Physical Examination

Findings reflect the secondary pulmonary involvement and may include fever, pulmonary crackles, muffled heart sounds (pleural effusion), and weight loss.

Radiography

- Thoracic radiographic abnormalities are primarily indicative of pulmonary complications and include localized alveolar, bronchial, or interstitial infiltrative patterns; lobar consolidation; or pleural effusion. Radiopaque esophageal foreign bodies may be identified. The caudal lung lobes are most commonly affected.
- A barium esophagram is required for definitive diagnosis. Contrast material will outline the communicating airway. Use a thin mixture of barium sulfate (20–30% wt/vol) to enhance filling of small fistulas.

▼ ***Key Point*** Do not use oral iodinated contrast material (e.g., Gastrografin, Squibb) because it is hypertonic and may cause pulmonary edema.

- Esophagoscopy and bronchoscopy can be performed, but a contrast esophagram is more reliable for detecting fistulas.

Treatment

- Treatment of esophageal fistulas requires surgery for esophagotomy, foreign body removal, fistula resection, and lobectomy.
- Perform culture and sensitivity testing of involved tissues for appropriate antibiotic therapy.

Prognosis

If severe complications such as pneumonia, pulmonary abscesses, and pleuritis are present, the prognosis is poor.

VASCULAR RING ANOMALIES

Etiology

Vascular ring anomalies are congenital malformations of the great vessels and their branches that entrap the intrathoracic esophagus and cause clinical signs of esophageal obstruction.

Persistent Right Aortic Arch

This malformation accounts for 95% of vascular ring anomalies in dogs and cats. Persistent right aortic arch (PRAA) occurs when the embryonic right rather than the left fourth aortic arch becomes the functional adult aorta. The ductus arteriosus continues to develop from the left side, forming a band that crosses over the esophagus to connect the main pulmonary artery and the anomalous aorta (Fig. 65-1). Esophageal compression occurs by the aorta on the right, the ligamentum arteriosum (remnant of the ductus arteriosus) dorsolaterally on the left, the pulmonary trunk on the left, and the base of the heart ventrally.

PRAA appears to have a familial tendency, because certain breeds (see Table 65-1), especially German shepherds and Irish setters, appear to be predisposed and multiple animals in a litter may be affected. The mechanism of inheritance may involve single or multiple recessive genes. Breeding of affected animals is not recommended.

Other Anomalies

Other anomalies that have been described include double aortic arch, persistent right ductus arteriosus (with normal left aortic arch), aberrant left or right subclavian arteries, and (in English bulldogs) esophageal compression by the left subclavian and brachiocephalic arteries.

Clinical Signs

- Affected animals are usually presented for regurgitation of solid food that began at the time of weaning. Regurgitation of undigested food commonly occurs immediately after eating but is sometimes delayed, as ingesta is retained in a large esophageal pouch that develops cranial to the obstruction. Liquids and semisolid food are preferentially retained because they can pass through the constricted area.
- Weight loss or failure to gain weight despite a good appetite is common.
- Cough and dyspnea suggest aspiration pneumonia.

Diagnosis

Regurgitation since weaning is very suggestive of a vascular ring anomaly. Most animals are presented by 6 months of age, although occasionally signs are mild and a diagnosis is not made until later in life. Differentiate vascular ring anomalies from other causes of regurgitation in young animals such as congenital megaesophagus and, less frequently, esophageal foreign bodies. Diffuse esophageal hypomotility (megaesophagus) occasionally complicates vascular ring anomalies in dogs.

Physical Examination

The cervical esophagus may be distended secondary to partial obstruction and development of a pouch. Cough, dyspnea, pulmonary crackles, and fever indicate aspiration pneumonia.

Radiography

- Survey thoracic radiographs often suggest a vascular ring anomaly. The dilated esophagus appears as a food- or fluid-filled density cranial to the heart, which tapers to normal at the base of the heart. In the ventrodorsal (VD) view of PRAA, the normal bulge of the aortic arch to the left is absent. Tracheal deviation consisting of a leftward curvature near the cranial border of the heart on the dorsoventral (DV) (or VD) radiographs is a consistent feature. Moderate to marked focal tracheal narrowing may also be seen on the DV (or VD) and lateral thoracic views.
- Perform a barium esophagram (see Chapter 4) to confirm the location of esophageal obstruction and severity of esophageal distention. Differential diagnoses for this radiographic appearance include an intramural stricture, segmental motility disorder, or congenital diverticulum.
- Fluoroscopy is useful to evaluate generalized esophageal hypomotility.
- Angiography is seldom necessary but in selected cases can be used for definitive confirmation of the type and location of vascular ring anomaly prior to surgery.

Endoscopy

- Endoscopy can distinguish a mural lesion from extraluminal compression. In animals with PRAA, the indentation in the esophagus caused by external

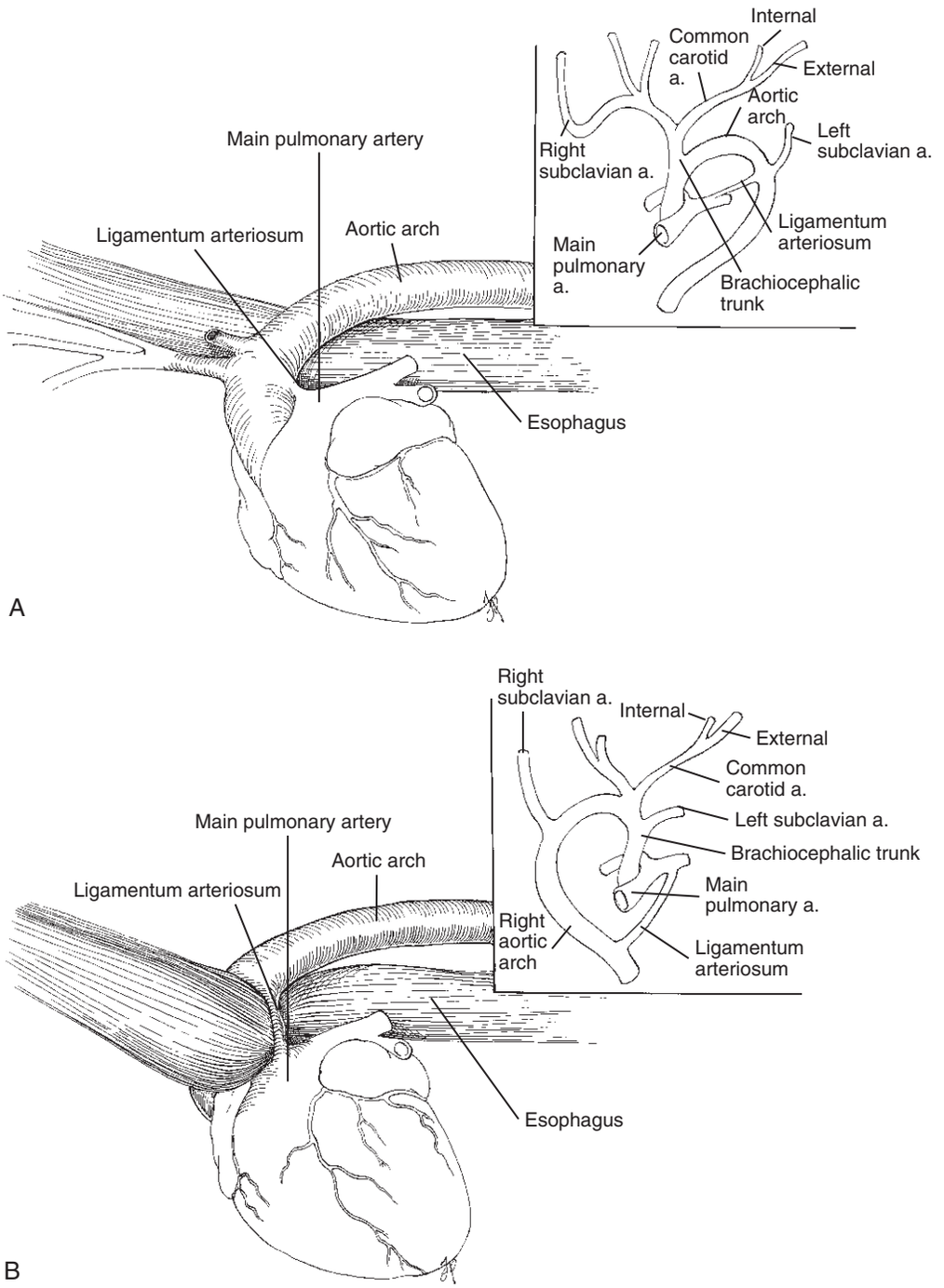

Figure 65-1. Persistent right aortic arch. *A,* Normal development of the aortic arch viewed from the animal's left side. Inset shows normal embryonic development of the great vessels from a dorsoventral view. *B,* When the embryonic right fourth aortic arch becomes the adult aorta, esophageal constriction occurs. Inset shows dorsoventral view of the vascular malformation.

compression from the ligamentum arteriosum is visible. The cranial thoracic esophagus is usually dilated.

- Endoscopy is also helpful to rule out cranial esophageal foreign bodies or hairballs (especially) that become lodged secondary to the PRAA.

Treatment

Definitive therapy for PRAA is surgical ligation and transection of the ligamentum arteriosum (see Chapter 66).

- If the animal is debilitated and malnourished, improve nutritional status before surgery. Give fre-

quent elevated feedings of small amounts of a semimoist or liquid diet. If this diet is poorly tolerated, consider feeding through a gastrostomy tube (see Chapter 3).
- Control aspiration pneumonia with antibiotics before surgery (see Chapter 163).
- Significant clinical improvement usually occurs after surgery, although mild esophageal distention often persists, especially if a large cranial diverticulum was present.
- Manage as described for megaesophagus if regurgitation persists.
- Recovery of normal esophageal function is more likely if surgery is performed at an early age and esophageal dilatation is not severe.

HIATAL DISORDERS

Anatomic abnormalities of the hiatus include hiatal hernia and gastroesophageal intussusception (GEI).

- A *sliding* hiatal hernia is a protrusion of any structure (usually the distal esophagus and stomach) through the esophageal hiatus of the diaphragm into the thorax.
- A *paraesophageal* hiatal hernia involves displacement of a portion of the stomach through a diaphragmatic defect adjacent to the esophageal hiatus and is rare in veterinary medicine.
- Differentiate hiatal hernia from GEI, in which the stomach (and occasionally other structures such as the spleen, proximal duodenum, pancreas, and omentum) invaginates or prolapses into the distal lumen of the esophagus. Hiatal hernias and GEI may be intermittent or persistent.

Etiology

Congenital or acquired enlargement of the esophageal hiatus or laxity of the surrounding ligaments may predispose to hiatal hernias and GEI.

Congenital Hiatal Disorders

- Most hiatal hernias are congenital and occur as a developmental defect of the diaphragmatic esophageal hiatus.
- Sliding hiatal hernia has been described in young Shar-Pei dogs. Concurrent megaesophagus or esophageal hypomotility, which resolved after surgical correction of the hernia, suggests that reflux esophagitis rather than a primary motility disorder was the underlying cause of these complications.

Acquired Hiatal Disorders

- Acquired hiatal hernias may occur secondary to high positive intra-abdominal pressure (e.g., blunt abdominal trauma or vomiting).
- Chronic upper airway obstruction (e.g., laryngeal disease or brachycephalic syndrome) can predispose to hiatal hernia since severe inspiratory dyspnea results in negative intrathoracic pressure, which may pull the stomach into the thorax. Bulldogs with severe manifestations of brachycephalic syndrome appear to be at increased risk for hiatal hernia.
- Reversible hiatal hernia and megaesophagus may be seen as a complication of tetanus in dogs.
- Congenital idiopathic megaesophagus predisposes to GEI, presumably due to decreased esophageal motility and decreased gastroesophageal sphincter pressure.

Clinical Signs

Small hiatal hernias or intussusceptions may not be associated with clinical signs unless complicated by reflux esophagitis. If the hernia or intussusception occurs intermittently, clinical signs also may be intermittent. Common signs include vomiting, regurgitation, hypersalivation, and weight loss. Dyspnea also is common and may be due to aspiration pneumonia or compression of the lungs secondary to large hernias.

Hiatal Hernia

Signs are due primarily to impaired gastroesophageal sphincter function, which predisposes to gastroesophageal reflux, reflux esophagitis, and segmental or diffuse esophageal hypomotility. Dogs and cats with asymptomatic hiatal hernia may become symptomatic after general anesthesia, when impaired gastroesophageal sphincter function predisposes to reflux esophagitis and esophageal stricture formation. If large portions of the stomach are displaced through the diaphragm, signs occur because of esophageal and gastric obstruction.

Gastroesophageal Intussusception

GEI can cause both esophagitis and esophageal obstruction. When a large portion of the stomach is intussusceipted, rapid clinical deterioration is evidenced by signs of dyspnea, hematemesis, profound depression, collapse, and sudden death.

Diagnosis

Shar-Pei dogs and brachycephalic breeds are predisposed to hiatal hernia, and GEI occurs most frequently in young male dogs. Regurgitation prior to the onset of GEI suggests that megaesophagus may be a predisposing factor. When GEI causes esophageal obstruction, the acuteness of onset and rapid progression to death often preclude an antemortem diagnosis.

Physical Examination

Findings often are unremarkable unless a large hernia or intussusception is causing esophageal obstruction. In this situation, dyspnea, collapse, and shock predominate. Evaluate for evidence of concurrent upper airway obstruction, which may worsen the hiatal hernia.

Radiography

Survey thoracic radiography can usually identify both hiatal hernia and GEI if they are large and persistently present. A soft tissue and gas density mass (the stomach) can be seen in the caudal dorsal mediastinum. The normal gastric gas bubble usually seen in the cranial abdomen may be diminished in size.

- Perform a barium esophagram to confirm a hernia or GEI and to distinguish masses arising from other mediastinal structures or the esophagus. With a hiatal hernia, the gastroesophageal junction and gastric rugae are visible cranial to the diaphragm but the linear relationship between the esophagus and the stomach is preserved. Gastroesophageal reflux also may be demonstrated. With GEI, gastric rugae are seen within the esophageal lumen and esophageal obstruction is present.
- Hiatal hernias and GEI that are small and reduce spontaneously are a diagnostic challenge. Because of their intermittent nature, they may not be identified routinely on either survey or contrast radiographs. Fluoroscopy is helpful to detect intermittent hiatal hernias and gastroesophageal reflux.

Endoscopy

Endoscopy can assess secondary reflux esophagitis and may confirm hiatal hernia or GEI.

- In hiatal hernia, findings include enlargement of the hiatal opening, cranial displacement and dilatation of the gastroesophageal sphincter, rugal folds of the stomach extending through the hiatus into the thoracic esophageal region as viewed from the esophageal and gastric retroflex positions, and evidence of reflux esophagitis.
- In GEI, the rugal folds of the invaginated stomach form a bulging mass in the lumen of the caudal thoracic esophagus.

Treatment

- Surgery is indicated for treatment of large hiatal hernias and intussusceptions (see Chapter 66). Emergency surgery is required for reduction of a large GEI, along with intensive fluid therapy for treatment of shock (see Chapter 3).
- Small intermittent hiatal hernias do not usually require surgery. Medical management of reflux esophagitis (see earlier in this chapter) and a low-fat canned or liquid diet fed 3 to 5 times per day (to minimize gastric volume and incidence of gastroesophageal reflux) usually controls clinical signs. In refractory cases, consider other causes of regurgitation and vomiting before surgical intervention.
- Surgical correction of upper airway obstruction (laryngeal disease, brachycephalic syndrome) may resolve clinical signs and radiographic detection of hiatal hernia in some patients, and it should be considered before performing surgical hernia repair.

PERIESOPHAGEAL OBSTRUCTION

Etiology

- Mass lesions arising from the periesophageal tissues may cause signs of esophageal disease, because esophageal compression leads to partial or complete obstruction.
- Examples include thyroid tumors (cervical esophagus), mediastinal tumors (e.g., lymph node, thymus, and heart base), lung tumors, and intrathoracic abscesses.

Clinical Signs

- Clinical signs associated with external compression of the esophagus by mass lesions (especially neoplasia) include chronic progressive regurgitation, dysphagia, and hypersalivation.
- Signs of esophageal disease may be overshadowed by signs reflecting involvement of other systems (e.g., pulmonary metastases and pleural and pericardial effusion), such as dyspnea, cough, and exercise intolerance.

Diagnosis

Radiography

- Survey thoracic radiographs usually identify an intrathoracic mass.
- If survey films are unremarkable, a barium esophagram is indicated to identify the location and severity of obstruction.

Endoscopy

Endoscopy determines the extent of esophageal obstruction and helps characterize whether it is extramural or intramural. A stenotic region with normal-appearing mucosa is indicative of extramural compression by a periesophageal mass rather than stricture or primary neoplasia of the esophagus.

Biopsy

The diagnosis depends on identifying the cause of the offending mass lesion with fine-needle aspiration or biopsy via thoracotomy.

Treatment

Treatment and prognosis are determined by the underlying cause of esophageal compression.

ESOPHAGEAL NEOPLASIA

Etiology

Primary esophageal neoplasms are rare. Malignant tumors of the esophagus include squamous cell carcinoma, osteosarcoma, fibrosarcoma, and undifferentiated carcinoma. Metastatic tumors occasionally involve the esophagus, but unless the tumor is large, clinical signs of esophageal disease are absent.

- Esophageal fibrosarcoma and osteosarcoma in dogs can develop after malignant transformation of esophageal granulomas associated with infection by the helminth parasite *S. lupi*. This parasite occurs in the southeastern United States. The life cycle involves a coprophagous beetle that is eaten by the dog or by a transport host (mouse, chicken, bird, reptiles) that is subsequently eaten by the dog.
- Squamous cell carcinoma is the most commonly reported esophageal tumor in cats.
- The most common benign esophageal tumor is leiomyoma.

Clinical Signs

- Animals with esophageal neoplasia have signs of chronic regurgitation, dysphagia, and ptyalism that are slowly but relentlessly progressive.
- Anorexia, weight loss, and cachexia result from inability to retain food or are secondary to the systemic effects of advanced neoplasia and metastasis.
- Signs associated with *S. lupi* infection are often subclinical until late in the disease and include anorexia, lethargy, regurgitation, and dyspnea (with large masses).

Diagnosis

Chronic progressive signs of obstructive esophageal disease in an older animal suggest esophageal neoplasia.

Physical Examination

- Findings may include weight loss and emaciation consistent with the secondary effects of chronic malnutrition.
- Cervical esophageal tumors may be palpable.
- Dyspnea may occur with a large intrathoracic mass or pulmonary metastatic disease.

Radiography

Survey thoracic radiographs may be normal or may reveal a mass in the region of the esophagus. With partial to complete esophageal obstruction, the esophagus may be dilated proximal to the mass and contain air, fluid, or food.

- Evaluate the lungs for metastases.
- Spondylitis of the caudal thoracic vertebrae or hypertrophic osteopathy may be associated with *S. lupi* esophageal granulomas.
- A barium esophagram can confirm the presence of a mass or obstruction, characterize the mass as esophageal or periesophageal in origin, and evaluate the extent of esophageal wall involvement.

Endoscopy and Biopsy

Endoscopy and biopsy are required for definitive diagnosis of esophageal neoplasia.

- If esophageal sarcoma is caused by *S. lupi* infection, adult worms may be seen protruding into the lumen of the esophagus from the affected tissue. *S. lupi* eggs may be detected on fecal sedimentation.
- Squamous cell carcinoma usually appears as a proliferative mass with an irregular, friable, ulcerated surface and causing variable obstruction of the lumen.
- Obstruction may cause the esophagus to be dilated with ingesta or fluid proximal to the tumor site.

Treatment

Successful treatment of esophageal neoplasia requires surgical resection of the tumor (see Chapter 66).

- For best results, it is important to make an early diagnosis before metastasis or extensive esophageal involvement has occurred. In many cases, the tumor is too extensive for complete surgical resection, and thus the prognosis is poor.
- Anthelmintic therapy for *S. lupi* infection includes the following:
  - Doramectin (Dectomax, Pfizer), which reportedly cured six dogs of spirocercosis, at 200 µg/kg SC at 14-day intervals for three doses or at 500 µg/kg PO daily for 6 weeks in refractory cases.
  - Although unproved, fenbendazole (50 mg/kg PO) or ivermectin (200 µg/kg, single oral dose) may be effective against larvae.
- Levamisole is not recommended because it sterilizes but does not kill adult *S. lupi* organisms.

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Chapter 66

Surgery of the Esophagus

Ronald M. Bright

In general, the signs of esophageal disease are related to loss of function, to obstruction, or to inflammation of the esophagus and the surrounding structures. Surgery on the esophagus probably requires more skill and precision than any other portion of the alimentary tract. The esophagus is constantly moving, lacks a serosal layer, and does not have omentum to help seal small leaks. If suture line reinforcement is necessary, adjacent muscle, diaphragmatic tissue, or pericardium may be used. Extra-abdominal movement of omentum on a pedicle through a rent in the diaphragm can also be used for this purpose.

ANATOMY

Upper Esophageal Sphincter

The upper esophageal sphincter is located at the proximal end of the esophagus. There is no obvious thickening of the esophageal tissue.

- Sphincter function is performed primarily by the cricopharyngeal muscle.
- Innervation of the cricopharyngeal muscle is from branches of the glossopharyngeal and vagus nerves.
- The blood supply is derived primarily from branches of the cranial thyroid artery.

Lower Esophageal Sphincter

The distal 2 cm of the esophagus is located intra-abdominally below the diaphragm and is thought to have a slightly thickened inner circular muscle that acts as a sphincter.

- Sling fibers from the lesser curvature of the stomach may reinforce the sphincteric function.
- The pinchcock effect of the diaphragmatic hiatus is thought to assist in preventing gastroesophageal reflux.
- Innervation is primarily from the vagus.
- The major portion of the blood supply is derived from the esophageal branch of the left gastric artery.

Body of the Esophagus

- The esophagus has a cervical and thoracic portion.
- The esophagus has four layers—adventitia, muscularis (striated in the dog, smooth muscle in the caudal one-third of the cat), a thin submucosal layer, and mucosa composed of stratified squamous epithelium.
- The blood supply is from the thyroid and esophageal branches of the carotid artery proximally; the bronchoesophageal artery supplies the thoracic and distal portion of the esophagus. A few branches from the left gastric artery are located just above and below the lower esophageal sphincter.

CRICOPHARYNGEAL ACHALASIA

- This rare form of dysphagia is characterized by inadequate relaxation of the cricopharyngeal muscle and affects primarily young animals.
- This condition has recently been determined to be an inherited condition in golden retrievers.

Preoperative Considerations

As described in Chapter 4, perform barium swallow fluoroscopy preoperatively to distinguish cricopharyngeal achalasia from other forms of oropharyngeal dysphagia and to evaluate motility of the body of the esophagus. Evaluate for aspiration pneumonia and treat accordingly.

Surgical Procedure (Cricopharyngeal Myectomy)

Objectives

- Surgically relieve the constriction by removing fibers of the cricopharyngeal muscle.
- Allow unobstructed movement of food from the pharynx to the esophagus while decreasing the incidence of aspiration pneumonia.

Equipment

- Standard surgical pack
- Gelpi or Weitlaner retractors
- Surgical suction and cautery

Technique

1. Place the animal in dorsal recumbency with the legs tied caudally.
2. Aseptically prepare the ventral portion of the neck, from the angle of the mandible to the manubrium.
3. Make a ventral midline cervical incision, starting just cranial to the larynx and extending caudally 15 to 20 cm.
4. Separate the sternohyoideus muscles to expose the trachea and cricothyroideus muscles.
5. Expose the dorsum of the trachea by rotating the larynx and trachea 180 degrees in either direction. If working on the dog's right side, pull the trachea to the right.
6. Remove a thin layer of connective tissue, exposing the dorsal aspect of the cricopharyngeal musculature.
7. Incise the cricopharyngeal musculature on its midline. Gently elevate the muscle from the underlying esophagus with meticulous and careful blunt dissection. Consider placing an inflated Foley catheter or endotracheal tube in the esophagus to help delineate the structures.
8. Elevate the cricopharyngeal muscle laterally and then cranially to the thyropharyngeal muscles.
9. Cut the halves of the muscle belly along their lateral attachments and remove the muscle (Fig. 66-1).
10. Allow the larynx and trachea to return to their normal position, and appose the sternohyoideus muscle with a continuous suture, using 4-0 synthetic absorbable suture.

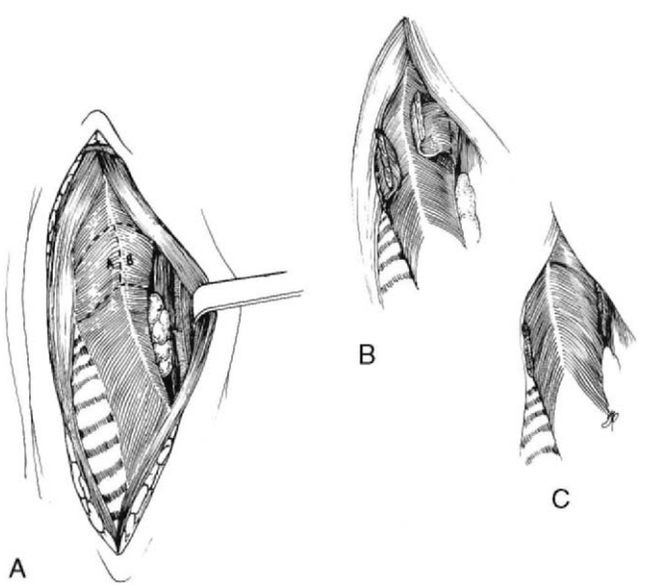

Figure 66-1. Myotomy of the cricopharyngeus muscle for cricopharyngeal achalasia. The cranial esophagus has been exposed via a ventral midline cervical approach. *A,* Rotate the esophagus so that the dorsal aspect is exposed and the cricopharyngeal muscles are seen. *B,* Initially incise on the midline (raphe) to separate the paired muscles. Use care not to perforate the esophagus. *C,* Make two longitudinal incisions laterally, one in each muscle belly, in the cricopharyngeal muscles. Remove each section of muscle.

Postoperative Care and Complications

Short-Term

- Give blenderized food for 48 hours.
- Slowly return to normal diet over the next 48 to 72 hours.
- If *oral phase dysphagia* is present (see Chapter 65), there may not be any improvement seen following surgery.
- If *pharyngeal phase dysphagia* is present (see Chapter 65) concurrently, a cricopharyngeal myectomy may worsen the animal's signs and the aspiration pneumonia.
- Hypomotility of the proximal esophagus may interfere with a successful outcome. Food and liquids pass more easily through the cricopharyngeal sphincter, but decreased clearance by the esophagus enhances the likelihood of stasis and retrograde movement of material into the trachea. Aspiration pneumonia continues to be a problem.

Long-Term

- If nutritional needs are aspiration pneumonia problems are not aggressively treated prior to surgery for cricopharyngeal achalasia, the failure rate is high. Careful section of patients for surgery of this condition is mandatory.

Prognosis

- If there is no concurrent oropharyngeal or esophageal neuromuscular disorder, the prognosis is fair to good.

VASCULAR RING ANOMALY

Preoperative Considerations

- Any young dog or cat with regurgitation should be suspected of having a vascular ring anomaly.
- Most animals with a vascular ring anomaly are presented to the veterinarian at the age of 4 to 10 weeks. Rarely, an animal may reach adulthood before a vascular ring anomaly is diagnosed.
- Persistent right aortic arch (PRAA) accounts for 95% of vascular ring anomalies in dogs.
- Rule out other causes of megaesophagus (see Chapter 65).
- Confirm the diagnosis by contrast esophagography and endoscopy of the esophagus.
- Fluoroscopy can evaluate motility of the esophagus above and below the site of constriction.
- Evaluate the lungs radiographically for aspiration pneumonia. If necessary, institute antibiotic therapy several days preoperatively.

- Debilitated animals may benefit from hyperalimentation via a gastrostomy tube (see Chapter 3) for 7 to 10 days before surgery.

Surgical Procedure

Objectives

- Relieve the constricted portion of the esophagus caused by the vascular ring.
- Allow unobstructed passage of food to the stomach.
- Avoid perforation of the esophagus.

Equipment

- Finochietto rib retractors
- Suction and cautery
- Right-angle forceps
- DeBakey thumb forceps
- Foley catheter or balloon dilator

Technique

1. Place the animal in right lateral recumbency.
2. Aseptically prepare the left lateral thoracic wall from three intercostal spaces above to five spaces below the fourth intercostal space.
3. To approach the vascular ring, perform a thoracotomy through the fourth intercostal space (see Chapter 167 for thoracotomy technique).
4. Identify the ligamentum arteriosus, which is a constricting band encircling the esophagus. In a PRAA, the aorta is on the animal's right side and cannot be seen through a left thoracotomy (see Fig. 85-1).
5. If a PRAA is not the problem, consider vascular anomaly variations, including a left subclavian artery originating from the brachiocephalic trunk and, less commonly, a double aortic arch.
6. Double-ligate (e.g., with 3-0 or 4-0 silk) and divide the constricting vessel.
7. Gently dissect the mediastinum and adventitia away from the esophagus 1 to 2 cm above and below the constricted portion. Dissect any restricting bands of tissue away from the esophagus.

▼ ***Key Point*** The esophageal wall usually is very thin; use great care to avoid perforation during dissection.

8. Pass a large Foley catheter or balloon dilator into the esophagus per os to further expand the esophagus at the site of constriction.

Closure

1. Administer a long-acting local anesthetic agent (e.g., mepivacaine) caudal to the head of the rib above and below the thoracotomy incision.
2. Place a chest tube before closure.
3. Close the thoracotomy incision routinely (see Chapter 167).

Postoperative Care and Complications

Short-Term

- Evacuate the pleural cavity and administer mepivacaine through the indwelling chest tube to control pain as necessary postoperatively. The chest tube usually can be removed within 24 hours.
- Regurgitation may continue to be a problem early in the postoperative period. Feeding blenderized food with the animal in a standing position may be necessary because of concurrent esophageal hypomotility.

Long-Term

- Amelioration of signs followed by a return of regurgitation several weeks after surgery may signal extraluminal scar formation acting as a constricting band.
- Repeated endoscopic balloon dilatation (see Chapter 65) of these strictures sometimes ameliorates signs.
- An esophagoplasty or resection of the stenotic segment may be necessary.

Prognosis

- The prognosis is good in most animals. Animals with severe dilatation of the esophagus cranial to the obstruction have a poor prognosis.
- Although not well documented, it is believed that the younger the patient at the time of surgical correction, the better the prognosis.
- The prognosis is thought to be better in animals in which preoperative fluoroscopy shows
  - Normal or near-normal motility of the esophagus above and below the constriction.
  - Absence of severe esophageal dilatation cranial to the obstruction.

ESOPHAGOTOMY

The most common indication for an esophagotomy is to remove a foreign body that could not be removed by intraluminal retrieval methods.

Preoperative Considerations

- Place a large-bore tube in the esophagus just before an esophagotomy to aspirate esophageal contents, act as a support while incising into the lumen of the esophagus, and help immobilize the esophagus.
- Treat concurrent aspiration pneumonia aggressively before and after esophagotomy.
- Although surgery of the esophagus carries a low risk of postoperative infection, some contamination occurs. Perioperative antibiotics are recommended (given 30 minutes before surgery and repeated once or twice). The antibiotic chosen should be effective against gram-positive pathogens (e.g., a cephalosporin).

Surgical Procedure

Objectives

- Gain access to the lumen of the esophagus to assist in the removal of a foreign body.
- Make the incision over healthy esophageal tissue.
- Handle esophageal tissues gently to preserve blood supply and optimize healing.
- Establish a watertight seal with closure.

Equipment

- Standard general surgery pack and suction unit
- Laparotomy pads to isolate the esophagus and prevent contamination of the surrounding tissues
- Fine-tipped needle holders to assist in delicate placement of sutures during closure
- Long-handled Metzenbaum scissors for thoracic esophagus dissection
- DeBakey thumb forceps

Technique (Cervical)

1. Make a ventral midline cervical incision extending from the manubrium to the larynx.
2. Retract the trachea and carotid sheaths gently to the right side.
3. Isolate the esophagus from surrounding structures with moistened laparotomy pads.
4. Following the insertion of a large-bore orogastric tube, make an incision into the esophagus.

Closure

1. A two-layer closure is preferred:
   a. The first layer incorporates the submucosa and mucosa; use 3-0 or 4-0 monofilament nonabsorbable sutures with the knots tied in the lumen.
   b. The second layer incorporates the muscle and adventitia. Use an absorbable synthetic suture for this layer.
2. Alternatively, close both layers with a single interrupted appositional suture pattern. Place sutures 2 to 3 mm deep and at intervals of 2 to 3 mm.
3. Irrigate the surgical field with a copious amount of sterile saline.
4. If infection is present or tissue trauma excessive, use a closed drainage system with silicone tubing, for 3 to 5 days.

Technique (Cranial Thoracic)

1. To approach the cranial thoracic esophagus (T2–T6), perform a right-sided third or fourth intercostal space thoracotomy.
2. Retract the cranial and middle lung lobes caudally with moistened sponges.
3. If necessary, dissect the azygos vein free and ligate.
4. Dissect the mediastinal pleura overlapping the esophagus to just above and below the proposed site of esophagotomy.

▼ ***Key Point*** Avoid trauma to the vagal nerve trunks located laterally along the esophagus.

Technique (Caudal Thoracic)

1. Perform a right-sided seventh or eighth intercostal space thoracotomy to gain exposure to the caudal one-half of the thoracic esophagus.

Closure

1. Closure of an esophagotomy incision is similar to that described under Cervical Technique.
2. Place a chest tube before thoracotomy closure.

Postoperative Care and Complications

- Remove the chest tube 24 to 48 hours postoperatively unless esophageal perforation and mediastinitis were present.
- Withhold all food and water (NPO) and give intravenous fluid therapy for at least 48 hours.
- If esophageal tissue was devitalized or compromised at the time of esophagotomy, it may be necessary to maintain the NPO period for several weeks.
- Ideally, use a gastrostomy tube for nutritional support during the NPO period (see Chapter 3).
- For the next 5 to 7 days, feed a blenderized diet. Gradually return to a normal diet by postoperative day 10.
- If infection was present at the time of esophagotomy, submit a tissue sample for culture and sensitivity testing and initiate appropriate antimicrobial therapy.

Prognosis

- The prognosis is good if the tissue was viable at the time of esophagotomy.
- If perforation has already occurred and infection is present, the prognosis is poor.

ESOPHAGEAL RESECTION AND ANASTOMOSIS

Indications for resection and anastomosis include foreign bodies, esophageal strictures, neoplasia, and granulomas.

Preoperative Considerations

▼ ***Key Point*** Some type of nutritional support (e.g., via gastrostomy tube) for patients undergoing an esophageal resection and anastomosis should always be part of the preoperative treatment strategy.

- If the site of anastomosis is unhealthy or compromised, a reinforcement or grafting technique may be necessary.
- Many patients requiring esophageal resection are dehydrated and malnourished and may have aspiration pneumonia. Ideally, correct these conditions before resection and anastomosis.

Surgical Procedure

Approaches to the various parts of the esophagus are described under Esophagotomy. Closure following anastomosis and resection is described here.

Objectives

- Resect the lesion and reappose the esophagus under minimal tension.
- Restore esophageal continuity while minimizing the risk of early postoperative leakage or later stricture formation.

Equipment

- Similar to that for esophagotomy plus intestinal non-crushing forceps

Technique—Closure

1. A two-layer closure, using a simple interrupted appositional suture pattern, is preferred (Fig. 66-2).
   a. Use non-crushing forceps (or fingers) to occlude esophageal ends during closure.
   b. Use multiple stay sutures to maintain alignment of the tissues.
2. Close the contralateral adventitial and muscular layers, using 3-0 or 4-0 synthetic non-absorbable sutures.
3. Appose the contralateral mucosal-submucosal layers with 3-0 or 4-0 monofilament non-absorbable sutures with the knot tied in the lumen; follow with closure of the ipsilateral mucosa-submucosa.
4. Close the ipsilateral superficial layers as in Step 2.
5. To relieve excessive tension across the suture line:
   a. A circular myotomy (including only the outer muscular layer) adjacent to the anastomosis can be performed. Injecting saline between the muscle layers helps to identify the outer layer.
   b. Mobilizing the stomach cranially through an enlarged hiatal opening can also help to reduce tension across the suture line.
6. If necessary, reinforce the sutures by bringing omentum on a pedicle through a small rent in the diaphragm or by using pericardial tissue or intercostal musculature.
7. Place a chest tube before thoracotomy closure.

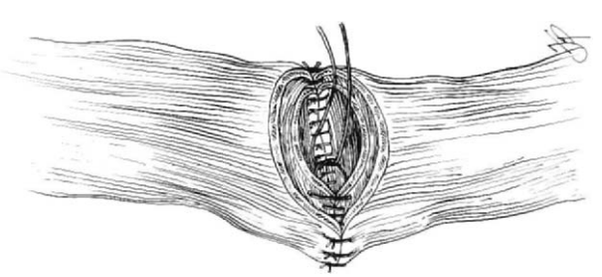

Figure 66-2. Esophageal resection and anastomosis. Close the esophageal layers in the following order: far wall, seromuscular layer; far wall, mucosal layer (knots in the lumen); near wall, mucosal layer (knots in the lumen); near wall, seromuscular layer.

Postoperative Care and Complications

Short-Term

▼ ***Key Point*** Bypass the esophageal anastomotic site and provide nutrition via gastrostomy tube for a minimum of 7 days.

- Monitor closely for fever, which often signals an infection secondary to leakage.
- Allow water consumption and return to oral feeding beginning on day 7. Retain the gastrostomy tube until normal food and water intake can be restored.

Long-Term

- Dysphagia or regurgitation occurring 3 to 6 weeks postoperatively probably indicates a stricture.
- Bougienage or balloon dilatation may be necessary to relieve the postoperative stricture (see Chapter 65 for discussion of esophageal stricture).

Prognosis

- Esophageal surgery of any kind carries a poorer prognosis than surgery on any other portion of the alimentary tract.
- If the anastomosis is done with precision and the tension across the suture line is minimal, fair to good results can be expected.
- Any compromise of the tissue at the anastomotic site carries a guarded to poor prognosis.

ESOPHAGOTRACHEAL/ESOPHAGOBRONCHIAL FISTULAS

Preoperative Considerations

- These fistulas usually are sequelae to a chronic foreign body.
- Most affected animals are high-risk patients because of severe bronchopneumonia.
- It may be necessary to sacrifice a lung lobe to achieve a cure.
- The use of gas anesthesia may cause the stomach to become overinflated if the endotracheal tube is located cranial to the fistula.

Surgical Procedure

Objectives

- Isolate the esophagus and the trachea or bronchus associated with the fistula.
- Close the abnormal communication between the alimentary and respiratory tracts.

Equipment

- General surgical pack
- Laparotomy pads
- Finochietto retractors
- TA stapler (U.S. Surgical Corporation, Norwalk, CT) (optional for lung lobectomy)
- Chest tube

Technique

1. If a lobectomy is contemplated, the approach is through the sixth or seventh intercostal space.
2. Isolate the esophagus and trachea or affected bronchus and dissect around the fistula. Obtain samples for culture and sensitivity testing.
3. Sever the fistula near its respiratory attachment; debride the opening and close using 3-0 or 4-0 non-absorbable sutures.
4. If necessary, enlarge the opening to the esophagus to remove the foreign body if it is still present. The wound is then debrided and the esophageal defect closed in two layers as described previously under Esophagotomy.
5. Remove the affected lung if it is irreversibly damaged.
6. Place a chest tube before the thoracotomy closure.

Postoperative Care and Complications

Short-Term

- Treat concurrent pneumonia, emphysema, or septicemia aggressively, and administer a broad-spectrum antibiotic pending culture and sensitivity testing results.
- If empyema is present, consider leaving the chest tube in for an extended period of time for ongoing evacuation of fluid from the pleural space (see Chapter 3).
- Maintain enteral feeding for an extended period of time via a tube gastrostomy to decrease the likelihood of leakage from the esophageal wound and allow healing of the esophagus.

Long-Term

- Stricture is always a potential sequela to esophageal surgery.

Prognosis

- In most cases, pulmonary involvement is significant, and the mortality rate is high.
- If the degree of pulmonary involvement and esophageal trauma is minimal, the prognosis is better.

ESOPHAGEAL DIVERTICULECTOMY

Preoperative Considerations

- Perioperative antibiotics are necessary to decrease the potentially deleterious effects of bacterial leakage.
- If regurgitation is severe, dehydration may occur; correct with fluid therapy before surgery.

Surgical Procedure

Objectives

- Resect the large diverticula and reconstruct the esophageal wall.
- Remove the primary cause of the diverticulum, including strictures or periesophageal adhesions.

Equipment

- General surgical pack
- Finochietto rib retractors
- Chest tube
- Non-crushing intestinal or vascular clamp

Technique

1. A left eighth intercostal space thoracotomy is used to approach most diverticula because of their epiphrenic location (just cranial to the diaphragm).
2. Isolate the diverticulum by blunt dissection down to its base.
3. Place a non-crushing clamp across the base of the diverticulum.
4. Excise the diverticulum below the clamp and close the esophagus in an open two-layer technique as described previously under Esophagotomy.
5. Place a chest tube before thoracotomy closure.

Postoperative Care and Complications

Short-Term

- Dietary restrictions are the same as those used following esophagotomy. A gastrostomy tube usually is not necessary.
- Monitor for elevated temperature and neutrophilia closely, because these suggest esophageal dehiscence and mediastinitis.
- Before discharge, perform contrast esophagography to evaluate esophageal motility.

Long-Term

- Stricture formation may be a sequela to extensive excision of the esophagus.
- Special dietary management may be necessary for the life of the animal if motility dysfunction remains.

Prognosis

- The prognosis is good if the underlying cause can be corrected.

ESOPHAGEAL STRICTURE REPAIR

Preoperative Considerations

▼ ***Key Point*** Attempt surgical correction of esophageal stricture only after bougienage or balloon dilatation (as described in Chapter 65) is unsuccessful.

- Cervical strictures carry less risk with surgical correction than do those involving the thoracic esophagus.
- Correction of fluid and electrolyte imbalances is imperative before any surgical procedure.

Surgical Procedure

Objectives

- Increase the size of the esophageal lumen by reconstructive procedures or resection.
- Resection of a lesion greater than 3 cm in length may require an esophageal lengthening procedure or a suture line reinforcement technique.

Equipment

- Standard general surgery pack
- Cervical location—Gelpi retractors; thoracic location—Finochietto retractors
- Chest tube (thoracic repair)
- Intestinal non-crushing clamps

Technique—Esophagoplasty

If the stricture is not too wide, a longitudinal full-thickness incision followed by a transverse closure (two-layer) may be adequate to increase lumen size. This is similar to Heineke-Mikulicz pyloroplasty (see Chapter 68).

Patch-Grafting Technique in Cervical Region

1. Resect a partial circumference stricture, leaving a defect.
2. Separate a belly of one of the paired sternohyoideus or sternocephalicus muscles from its attachment to the other belly and reflect it laterally.
3. Transpose the muscle to lie deeply against the esophageal defect. Suture the muscle to the edges of the defect. Be sure that the muscle fills the entire defect.
4. The muscle graft must be mobile enough and of sufficient width to prevent postoperative stricture.

Resection and Anastomosis

This is described previously under Esophageal Resection and Anastomosis.

Postoperative Care and Complications

Short-Term

- Monitor signs of infection that may suggest leakage from the surgical site; the more extensive the resection, the more likely that signs of early leakage will occur.
- Placement of a gastrostomy tube is probably necessary in most cases to prevent leakage and enhance esophageal healing.

Long-Term

- Stricture is likely to recur.
- Lifelong tube gastrostomy to bypass the stricture may be necessary if surgery fails and if the owner is willing to maintain nutrition by this method.

Prognosis

- The more extensive the surgery, the poorer the prognosis.
- Less aggressive procedures (e.g., esophagoplasty) carry a better prognosis.

HIATAL HERNIA

Preoperative Considerations

▼ ***Key Point*** The radiographic presence of a hiatal hernia does not by itself indicate the need for surgical repair.

- The reflux esophagitis that results from hiatal hernia can be managed successfully in most cases with medical therapy alone (see Chapter 65).
- Sphincter reinforcement procedures (e.g., fundoplication) probably are not indicated in most cases of hiatal hernia, because incompetence of the lower esophageal sphincter is seldom a factor in dogs and cats (in contrast to humans).
- Treat gastroesophageal intussusception using similar surgical techniques as described next.

Surgical Procedure

Objectives

- Restore the anatomic relationship of the stomach, diaphragm, and distal esophagus.
- Decrease the size of the enlarged hiatus.
- "Fix" the distal esophagus and stomach to structures below the diaphragm.

Equipment

- General surgery pack
- Abdominal self-retaining retractors
- 28-French orogastric tube
- Malleable (ribbon) retractors

Technique

1. Place the animal in dorsal recumbency with the forelimbs gently drawn forward.
2. Aseptically prepare the ventral midline from the mid-sternum to 2 to 3 cm cranial to the pubis.
3. Pass a 28-French orogastric tube into the stomach per os.
4. Incise the skin and underlying tissues from just below the xiphoid to several centimeters caudal to the umbilicus.
5. Cover the left side of the liver with a saline-soaked laparotomy pad and retract the liver to the right and caudally with a wide malleable retractor.
6. Evaluate the esophageal hiatus for size. Gently dissect the surrounding tissue to expose the margins of the hiatus. Identify and protect the vagus nerves.
7. While an assistant places caudal traction on the stomach, plicate the hiatus with 1-0 or 2-0 non-absorbable sutures (Fig. 66-3).
8. When plication is completed, it should be possible to insert two fingers through the hiatus.

Figure 66-3. Hiatal plication for hiatal hernia. Place the stomach in its normal position and put slight caudal traction on the stomach to expose the distal esophagus and esophageal hiatus. Plicate the esophageal hiatus with non-absorbable sutures, then perform an esophagopexy by placing sutures from the diaphragm to the esophageal wall, being careful not to penetrate the lumen and not to injure the vagus nerves. Perform a pexy of the fundus to the interior body wall *(insets)*. Incise the seromuscular layer of the fundus and then incise the peritoneum and underlying muscle adjacent to the fundic incision. Suture the stomach wall to the body wall as shown.

9. Perform esophagopexy by placing 2-0 non-absorbable sutures between the diaphragm and the lateral aspect of the distal esophagus as it passes through the hiatus; incorporate the muscle layers of the esophagus (see Fig. 66-3).
10. Fix the fundus of the stomach to the left abdominal wall by performing an incisional gastropexy.
11. Make an incision 3 to 4 cm long through the serosa and muscular layers of the stomach. Make a similar incision in the peritoneum and transversalis musculature (see Fig. 66-3).
12. Appose the margins of the two surgical wounds, using six to eight size 1-0 non-absorbable sutures.

Postoperative Care and Complications

Short-Term

- Feed a gruel diet for 3 to 5 days. A return to a normal ration usually is possible thereafter.
- Some animals may need to be fed from an elevated position for an indefinite period of time.
- If severe esophagitis was present before surgery, continue medical therapy for reflux esophagitis (see Chapter 65) with a systemic antacid postoperatively.
  - Omeprazole (0.7 mg/kg PO once daily) is the preferred antacid. Ranitidine (2–4 mg/kg PO q8–12h) or cimetidine (5 mg/kg PO q8h) can be substituted.
  - Administer metoclopramide (0.2–0.4 mg/kg PO q8h) or cisapride (0.5–0.7 mg/kg PO q8h) to most patients for 2 to 3 weeks postoperatively.
- Some dysphagia is common for several days following surgery. However, unrelenting dysphagia suggests that the hiatus has been narrowed too much. Reoperation is necessary in those cases that do not respond to medical therapy and when there are signs of dysphagia beyond 1 week.

Long-Term

- Perform esophagography if signs of regurgitation continue in spite of surgery and follow-up medical therapy.
- If failure of the "pexy" procedure or if incompetence of the lower esophageal sphincter is suspected, surgical intervention is necessary.
  - If a sphincter-reinforcement procedure is indicated, perform the Nissen fundoplication (Fig. 66-4).

Prognosis

- The prognosis is good if aspiration pneumonia is controlled.
- Chronic reflux esophagitis associated with a hiatal hernia may cause various degrees of esophageal stricture. If the pathology is advanced to this degree, the prognosis is poor.

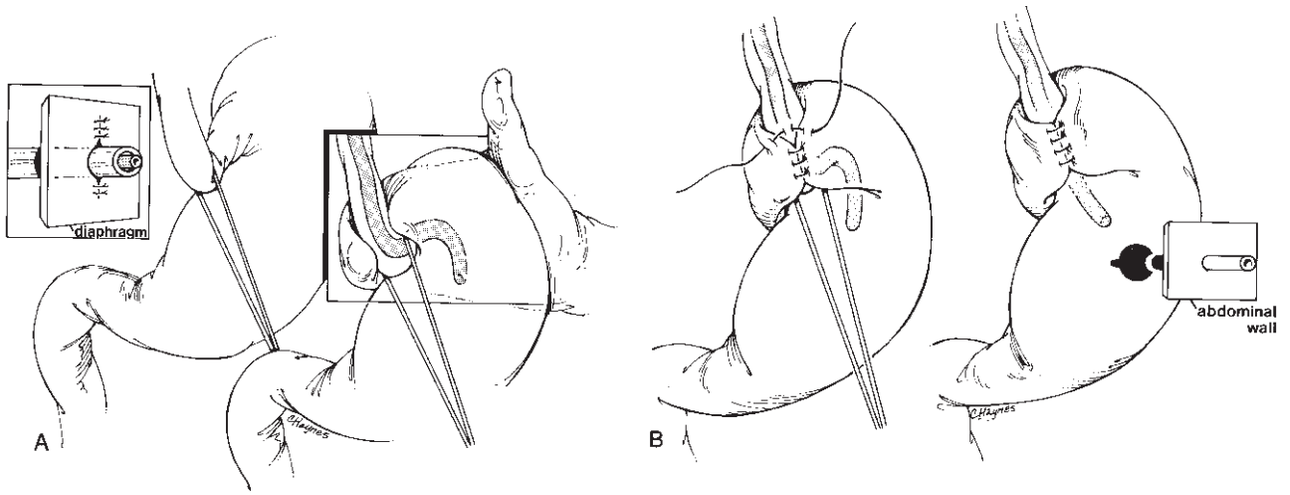

Figure 66-4. Surgical treatment of hiatal hernia. *A,* Place traction on the distal esophagus and wrap the fundus around the esophagus. *B,* Plicate the fundus around the distal esophagus and place a tube gastrostomy.

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Chapter 67

Diseases of the Stomach

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VOMITING

Vomiting is a common clinical sign associated with many gastrointestinal (GI) and non-gastrointestinal (non-GI) disorders of dogs and cats. Vomiting is a central nervous system reflex that is integrated in the vomiting center of the brain stem. Afferent stimuli can originate from the cerebral cortex, chemoreceptor trigger zone, pharynx, peritoneum, or abdominal viscera. Vomiting must be differentiated from regurgitation, which is the passive expulsion of undigested food indicating a pharyngeal (swallowing) or esophageal disorder (see Chapter 65).

The metabolic consequences of vomiting vary, depending on the volume and composition of the expulsed fluid. Mild vomiting of short duration usually is not accompanied by overt fluid, electrolyte, or acid-base imbalances. Frequent or profuse vomiting can cause metabolic complications such as dehydration; electrolyte imbalances such as hypokalemia, hyponatremia, and hypochloremia; and acid-base imbalances such as metabolic acidosis or metabolic alkalosis. Metabolic alkalosis is most likely to occur in dogs and cats with vomiting secondary to pyloric obstruction. Other potential complications of vomiting include aspiration pneumonia and reflux esophagitis.

Etiology

Vomiting is a clinical sign, rather than a diagnosis, and can be associated with numerous GI and non-GI disorders (Table 67-1).

▼ ***Key Point*** Remember that non-GI disorders commonly cause vomiting; do not overlook these before evaluating for primary GI causes of vomiting.

Clinical Signs

- Vomiting frequently is preceded by nausea (evidenced by hypersalivation, licking of the lips, repeated swallowing), retching, and abdominal contractions.
- Vomitus consists of stomach and duodenal contents such as food, mucus, and foamy or bile-stained fluid with a neutral or acidic pH.
- The term *hematemesis* is used when vomitus contains blood flecks, blood clots, or brown coffee grounds–like material (digested blood).
- Vomitus may contain hair, plant material, or other ingested foreign material that can irritate the stomach.
- Vomiting of undigested or partially digested food more than 12 hours after eating suggests delayed gastric emptying (functional or mechanical).
- Projectile vomiting (the forceful ejection of vomitus from the mouth that may be expelled a considerable distance) usually indicates gastric outlet or upper small bowel obstruction.
- Other clinical signs may be present depending on the underlying cause of vomiting and the presence of complications such as dehydration or electrolyte and acid-base imbalances.

Diagnosis

The diagnostic approach to vomiting is directed toward identifying the underlying disorder (see Table 67-1) and is influenced by whether vomiting is acute or chronic and by the associated historical and physical findings.

Acute Vomiting

Acute vomiting is a common problem in dogs and cats and may be caused by benign, self-limiting disorders such as acute gastritis or serious life-threatening diseases such as acute pancreatitis, intestinal obstruction, or acute renal or hepatic failure (see Table 67-1).

- Extensive diagnostic testing is not necessarily warranted in every dog or cat with acute vomiting, because nonspecific, self-limiting acute gastritis is a common cause of acute vomiting.
- Base the decision to perform further testing in an acutely vomiting dog or cat on historical and physical findings.
  - Further evaluation is usually warranted at initial presentation if abnormal physical findings are detected, such as fever, lethargy, depression,

Table 67-1. CAUSES OF VOMITING IN DOGS AND CATS

Acute Vomiting (<1 wk)	Chronic Vomiting (>1–2 wk)
Gastrointestinal Disorders	*Gastrointestinal Disorders*
Diet-related	Diet-related
Sudden diet change	Food intolerance
Food intolerance or allergy	Food allergy
Dietary indiscretion (e.g., garbage)	Chronic gastritis
Acute gastritis or enteritis	Lymphocytic-plasmacytic
Ingested bacterial enterotoxins	Eosinophilic
Foreign bodies (e.g., bones, plants, plastic, rocks, hairballs)	Granulomatous (e.g., pythiosis)
Ingested chemical irritants or toxins	Foreign bodies (including hairballs)
Drug-induced (e.g., aspirin and other NSAIDs, glucocorticoids, antineoplastics, erythromycin)	Parasites (*Ollulanus*, *Physaloptera*)
Viral enteritis (e.g., canine parvovirus, feline panleukopenia, canine distemper)	Reflux gastritis
Bacterial infection (e.g., *Helicobacter* spp.)	Hypertrophic gastropathy
Parasites (e.g., *Physaloptera*)	Gastrointestinal ulceration
Gastric or intestinal obstruction	Gastric neoplasia
Foreign bodies	Gastric outflow obstruction
Intestinal volvulus	Foreign bodies
Intestinal intussusception	Gastric neoplasia
Gastric dilatation-volvulus	Gastric polyps
Nongastrointestinal Disorders	Hypertrophic gastropathy
Acute pancreatitis	Pyloric stenosis
Acute renal failure	Chronic gastritis
Acute hepatic failure	Granuloma (pythiosis)
Ketoacidotic diabetes mellitus	External compression
Pyometra	Partial gastric dilatation-volvulus
Prostatitis	Gastric motility disorder
Peritonitis	Hiatal hernia
Drug-induced (e.g., cardiac glycosides, narcotics, antineoplastics)	Diaphragmatic hernia
Sepsis	Chronic colitis
CNS disorders (inflammation, edema)	Obstipation
Motion sickness	Partial distal intestinal obstruction
Vestibular disease	*Nongastrointestinal Disorders*
	Renal failure
	Hepatic disease
	Hypoadrenocorticism
	Hyperthyroidism (feline)
	Chronic pancreatitis (feline)
	Heartworm (feline)
	CNS disorders (e.g., inflammatory, neoplastic, visceral epilepsy)
	Lead toxicity
	Sialadenosis

CNS, central nervous system; NSAIDs, nonsteroidal anti-inflammatory drugs.

weakness, dehydration, or palpable abdominal abnormalities.
  - A history of possible GI foreign body exposure may warrant abdominal radiographs even if the physical examination is normal.
- If the history and physical examination are unremarkable, further diagnostic evaluation may be postponed and symptomatic therapy may be given on an outpatient basis.
- If vomiting does not resolve in 2 to 3 days or if additional clinical signs develop, further evaluation is indicated.

Chronic Vomiting

Chronic or persistent vomiting is always an indication for further workup.

History

Perform a complete history. Determine the past medical and deworming history, vaccination status, diet, and any recent exposure to medications, toxins, plants, string or other foreign bodies, garbage, or other sick animals.

Characterize vomiting as to duration, frequency, progression, relationship to eating, and other specific features (e.g., presence of hematemesis, foreign material, or partially digested food). Determine if there are other associated clinical signs.

- Is the appetite decreased or increased?
- Has there been weight loss?
- Has there been a change in attitude (depression)?
- Has there been any diarrhea?
- Is polyuria or polydipsia present?
- Is there a history of cough or dyspnea?

Physical Examination

Perform a complete physical examination. However, physical findings are often unremarkable in animals with gastric disorders.

- Perform a complete oropharyngeal examination to detect a sublingual string foreign body (especially in cats).
- Palpate the GI tract for masses, foreign bodies, trichobezoars, thickenings, distention, plication, or pain.
- Evaluate for evidence of non-GI causes of vomiting (e.g., lumpy, enlarged, or small kidneys with renal failure; cranial abdominal pain and fever with pancreatitis; icterus or hepatomegaly with liver failure; or palpable thyroid nodule with feline hyperthyroidism).
- Perform a digital rectal examination to evaluate the character of the feces (e.g., presence of melena, foreign material, blood, and mucus) and to obtain a sample for fecal evaluation.
- Evaluate for systemic effects or complications of vomiting (e.g., dehydration, weakness, and cachexia).
- Findings that suggest potentially serious underlying disease include hematemesis, weakness, severe depression, anorexia, abdominal mass, fever, abdominal pain, abdominal distention, dehydration, and shock.

Laboratory Evaluation

When further diagnostic testing is indicated, a stepwise strategy is recommended.

- Perform routine hematology, biochemistries (including serum amylase and lipase in dogs; serum pancreatic lipase immunoreactivity [PLI] in dogs and cats), urinalysis, survey abdominal radiographs, and miscellaneous ancillary tests, such as serum thyroxine (T_4) in cats greater than 6 years of age, feline leukemia virus (FeLV) antigen test, and feline immunodeficiency virus (FIV) antibody test, as indicated by the history and physical examination. These evaluations are necessary to rule out non-GI disorders that cause vomiting before evaluating for primary GI disorders with contrast radiology, endoscopy, or exploratory laparotomy.
- Routine blood tests are also helpful to detect and characterize metabolic complications of vomiting such as dehydration and electrolyte imbalances.
- Perform a fecal flotation test to diagnose GI parasitism, especially if vomiting is accompanied by diarrhea.
- Evaluate cats for heartworm disease in endemic areas, since vomiting is a frequent presenting sign in cats.
- Perform a fecal occult blood test to detect occult GI bleeding when blood loss is suspected but overt melena is absent.

Radiography

Perform routine ventrodorsal and lateral abdominal radiographs to identify radiopaque foreign bodies, gastric or intestinal obstruction, and abdominal masses or abnormalities of the kidneys, liver, and pancreas.

- Perform barium contrast radiography to evaluate for GI causes of vomiting such as radiolucent foreign bodies, obstruction, and mural thickening or irregularity. Use barium administered by stomach tube as recommended in Chapter 4.
- Barium mixed with food may be better than liquid barium to detect gastric retention disorders.
- Double air-barium contrast gastrography is also useful.
- Use aqueous iodide contrast (iohexol; Omnipaque, Amersham Health) rather than barium if perforation is suspected.
- Barium-impregnated plastic spheres (BIPS) are an alternative to liquid barium for evaluating gastric emptying and GI transit times.

Ultrasonography

Perform abdominal ultrasonography to evaluate for non-GI disorders associated with vomiting that are suspected based on initial blood test results (e.g., pancreatitis and hepatic or renal disease). Ultrasonography may also be helpful to evaluate for primary GI disorders such as intussusception, GI masses, and gastric outflow obstruction.

Endoscopy

Endoscopy of the stomach and proximal duodenum is a non-invasive technique for evaluation of primary upper GI disorders associated with vomiting. Endoscopy is used to visually examine the GI lumen, obtain biopsies, remove foreign bodies, and collect intraluminal juices.

- Endoscopy requires general anesthesia and a flexible fiberoptic endoscope. Appropriate endoscopes for use in evaluating the GI tract of dogs and cats are 100 to 150 cm long with a 7.5- to 9.4-mm-diameter shaft, 2.0- to 2.8-mm biopsy channel, four-way angulation of the tip, and flush and suction capabilities.
- Routinely evaluate the esophagus, stomach, pylorus, and proximal duodenum. Perform mucosal biopsies in all cases because abnormal histologic findings may be present despite a normal gross appearance.

Exploratory Laparotomy

- Exploratory laparotomy is sometimes indicated for diagnosis or treatment of primary GI disorders, especially when endoscopy is not available.
- Obtain full-thickness gastric and intestinal biopsies (see Chapters 68 and 70).

Treatment

Treatment strategies in the vomiting animal are directed toward the following:

- Correction of the underlying cause of vomiting, whenever possible.
- Symptomatic and supportive therapy of vomiting and its metabolic complications.
- Surgery is indicated to remove large gastric foreign bodies, excise localized tumors and deep ulcers, and correct gastric outflow obstruction.

Fluid Therapy

- Give fluids parenterally because vomiting usually precludes adequate oral intake of fluid. Subcutaneous fluid administration can be used to treat mild dehydration in the absence of other systemic signs, but IV fluid therapy is preferred for animals with moderate to severe dehydration. Daily fluid therapy requirements in the vomiting dog or cat depend on the degree of dehydration, ongoing fluid losses, and maintenance needs (see Chapter 5).
- Ideally, base the choice of replacement fluid on serum electrolyte concentrations and blood gas analysis, because the electrolyte and acid-base changes that occur secondary to vomiting may vary considerably. In the absence of such information, use a balanced electrolyte solution such as lactated Ringer's solution,

Plasma-Lyte 148, or 0.9% saline. Additional potassium supplementation (see Chapter 5) usually is necessary because hypokalemia is a common complication of vomiting.
- If metabolic acidosis is present, use an alkalinizing solution such as lactated Ringer's solution or Plasma-Lyte 148. Sodium bicarbonate administration is necessary only in the treatment of severe metabolic acidosis (pH < 7.1–7.2) (see Chapter 5).
- Hypochloremic metabolic alkalosis is most likely to occur with pyloric obstruction. Give 0.9% saline supplemented with potassium chloride.
- For a comprehensive discussion of fluid therapy, refer to Chapter 5.

Dietary Management of Acute Vomiting

- Restrict oral intake of food to minimize vomiting and further fluid loss. Withhold food for at least 12 to 24 hours.
- If vomiting resolves, offer a bland, digestible, moderately fat-restricted diet such as chicken and rice, low-fat cottage cheese and rice, or a commercially available veterinary diet that meets these requirements.
- After 2 to 3 days on the bland diet, gradually reintroduce the animal's routine diet over a period of 2 to 3 days.

Antiemetics

Antiemetics are used for symptomatic control of acute vomiting on a short-term basis or to control profuse vomiting that results in fluid, electrolyte, or acid-base disturbances.

Phenothiazines

Phenothiazine derivatives are broad-spectrum, central-acting antiemetics that inhibit the chemoreceptor trigger zone (CRTZ) at low doses and depress the vomiting center at higher doses. Phenothiazines, especially chlorpromazine (0.5 mg/kg SC, IM, or IV q6–8h), and prochlorperazine (0.5 mg/kg SC, IM, or IV q6–8h) are the most widely used antiemetics.

- Hypotension, a potentially serious side effect, is caused by alpha-adrenergic receptor blockade. Consequently, use phenothiazines cautiously in patients with preexisting dehydration.
- Sedation may occur because of concurrent tranquilizing properties.
- Phenothiazine derivatives decrease the seizure threshold and should not be used in animals with seizure disorders.
- Phenothiazine derivatives are the most effective central-acting antiemetic in cats, regardless of the underlying cause.

Metoclopramide

Metoclopramide (Reglan, Robins) (0.2–0.4 mg/kg PO, IM, or SC q8h or 1–2 mg/kg q24h as a constant-rate IV infusion) possesses both central and peripheral antiemetic properties. Central effects are attributed to antidopaminergic activity at the CRTZ and at higher doses, antagonism of 5-hydroxytryptamine type 3 (5-HT_3) serotonergic receptors. The peripheral antiemetic effect is due to its stimulant effect on GI motility.

- Metoclopramide promotes gastric emptying by increasing the tone and amplitude of gastric contractions and relaxation of the pylorus (Fig. 67-1). Because gastric relaxation and retroperistalsis are key events preceding vomiting, their inhibition may account in part for the drug's peripheral antiemetic effect.
- Metoclopramide is indicated for broad-spectrum antiemetic therapy. It is frequently used to prevent chemotherapy-induced nausea and vomiting.
- It is indicated for control of vomiting associated with parvoviral gastroenteritis because this disorder may be complicated by delayed gastric emptying.
- Metoclopramide may not be as useful a central-acting antiemetic in cats as in dogs because D_2 dopamine receptors are less important in mediating vomiting in cats.
- Metoclopramide should not be used in animals with seizures or those receiving phenothiazines, butyrophenones, narcotics, or anticholinergic drugs.
- Decrease the dose in renal failure.

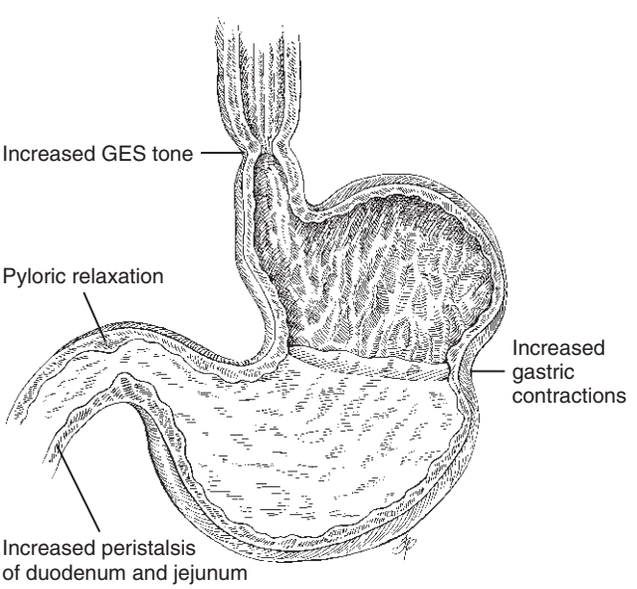

Figure 67-1. Effects of promotility agents such as cisapride and metoclopramide on the gastrointestinal tract. Promotility drugs increase gastroesophageal sphincter (GES) tone and promote gastric emptying by coordinating increased gastric contractions with pyloric relaxation and increased intestinal peristalsis.

Serotonin Antagonists

Ondansetron (Zofran, GlaxoSmithKline) (0.1–0.2 mg/kg SC q8h, 0.5 mg/kg IV loading dose, and 0.5 mg/kg IV infusion q1h or 0.5–1.0 mg/kg PO q6–12h) and dolasetron (Anzemet, Aventis Pharmaceuticals) 0.6 mg/kg q24h (prevention of nausea and vomiting) or 1 mg/kg q24h (control of vomiting) represent a relatively new class of antiemetics known as 5-HT_3 serotonergic receptor antagonists. The site of antiemetic action is the CRTZ and vagal afferent neurons in the intestinal tract.

- They are especially effective for control of chemotherapy-induced vomiting in dogs and cats but are also useful to control vomiting associated with parvoviral enteritis and acute pancreatitis.
- Because they are expensive, ondansetron or dolasetron are not used as first-choice general antiemetics.
- Side effects in dogs include sedation, lip licking, and head shaking.

Butorphanol

Butorphanol (Torbutrol, Fort Dodge), an opiate receptor antagonist, has antiemetic activity presumed to be due to decreased sensitivity of the vomiting center to chemical stimuli. It is effective in controlling vomiting in dogs treated with chemotherapy (especially Cisplatin) at a dose of 0.4 mg/kg IM.

- The only side effect is mild sedation.
- Concurrent analgesic effects may make it a good choice as an antiemetic in dogs with acute pancreatitis.
- Butorphanol can be given as a constant-rate IV infusion (0.1 mg/kg/hr) for control of vomiting in dogs.
- Antiemetic efficacy in cats is unknown.

Anticholinergic Drugs

Avoid the use of anticholinergic drugs such as isopropamide, atropine, and aminopentamide (Centrine, Fort Dodge) for routine symptomatic control of vomiting.

- Although anticholinergics may decrease peripheral afferent stimulation of the vomiting center by relieving GI smooth muscle spasms or inhibiting intestinal secretions, their side effects include xerostomia, mydriasis, tachycardia, urinary retention, ileus, and gastric retention.
- Because delayed gastric emptying caused by anticholinergics can in itself cause vomiting, these drugs should not be used any longer than 3 days in a vomiting patient.

ACUTE GASTRITIS

Acute gastritis is a common disease in dogs and cats. It is usually a mild, self-limiting condition that rarely warrants biopsy confirmation. Clinical diagnosis of acute gastritis often is made when acute vomiting occurs without apparent cause and resolves on its own in 24 to 48 hours.

Etiology

There are numerous potential etiologies of acute gastritis (see Table 67-1), but the cause often is not determined. Possible causes include the following:

- *Dietary indiscretion* is frequently associated with acute gastritis and vomiting. Gastritis is most likely due to ingestion of rancid or spoiled foods that contain fermentation byproducts, bacterial enterotoxins, or mycotoxins.
- *Foreign body ingestion* (e.g., rocks, aluminum foil, small toys, food wrappings, or plastic) can cause mechanical irritation of the gastric mucosa.
- *Ingested plant material* including grass and house plants is a common cause of acute gastritis.
- *Chemical irritants or toxins* (e.g., fertilizers, herbicides, cleaning agents, and heavy metals such as lead) can cause gastric irritation.
- *Drugs* (e.g., aspirin, nonsteroidal anti-inflammatory drugs, and glucocorticoids) can cause acute gastritis, which is frequently accompanied by erosions and ulceration. Antibiotics and chemotherapeutic drugs can also cause acute gastritis, anorexia, and vomiting.
- *Viral infections* such as canine parvovirus, feline panleukopenia, or canine distemper can cause lesions of gastritis in addition to more diffuse intestinal and systemic involvement.
- *Bacterial infections* causing gastritis are uncommon. Gastric spiral bacteria (*Helicobacter* spp.) may play a role in gastritis in some dogs and cats, but these bacteria are also present in many clinically healthy animals.
- *Parasitic infections* of the stomach are uncommon. *Physaloptera* spp. infect dogs and cats but the infection is not consistently associated with clinical signs. *Ollulanus tricuspis* is a cause of chronic gastritis in cats.
- *Systemic disorders* such as uremia, liver disease, neurologic disease, shock, stress, and sepsis may cause secondary gastritis by altering the gastric mucosal barrier, mucosal blood flow, or gastric acidity.

Clinical Signs

- Acute onset of nausea and vomiting
- Acute anorexia, lethargy, and diarrhea (from concurrent enteritis)

Diagnosis

Because acute gastritis is usually self-limiting, diagnostic evaluations are not usually warranted unless specific historical or physical findings suggest a more serious problem. Response to supportive therapy in 1 to 3 days indirectly supports the diagnosis of uncomplicated acute gastritis as the cause of vomiting.

History

Acute vomiting in an otherwise healthy animal suggests the possibility of acute gastritis. Perform a detailed historical evaluation including recent exposure to drugs or other sick animals and the potential for dietary indiscretion.

Physical Examination

The physical examination is usually unremarkable except for dehydration in severe cases.

Treatment

Identify and treat underlying causes when possible.

Dietary Restriction

- Withhold food for 12 to 24 hours.
- Reintroduce food when vomiting has ceased for longer than 24 hours. Offer a bland, digestible, moderately fat-restricted diet such as chicken and rice, low-fat cottage cheese and rice, or a commercially available veterinary diet that meets these requirements.
- After 2 to 3 days on the bland diet, gradually reintroduce the animal's routine diet over a period of 2 to 3 days.

Maintenance of Hydration

- For oral hydration, offer ice cubes, small amounts of water, or an oral glucose and electrolyte solution such as Pedialyte (Ross). Give at frequent intervals to provide daily maintenance requirements.
- Parenteral fluid therapy is indicated to treat dehydration (see the previous discussion of fluid therapy in the vomiting patient and refer to Chapter 5).

Medical Therapy

- Consider using antiemetics for short-term symptomatic control of vomiting (see the previous section on antiemetics) and acid control therapy (see the later section, "Gastroduodenal Ulceration").
- If vomiting does not resolve in 1 to 3 days, pursue further diagnostic evaluation (see under "Vomiting").

GASTRIC FOREIGN BODIES

Gastric foreign bodies are most common in dogs owing to their dietary habits and indiscriminant chewing behavior.

Etiology

Gastric foreign bodies cause clinical signs because of mechanical irritation (e.g., acute or chronic gastritis) or gastric outflow obstruction.

- Gastric foreign bodies frequently seen in dogs include needles, coins, stones, sticks, peach pits, plastic, aluminum foil, cloth, rubber balls, and small toys.
- String and other linear foreign bodies are more likely in cats.

Clinical Signs

Most dogs and cats with a gastric foreign body are presented for acute onset of vomiting. However, if the foreign body goes undiagnosed initially, chronic vomiting may be the primary complaint. Additional clinical signs may be seen if systemic absorption of a toxic component occurs. For example:

- Zinc-induced hemolytic anemia has been described secondary to ingestion of zinc-containing nuts and bolts or pennies minted in 1983 or later.
- Lead-containing foreign bodies may be associated with significant lead absorption and toxicity.
- Neurologic signs due to absorption of aluminum also have been described.

Diagnosis

Consider gastric foreign bodies in all animals with acute vomiting and a history of chewing on foreign objects.

Physical Examination

This is often unremarkable except when gastric foreign bodies are very large and palpable.

Radiography

Abdominal radiographs can identify radiopaque objects (e.g., coins, needles, and other metal objects), radiodense objects, and evidence of gastric outflow obstruction (gas-, fluid-, or food-distended stomach). A barium contrast gastrogram may be necessary to detect radiolucent gastric foreign bodies.

Endoscopy

Endoscopy can confirm a suspected gastric foreign body and, more important, can remove most objects noninvasively. For this reason, endoscopy often is preferable to barium-contrast radiography, unless general anesthesia is contraindicated.

Treatment

When a gastric foreign body is identified radiographically, consider whether immediate removal is necessary.

- Remove the object promptly if it is large, sharp, or potentially toxic (e.g., pennies, nuts and bolts, and lead objects) or if the animal is persistently vomiting, anorexic, or dehydrated.
- Small, non-toxic foreign bodies may pass through the GI tract uneventfully and thus can be managed conservatively if the animal is not symptomatic. Allow a

period of 7 to 10 days while periodically repeating radiographs to monitor progress. If clinical signs develop, immediate removal is recommended.
- Bones are rapidly decalcified and softened, and they do not require removal from the stomach.

Endoscopic Removal

Attempt endoscopic removal of gastric foreign bodies before gastrotomy, because most foreign bodies can be removed in this manner.

Preparation

- Fast the animal 8 to 12 hours before anesthesia to be sure that the stomach is empty, because food can obscure the endoscopic view. Correct fluid, electrolyte, and acid-base imbalances before general anesthesia.
- Repeat abdominal radiographs immediately before induction of anesthesia to confirm that the object remains in the stomach. This avoids an unnecessary procedure if the object has already entered the intestinal tract and is beyond the reach of the endoscope.

Procedure

The key to removing foreign bodies endoscopically is to get a firm grip on the object, using a grasping forceps or a basket retrieval instrument.

- Use forceps for retrieval of needles, coins, and small, soft objects. To remove the foreign body, grasp the object, pull it up near the end of the endoscope, and remove the endoscope, instrument, and foreign body as one unit.
- Use the basket for retrieval of small, round objects such as marbles or stones that cannot be grasped with the forceps. Large smooth objects are also removed with a basket, but they can be especially difficult to maneuver back through the gastroesophageal sphincter (or upper esophageal sphincter).
- Use an overtube (a plastic tube that fits over the shaft of the endoscope and can be advanced over the end of the endoscope) to protect the esophageal mucosa when sharp or pointed objects are withdrawn. An overtube is also useful to assist removal of objects through the gastroesophageal sphincter by maintaining sphincter dilatation.
- After removing the foreign body, perform a thorough examination of the stomach to look for other objects or mucosal lesions. This should be done even if only one object is seen radiographically, because radiolucent objects may not have been detected or multiple objects may have previously adhered to each other, appearing as one. If food obscures the endoscopic view, reposition the animal in the alternate lateral position or in the ventral dorsal position.

Gastrotomy

If endoscopic equipment is unavailable or the object cannot be retrieved endoscopically, gastrotomy is indicated (see Chapter 68).

Postoperative Care and Complications

- Food and water can be given orally 12 to 24 hours after foreign body removal.
- If mucosal injury is severe, treat as for gastric ulcer (see the next section).

GASTRODUODENAL ULCERATION

For the purposes of this discussion, gastroduodenal ulceration is defined as mucosal defects associated with bleeding, which includes petechiae, erosions, and ulcers. Clinical recognition of gastroduodenal ulceration as a complicating factor in many disorders is becoming more common, most likely due to the increased use of endoscopy.

Etiology

Many disorders have been associated with gastroduodenal ulceration (Table 67-2). Ulceration is more likely when two or more risk factors are present. General mechanisms of gastroduodenal ulceration include direct damage to the gastric mucosal barrier, increased gastric acid secretion, delayed gastric epithelial renewal, and decreased gastric mucosal blood flow.

Nonsteroidal Anti-Inflammatory Drugs

Nonsteroidal anti-inflammatory drugs (NSAIDs) (see Table 67-2) are frequent causes of gastric ulceration. These drugs inhibit prostaglandin synthesis, which decreases mucosal blood flow and alters gastric mucus production, thus predisposing to ulceration. Dogs are more susceptible to the ulcerogenic effects of NSAIDs than are humans.

- Both gastric hemorrhage and large perforating ulcers may occur. A predilection for ulceration of the pyloroantral region has been recognized.
- Ulceration is most likely to occur when NSAIDs are given to animals with other risk factors (see Table 67-2).
- Newer NSAIDs that preferentially inhibit cyclooxygenase-2 (COX-2) rather than COX-1 enzymes such as carprofen (Rimadyl, Pfizer), etodolac (EtoGesic, Fort Dodge), deracoxib (Deramaxx, Novartis), meloxicam (Metacam, Merial), and tepoxalin (Zubrin, Schering-Plough) are much less likely to cause GI bleeding. However, they should not be used in the presence of ulcers or inflammatory GI disease or concurrently with glucocorticoids.

Table 67-2. RISK FACTORS FOR GASTRODUODENAL ULCERATION

Drug-induced Gastrointestinal Damage
Nonsteroidal anti-inflammatory drugs
Aspirin
Carprofen*
Deracoxib*
Etodolac*
Flunixin
Ibuprofen
Indomethacin
Ketoprofen
Meloxicam*
Naproxen
Phenylbutazone
Piroxicam
Tepoxalin*
Glucocorticoid drugs
Infiltrative Disease
Gastric neoplasia
Lymphoma
Adenocarcinoma
Leiomyoma; leiomyosarcoma
Eosinophilic gastroenteritis
Lymphocytic plasmacytic gastroenteritis
Gastric pythiosis
Systemic Disorders
Liver disease
Renal failure
Mast cell tumor
Spinal cord disease
Hypoadrenocorticism
Gastrinoma (Zollinger-Ellison syndrome)
Lead poisoning
Cyclic hematopoiesis (gray collies)
Stress conditions
Severe illness
Major surgery
Hypotension and shock
Trauma
Intensive exercise (racing sled dogs)

*COX-2 selective NSAIDs are less likely to cause gastrointestinal hemorrhage and ulceration.

Glucocorticoids

Glucocorticoid therapy has been associated with gastric erosions and bleeding but usually only when combined with other risk factors for ulceration such as NSAIDs or in dogs with spinal cord disease (see Table 67-2). Dexamethasone, especially at high doses, is more likely to cause GI bleeding than is prednisolone.

Chronic Gastritis

Various forms of chronic gastritis may be complicated by mucosal ulcerations, particularly eosinophilic gastritis, lymphocytic-plasmacytic gastritis, granulomatous gastritis, and gastric pythiosis (see the "Chronic Gastritis" section).

Hepatic Disease

Hepatic diseases of all types are commonly associated with ulceration (duodenal more commonly than gastric). Potential mechanisms include decreased mucosal blood flow secondary to portal hypertension, decreased gastric epithelial cell turnover associated with negative nitrogen balance and hypoalbuminemia, increased gastric acid secretion due to impaired degradation of a secretagogue (possibly histamine), or stimulation of gastrin release by increased serum bile acids. Coexisting coagulopathies magnify GI blood loss.

Renal Failure

Renal failure may be associated with GI hemorrhage and ulceration. Multiple factors probably contribute, including decreased mucosal blood flow due to diffuse vascular injury, gastroduodenal reflux, acidosis, and increased concentrations of gastrin with hypersecretion of gastric acid.

Neurologic Disease

Neurologic disease can predispose to GI ulceration, especially in dogs with spinal cord disease that are receiving corticosteroids. Lower GI bleeding and hematochezia appear to be more common than upper GI bleeding. Colonic perforation, septic peritonitis, and sudden death have been reported.

Gastric Neoplasia

Gastric tumors, especially lymphoma and adenocarcinoma, frequently cause mucosal ulceration and hemorrhage (see the "Gastric Neoplasia" section).

Mast Cell Tumors

Cutaneous mast cell tumors can cause GI ulceration through the release of histamine that induces gastric acid hypersecretion. Perform a thorough search for cutaneous masses in all animals with GI bleeding and ulceration to identify a predisposing mast cell tumor.

Gastrinoma

This rare gastrin-producing tumor, arising from the amine precursor uptake and decarboxylation (APUD) cells of the pancreas, causes gastric acid hypersecretion and gastroduodenal ulceration (Zollinger-Ellison syndrome).

- Suspect gastrinoma when ulceration is associated with gastric mucosal hypertrophy or when ulcers respond to medical management but relapse when therapy is discontinued and no underlying cause can be identified.
- Diagnosis is made by documenting hypergastrinemia and identifying the tumor on surgical exploration.
- Most pancreatic gastrinomas are small (<2 cm) and have metastasized to regional lymph nodes and the liver at the time of diagnosis.
- Tumor cytoreduction may be a useful palliative procedure to temporarily control clinical signs along with medical therapy to control ulceration (see "Treatment" in this section).

Stress Conditions

Severe illness, major surgery, trauma, shock, sepsis, hypotension, and exercise (in racing sled dogs) predispose to gastroduodenal bleeding and ulceration. Acutely ill, intensive-care patients are most at risk. Consider a presumptive diagnosis of gastroduodenal ulceration when vomiting or hematemesis occurs in this clinical setting.

Clinical Signs

Clinical signs of gastroduodenal ulcers include anorexia, vomiting, melena, anemia, abdominal pain, and weight loss.

- The vomitus may contain digested blood (coffee-grounds appearance) or fresh blood with clots. Overt hematemesis and melena may not be consistently observed by the owner. Weakness associated with blood loss anemia may occur.
- Ulcer perforation and septic peritonitis are suggested by acute onset of abdominal pain, depression, collapse, and shock. However, early gastroduodenal perforation may be present in animals without dramatic signs of acute abdomen.

Diagnosis

Perform a detailed history. Determine if any ulcerogenic drugs have been administered recently (see Table 67-2).

Physical Examination

- Palpate the abdomen for abdominal pain.
- Evaluate the mucous membranes for evidence of anemia.
- Perform a rectal examination to evaluate for melena.
- If hematemesis and melena are present, evaluate the skin and mucous membranes for hemorrhages, which may suggest that GI bleeding is secondary to a systemic abnormality of hemostasis.
- Perform a thorough examination for cutaneous masses that may be mast cell tumors.

Laboratory Evaluation

Complete Blood Count

Perform a complete blood count (CBC) to assess for anemia.

- Acute GI bleeding is associated with a normocytic normochromic regenerative anemia, whereas chronic blood loss is characterized by iron deficiency and microcytic hypochromic anemia (see Chapter 22).
- With peracute GI bleeding, nonregenerative anemia may be detected initially until the bone marrow has adequate time to respond (3–5 days).
- Iron deficiency is further characterized by decreased serum iron concentration and decreased percentage saturation.
- With active bleeding, anemia is accompanied by hypoproteinemia.
- Neutrophilia and left shift may be seen with severe inflammation and ulcer perforation.

Other Laboratory Tests

- Perform a biochemistry profile to identify underlying liver disease, renal failure, and hypoadrenocorticism (see Chapter 33). Decreased total protein and albumin levels are common with blood loss, but liver disease, renal disease, and malnutrition also may contribute to these changes.
- Evaluate for dehydration and electrolyte imbalances secondary to vomiting.
- Perform blood gas analysis to assess acid-base imbalances.
- Perform a urinalysis to screen for underlying systemic disorders.
- If GI blood loss is suspected and the stool is grossly normal, perform a fecal occult blood test. Perform a fecal flotation to diagnose hookworm infection as a cause of GI blood loss.
- Screen for underlying bleeding disorders with evaluations such as one-stage prothrombin time, activated partial thromboplastin time, platelet count, fibrinogen, and fibrin degradation products (FDPs) (see Chapter 23).
- Perform fine-needle aspiration (or biopsy) of any cutaneous masses to diagnose mast cell tumor.
- If gastrinoma is suspected, evaluate a fasting serum gastrin concentration and measure gastrin after a provocative secretin injection.

Radiography

- Survey abdominal radiographs usually are unremarkable unless ulcer perforation results in pneumoperitoneum or peritoneal effusion (peritonitis).
- A GI contrast study usually outlines large ulcers but is an insensitive method for detecting small ulcers and erosions. If perforation is suspected, use a water-soluble non-ionic iodide contrast agent, such as iohexol (Omnipaque, Amersham Health) rather than barium.

Abdominocentesis

If ulcer perforation is suspected, perform abdominocentesis to detect septic peritonitis. Submit a sample for bacterial culture and antibiotic sensitivity testing.

Endoscopy

Endoscopy is indicated to characterize the location and severity of upper GI bleeding and for visual confirmation of ulceration.

▼ ***Key Point*** Endoscopy is the most reliable procedure for detection of gastric mucosal ulcers and erosions and is preferred over contrast radiography, unless general anesthesia is contraindicated.

- Concurrent gastric mucosal thickening or mass lesions suggest an underlying neoplastic or inflammatory disorder.
- Perform mucosal biopsies, regardless of the gross appearance, to identify predisposing causes such as gastritis or gastric neoplasia.
- If perforation is suspected, perform exploratory laparotomy.

Laparotomy

Laparotomy can be used to diagnose and resect gastroduodenal ulcers.

- Evaluate other abdominal organs, including the kidneys and liver.
- Carefully examine the pancreas to identify gastrinoma nodules.

Treatment

The goals of management of gastroduodenal ulceration include the following:

- Eliminate or control predisposing factors (see Table 67-2).
- Correct fluid, electrolyte, and acid-base imbalances.
- Control any GI bleeding and correct resulting anemia. If the packed cell volume (PCV) is less than 15%, give a blood transfusion (see Chapters 3 and 22).
- Control gastric acid secretion (Fig. 67-2).
- Promote mucosal cytoprotection.

Agents That Control Gastric Acid Secretion

Antacids

Antacids can effectively neutralize gastric acid secretion; however, H_2 blockers or proton pump inhibitors are preferred because of their ease of administration and greater potency (Table 67-3).

H_2 Blockers

These drugs are most commonly used to control acid secretion. They inhibit basal, nocturnal, and meal-stimulated acid secretion by blocking the H_2 receptors on gastric parietal cells (see Fig. 67-2). Several H_2 blockers (e.g., cimetidine, ranitidine, famotidine, and nizatidine) are available that are equally effective but differ in potency, frequency of administration, and potential to inhibit hepatic P-450 enzymes (see Table 67-3).

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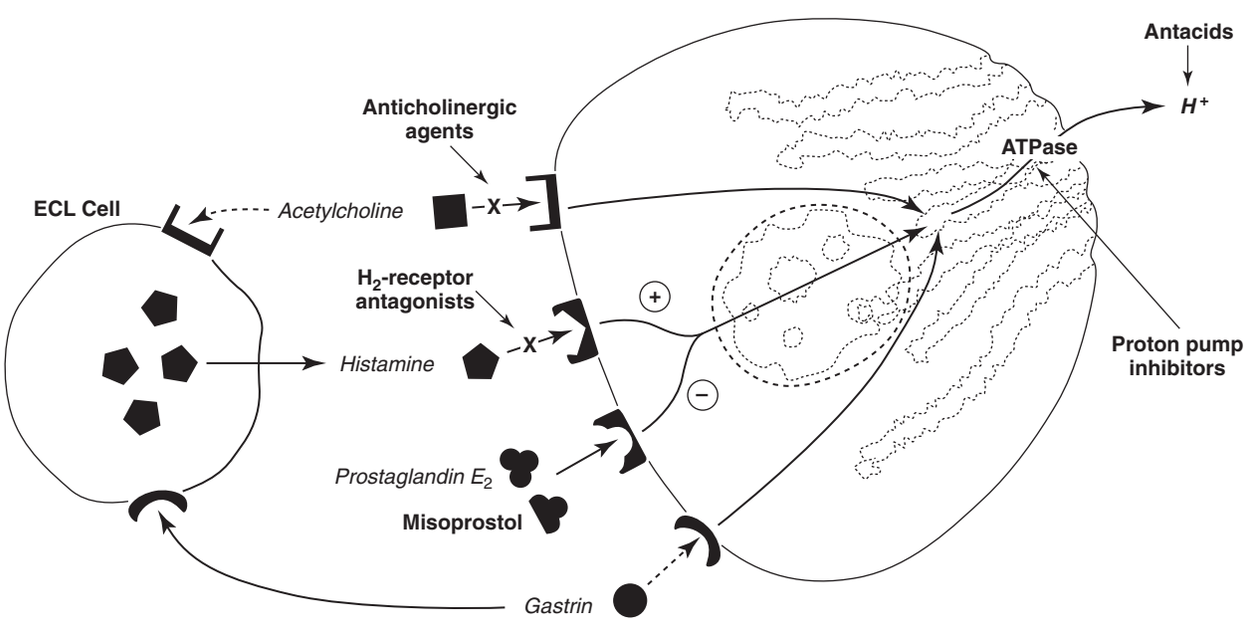

Figure 67-2. Representation of a gastric parietal cell showing the site of action of various therapeutic agents used to decrease gastric acid secretion. H_2 antagonists (blockers) competitively inhibit acid secretion stimulated by histamine, which is released from nearby enterochromaffin-like (ECL) cells by gastrin stimulation. Acetylcholine also indirectly stimulates histamine release from the ECL cells. Use of anticholinergic drugs to inhibit acid secretion is limited by systemic side effects. Prostaglandin (PGE_2) analogues, such as misoprostol, inhibit acid secretion by blocking histamine-induced cyclic adenosine monophosphate production. Proton pump inhibitors such as omeprazole and pantoprazole have broad-spectrum antisecretory activity because they interrupt the final common pathway of acid secretion by inhibiting hydrogen potassium adenosine triphosphatase. Antacids neutralize luminal gastric acid.

Table 67-3. DRUGS USED FOR TREATMENT OF GASTRIC DISEASE

	Product (Manufacturer)	Preparations	Dosage	Special Indications	Comments*
H_2 Receptor Blocker					
Cimetidine	Tagamet (GlaxoSmithKline)	Syrup: 60 mg/ml Tabs: 100 mg (OTC), 200 mg (OTC), 300 mg, 400 mg, 800 mg Injectable: 150 mg/ml	5–10 mg/kg PO or IV q6–8h	Decreases gastric acid secretion	Inhibits hepatic P-450 drug metabolizing enzymes. Decrease the dose of the following drugs if used concurrently: lidocaine, beta-blockers, calcium channel blockers, theophylline, diazepam, metronidazole, quinidine, phenytoin, warfarin. Does not decrease hepatic blood flow. Simultaneous oral administration of cimetidine and sucralfate or cimetidine and metoclopramide is acceptable if using the higher dose range for cimetidine. Separate oral administration from antacids by ≥1 hr. Decrease dosage in renal failure
Ranitidine	Zantac (GlaxoSmithKline)	Syrup: 15 mg/ml Tabs: 75 mg (OTC) 150 mg, 300 mg Injectable: 25 mg/ml	2.0 mg/kg PO or IV q8–12h (dog); 2.5 mg/kg IV q12h or 3.5 mg/kg PO q12h (cat)	Decreases gastric acid secretion. Preferred over cimetidine when concurrently administering drugs dependent on hepatic metabolism.† Less frequent administration than cimetidine. Promotes gastric emptying	4–10 times as potent as cimetidine. Minimal inhibition of hepatic P-450 enzymes. No effect on hepatic blood flow. Separate oral administration from antacids by ≥1 hr. Decrease dose in renal failure. Stimulates GI motility (stomach, small intestine, colon) by inhibiting acetylcholinesterase activity
Famotidine	Pepcid (Merck)	Liquid: 8 mg/ml Tabs: 10 mg (OTC), 20 mg, 40 mg Injectable: 10 mg/ml	0.5–1.0 mg/kg PO or IV q12–24h	Decreases gastric acid secretion. Preferred over cimetidine when concurrently administering drugs dependent on hepatic metabolism.† Once-a-day dosing convenience	20–50 times as potent as cimetidine. No inhibition of hepatic drug metabolizing enzymes and no effect on hepatic blood flow. Decrease dose in renal failure
Nizatidine	Axid (Lilly)	Tabs: 75 mg (OTC) Caps: 150 mg, 300 mg	2.5–5.0 mg/kg PO q24h	Decreases gastric acid secretion. Promotes gastric emptying. Once-a-day dosing	Similar potency as ranitidine. No effect on hepatic P-450 enzymes. Stimulates gastric emptying at antisecretory doses by inhibiting acetylcholinesterase activity, similar to ranitidine

Mucosal Protectant

Sucralfate	Carafate (Axcam Scandipharm)	Tabs: 1 g Liquid: 1 g/10 ml	1 g: large dogs, 0.5 g: small dogs, 0.25 g: cats PO q8–12h	GI erosions or ulcers; NSAID-induced gastritis; reflux esophagitis (susp)	Safe local-acting drug. Potential for nonspecific binding with impaired absorption of simultaneously administered oral drugs. No effect (in dogs) on absorption of the following drugs: digoxin, quinidine, propranolol, aminophylline, diazepam, imipramine, and chlorpromazine. Minor effect on cimetidine absorption, not clinically significant at higher doses of cimetidine (and other H_2 blockers?). Separate phenytoin, tetracycline, and fluoroquinolone antibiotics from sucralfate by ≥2 hr. Antacids interfere with sucralfate binding; give antacids ≥30 min after sucralfate. Contains aluminum—use cautiously in renal failure. Side effect: constipation
Omeprazole	Prilosec (Astra-Zeneca)	Caps: 10 mg, 20 mg, 40 mg (delayed-release with enteric coating) Tabs: 20 mg (OTC) Tabs: 20 mg, 40 mg (with enteric coating)	0.75–1.0 mg/kg PO q12–24h	Severe GI ulceration, unresponsive to H_2 blockers; severe reflux esophagitis, unresponsive to metoclopramide and H_2 blockers; gastrinoma (Zollinger-Ellison) syndrome)	Inhibits subset of hepatic P-450 drug metabolizing enzymes. Decrease the dose of concurrently administered diazepam and phenytoin but not theophylline or propranolol. 2–7 times as potent as cimetidine. No dose adjustment necessary in hepatic or renal failure. Do not administer partial tablet or capsule unless dissolved in HCO_3§
Pantoprazole	Protonix (Wyeth-Ayerst)	Injectable: 4 mg/ml	0.7–1.0 mg/kg PO or IV q24h	Same as omeprazole	Injectable alternative to omeprazole

Prostaglandin Analog

Misoprostol‡	Cytotec (Searle)	Tabs: 100 µg, 200 µg	3–5 µg/kg PO q6h	Prevention of NSAID-induced GI injury	Gastric mucosal cytoprotection at low doses, inhibits gastric acid secretion at higher doses. Side effects: diarrhea, abortion

Promotility Agent

Metoclopramide	Reglan (Robins)	Syrup: 1 mg/ml or 10 mg/ml Tabs: 5 mg, 10 mg Injectable: 5 mg/ml	0.2–0.4 mg/kg PO, IM, or SC 30 min before eating, q8h or 1–2 mg/kg/24 h given in fluids as constant-rate infusion	Central antiemetic (CRTZ) for drug-induced vomiting, parvoviral enteritis, and uremic gastritis; promotility for reflux esophagitis, functional gastric emptying disorder, recurrent gastric hairballs, reflux gastritis, gastric stasis 2° to gastric surgery, ileus	Side effects: anxiety, agitation, tremors, twitching, constipation. Contraindicated in patients with mechanical gastric outflow obstruction or epilepsy. Should not be used in combination with phenothiazines, butyrophenones, or narcotics. Atropine or other anticholinergic drugs antagonize effects of metoclopramide. When oral metoclopramide is given simultaneously with oral cimetidine, decreased cimetidine absorption occurs. Probably not clinically significant if cimetidine given at higher dosage range. Decrease dose in renal failure. Metoclopramide is physically incompatible when mixed with cephalothin sodium, sodium bicarbonate, chloramphenicol sodium succinate, or tetracycline. Light sensitivity of metoclopramide occurs in dextrose solutions after 24 hr

Table continued on following page

Table 67-3. DRUGS USED FOR TREATMENT OF GASTRIC DISEASE—cont'd

	Product (Manufacturer)	Preparations	Dosage	Special Indications	Comments*
Cisapride	Propulsid (Janssen)	Available through compounding pharmacies	0.25–0.5 mg/kg PO q8–12h (dogs); 2.5–5 mg PO q8–12h (cats)	Same promotility indications as metoclopramide but has no central antiemetic effect; has effects on motility of distal small bowel and colon; megacolon in cats, idiopathic megaesophagus in cats	5-HT_4 agonist. Decrease dose in hepatic but not renal failure. Taken off the U.S. market due to fatal arrhythmias in humans
Prucalopride	(Janssen)	Not yet approved		Delayed gastric emptying, constipation	5-HT_4 agonist similar to cisapride. Promotility effects on stomach and colon
Tegaserod	Zelnorm (Novartis)	Tabs: 2 mg, 6 mg	0.05–0.1 mg/kg PO q12h (dogs)	Ileus, pseudoobstruction, constipation	5-HT_4 agonist similar to cisapride. Promotility effects primarily on intestine and colon (not stomach)
Erythromycin	Many	Liquid: 25, 50, and 100 mg/ml Tabs: 250 mg, 333 mg, 500 mg Caps: 125 mg, 250 mg Injectable: 100 mg/ml	0.5–1.0 mg/kg PO q8h	Reflux esophagitis; delayed gastric emptying; postoperative ileus (dogs)	Increases gastroesophageal sphincter pressure. Promotes gastric emptying and small intestine transit by a motilin-like effect. Promotility effects occur at lower dose than the antimicrobial dose
Antacids					
Many available (OTC)	Maalox (Al + Mg) Quick Dissolve Maalox ($CaCO_3$) Mylanta II (Al + Mg + simethicone) Amphojel (AlOH) Tums tabs ($CaCO_3$)	Tabs and liquid	1–2 tabs or 5–10 ml PO q4–6h	Safe and inexpensive treatment of GI ulceration	Potency varies between products. Crush tablets for maximum effectiveness. Difficult to administer in animals. Potential side effects: constipation (AlOH, $CaCO_3$), diarrhea (Mg salts), hypernatremia and alkalosis ($NaHCO_3$), hypercalcemia and acid rebound ($CaCO_3$), phosphate depletion (AlOH); impaired excretion of aluminum and magnesium in renal failure; nonspecific binding of concurrently administered drugs (e.g., cimetidine, ranitidine); interference with binding of sucralfate to GI ulcers

*All drugs that decrease gastric acidity could potentially decrease absorption of orally administered drugs that are weak bases (e.g., ketoconazole), and increase absorption of durgs that are weak acids (e.g., diazepam, aspirin, furosemide).

†Examples include lidocaine, propranolol, theophylline, diazepam, phenytoin, metronidazole, and warfarin.

‡Limited experience with use in cats.

§To prepare as oral suspension, dissolve 20 mg capsule or tab in 10 ml of 8.4% HCO_3 to make a 2 mg/ml solution; good for 7 days.

CRTZ, chemoreceptor trigger zone; GI, gastrointestinal; NSAID, nonsteroidal anti-inflammatory drug; OTC, over the counter (nonprescription); susp, suspension; 5-HT_4 (serotonin) agonist.

Famotidine is typically the first choice H_2 blocker because it does not inhibit hepatic drug metabolism, it can be given once a day, and it is available in dosing formulations that are easy to use in dogs and cats. In humans, acid suppression declines during continuous use of H_2 blockers due to pharmacologic tolerance. Whether this phenomenon reduces the long-term effectiveness of H_2 blockers for acid control in dogs and cats remains to be determined.

Proton Pump Inhibitors

Omeprazole (Prilosec, AstraZeneca) is a potent inhibitor of gastric acid secretion that acts by inhibiting hydrogen-potassium adenosine triphosphatase (ATPase) (the proton pump) of the gastric parietal cell (see Fig. 67-2). This drug has broad-spectrum antisecretory activity because the proton pump is the final common pathway for HCl production, regardless of initiating stimulus. Because of its long duration of action, omeprazole can be given on a once-daily basis (see Table 67-3).

Agents That Promote Mucosal Cytoprotection

Sucralfate

Sucralfate (Carafate, Axcan Scandipharm) is an aluminum salt that selectively binds to injured gastroesophageal mucosa, forming a protective "bandage." Sucralfate neutralizes acid, inactivates pepsin, adsorbs bile acids and pancreatic enzymes, and stimulates local prostaglandins, which are cytoprotective. It is a safe drug with minimal systemic absorption.

▼ ***Key Point*** For initial treatment of gastric ulcers and erosions, combine an H_2 blocker for acid control with sucralfate for mucosal cytoprotection.

Misoprostol

Misoprostol (Cytotec, Searle) is a synthetic prostaglandin analogue that at low doses (3–5 µg/kg) is cytoprotective and at high doses (10 µg/kg) has antisecretory activity (see Fig. 67-2). The primary indication for use of misoprostol in dogs is to prevent NSAID-induced gastric injury. Side effects of misoprostol (especially at the higher dose) include diarrhea and abortion (see Table 67-3).

Antibiotic Therapy

Give systemic antibiotics when ulcer perforation is suspected or confirmed. Select the antibiotic based on results of culture and sensitivity testing of abdominal fluid or affected tissue. Give parenteral ampicillin or amoxicillin combined with enrofloxacin while awaiting culture results.

Laparotomy

Emergency exploratory laparotomy is indicated when perforation of a gastroduodenal ulcer is suspected or confirmed (see Chapter 76 for detailed description of treatment for peritonitis). Correct fluid, electrolyte, and acid-base imbalances as rapidly as possible before surgery. Treat shock as described in Chapter 156.

Prevention

- COX-2 selective NSAIDs are less likely to be associated with GI bleeding and ulceration than are nonselective NSAIDs like aspirin. Use recommended doses and monitor for occult bleeding, melena, or vomiting to detect early GI bleeding. Do not give glucocorticoids concurrently.
- A wash-out period of 7 days is recommended when switching from one NSAID to another or when discontinuing an NSAID and starting glucocorticoid therapy (or vice versa).
- Misoprostol has been shown to prevent aspirin-induced gastric injury in dogs. Omeprazole also provides some protection against the development of aspirin-induced GI damage in dogs, but cimetidine appears to be ineffective. Once NSAID-induced GI injury occurs, omeprazole is probably more effective for ulcer healing than is misoprostol.
- Use of an H_2 blocker, sucralfate, or omeprazole to prevent ulceration in dogs given glucocorticoids has not been proven to be effective but is widely recommended.
- Pretreatment with omeprazole, misoprostol, cimetidine, or sucralfate is not effective in preventing GI bleeding in dogs with spinal cord disease treated with glucocorticoids.
  - Consider the use of omeprazole or H_2 blockers, if multiple risk factors are present or if any degree of GI bleeding would be poorly tolerated by the patient.

CHRONIC GASTRITIS

Chronic gastritis is a common cause of chronic and episodic vomiting in dogs and cats. Chronic gastritis is classified based on histologic features such as type of inflammatory infiltrate and the presence of fibrosis, atrophy, or mucosal hypertrophy. The most common histologic category is lymphocytic-plasmacytic gastritis, which is a nonspecific tissue reaction to many insults.

Etiology

Regardless of the initial insult, release of inflammatory mediators and vasoactive compounds lead to disruption of the normal gastric mucosal barrier, allowing back diffusion of gastric acid and pepsin. Subsequent inflam-

mation further stimulates acid secretion, which, in turn, promotes further mucosal injury, altered cell membrane permeability, and decreased microvascular blood flow. The end result is varying degrees of gastric erosion, ulceration, hemorrhage, edema, and necrosis.

Idiopathic Chronic Gastritis

The underlying etiology of chronic gastritis is seldom determined. Possible causes include all factors capable of causing acute gastritis (see Table 67-1) in which repeated or persistent exposure occurs.

- In cats, lymphocytic-plasmacytic gastritis is often accompanied by diffuse inflammatory bowel disease (see Chapter 69).
- Gastroduodenal ulcerations may be associated with secondary lymphocytic-plasmacytic gastritis that resolves after ulcer therapy. Conversely, lymphocytic-plasmacytic gastritis may be complicated by gastric erosions and ulcerations.
- Eosinophilic gastritis is discussed later in this chapter.

Physaloptera Infection

The nematode parasite, *Physaloptera rara,* inhabits the stomach and duodenum of dogs and cats and is an infrequent cause of lymphocytic-plasmacytic gastritis and chronic intermittent vomiting. In most infections, only one to five worms are found in the stomach of the host.

- Embryonated eggs passed in the feces are ingested by an intermediate host (cockroach, cricket, or beetle) in which infected larvae develop. Infection occurs when a dog or cat ingests an intermediate or transport host (rodent or snake).
- Diagnosis of *Physaloptera* spp. is difficult. Fecal flotation using either sodium dichromate or magnesium sulfate solution is often recommended, but eggs may not be detected due to the small number of parasites, low fecundity of the female nematodes, and presence of single-sex infection. The clinical diagnosis is usually made by endoscopic detection of the adult worms attached to the stomach mucosa.

Ollulanus Infection

O. tricuspis is a nematode infection of cats associated with chronic fibrosing gastritis.

Pythium Infection

Pythium insidiosum is a fungal infection that can lead to pyogranulomatous gastritis in dogs.

Helicobacter Infection

Gastric spiral bacteria (*Helicobacter* spp.) are a common finding in apparently healthy dogs and cats without clinical signs of GI disease. *Helicobacter* spp. may play a role in chronic gastritis in some dogs and cats, but there is little information on the relationship of *Helicobacter* to gastric disease in these species.

Enterogastric Reflux

Reflux gastritis (or bilious vomiting syndrome) refers to gastric mucosal damage caused by persistent enterogastric reflux of potentially damaging constituents such as bile and pancreatic enzymes. Inappropriate pyloric relaxation predisposes to excess reflux, and impaired gastric motility contributes to delay in clearing previously refluxed material from the stomach. Reflux gastritis is a poorly documented clinical entity in dogs.

Clinical Signs

- Animals with *chronic gastritis* have intermittent vomiting, usually over a period of weeks to months. Vomiting is not consistently associated with eating. Hematemesis and melena may occur if gastritis is associated with mucosal erosions or ulcers.
- Other signs such as depression, anorexia, weight loss, and abdominal pain are present less frequently.
- Signs of *reflux gastritis* include nausea, vomiting of bile-stained fluid or foam early in the morning when the stomach is empty, and abdominal pain. Most animals are otherwise healthy and do not usually vomit any other time of day.

Diagnosis

Confirmation of chronic gastritis requires a gastric mucosal biopsy, obtained by endoscopy or laparotomy.

History and Physical Examination

Obtain a complete history, emphasizing potential exposure to ingested drugs, foreign bodies, chemicals, irritants, and unusual diets (see Table 67-1).

- Response to previous therapy (e.g., a change in diet) may indirectly suggest a dietary intolerance or allergy.
- The physical examination often is unremarkable.

Laboratory Evaluation

- A CBC, biochemical profile, and urinalysis are indicated to exclude non-GI causes of vomiting and to characterize any fluid, electrolyte, or acid-base imbalances resulting from vomiting.
- Test results usually are normal in animals with chronic gastritis unless vomiting is profuse, mucosal erosions or ulcers cause blood loss anemia, or inflammation of the antral and pyloric region results in gastric outflow obstruction.

Radiography

- Survey abdominal radiographs usually are unremarkable.

- Upper GI contrast studies may be normal or show thickening of gastric rugal folds, mucosal irregularity, mass lesions, or delayed gastric emptying. These findings are nonspecific, and gastric biopsy is required to distinguish chronic gastritis from other disorders such as gastric neoplasia.

Endoscopy

Endoscopy is used to obtain mucosal biopsies and is the diagnostic method of choice for confirming chronic gastritis.

- Endoscopically, the gastric mucosa may appear grossly normal or show thickened rugae, mucosal irregularity or friability, hemorrhage, ulceration, or firm areas of fibrosis.
- Severe chronic gastritis may have a diffuse nodular appearance that must be differentiated from gastric lymphoma.

▼ ***Key Point*** Always obtain biopsies because histologic changes in chronic gastritis may be present despite a normal endoscopic appearance.

- Carefully examine the entire gastric and proximal duodenal mucosa for adult *Physaloptera,* which appear as white, 1-cm-long nematodes that may be attached to the mucosa or living free on the mucosal surface. Often only one worm is present. Remove any worms observed by use of the grasping forceps.
- If *O. tricuspis* is suspected, aspirate gastric juice for microscopic examination for adult and larval forms.
- Gastric foreign bodies can be detected and removed.
- In patients with reflux gastritis, large amounts of bile-stained fluid may be present in the stomach and the pylorus may appear wide open.

Laparotomy

- Perform laparotomy to obtain full-thickness gastric biopsies and to correct associated gastric outflow obstruction.
- Full-thickness biopsy may be necessary to differentiate severe lymphocytic gastritis diagnosed by endoscopic biopsy from gastric lymphoma.

Treatment

Eliminate underlying causes of gastritis whenever possible.

- Discontinue implicated drugs (e.g., aspirin).
- Remove gastric foreign bodies.
- Treat *Physaloptera* infections with fenbendazole (50 mg/kg/day PO for 3 days) or pyrantel pamoate (15 mg/kg PO initially and repeat in 2–3 weeks).
- Treat *O. tricuspis* infections with fenbendazole (50 mg/kg/day PO for 3 days) or pyrantel pamoate.
- Avoid further exposure to plants, chemicals, and other irritants.
- In most cases, a specific cause of gastritis cannot be identified, and therefore specific therapy is unavailable.

Dietary Trials

Perform dietary trials in all animals with chronic gastritis because dietary factors or antigens could be the inciting cause. Continue dietary trials for at least 2 to 4 weeks before assessing response to therapy. Feed a controlled diet that is easily digestible, carbohydrate based, and moderately fat restricted. Give frequent small meals. Avoid high-fiber diets or the feeding of only one large meal per day.

- If gastritis is mild, dietary modification may be all that is required to control clinical signs.
- Commercial or homemade hypoallergenic diets (single-protein or novel-protein source) are beneficial in some cases.
- Reflux gastritis often responds to frequent feedings or feeding of a late bedtime meal. Food may be effective because it buffers refluxed duodenal contents and stimulates gastric motility. Metoclopramide also may be effective (see "Gastric Motility Disorders" and Table 67-3).

H_2 Blockers

Reduction of acid secretion with H_2 blockers (discussed previously) may be useful in animals with chronic gastritis even if gross mucosal erosions or ulcerations are absent (see Table 67-3). A 2-week trial is recommended, but long-term therapy may be required, depending on clinical response. Ranitidine and nizatidine also promote gastric emptying, which may be useful for secondary motility disorders that may accompany chronic gastritis.

Anti-inflammatory or Immunosuppressant Drugs

Prednisolone

- If no response is obtained with dietary control and H_2 blocker therapy, give prednisolone (0.5–1 mg/kg PO q12h) for a 2-week trial period.
- If remission occurs, taper this dose over a period of 6 to 8 weeks and maintain alternate-day therapy using the lowest effective dose.

Azathioprine

- Azathioprine (Imuran, Glaxo Wellcome), an immunosuppressive drug, may be useful for treatment of chronic gastritis in dogs that have not responded to prednisolone or when glucocorticoid side effects are a problem.
- The initial dose for dogs is 2 mg/kg PO q24h. The dose can be tapered after a clinical response is obtained, usually by giving the same dose on an alternate-day basis.

- Because of azathioprine's ability to suppress the bone marrow, periodically monitor the CBC to detect neutropenia and thrombocytopenia. Other potential side effects include pancreatitis and hepatotoxicity.
- Azathioprine has been recommended at a lower dose (0.3 mg/kg PO q48h) in cats. However, chlorambucil is a safer alternative (see below).

Chlorambucil

- Chlorambucil, an alkylating antineoplastic or immunosuppressive agent, can be used in cats that fail to respond to corticosteroids. The dose is 20 mg/m^2 PO once every 2 to 3 weeks (refer to Chapter 26 for conversion of body weight to body surface area in m^2).
- Side effects are uncommon but may include myoclonus, cytopenia, and hepatotoxicity.

Promotility Drugs

- Secondary motility disorders may accompany chronic gastritis. If postprandial vomiting occurs, add metoclopramide, or cisapride to the above therapy (see Table 67-3 and Fig. 67-1).

Antibacterial Drugs for Helicobacter

- Although the clinical significance of gastric spiral bacteria (*Helicobacter* spp.) in dogs and cats is unclear, treatment is justified empirically when chronic gastritis is associated with large numbers of spiral bacteria on biopsy.
- Therapy for *Helicobacter* spp. has been extrapolated from human medicine. Single antibiotics are not effective and resistance rapidly develops; thus, effective treatment usually requires "triple therapy" with a combination of three antibiotics or a combination of two antibiotics plus an acid reducer such as omeprazole or an H_2 blocker for potentiation. Antimicrobials commonly used in various combinations include clarithromycin, amoxicillin, metronidazole, tetracycline, and bismuth.
- Only a few controlled therapeutic trials have been done in dogs and cats. It appears that some of the treatment regimens effective for eradicating *Helicobacter pylori* in humans only transiently suppress *Helicobacter* in dogs and cats without eliminating the infection; thus, the optimal treatment protocol for dogs and cats is not yet known.
- The combination of clarithromycin (7.5 mg/kg PO q12h), amoxicillin (20 mg/kg PO q12h), and metronidazole (10 mg/kg PO q12h) for 14 days successfully eliminated *Helicobacter* in 100% of cats in one study and can be used to treat dogs.
- Other commonly used (but unproven) treatments for *Helicobacter* in dogs include the combinations of clarithromycin, amoxicillin, and omeprazole—or amoxicillin, metronidazole, and famotidine—given for 14 to 21 days.

Prognosis

The prognosis for chronic gastritis is variable. If the underlying cause can be identified and corrected, the prognosis for recovery is good. In animals with idiopathic chronic gastritis, long-term dietary and medical management may be required.

EOSINOPHILIC GASTRITIS AND GRANULOMA

Eosinophilic gastritis is characterized by diffuse or focal infiltration of mature eosinophils into the mucosa, submucosa, or muscularis. Variable increases in lymphocytes, plasma cells, and neutrophils may also occur.

- Eosinophilic inflammation of the stomach in dogs occurs as two distinct pathologic forms:
  - Diffuse eosinophilic infiltration of the gastric mucosa and submucosa is most common and is usually associated with generalized eosinophilic gastroenterocolitis.
  - Single or multiple eosinophilic granulomatous lesions (scirrhous eosinophilic gastritis) with transmural eosinophilic inflammation, severe arteritis, and fibrosis occur less frequently.
- In cats, eosinophilic gastritis is usually a manifestation of inflammatory bowel disease, which is similar to eosinophilic gastroenterocolitis in dogs. Rarely, eosinophilic gastroenteritis in cats is associated with hypereosinophilic syndrome (see Chapter 69).

Etiology

The cause of eosinophilic gastritis or granuloma in dogs is unknown. The presence of increased numbers of circulating and tissue eosinophils suggests an allergic or immunologic hypersensitivity, possibly in response to dietary components or parasites.

- Food allergy or hypersensitivity has been proposed but not proven as a cause of eosinophilic gastritis in dogs.
- Microfilariae have been observed on histologic sections in a dog with diffuse eosinophilic gastritis.
- Eosinophilic gastroenteritis with multiple focal eosinophilic granulomas has been described in German shepherds with visceral larva migrans but is not an important clinical cause of eosinophilic gastroenteritis.

Clinical Signs

Dogs with eosinophilic gastritis usually have signs of chronic vomiting, anorexia, and weight loss.

- Eosinophilic gastritis is more likely to be associated with mucosal ulceration and bleeding (suggested by hematemesis and melena) than are other types of chronic gastritis.

- Additional clinical signs may be present if gastritis is a component of diffuse eosinophilic gastroenterocolitis. Small intestinal involvement is characterized by malabsorption and voluminous watery diarrhea, whereas colonic or rectal involvement is characterized by bloody-mucoid diarrhea with tenesmus (see Chapter 69).

Diagnosis

Determine previous diets and clinical responses to dietary changes. A history of dramatic response to previous corticosteroid therapy is consistent with but not specific for eosinophilic gastritis.

Physical Examination

- Weight loss is common.
- Less common findings include pain on palpation of the stomach, or the stomach may feel diffusely rigid and firm. With large focal granulomas, a mass in the stomach wall may be palpated.
- Additional findings that indicate more extensive intestinal involvement include focal or diffuse thickening of the small intestine or colon or mesenteric lymphadenopathy.

Laboratory Evaluation

- A hemogram often reveals eosinophilia, but not in all cases.
- Gastric erosions and ulcerations can cause anemia and hypoproteinemia.
- Heartworm and fecal flotation tests are indicated to identify underlying parasitism.

Radiography and Ultrasonography

- Abdominal radiography is usually normal unless gastric outflow obstruction occurs secondary to transmural involvement or granuloma formation at the antral or pyloric region.
- Contrast radiography may demonstrate irregularity of the gastric mucosa or diffuse or focal thickening of the gastric wall.
- With concurrent intestinal involvement, associated radiographic changes may be identified.
- Abdominal ultrasonography may identify gastric wall thickening, masses, or enlarged mesenteric lymph nodes.

Endoscopy

- Visual endoscopic findings are nonspecific and may mimic other inflammatory and neoplastic diseases. The gross appearance may be normal in some cases.
- Involved areas of the stomach may appear diffusely thickened, with hemorrhages, erosions, or ulcers. Granulomas appear as focal mass lesions.
- Endoscopy is the preferred initial method for biopsy rather than laparotomy, unless mechanical obstruction requiring surgical decompression is present. Obtain multiple biopsies from the stomach and duodenum.
- Cytologic examination of mucosal biopsies reveals increased numbers of eosinophils.
- A disadvantage of endoscopically obtained biopsies is that the depth of the biopsy generally is limited to the mucosa, and deeper layers may be predominantly involved in eosinophilic gastritis.

Laparotomy

- Exploratory laparotomy may reveal diffuse or focal thickening in affected regions of the stomach and GI tract.
- Diffuse involvement of the stomach wall or large focal granulomas may grossly resemble neoplasia.
- Regional lymphadenopathy is common.

Treatment

The treatment of choice for eosinophilic gastritis in dogs is glucocorticoid therapy combined with dietary management.

- If a broad-spectrum anthelmintic has not been administered recently, before initiating glucocorticoids, treat with fenbendazole (Panacur, Intervet), 50 mg/kg daily for 3 days, to eliminate undetected GI parasites as a potential cause of the clinical signs.
- Treatment of eosinophilic gastritis in cats that is a manifestation of hypereosinophilic syndrome is discussed in Chapter 69. Eosinophilic gastritis or gastroenteritis in cats that is associated with focal GI involvement and resembles canine eosinophilic gastroenterocolitis can be managed as outlined next for dogs.

Anti-inflammatory and Immunosuppressant Therapy

- Administer prednisolone, 0.5 to 1 mg/kg PO q12h. Response is prompt and dramatic, usually occurring within 24 to 48 hours.
- Gradually taper the dosage over the following 6 to 8 weeks, decreasing to once daily (given in the morning) and then to alternate days. If the initial treatment period is too short, relapse may occur. If relapse does not occur while tapering the dosage, discontinue therapy at the end of the 6- to 8-week period. Continue to monitor for relapse.
- If side effects are a problem or if higher dosage or continued daily therapy is required, give azathioprine concurrently, as described previously for chronic gastritis.

Dietary Recommendations

Because food hypersensitivity is a potential cause of eosinophilic gastritis, consider a trial with a hypoallergenic diet. Some animals with eosinophilic gastritis may respond to a hypoallergenic diet alone. Institute a

dietary trial even if corticosteroids are being given, because it may decrease the dose of corticosteroids required to control clinical signs.

- Suggested hypoallergenic diets include select protein or novel protein commercial diets consisting of lamb, egg, fish, rabbit, duck, kangaroo, or venison. An alternative approach is to use a diet containing hydrolyzed proteins, which may be less antigenic (Prescription Diet z/d, Hill's, or HA Diet, Purina).
- Choose a protein and carbohydrate source that has not been a part of the animal's diet in the past 6 months.
- Feed the diet exclusively for at least 3 to 4 weeks before determining effectiveness.
- If a hypoallergenic diet is ineffective, try a controlled diet that is easily digested, carbohydrate based, and moderately fat restricted.

Surgery

Perform surgical resection of obstructing granulomas at the antral and pyloric region and follow up with glucocorticoid therapy.

Prognosis

The prognosis for eosinophilic gastritis in dogs is good. Most dogs respond to therapy and many have complete resolution of clinical signs on a long-term basis. In others, relapses occur, and a hypoallergenic diet or corticosteroid therapy is required on a long-term basis.

GASTRIC OUTFLOW OBSTRUCTION

Etiology

Gastric outflow obstruction most commonly is caused by mural, mucosal, and luminal abnormalities involving the antral and pyloric regions of the stomach (see Table 67-1). External compression of the gastric outflow tract is identified less frequently. Common causes of outflow obstruction include the following:

- Foreign bodies often lodge in the pylorus and cause partial or complete outflow obstruction.
- Chronic hypertrophic pyloric gastropathy (CHPG) is a benign disorder of middle-aged to older small-breed dogs that frequently results in outflow obstruction (see "Hypertrophic Gastropathy").
- Pyloric stenosis is hypertrophy of the circular muscle fibers of the pylorus. Congenital pyloric stenosis occurs in young dogs and cats. Acquired muscular pyloric stenosis is sometimes a component of CHPG in older animals.
- Chronic gastritis, especially eosinophilic gastritis and granuloma, that involves the antral and pyloric region can result in outflow obstruction.
- Obstructing granulomas may be a manifestation of fungal gastritis caused by pythiosis or histoplasmosis.
- Gastric ulcers at the pylorus may cause outflow obstruction.
- Gastric neoplasia, especially adenocarcinoma, can obstruct outflow (see under "Gastric Neoplasia").
- Gastric dilatation-volvulus (GDV) is a frequent cause of acute outflow obstruction and is discussed later in this chapter.
- Extrinsic outflow compression may be caused by hepatic or pancreatic inflammation, abscesses, and neoplasia; marked regional lymphadenopathy; and diaphragmatic hernia with gastric displacement.

Clinical Signs

- Vomiting is a consistent sign of gastric outflow obstruction. Typically, undigested food is present in the vomitus greater than 12 hours after eating (the stomach normally empties by 8–10 hours after eating).
- Bile staining of vomitus is usually absent.
- Projectile vomiting suggests gastric outflow obstruction.
- Complete obstruction results in severe, profuse vomiting.
- Abdominal distention caused by an enlarged fluid- or food-filled stomach may occur, especially after eating.
- Anorexia may occur because of a sense of fullness from gastric overdistention.
- Belching may indicate an attempt to release gas from the stomach.
- Weight loss and dehydration may result from chronic vomiting.

Diagnosis

History and Signalment

The history and signalment often indicate a possible underlying cause.

- Persistent vomiting since weaning in young animals suggests congenital pyloric stenosis.
- Acute onset of vomiting in young animals may indicate a foreign body.
- Chronic vomiting with hematemesis is seen with gastric neoplasia, chronic gastritis, and gastric ulcer.
- Chronic intermittent vomiting over weeks to months in middle-aged and older small-breed dogs is consistent with CHPG.
- Acute onset of non-productive retching and gagging accompanied by abdominal distention in large-breed dogs suggests GDV.

Physical Examination

The examination may be unremarkable, or potential findings can include abdominal distention and signs associated with metabolic abnormalities secondary to profuse vomiting, such as weakness and dehydration.

Laboratory Evaluation

- Laboratory findings usually are unremarkable unless profuse vomiting results in fluid, electrolyte, and acid-base disturbances such as dehydration, hypokalemia, hyponatremia, hypochloremia, or metabolic alkalosis.
- Other laboratory findings are variable and depend on the underlying cause of obstruction.

▼ ***Key Point*** Always consider gastric outflow obstruction in vomiting animals with hypochloremic metabolic alkalosis.

Radiography and Ultrasonography

Survey Abdominal Radiography

- The finding of a distended fluid-filled stomach or food present in the stomach greater than 12 hours after eating suggests delayed gastric emptying. The stomach normally empties by 8 to 10 hours after eating; however, emptying times up to 16 hours can be normal in some dogs, especially when fed dry food.
- Identification of the underlying cause of delayed gastric emptying requires further evaluation with contrast radiography, ultrasonography, endoscopy, or exploratory laparotomy.

Barium Contrast Gastrography

- A contrast gastrogram is useful to further evaluate gastric emptying. Liquid barium normally begins to leave the stomach in 5 to 15 minutes, and the stomach is usually empty within 30 to 60 minutes in cats and 1 to 2 hours in dogs.
- The presence of barium in the stomach after 12 to 24 hours confirms delayed gastric emptying.
- Contrast studies can provide important information about the cause of delayed gastric emptying. Potential findings include foreign bodies, thickening or mass lesions of the antral and pyloric region, and narrowing of the pyloric canal (the "beak" sign).

Fluoroscopy and Ultrasonography

Fluoroscopy and ultrasonography may provide information about the outflow tract including intrinsic thickening of the wall of the pyloric antrum or extrinsic compression of the antrum and pylorus by hepatic and pancreatic lesions.

Endoscopy

Endoscopy is useful to identify and remove foreign bodies and to evaluate the antral and pyloric region for outflow obstruction. Fast the patient with suspected delayed gastric emptying for at least 24 hours before endoscopy to ensure that the stomach is empty. If large volumes of fluid are still present, aspirate the fluid through the endoscope to improve visualization.

- Foreign bodies, masses, mucosal proliferations (e.g., CHPG) or thickenings, and ulcers can readily be identified at endoscopy.
- Endoscopic biopsies of affected tissues can be obtained; however, if mechanical outflow obstruction is detected, immediate surgical relief of obstruction and full-thickness biopsies are preferred.
- If the outflow area looks normal and the endoscope is readily passed through the pylorus into the duodenum, mechanical outflow obstruction is much less likely. However, extrinsic compression of the outflow region cannot be fully appreciated with endoscopy and may require an exploratory laparotomy.
- An alternative consideration when the pylorus appears normal is that delayed gastric emptying is caused by a functional motility disturbance (see under "Gastric Motility Disorders") of the stomach rather than by mechanical outflow obstruction.

Treatment

- Give appropriate fluid therapy to correct fluid, electrolyte, and acid-base disturbances before general anesthesia for surgery or endoscopy. Because metabolic imbalances are variable, base the choice of fluid composition on results of electrolyte and blood gas analysis (see the previous discussion of fluid therapy under "Vomiting").
- Metabolic alkalosis may occur secondary to outflow obstruction; manage with non-alkalinizing solutions such as 0.9% saline or Ringer's solution, supplemented with potassium chloride, as described in Chapter 5.
- Surgery is indicated for definitive treatment of gastric outflow obstruction (see Chapter 68).
- If gastric stasis persists after surgical relief of outflow obstruction, give a gastric promotility drug such as metoclopramide, cisapride, or erythromycin to improve gastric emptying (see Fig. 67-1 and Table 67-3). Promotility drugs such as these are contraindicated in the presence of mechanical outflow obstruction.

GASTRIC MOTILITY DISORDERS

Gastric motility disorders that result in weak or ineffective gastric contractions can cause delayed gastric emptying in dogs and cats. These disorders are not well documented in veterinary medicine. Currently, the diagnosis of a gastric motility disorder is presumptive and is based on clinical findings consistent with delayed gastric emptying in the absence of an obstructive lesion.

Etiology

The causes and pathophysiologic mechanisms of gastric motility disorders are poorly understood. Gastric motility is dependent on normal electrical and mechanical

activity of the stomach. Control of gastric motility and emptying is influenced by hormones, autonomic nervous input, and composition of the food. Emptying is prolonged as the fat and protein content, acidity, osmolality, and viscosity of the gastric contents increase.

The following factors may be associated with functional delays in gastric emptying:

- Drug therapy with anticholinergic drugs, adrenergic agonists, or narcotic analgesics can delay gastric emptying.
- Inflammatory lesions such as gastritis, gastric ulcers, *Physaloptera* infection, and parvoviral gastroenteritis can alter gastric motility.
- Acute abdominal inflammation caused by pancreatitis and peritonitis can alter gastric motility.
- Nervous inhibition associated with stress, trauma, pain, or psychogenic input may cause a transient delay in gastric emptying due to increased sympathetic stimulation.
- Metabolic disturbances such as hypokalemia, endotoxemia, and hypothyroidism may delay gastric emptying.
- Neurogenic causes of delayed gastric emptying include dysautonomia and vagal nerve damage.
- Dogs recovering from GDV commonly have gastric myoelectrical and motor abnormalities.
- Prolonged gastric obstruction may be complicated by secondary motility dysfunction.
- In many cases, functional gastric emptying disorders are idiopathic. These disorders may be associated with abnormal gastric electrical conduction disturbances such as tachyarrhythmias.
- Recurrent trichobezoar formation in cats may be related to abnormal migrating motor complexes that impair gastric emptying of indigestible material during fasting.

Clinical Signs

The clinical signs of a gastric motility disorder causing delayed gastric emptying are similar to those of gastric outflow obstruction. These include the following:

- Vomiting of undigested food more than 12 hours after eating
- Abdominal distention and discomfort after eating
- Anorexia and belching

Diagnosis

Perform a complete history to determine if anticholinergics, narcotics, or adrenergic agonists are currently being administered or if other predisposing influences on gastric motility are present.

Laboratory Evaluation

Perform routine screening tests including a CBC, biochemical profile, and urinalysis to detect predisposing metabolic abnormalities. For example, neutropenia associated with acute onset of vomiting, bloody diarrhea, and gastric retention and hypomotility in a young dog suggests parvoviral gastroenteritis.

Radiography

- Perform abdominal radiographs. Delayed gastric emptying is suggested by the finding of a distended fluid-filled stomach or food present in the stomach greater than 12 hours after eating.
- Perform a contrast gastrogram to assess gastric emptying, as described previously under "Gastric Outflow Obstruction." Normal gastric emptying of barium does not exclude a gastric motility disorder because it evaluates only the ability of the stomach to empty liquids and not solids. In functional gastric motility disorders, the gastric outflow region appears normal, but barium may not leave the stomach in a timely fashion.
- Commercially available BIPS have also been used to evaluate gastric emptying time.

Endoscopy

- Endoscopy is a useful non-invasive method to exclude mechanical outflow obstruction as a cause of delayed gastric emptying.
- Fast the patient for at least 24 hours before endoscopy to ensure that the stomach is empty. Large volumes of fluid are often present and should be aspirated through the endoscope to improve visualization.
- In idiopathic gastric motility disorders, the gastric mucosa and pyloric outflow area appear normal. If gastritis is a predisposing cause, gross and microscopic changes will be detected.

Electrogastrogram

Electrogastrograms have been used on a research basis to document abnormal gastric electrical rhythms and may have clinical applications in the future.

Treatment

Whenever possible, identify and correct the underlying cause of a gastric motility disorder. For example, discontinue any anticholinergic drug therapy.

Dietary Management

Diet is an important aspect of treatment for chronic gastric motility disorders.

- Use a diet that is low in fat and high in digestible carbohydrate.
- Feed small amounts at frequent intervals.
- Modify the consistency of the diet. In many instances, the more liquid the diet, the better it empties from the stomach.

Promotility Therapy

The treatment for idiopathic gastric motility disorders is a motility modifier such as metoclopramide, cisapride, erythromycin, or the H_2 blockers ranitidine or nizatidine (see Table 67-3). The effects of metoclopramide and cisapride on the stomach are shown in Figure 67-1.

Metoclopramide

- Although metoclopramide, a dopaminergic antagonist, has traditionally been used as a first choice gastric promotility drug, its effectiveness in promoting gastric emptying may be overstated.
- Give metoclopramide one-half hour before meals at a dose of 0.2 to 0.4 mg/kg PO q8h.

Cisapride

- Cisapride, a serotonergic (5-HT_4) agonist, appears to be more effective than metoclopramide for gastric emptying, but availability of cisapride is limited to compounding pharmacies. Cisapride was taken off the market because of fatal ventricular arrhythmias that occurred in humans but have not been documented in dogs and cats. Cisapride lacks the broad-spectrum central antiemetic effects of metoclopramide.
- Administer cisapride one-half hour before meals at a dosage of 0.25 to 0.5 mg/kg PO q8–12h in dogs and at a dosage of 2.5 to 5.0 mg PO q8–12h in cats.

Other Serotonin Agonist Drugs

- Tegaserod (Zelnorm, Novartis) is a newly marketed 5-HT_4 agonist. However, the intestine and colon are the predominate site of its promotility effects and it may not be useful for treatment of delayed gastric emptying.
- Prucalopride (Janssen Pharmaceutical), another 5-HT_4 agonist, is more likely to be indicated in the treatment of delayed gastric emptying in dogs, but it is not yet available.

Ranitidine and Nizatidine

The H_2 blockers, ranitidine and nizatidine, also have gastric prokinetic effects in dogs and cats (see Table 67-3).

Erythromycin

The antibiotic erythromycin has a prokinetic effect on the stomach of dogs, mimicking the effects of the hormone motilin. The promotility effect occurs at lower doses (0.5–1.0 mg/kg PO or IV q8h) than the antimicrobial effect.

HYPERTROPHIC GASTROPATHY

The term *hypertrophic gastropathy* is used to describe a heterogeneous group of poorly understood disorders associated with focal, multifocal, or diffuse hypertrophic changes of the gastric mucosa of dogs. Hypertrophic gastropathy appears to be quite rare in cats. Various other names have been used, including CHPG, hypertrophic gastritis, gastric polyps, and acquired pyloric stenosis or hypertrophy. These disorders may be variations of the same disease process. Microscopic changes are variable and include hyperplasia of mucosal epithelial cells, glandular hypertrophy, variable inflammatory infiltrates, and mucosal ulceration.

The most commonly recognized form of hypertrophic gastropathy in dogs is a benign disorder associated with mucosal hypertrophy of the antral and pyloric region, resulting in gastric outflow obstruction. Some affected dogs have a component of pyloric muscular hypertrophy. This disorder has been termed *chronic hypertrophic pyloric gastropathy* (CHPG).

Etiology

Little is known about the underlying etiology and pathophysiologic mechanisms of hypertrophic gastropathy; thus, the disease is idiopathic in most cases. Environmental, hormonal, genetic, and immune-mediated mechanisms may play a role.

- Chronic irritation associated with aspirin therapy can result in focal gastric hypertrophy.
- Hormones such as gastrin, cholecystokinin, acetylcholine, and histamine can be trophic to the gastric mucosa. Causes of hypergastrinemia such as chronic renal failure, chronic gastric distention, liver disease, gastrin-secreting tumors, and idiopathic hypertrophy of the antral G-cells (gastrin-secreting cells) may be important considerations in some cases.
- Basenji dogs have hypertrophic gastritis in association with immunoproliferative enteropathy; genetic, immune-mediated, and hormonal (gastrin) factors may play a role.
- Hypertrophic gastritis involving the body of the stomach has been described in the Drentse patrijshond breed of dog. Affected dogs also have red blood cell stomatocytosis and hemolytic anemia.
- Hyperplastic polyps involving the pylorus have been described in young, related French bulldogs with chronic vomiting and gastric outflow obstruction.
- CHPG is most common in highly excitable, nervous small-breed dogs; underlying neuroendocrine or stress-related mechanisms have been proposed.

Clinical Signs

Chronic vomiting is the most consistent clinical sign. Anorexia, weight loss, abdominal distention, and belch-

ing are less frequent signs. Vomiting occurs at variable intervals after eating.

- If hypertrophic changes cause outflow obstruction, undigested food may be present in the vomitus greater than 12 hours after eating.
- Hematemesis and melena may be detected in association with mucosal ulceration.
- Dogs with CHPG often are otherwise healthy and are presented because of chronic intermittent vomiting for a duration of weeks to months (sometimes years).
- Basenji dogs with immunoproliferative enteropathy and hypertrophic gastritis usually have concurrent chronic diarrhea, anorexia, and weight loss.

Diagnosis

Hypertrophic gastropathy is most common in middle-aged or older small-breed dogs such as Lhasa apsos, Shih Tzus, and miniature poodles. Males are affected more commonly than females. A history of chronic intermittent vomiting is typical.

Physical Examination

- Potential findings include weight loss and abdominal distension due to a fluid- or food-filled stomach.
- If significant GI blood loss occurs, pale mucous membranes due to anemia may be detected.

Laboratory Evaluation

- Laboratory evaluation often is unremarkable.
- If profuse vomiting has occurred, laboratory findings may reflect dehydration or electrolyte imbalances. Metabolic alkalosis may occur secondary to gastric outflow obstruction.
- If hypertrophic gastropathy is associated with gastric ulceration, evaluate serum gastrin concentration to detect underlying hypergastrinemia (e.g., gastrinoma).
- Iron deficiency anemia may result from chronic GI blood loss.

Radiography and Ultrasonography

- Perform survey abdominal radiographs to detect a fluid-filled distended stomach or food remaining in the stomach greater than 12 hours after eating. These findings are consistent with a gastric retention disorder.
- Perform a contrast gastrogram (see under "Gastric Outflow Obstruction"). Findings consistent with CHPG include delayed gastric emptying, filling defects in the antral and pyloric region due to hypertrophied mucosa, and narrowing of the pyloric canal. With other types of hypertrophic gastropathy, potential findings include focal, multifocal, or diffusely thickened gastric rugae. Radiographic features of hypertrophic gastropathy are not specific and mimic other inflammatory and infiltrative disorders.
- Ultrasonography can demonstrate thickening of the gastric wall at the antral and pyloric region.

Endoscopy

- Endoscopy can confirm focal, multifocal, or diffusely thickened mucosal folds. Moderate gastric distention with air is required so that normal-sized gastric rugal folds do not appear falsely thickened.
- With CHPG, the lesions predominantly involve the antrum and pyloric region, causing partial or complete pyloric obstruction. Hypertrophied mucosa may form polypoid masses. Mucosal ulceration or hemorrhage is not typical.
- Endoscopically obtained biopsies are inadequate to diagnose hypertrophic gastropathy because they are too superficial to demonstrate the lesion.

Surgery

- Definitive diagnosis of hypertrophic gastritis requires full-thickness biopsies obtained surgically.
- Excisional biopsies are indicated when possible to help relieve the obstruction.

Treatment

- Surgical excision of abnormal tissue and relief of outflow obstruction is the treatment of choice for CHPG (see Chapter 68). Response to surgery is usually good to excellent, and most dogs are clinically normal after relief of obstruction. If gastric atony persists after surgery, a promotility drug such as cisapride or metoclopramide may be needed.
- If hypertrophic gastropathy is associated with gastric erosions or ulcerations, institute antiulcer therapy with H_2 blockers and sucralfate as described under "Gastroduodenal Ulceration."
- When hypertrophic gastropathy is accompanied by a significant inflammatory infiltrate, consider treatment with prednisolone as described under "Chronic Gastritis."
- For treatment of basenji dogs with hypertrophic gastritis and immunoproliferative enteropathy see Chapter 69.

GASTRIC NEOPLASIA

The clinical presentation of gastric neoplasia in dogs and cats is influenced by the size and location of the tumor, whether it is benign or malignant, and whether it is associated with outflow obstruction, altered gastric motility, or mucosal ulceration and bleeding.

Etiology

Malignant Neoplasia

▼ ***Key Point*** Gastric adenocarcinoma is the most common gastric neoplasm in dogs.

- In dogs, gastric adenocarcinoma occurs most commonly in the antral and pyloric region and may appear as a raised plaque or mass with a central ulcerated area or as a diffuse infiltration of the gastric wall. Metastases to the regional lymph nodes, liver, adrenals, and lungs are common. Gastric adenocarcinoma is rare in cats.

▼ ***Key Point*** Lymphoma is the most common gastric neoplasm in cats.

- Cats with gastric lymphoma usually are FeLV negative. Lymphoma may appear as multiple, raised, white mucosal masses or as diffuse infiltration of the gastric wall. Mucosal ulceration is common.
- Other, less common primary malignant neoplasms include leiomyosarcoma and fibrosarcoma.

Benign Neoplasia

- Benign adenomatous polyps occur infrequently in dogs and cats. Polyps probably develop in response to chronic gastric mucosal damage or irritation. They appear as single or multiple, pedunculated or polypoid nodules that vary in size from millimeters to centimeters. A predilection for the proximal duodenum within 1 cm of the pylorus has been noted in cats. Clinical signs usually are absent unless pyloric obstruction occurs. Polyps usually are an incidental finding at endoscopy or necropsy.
- Leiomyomas are the second most common gastric tumor in dogs. These tumors arise from the muscle layers of the gastric wall; clinical signs may be absent unless the mechanical effects of the mass alter motility or cause outflow obstruction. A predilection for the gastroesophageal junction has been noted. Mucosal ulceration occasionally occurs.

Clinical Signs

Malignant Neoplasia

Dogs and cats with malignant gastric neoplasia are usually presented because of chronic progressive vomiting.

- If pyloric outflow obstruction occurs, clinical signs reflect delayed gastric emptying.
- Hematemesis and melena are common with adenocarcinoma because of mucosal ulceration. Other signs include anorexia, weight loss, and chronic debilitation.

Benign Neoplasia

Clinical signs may be absent with benign neoplasms or polyps unless pyloric obstruction occurs.

Diagnosis

Gastric neoplasia is an important consideration in older dogs and cats with a history of chronic progressive vomiting and hematemesis.

Physical Examination

- Findings often include weight loss and cachexia.
- Palpable abnormalities of the stomach usually are absent, although, rarely, a gastric mass may be palpable.
- Pale mucous membranes and melena are associated with mucosal ulceration and blood loss anemia.
- Gastric perforation and peritonitis are associated with abdominal distention, pain, collapse, and shock.
- Additional findings such as ascites, jaundice, and dyspnea reflect metastatic disease.

Laboratory Evaluation

Laboratory evaluation is variable and depends on secondary complications such as blood loss anemia, perforation, metastatic disease, and metabolic complications of vomiting. Paraneoplastic hypoglycemia may occur in dogs with gastric leiomyosarcoma.

Radiography

- Survey abdominal radiographs may be unremarkable or suggest outflow obstruction, a thickened gastric wall, or mass lesions.
- Barium contrast radiography often reveals mass lesions, filling defects, ulcers, and diffuse thickening of the gastric wall. Rigidity of the gastric wall seen repeatedly on sequential radiographs suggests an infiltrative lesion.
- Delayed gastric emptying can result from pyloric outflow obstruction.
- Perform thoracic films to screen for pulmonary metastases.

Endoscopy

Endoscopy is useful to confirm lesions suggested on radiography and to obtain biopsies of affected tissues. Gastric neoplasia that does not involve the mucosa or results in a mass effect can be difficult to detect endoscopically, and a full-thickness biopsy obtained surgically is often necessary.

- Adenocarcinoma may appear as raised plaques, polypoid lesions, or a diffuse infiltrating lesion. Mucosal ulceration is common.

- Gastric lymphoma appears as single or multiple white nodules or as diffuse infiltration of the mucosa with irregular thickening of the mucosal folds. With diffuse infiltration of the gastric wall, the stomach may lack distensibility.
- Leiomyomas are smooth mass lesions with a normal overlying mucosa unless complicated by ulceration.
- Polyps appear as small, smooth, or raspberry-like masses on a stalk.

Surgery

Surgical exploration is an important diagnostic method for gastric neoplasia.

- Palpate all areas of the stomach to identify affected areas.
- Obtain full-thickness biopsies.
- Evaluate regional lymph nodes and the liver for metastases.

Treatment

- The treatment of choice for gastric neoplasia is surgical resection of the tumor by partial gastrectomy (see Chapter 68). Because the antral and pyloric regions are often involved, a gastroduodenostomy or gastrojejunostomy may be necessary.
- For treatment of lymphoma, use chemotherapy as described in Chapters 26 and 27, with or without prior surgical resection of large solitary gastric masses.

Prognosis

- The prognosis for benign neoplasms after surgical removal is good.
- The prognosis for adenocarcinoma is poor.
- Some cats with lymphoma localized to the stomach may have a good to excellent response to chemotherapy.

GASTRIC DILATATION-VOLVULUS

GDV is an acute, life-threatening disorder that is a medical and surgical emergency. Early recognition and treatment are essential for a successful outcome. Gastric dilatation refers to distention of the stomach, usually with swallowed air. Gastric dilatation may or may not be complicated by volvulus. GDV occurs when the stomach rotates on its long axis, resulting in complete gastric outflow obstruction. Concurrent obstruction of the gastroesophageal junction precludes relief of fluid and gas accumulation by vomiting or belching. Massive gastric distention impairs venous return through the portal vein and caudal vena cava, causing hypovolemic and endotoxic shock. Passive congestion of the abdominal viscera predisposes to local acidosis and disseminated intravascular coagulation (DIC). The spleen often is displaced concurrently, causing splenic vascular occlusion, congestion, and splenomegaly. Strangulation necrosis of the gastric wall eventually occurs secondary to twisting of the stomach.

Etiology

The cause of GDV is unknown.

- An anatomic predisposition may play a role; large-breed, deep-chested dogs are most commonly affected, and the disorder is rare in small dogs and cats.
- Whether gastric distention due to excess swallowed air precedes volvulus is not known, but if this theory is true, it suggests causes of aerophagia such as gulping of food and water may be important.
- Risk factors for GDV include increasing age, having a first-degree relative affected by GDV, lean body conformation, rapid eating, eating from a raised bowl, eating one meal daily, exercise, stress after a meal, and a fearful temperament.

Clinical Signs

- Acute onset of abdominal distention with tympany
- Non-productive retching
- Salivating, restlessness, and respiratory distress

Diagnosis

Consider GDV in the differential diagnosis of any large-breed, deep-chested dog with acute onset of abdominal distention.

Physical Examination

Examination usually reveals abdominal distention that is tympanitic on percussion and findings indicative of hypovolemia and/or shock, such as increased heart rate, weak femoral pulses, decreased capillary refill time, and pale oral mucous membranes.

Laboratory Evaluation

- After initial stabilization (see "Initial Medical Management") submit blood for a CBC and biochemical evaluation to characterize secondary metabolic imbalances and to identify any other coexistent abnormalities.
- Hypokalemia is the most common electrolyte abnormality in dogs with GDV. Although serum potassium concentration may be normal initially, hypokalemia frequently develops after aggressive fluid therapy and, if surgery is necessary, postoperatively. Prevention of hypokalemia may decrease the frequency of postoperative cardiac arrhythmias and muscle weakness.

- Because a variety of acid-base imbalances may occur secondary to GDV, repeated laboratory assessment and frequent monitoring of blood gases and electrolyte concentrations are recommended.
- Metabolic acidosis is most common and occurs because of decreased effective circulating blood volume, arterial hypoxemia, and lactic acid accumulation.
- Metabolic alkalosis, respiratory alkalosis, respiratory acidosis, and mixed acid-base disorders may also develop.

Radiography

Perform abdominal radiography only after the patient is stabilized medically (see the next section). Minimize stress to the patient during the procedure.

▼ ***Key Point*** Right lateral and ventrodorsal radiographic views of the abdomen are the most useful for diagnosing GDV.

- Radiographic findings suggestive of GDV include overdistention of the stomach with gas, pyloric displacement dorsally and to the left, gastric fundic displacement caudally and to the right, and compartmentalization of the stomach on the lateral view. Splenomegaly is also seen.
- Pneumoperitoneum suggests gastric perforation and requires immediate surgery.
- Thoracic radiography is not essential but may demonstrate microcardia (due to hypovolemia), megaesophagus, or aspiration pneumonia.
- In cases of intermittent bloating or failure of surgical correction following tube decompression, perform a contrast gastrogram (see Chapter 4) to identify malposition of the stomach.

Initial Medical Management

Decompress the Stomach by Orogastric Intubation

- Sedation may be necessary to pass an orogastric tube. Give diazepam (0.1 mg/kg IV slowly) alone or in combination with butorphanol (0.5 mg/kg IV). An alternative is the combination of diazepam-ketamine (50:50), 1 ml/10 kg IV.
- Perform gastric decompression by passing a well-lubricated large-bore orogastric tube. Remove all air and fluid from the stomach and lavage the stomach with 4 to 5 L of warm saline or water. Repeat orogastric decompression as needed during the stabilization period.
- If orogastric decompression is not possible with a tube, use several 18-gauge needles to trocarize the distended stomach. Following decompression with needle trocarization, a subsequent attempt to pass the orogastric tube often is successful.

Place an Intravenous Catheter and Administer Fluids

- While decompression is being performed, place a large-bore catheter in each cephalic vein.
- Treat for shock as described in Chapter 156. Give isotonic crystalloid fluids such as lactated Ringer's solution at an initial rapid rate of 90 ml/kg for the first hour. After shock is controlled and dehydration is corrected, lower to a maintenance rate of administration. Add potassium chloride to the fluid (30 to 40 mEq KCl per liter of fluid) after the initial shock dose of fluids has been given. When blood gas analysis is not available, routine addition of $NaHCO_3$ to fluids is not recommended, because many dogs with GDV have relatively normal blood pH at presentation. Correction of volume depletion and mild metabolic acidosis by lactated Ringer's solution is sufficient unless severe metabolic acidosis is present.
- Alternatively, administer small-volume fluid therapy using 7% NaCl (5 ml/kg) in 6% dextran 70 (HS/D70) (see Chapter 156). Give over 5 to 10 minutes and follow with 20 ml/kg/hr of 0.9% NaCl.
- Place a Foley catheter in the bladder to monitor urine output.

Control Infection and Endotoxemia

- To treat endotoxemia, give prednisolone sodium succinate (10 ml/kg IV). Give a single dose of flunixin meglumine (Banamine, Schering), 1 mg/kg IV, during the initial phase of therapy.
- Give a broad-spectrum antibiotic (cefmetazole, 15 mg/kg IV) or a combination drug therapy (cefazolin, 20 mg/kg IV, and enrofloxacin, 5–10 mg/kg IV).

Monitor and Treat Cardiac Arrhythmias

- Ventricular arrhythmias are the most common.
- To treat ventricular arrhythmias, give a bolus of lidocaine (1–2 mg/kg) IV while monitoring the electrocardiogram. If no conversion is noted within 3 to 5 minutes, repeat this dose. For a comprehensive discussion of diagnosis and treatment of arrhythmias, see Chapter 145.
- If only temporary conversion occurs, start a lidocaine drip. A maintenance effect is achieved with a constant rate infusion of lidocaine at a dosage of 40 to 60 µg/kg/min added to the IV fluids. Lidocaine's effectiveness may be impaired in the presence of hypokalemia.
- If lidocaine boluses are ineffective for controlling ventricular arrhythmias, consider giving procainamide (10–15 mg/kg IM q6h) or quinidine sulfate (6–15 mg/kg IM q6h). If arrhythmias are controlled with parenteral administration of procainamide or quinidine, an oral antiarrhythmic can later be substituted, as described in Chapters 145 and 146.

Surgical Management

Surgical management of GDV is detailed in Chapter 68. The goals of surgical intervention for acute GDV include the following:

- Repositioning of the stomach and spleen
- Resecting devitalized gastric and splenic tissue
- Permanently fixing the stomach (pyloric antrum) to the right abdominal wall to prevent future recurrences of volvulus (see Chapter 68)

Prevention

If medical therapy alone is successful and no evidence of gastric volvulus is detected subsequently on a contrast gastrogram, there is still a 70% to 75% likelihood that the dog will have another episode of GDV. Owner education can help lessen the probability of recurrence.

Instruct the owner to do the following:

- Feed the dog frequent, small portions of food 3 to 5 times per day.
- Limit water intake and do not allow access to water for 1 hour after eating.
- Restrict exercise for at least 1 hour after eating, because this may predispose to GDV.
- Be aware of the early warning signs of GDV (e.g., depression, restlessness, belching, excessive flatulence, and abdominal enlargement), especially when there is a change in the dog's environment—for example, when the dog is boarded or hospitalized, or when a new adult, child, or pet is introduced into the household.
- Consider prophylactic gastropexy in high-risk dogs (see Chapter 68).

SUPPLEMENTAL READING

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Chapter

68 Surgery of the Stomach

Ronald M. Bright

Retrieval of foreign bodies is the most common reason for surgery on the stomach. Surgery of the pylorus is most often indicated for some forms of gastric outflow obstruction. The most common sign related to surgical disease of the stomach is emesis. The stomach has an excellent blood supply and heals rapidly (10–14 days).

ANATOMY

Stomach

- The stomach is a musculoglandular organ capable of undergoing a great amount of distention.
- The stomach is a C-shaped, partially coiled, bulging tube.
- The stomach lies in a transverse plane. The larger part of the stomach (fundus) lies to the left of the midline.
- The esophageal entrance and duodenal exit are dorsal—the former lying to the left of the midline, the latter to the right.
- In the fasting dog, the stomach does not extend caudally beyond the costal arch and is rarely palpable.
- The stomach is divided into four regions: cardia, fundus, body (corpus), and pylorus.
- The stomach has four tunics: mucosa, submucosa, muscularis, and serosa. The submucosa and mucosa layers are easily separated from the overlying seromuscular layers.
- The blood supply to the distal stomach is from a branch of the hepatic artery, giving rise to the right gastric and gastroepiploic arteries.
- The splenic artery gives rise to the left gastroepiploic artery, which supplies the greater curvature.
- The left gastric artery supplies blood to the lesser curvature of the stomach and the distal esophagus.
- Veins are satellites to the arterial branches. Most blood drains from the left side of the stomach via the gastrosplenic vein and from the right side via the gastroduodenal vein. These veins ultimately drain into the portal vein.
- The major innervation is parasympathetic from the vagi and sympathetic from the celiac plexus.

Omentum

- The greater omentum extends caudally from the greater curvature of the stomach to the urinary bladder, forming a double-layered cover of the small intestine.
- A splenic portion of the omentum attaches to the greater curvature to the spleen and a smaller portion attaches to the pancreas.
- The lesser omentum extends from the lesser curvature of the stomach and attaches to the diaphragm, liver, and duodenum.
- The hepatoduodenal and hepatogastric ligaments are loose attachments between the respective components.

Pylorus

- The pylorus is composed of two segments, the antrum and the canal. The antrum is a narrow funnel-shaped chamber leading to the narrowed pyloric canal.
- The inner circular muscle layer is thickened in the pyloric region and functions as a powerful sphincter. An outer longitudinal muscle layer is also present.
- The pylorus has two major functions—to control the emptying of solid food once it becomes reduced to an appropriate size and to prevent excessive duodenogastric reflux.

GASTROTOMY

Preoperative Considerations

▼ ***Key Point*** Serious water and electrolyte abnormalities often accompany conditions that affect the stomach and require gastrotomy. Initiate fluid and electrolyte resuscitation before gastrotomy.

- The most common indication for gastrotomy is to retrieve foreign bodies.
- Endoscopic retrieval of gastric foreign bodies is preferred. When this approach fails, a gastrotomy is indicated.

Surgical Procedure

Objectives

- Access to and exposure of intraluminal contents.
- Collection of biopsy specimens.
- Avoidance of contamination of the peritoneal cavity.

Equipment

- General surgical pack
- Babcock forceps (optional)
- Abdominal self-retaining Balfour retractors
- Laparotomy pads

Technique

1. Make a cranial ventral midline abdominal approach, with the skin incision extending from the xiphoid to the umbilicus.
2. Exteriorize the stomach and isolate it from the other abdominal organs using moistened laparotomy pads.
3. Place two Babcock forceps or two stay sutures 10 to 15 cm apart on a hypovascular area of the stomach, halfway between the lesser and greater curvature.
4. Make a stab incision into the lumen with a #11 blade.
5. Use suction to remove liquids from the stomach.
6. Extend the stab incision with scissors.
7. Do a visual and tactile exploration of the entire stomach.

Closure

1. The first layer is a continuous inverting horizontal mattress (Connell) suture pattern involving only the submucosal and mucosal layers. A simple continuous suture pattern can be substituted. Synthetic 3-0 absorbable suture material is preferred. Use of chromic gut suture material is discouraged, because it breaks down too rapidly when coming in contact with the lumen of the stomach.
2. Close the second layer with a vertical (Lembert) or horizontal (Cushing) continuous inverting pattern.
3. If the gastrotomy closure is likely to incorporate diseased or devitalized tissue, suture a section of vascularized omentum or a serosal patch, employing a loop of jejunum over the wound for additional reinforcement.

Postoperative Care and Complications

Short Term

- Give no food for 24 hours; water is allowed ad libitum.
- Monitor the patient for leakage, especially if the gastrotomy closure involves diseased tissue (neoplasia).
- Emesis may be noted once or twice following gastric surgery and treatment is usually not required.
- Systemic antacids are indicated if ulcers or severe gastritis is observed during surgery (see Chapter 67).

Prognosis

- Good to excellent if the reason for surgery is related to a foreign body.

PARTIAL GASTRECTOMY RELATED TO GASTRIC DILATATION-VOLVULUS

Preoperative Considerations

- Gastrectomy in patients with dilatation-volvulus is a high-risk procedure.
- Initially, attempt to stabilize metabolic abnormalities but rapidly proceed with surgery because gastric rupture may occur.

Surgical Procedure

Objectives

- Resect non-viable gastric tissue and restore gastric continuity.
- Use a stapling technique, if possible, to expedite this high-risk procedure.

Equipment

- General pack
- LDS stapler (U.S. Surgical, Norwalk, CT) (optional)
- TA stapler (U.S. Surgical, Norwalk, CT) (optional)
- Abdominal self-retaining retractor
- Laparotomy pads
- Non-crushing straight Doyen intestinal clamps

Technique

1. The approach to the stomach is similar to that for a gastrotomy.
2. Non-viable tissue is recognized by its lack of bleeding on cut surfaces, bluish-black or greenish discoloration, and severe thinning of the stomach wall on palpation.

▼ ***Key Point*** Do not rely on the appearance of the mucosa alone to determine if full-thickness stomach wall necrosis has occurred.

3. Ligate and divide the appropriate short gastric vessels. LDS stapler apparatus is optimal. This procedure may not be necessary because these vessels are frequently torn.
4. After placement of stay sutures, apply intestinal forceps 2 lateral to the junction of viable and non-viable tissue. The tips of the forceps meet at an approximately 45-degree angle.
5. Use a #10 scalpel blade to cut along the intestinal clamps, leaving a 1-cm margin of healthy tissue outside the intestinal clamps.

Alternate Method of Resection

1. Place a TA stapler parallel to the junction of viable and non-viable tissue, leaving a 1-cm width of normal tissue.
2. After the stapler is engaged and the staples are placed in the tissue, cut the stomach wall next to the blade of the stapler and remove the necrotic tissue.

Closure

1. Without a stapler, the closure is similar to that for a gastrotomy incision.
2. With a stapler, perform the closure before cutting the non-viable tissue away from the TA stapler's blade.
3. Close the abdomen routinely. If gastric rupture has occurred, the abdomen may be left partially open as in treating peritonitis (see Chapter 76).

Postoperative Care and Complications

Short Term

- Refer to the discussion of gastric dilatation-volvulus surgery for postoperative management of metabolic problems.
- Delay feeding for 24 hours.
- Monitor very closely for signs of gastric leakage (fever, vomiting, pneumoperitoneum, peritonitis), especially during the first 96 hours postoperatively.

▼ ***Key Point*** When a partial gastrectomy is performed during surgical therapy for gastric dilatation-volvulus complex, the mortality rate ranges from 30% to 60%.

PARTIAL GASTRECTOMY (DISTAL STOMACH)

Preoperative Considerations

▼ ***Key Point*** Attempts to define the extent and nature of the disease (benign polyp, malignancy, fungal disease, chronic gastric ulcer) by radiography and endoscopic biopsy are extremely important when planning surgical therapy.

Many animals with gastric neoplasia are old and debilitated and are at greater risk during surgery than others.

Surgical Procedure—Partial Gastrectomy and Gastroduodenostomy (Billroth I)

Objectives

- To remove diseased tissue that is benign or, if malignant, is limited to the antrum and/or body of the stomach.
- To correct failed pyloroplasty procedures.
- To maintain an adequate outflow lumen.

Equipment

- Same as that for partial gastrectomy associated with the gastric dilatation-volvulus complex
- GIA stapler (U.S. Surgical, Norwalk, CT)—recommended if a stapler technique is used
- Large straight intestinal clamps

Technique

1. Place the dog in dorsal recumbency with surgical preparation similar to that for gastrotomy.
2. Stapling devices (e.g., the GIA stapler) can be substituted for more traditional suturing techniques.
3. If the diseased tissue is limited to the pylorus, a modification of a Billroth I (von Haberer) technique can be done (Fig. 68-1).
4. If a partial gastrectomy is performed to control ulcer disease, resect the entire antrum.
5. More extensive resection of the pylorus or distal stomach can be done and reconstructed with the original Billroth I (Shoemaker) procedure (see Fig. 68-1).

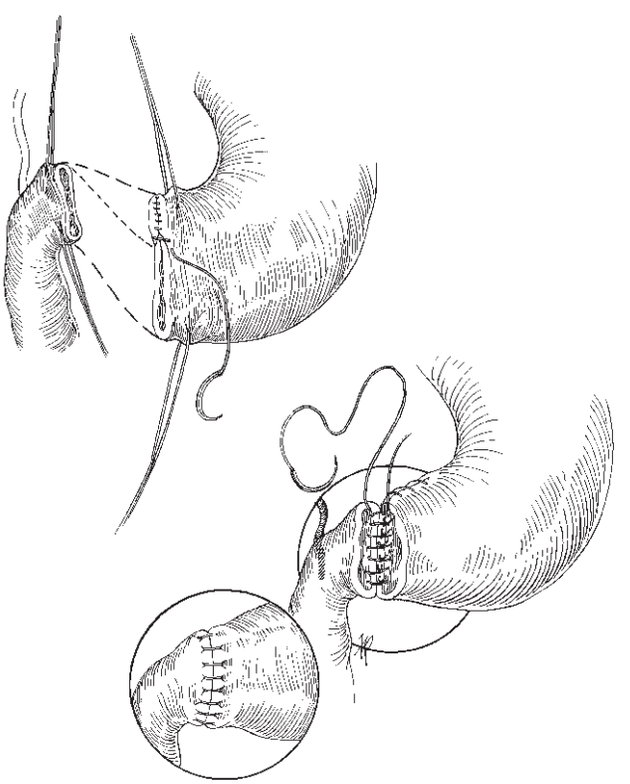

Figure 68-1. Partial gastrectomy with a Billroth I (gastroduodenostomy) repair. *Above,* Lesser curvature of the stomach is closed until lumen disparity is corrected. *Below,* Closure with single interrupted sutures.

6. After the line of resection is determined, ligate and divide the blood vessels supplying the lesser and greater curvature and attached omentum.
7. Mobilize the pylorus after incising the gastrohepatic ligament. Avoid cutting the common bile duct and hepatic arteries.
8. Isolate the area to be resected from the abdominal cavity with moistened laparotomy sponges.
9. Place large, straight non-crushing intestinal forceps above and below the proposed lines of incision.

Closure

1. Use a single-layer interrupted appositional suture pattern to appose the stomach and duodenum. With unequal lumen sizes, first close the lesser curvature side of the stomach until the lumen disparity is corrected (see Fig. 68-1, *top*).
2. Appose the back (far) wall first, placing the knots into the lumen. Synthetic 3-0 absorbable suture (e.g., polydioxanone [PDS]) is recommended.
3. Then appose the near wall.

Surgical Procedure—Partial Gastrectomy and Gastrojejunostomy (Billroth II)

Objectives

- Resect a significant portion of the diseased stomach and all or part of the duodenum.
- Remove the duodenum distal to the common bile duct opening.
- Reestablish continuity of the stomach with the small intestine with a gastrojejunostomy.
- Restore a biliary connection to the duodenal or jejunal stump via a cholecystenterostomy.

Equipment

- Same as that for the Billroth I.

Technique

1. Ligate and divide the appropriate vessels and the common bile duct.
2. Close the duodenal or jejunal stump with a simple interrupted appositional suture pattern using 3-0 synthetic absorbable suture material or a TA stapler.
3. The original Billroth II reconstruction is done by closing the gastric stoma followed by a side-to-side anastomosis of the jejunum to an incision made in the ventral aspect of the stomach (Fig. 68-2).
4. Use a simple interrupted appositional suture pattern to appose the gastric and jejunal segments.
5. For more extensive resections, appose the entire width of the gastric stump to a longitudinal incision made in the jejunum (Fig. 68-3).
6. Use a suture pattern as described in Step 4 for closure.

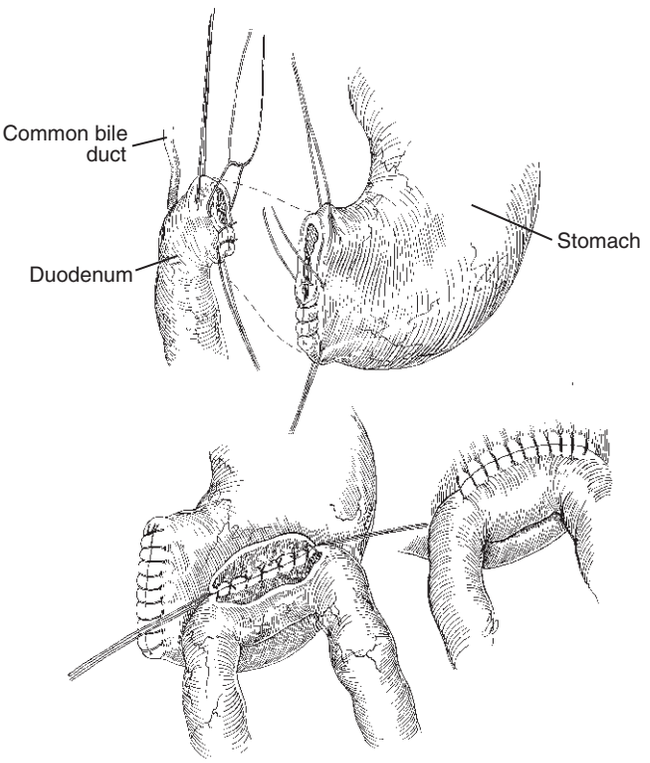

Figure 68-2. Billroth II procedure with side-to-side gastrojejunostomy.

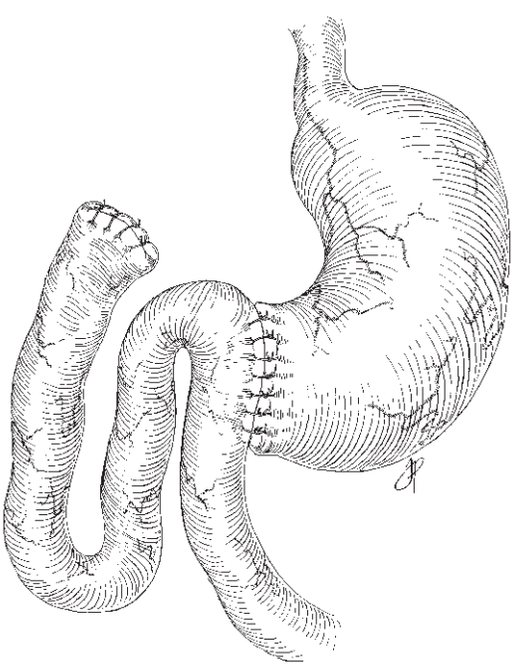

Figure 68-3. Billroth II with anastomosis of the entire gastric stump to a longitudinal incision of the jejunum.

7. Perform a cholecystenterostomy to complete the procedure (see Chapter 72).
8. Place a jejunostomy tube to provide nutrition in the debilitated patient.

Postoperative Care and Complications

Short Term

- Monitor for fever and abdominal pain as early signs of leakage peritonitis.
- Withhold food and water by mouth for 24 hours.
- Offer small amounts of food by mouth (per os) 24 hours after surgery.
- Dumping syndrome (passage of undigested food directly into the jejunum) may initially be a problem.

Long Term

- Dumping syndrome, due to disruption of the normal storage function of the stomach and rapid movement of ingested food into the small intestine, may cause chronic postprandial discomfort, vomiting, and diarrhea.
- Alkaline reflux gastritis may result from disruption of the pyloric sphincter.
- After extensive gastrectomy, multiple small feedings are necessary.

Prognosis

- Good—if the underlying disease is benign or inflammatory.
- Poor—if malignancy is the indication for surgery.

PYLOROMYOTOMY

Preoperative Considerations

- Delay pyloromyotomy until hypochloremic, hypokalemic metabolic alkalosis, which often accompanies the conditions requiring pyloromyotomy, is corrected.
- Direct fluid therapy toward restoring electrolyte *and* water abnormalities.
- In the younger dog or cat, add dextrose to the fluid therapy regimen in an attempt to maintain euglycemia.
- Food and water may be retained in the patient's stomach with outflow obstruction. Therefore, following sedation, place an orogastric tube into the stomach and evacuate the stomach contents.

▼ ***Key Point*** Pyloromyotomy will *not* effectively relieve outflow obstruction caused by mucosal hypertrophy. Pyloromyotomy is primarily indicated for dogs with muscular hypertrophy only (see Chapter 67).

Surgical Procedure

Objectives

- Increase the lumen diameter of the pylorus to enhance gastric emptying.

Equipment

- General surgery pack
- Abdominal self-retaining retractor
- Laparotomy sponges
- Babcock forceps

Technique

1. Place the dog in dorsal recumbency and aseptically prepare for a cranial midline abdominal incision.
2. Incise the skin and underlying tissues to allow an opening to the abdominal cavity extending from the xiphoid to 4 to 5 cm below the umbilicus.
3. Partially incise the gastrohepatic ligament to allow the pylorus to be mobilized.
4. Isolate the stomach with laparotomy sponges.
5. Place a stay suture or a Babcock forceps 3 to 5 cm proximal and distal to the pyloric ring.
6. Make an incision 4 to 5 cm long into a hypovascular area of the serosa overlying the pyloric antrum and canal and extend it distally into the proximal duodenum. The pylorus is at the midpoint of the incision (Fig. 68-4, *top*).
7. Gently incise or dissect away all muscle fibers, using a curved hemostat, to allow the submucosa and mucosa to bulge (see Fig. 68-4, *middle* and *bottom*).
8. Gently replace the stomach into the abdomen.
9. Perform routine ventral abdominal closure.

Postoperative Care and Complications

Short Term

- Treat emesis lasting more than 6 to 8 hours postoperatively with metoclopramide, 0.2 to 0.4 mg/kg subcutaneously (SC) q6h as needed, or constant-rate intravenous (IV) infusion of metoclopramide at 1 to 2 mg/kg/day, which is most effective.
- Maintain fluid therapy for 36 to 48 hours postoperatively.
- Perform frequent monitoring of the packed cell volume, albumin, and blood glucose values, especially in the very young animal.
- Monitor electrolyte values closely in all animals for the first 24 hours.
- Begin feeding soft food 24 hours after surgery unless vomiting continues.

Long Term

- Emesis may continue with little to no improvement noted. This sign may suggest a need to reoperate and perform a more extensive procedure (e.g., pyloroplasty).

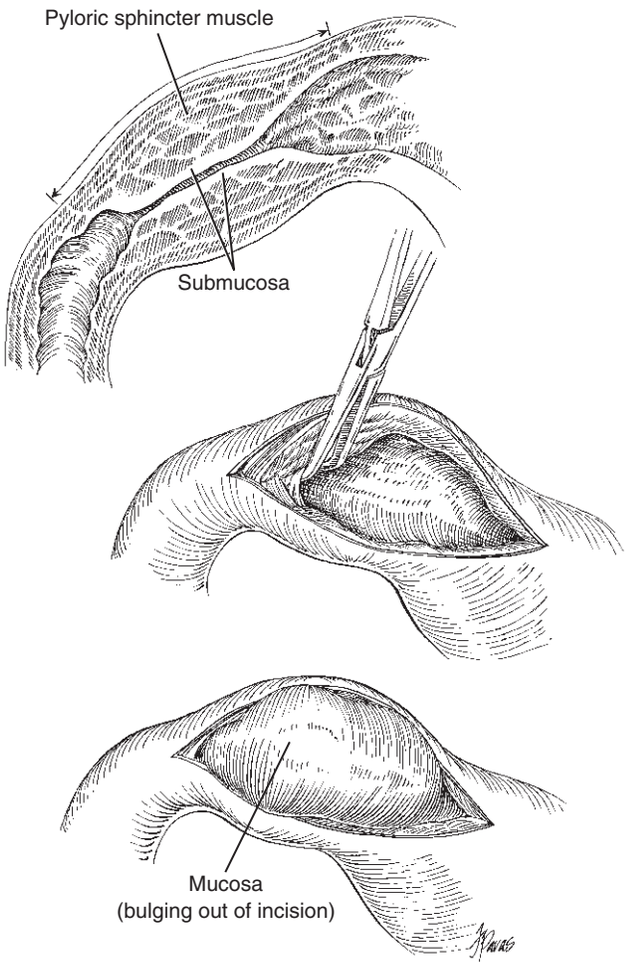

Figure 68-4. Technique for pyloromyotomy.

- Signs of vomiting may recur several days or weeks following surgery. If other causes of vomiting are not identified, reoperation may be necessary.

Prognosis

- Because the underlying disease in most cases is benign, the prognosis is good to excellent.

PYLOROPLASTY

Preoperative Considerations

- See under "Pyloromyotomy."
- Pyloroplasty is indicated for pyloric hypertrophy involving muscle and mucosa or mucosa alone (see Chapter 67). Dogs with severe pyloric hypertrophy may require the Billroth I procedure (see previous discussion).
- Manual and visual inspection of the lumen of the distal stomach, pylorus, and proximal duodenum is possible with a pyloroplasty.

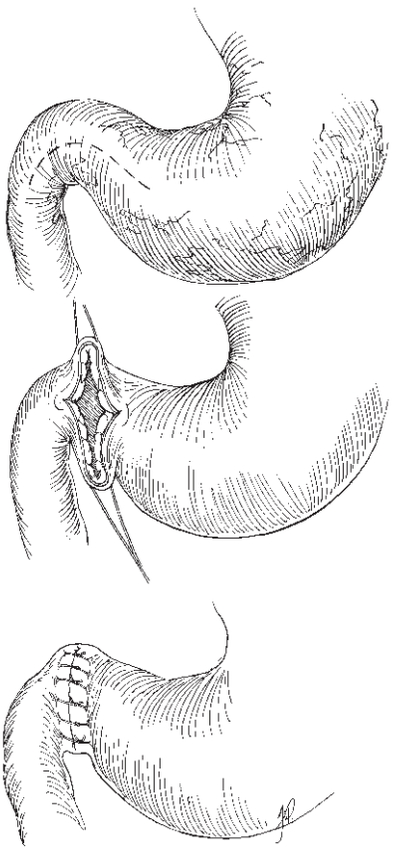

Figure 68-5. Technique for Heineke-Mikulicz pyloroplasty.

Surgical Procedure

Objectives

- Inspect the distal stomach and pylorus for abnormalities.
- Increase the diameter of the gastric outflow tract.

Equipment

- See under "Pyloromyotomy."

Heineke-Mikulicz Pyloroplasty

Technique

1. Place temporary stay sutures or Babcock forceps on the antrum and proximal duodenum proximal and distal to the pyloric ring.
2. Make a full-thickness stab incision into the pylorus using a #11 Bard-Parker scalpel blade. Place a suction tip into the stomach to evacuate contents and bile.
3. Extend the incision with scissors to 1 to 2 cm above and below the pylorus (Fig. 68-5).
4. Remove the stay sutures or Babcock forceps.
5. Close the longitudinal incision transversely with 3-0 synthetic absorbable sutures in a simple interrupted appositional pattern. Stay sutures can be placed on

both sides of the incision to help orient the tissues for closure.
6. Routine abdominal closure follows warm saline lavage of the surgical site.

Y-U Pyloroplasty (Antral Flap Advancement)

Technique

1. Mobilize the pylorus as described under Pyloromyotomy.
2. Place temporary stay sutures 4 to 5 cm above and below the pylorus.
3. Make a Y-shaped incision through the seromuscular tissue overlying the pylorus and distal stomach (Fig. 68-6).
4. Each limb of the Y is approximately 3 to 4 cm in length depending on the size of the animal.
5. The base of the Y extends a small distance (3–4 mm) into the antrum proximal to the pylorus.
6. Trim the V-shaped antral flap to a U-shape. Save the resected tissue and submit for histopathology.
7. Thoroughly palpate and visually examine the stomach and proximal duodenum.
8. Excise hypertrophied tissue via a submucosal resection. Close adjacent mucosa/submucosa in a continuous pattern with 3-0 or 4-0 synthetic absorbable suture.
9. Begin pyloroplasty closure by suturing the base of the U-shaped flap distally to the proximal duodenum with 3-0 or 4-0 synthetic absorbable suture (see Fig. 68-6).
10. A simple interrupted appositional pattern is recommended. If necessary, preplace the sutures to ensure accuracy.
11. Appose the lesser curvature limb of the Y, followed by the greater curvature limb (see Fig. 68-6).

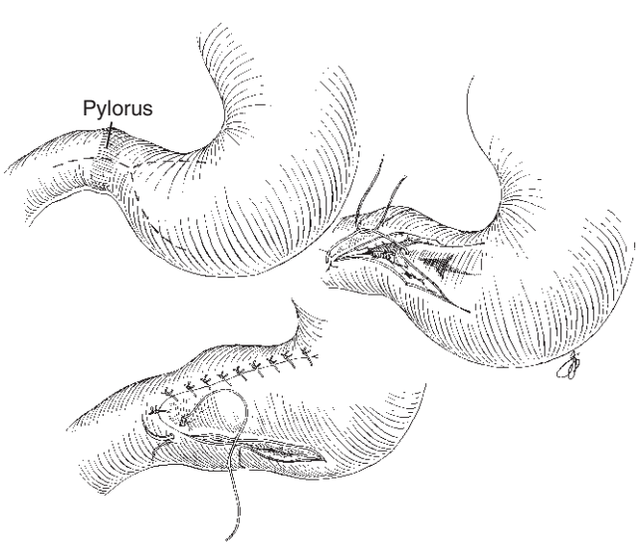

Figure 68-6. Technique for Y-U pyloroplasty.

Postoperative Care and Complications

Short Term

- Same as that for pyloromyotomy.

Long Term

- Emesis containing a significant amount of bile several weeks after surgery may suggest duodenogastric reflux. Consider treatment with metoclopramide.
- Alkaline reflux gastritis resulting from duodenogastric reflux may require long-term therapy with metoclopramide or cisapride to promote normal gastric emptying and an H_2 blocker for acid control.

Prognosis

- Good—if the disease being treated is benign.

ACUTE GASTRIC DILATATION-VOLVULUS

Preoperative Considerations

- Aggressive fluid therapy, cardiac arrhythmia therapy, and orogastric decompression are necessary before any surgical intervention (see Chapter 67).
- Stabilization of most patients can be accomplished in 2 to 3 hours.
- Complicating gastric perforation is considered a surgical emergency.
- Risk factors recently described by Glickman and colleagues (see "Supplemental Reading") are encouraging many surgeons to perform a prophylactic gastropexy in those dogs that are considered to be at great risk for gastric dilatation-volvulus. Some of the more important risk factors include rapid eating, hyperactivity, lean body conformation, aggressive nature, first-degree relative with known gastric dilatation-volvulus, and signalment (Great Dane breed).

Surgical Procedure

Objectives

- Reposition stomach and spleen to their normal anatomic relationship.
- Fix ("pexy") the stomach (pyloric antrum) to the right abdominal wall to prevent future episodes of volvulus.
- Resect devitalized tissue (spleen, stomach).

Equipment

- General surgical pack
- Self-retaining abdominal retractor (Balfour)
- Foley catheter (22–26-French)
- Orogastric tube

Technique

1. Place the dog in dorsal recumbency and surgically prepare from the mid-sternum to 6 to 8 cm below the umbilicus. If a tube gastropexy is used, prepare the right side of the abdominal wall aseptically, halfway up the side of the thoracic and abdominal wall that corresponds with the length of the midline incision.
2. Gently place an orogastric tube into the esophagus and advance it until there is resistance.
3. Derotate the stomach by grasping the pylorus and duodenum, usually located near the gastroesophageal junction, and elevating them to the right side of the body.
4. The fundus, usually on the right side, is depressed and rotated to the left side while the pylorus is being repositioned.
5. Place the orogastric tube within the stomach and perform stomach decompression.
6. Assess the viability of the stomach, and resect necrotic tissue if necessary (see discussion of "Partial Gastrectomy Related to Gastric Dilatation-Volvulus").
7. Splenectomy is usually not done unless there is evidence of splenic torsion or necrosis.
8. Perform a gastropexy procedure on the right side of the dog (regardless of the technique employed). Each of the gastropexy techniques described subsequently is effective. The technique chosen depends on the surgeon's preference.

Tube Gastropexy (22–26-French Foley Catheter)

Technique

1. Tube gastropexy is not considered to be an acceptable "pexy" technique unless it is done concurrently with a partial gastrectomy. Under these circumstances, the tube gastrostomy may be beneficial to wound healing by keeping the remaining stomach decompressed.
2. Place a full-thickness pursestring suture in the midantrum area using 2-0 or 3-0 non-absorbable suture. This suture is left untied (Fig. 68-7).
3. Pull the tip of a Foley catheter through a small right paracostal incision using Carmalt forceps, approximately 4 cm caudal to the costal arch and 4 cm lateral to the incision.
4. Make a stab incision into the middle of the pursestring suture area and advance the tip of the Foley catheter through this and into the stomach (see Fig. 68-7).
5. Inflate the balloon portion of the catheter.
6. Draw the pursestring suture tightly and tie it.
7. Move the stomach to the abdominal wall with traction on the Foley catheter.
8. Preplace six to eight interrupted sutures between the stomach, being sure to penetrate to the submucosa and the abdominal wall. Use nonabsorbable #1 or 1-0 suture material (see Fig. 68-7).

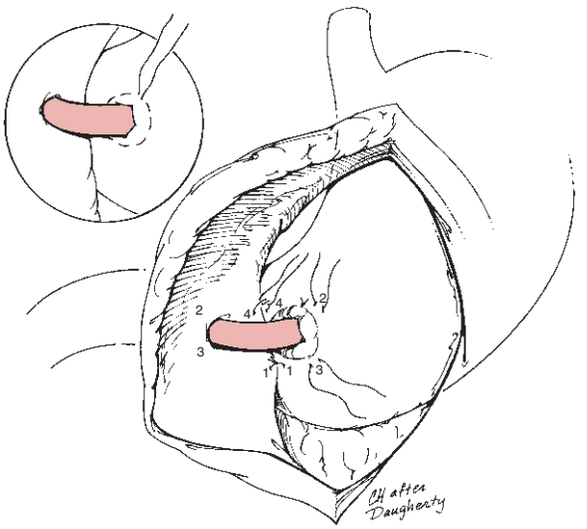

Figure 68-7. Technique for tube gastropexy in the treatment of gastric dilatation-volvulus. *Inset,* Place an untied pursestring suture in the midantrum area. Place a Foley catheter through the body wall, into the pyloric antrum. Connect the stomach and abdominal wall with interrupted sutures. In the figure, points 1 are connected, as are points 2 to each other, and so forth. (Drawing by Carol Haynes, after Daugherty.)

9. Tie the sutures starting dorsally and ending ventrally.
10. Affix the catheter to the skin with a traction suture.

Circumcostal Gastropexy

Technique

1. Place two retention sutures using 1-0 or 2-0 nonabsorbable suture material in the antrum approximately 6 cm apart and midway between the lesser and greater curvature.
2. Make a 3 × 3 cm incision through the seromuscular layer forming an I-shaped configuration (Fig. 68-8, *inset*).
3. The seromuscular flaps are formed by careful dissection between the muscular and submucosa tunics. Place two stay sutures on each flap.
4. Isolate the 11th or 12th rib ventral to the costochondral junction and rotate it laterally with two towel clamps placed 6 cm apart.
5. Expose a 4- to 5-cm length of the rib by incising through the peritoneum and muscle.
6. By blunt dissection remove all tissue attached to the rib.
7. Pass one arm of each stay suture under the rib.
8. Place another stay suture midway down the seromuscular flap found on the greater curvature side. This placement helps pull this flap around the exposed rib.
9. Once the flap is pulled around the rib, tie the two retention sutures.

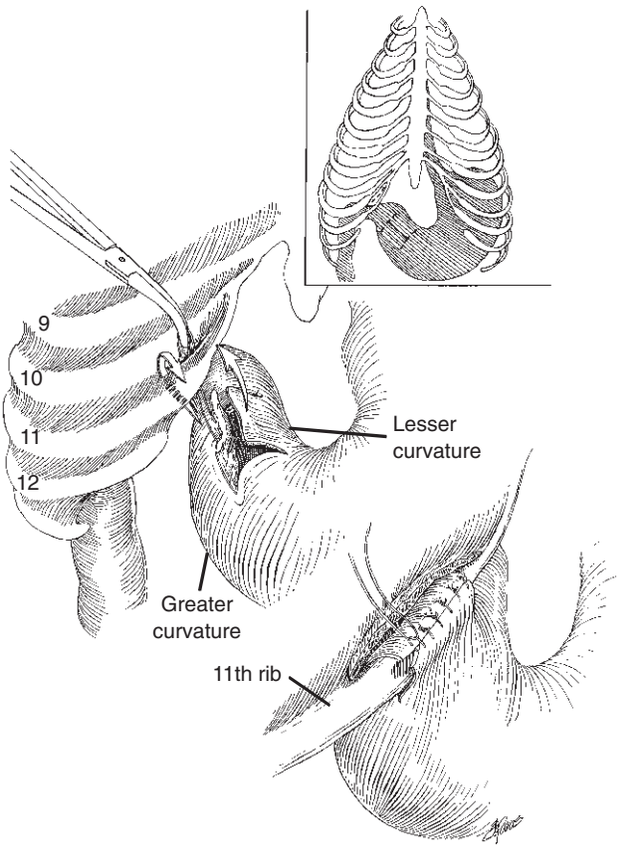

Figure 68-8. Technique for circumcostal gastropexy (for gastric dilatation-volvulus).

10. Suture the seromuscular flap to the opposite flap using 2-0 synthetic absorbable or non-absorbable suture (see Fig. 68-8). Use a simple interrupted full-thickness suture pattern.
11. Suture the peritoneum and musculature on the lateral aspect of the completed flap repair to the seromuscular layer of the stomach with six to eight sutures. This bridges and supports the seromuscular flap suture line.

Belt Loop Gastropexy

Technique

1. A belt loop of muscle is produced by making two parallel transverse incisions 2 to 3 cm apart and 2 to 3 cm in length through the peritoneum and fascia of the transversus abdominis muscle.
2. Bluntly separate the muscle fibers with scissors (Fig. 68-9*A*).
3. Make a 2 × 4 cm tongue-shaped seromuscular flap with the base of the flap along the greater curvature of the antrum (Fig. 68-9*B*).
4. A branch of the gastroepiploic artery is centered at the base of the flap.

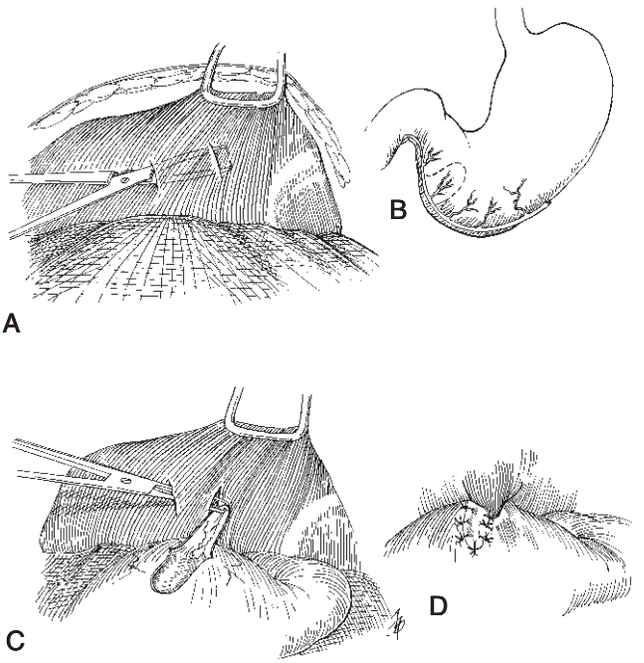

Figure 68-9. Technique for belt loop gastropexy (for gastric dilatation-volvulus). See text for details.

5. When creating the flap, make the base a little wider than the tip of the tongue-shaped flap.
6. Pass the stomach flap through the belt loop in a cranial-to-caudal direction (Fig. 68-9*C*).
7. The flap is now repositioned over its original anatomic location and reattached to adjacent seromuscular tissue with 1-0 monofilament synthetic absorbable or non-absorbable suture (Fig. 68-9*D*).

Muscle Flap Gastropexy

Technique

1. Make a U-shaped incision through the peritoneum and transversus abdominis muscle caudal to the 13th rib on the right lateral side.
2. Undermine and reflect the muscle flap ventrally.
3. Preplace two horizontal mattress sutures using 1-0 non-absorbable material from the base of the U through the seromuscular layer of the antrum and draw the antrum laterally to the right abdominal wall (Fig. 68-10*A*).
4. Tie the sutures and secure them against the body wall (Fig. 68-10*B*).
5. Secure the remaining base of the U to the stomach wall employing a simple continuous suture pattern (Fig. 68-10*C*).
6. Bring the muscle flap to the gastric surface, advancing it a few millimeters beyond the previous suture line.
7. Suture the flap with the same material to the stomach wall to close the myotomy (Fig. 68-10*C*).

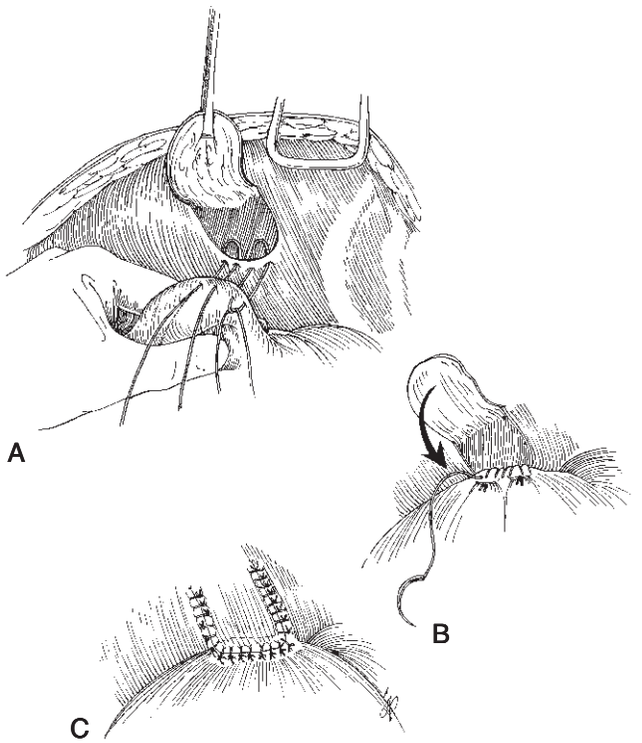

Figure 68-10. Technique for muscle flap gastropexy (for gastric dilatation-volvulus). See text for details.

Incisional Gastropexy

Technique

1. Refer to the incisional gastropexy procedure as described for hiatal hernia in Chapter 66.
2. An incisional gastropexy for gastric dilatation-volvulus differs by always being done on the right side (i.e., antrum to right side of body wall), as for the other gastropexy techniques described here.

Prophylactic Gastropexy

Technique

1. This can be done in a female dog at the time of sterilization by extending the incision cranially.
2. In the older sterilized bitch or male dog, a laparoscopic or laproscopic-assisted technique can be used.
3. The laparoscopic-assisted technique includes two small incisions, one just caudal to the umbilicus (2–3 cm) and the other approximately 3 to 4 cm caudal to the last rib and just lateral to the rectus abdominus muscle.
4. The midline incision allows a trochar cannula (10–12 mm in diameter) to be placed followed by the peritoneal infusion of carbon dioxide. Place a camera and light source through this cannula. Place the other trochar cannula through the small incision behind the right rib. Insert the Babcock forceps through this cannula.
5. Identify the antrum and pull to the incision behind the last rib using the Babcock forceps. Extend this incision to 4 to 6 cm in length to allow the pyloric antrum to be partially exteriorized.
6. Place two stay sutures in the antrum to allow a 4- to 5-cm seromuscular incision to be made between the sutures.
7. Suture the cut edges of the seromuscular layer to the peritoneum and transversus abdominus muscle. Suture the overlying abdominal oblique muscles and subcutaneous tissue and skin to close the incision. Close the midline linea alba incision routinely.

Postoperative Care and Complications

Short Term

- Monitor closely for a minimum of 4 days for cardiac arrhythmias, especially ventricular arrhythmias (see Chapter 145 for details of treatment); hemodynamic abnormalities or circulatory collapse; recurrent gastric retention; and gastric perforation with subsequent peritonitis.
- Maintain fluid therapy and supplement with potassium for a minimum of 48 hours.
- Monitor serum electrolyte, blood gas, hematocrit, total protein, urinary output, and central venous pressure values as necessary.
- Promote gastrointestinal motility with metoclopramide, 0.2 to 0.4 mg/kg SC or PO q6–8h. Treat with systemic antacids and sucralfate (see Chapter 67) if ulceration or necrosis was present at surgery, or if vomiting of bloody fluid is present postoperatively.
- Maintain tube gastropexy under a soft padded bandage so that chewing or dislodgement of the tube is prevented.
- The tube can be used for decompression and administration of fluids, gruel, and medication.
- Feeding can resume 24 to 48 hours after surgery.

Long Term

- Remove the tube (tube gastropexy) 5 to 7 days after placement. Allow the fistula to heal by second intention (contraction and epithelialization).
- Wean the animal slowly off antiarrhythmic drugs if cardiac arrhythmia was a problem and so treated.
- Encourage three to four feedings per day at home.

Prognosis

- Fair to good if partial gastrectomy is not indicated.
- Grave to poor when partial gastrectomy is done.

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Chapter 69

Diseases of the Intestines

Robert G. Sherding / Susan E. Johnson

DIARRHEA

Diarrhea results from excessive fecal water content and is the most important clinical sign of intestinal disease in the dog and cat. It is characterized by an abnormal consistency and increase in frequency, fluidity, and volume of feces. The pathogenesis involves derangement of transmucosal water and solute fluxes caused by abnormal digestion, absorption, secretion, permeability, motility, or a combination of these.

Acute versus Chronic Diarrhea

For initial management of diarrhea, consider whether diarrhea is acute or chronic (based on history).

Acute Diarrhea

Acute diarrhea is characterized by sudden onset and short duration (3 weeks or less) of watery or watery-mucoid diarrhea. Diarrhea may be overtly bloody when associated with loss of mucosal integrity. Inappetence, lethargy, and vomiting are frequently associated signs; fever, abdominal pain, and significant dehydration suggest more serious intestinal disease.

- Preliminary diagnostic considerations for diarrhea in the dog and cat should include diet (indiscretion, intolerance, hypersensitivity), medication side effects, toxicity, intestinal parasites (helminths, protozoa), enteric viruses, enteropathogenic bacteria, and a variety of systemic or metabolic disturbances.
- Although there are exceptions, acute diarrhea associated with diet, parasites, and medications generally tends to be mild and self-limiting, whereas acute diarrhea that is severe and life-threatening occurs most frequently in young animals with infectious enteritis (e.g., parvoviral enteritis).
- Diagnostic evaluations in acute diarrhea need not be extensive. Because treatment is mainly supportive and nonspecific, many animals can be managed without determination of a definitive diagnosis. Nevertheless, it is important to identify parasites and enteropathogens that require specific treatments and to identify surgical diseases (e.g., foreign bodies and intussusception).
- Treatment of acute diarrhea is based on rehydration therapy and dietary modification. Symptomatic therapy with antidiarrheal agents may be considered. Nonspecific or mild acute diarrhea often is self-limiting in a day or two without treatment or with restricted food intake.

Chronic Diarrhea

- Diarrhea is categorized as chronic if it has been persistent (3–4 weeks or longer) or has a pattern of episodic recurrence. Chronicity generally excludes simple dietary indiscretion, intoxication, and viral enteritis as causes.

▼ ***Key Point*** Base management of chronic diarrhea on diagnosis rather than symptomatic treatment. Specific intervention or treatment usually is necessary, requiring a specific diagnosis or functional and histopathologic characterization.

- The first step in management is to classify the diarrhea as large or small bowel in origin, based on the history and physical examination. Diagnostic tests and procedures include routine hematologic and serum chemistry evaluations, tests of enteropancreatic function, fecal examinations, radiography, ultrasonography, and endoscopy. Biopsy of the small or large intestine may be necessary.

Small Bowel versus Large Bowel

The anatomic localization of the disease process to the small or large bowel is based on the patient's defecation pattern and fecal characteristics (frequency, volume, consistency, color, odor, composition) (Table 69-1). This distinction is most useful in dogs for determining the direction of subsequent diagnostic evaluations. Diffuse diseases of the gastrointestinal (GI) tract may produce concurrent small and large bowel signs and, sometimes, gastric signs such as vomiting.

Small Bowel Diarrhea

Chronic small bowel diarrhea can be associated with maldigestion and malabsorption and is characterized by

Table 69-1. SMALL BOWEL VERSUS LARGE BOWEL DIARRHEA

Observation	Small Intestine	Large Intestine
Frequency of defecation	Normal to slightly increased	Very increased
Fecal output	Large volumes	Small volumes frequently
Urgency or tenesmus	Absent	Present
Dyschezia	Absent	Present with rectal disease
Mucus in feces	Absent	Present
Exudate (WBC) in feces	Absent	Present sometimes
Hematochezia (red blood)	Rare	Frequent
Melena (digested blood)	Present sometimes	Absent
Steatorrhea	Present sometimes	Absent
Flatulence and borborygmus	Present sometimes	Absent
Weight loss	Present sometimes	Rare
Vomiting	Present sometimes in dogs; frequent in cats	Occasional

WBC, white blood cells.

a high volume without urgency, tenesmus, or marked increase in frequency. Weight loss and decline in body condition (malnutrition) may occur.

- Because of unabsorbed nutrients that are degraded and fermented by intestinal bacteria, the feces are rancid and foul-smelling and the increased production of luminal gas by bacteria results in excessive flatulence and borborygmus.
- Steatorrhea (feces containing an excess of unabsorbed fat) can occur in maldigestive and malabsorptive small bowel diarrhea. In extreme cases, the feces may appear oily, greasy, and pale. Hair around the perineum may also have an oily texture from contact with fatty feces.
- Small bowel diarrhea is generally free of grossly visible mucus or blood. When there is bleeding from a lesion in the proximal GI tract, the blood pigment becomes dark black during transit (melena). In the absence of gastric bleeding, melena generally indicates small intestinal parasitism (e.g., hookworms), infection (viral, bacterial, fungal), ulceration (e.g., drug induced), severe inflammation, or neoplasia.

Large Bowel Diarrhea

Large bowel diarrhea is characterized by frequent urges to defecate (usually greater than 3 times normal frequency), with each defecation producing small quantities of feces that often contain excessive mucus and sometimes fresh red blood.

- Urgency resulting from irritability or inflammation of the distal colon causes frequent premature expulsions of small quantities of feces that would otherwise be insufficient to trigger the defecation reflex. Lapses in housetraining ("accidents") may be caused by urgency and inability to control urges to defecate.
- Straining (tenesmus) may be noted as the patient remains in position for a prolonged time after defecation or makes repeated attempts to defecate within a few minutes. These attempts may produce little or no feces or sometimes just a few drops of mucus, exudate, and blood.
- Because many colonic diseases are associated with mucosal injury, inflammation, or ulceration, abnormal fecal constituents are frequently found in large bowel diarrhea, including (1) fresh red blood (hematochezia) that originates from sites of erosion or ulceration, (2) mucus that originates from the abundant goblet cells in the colon that respond to mucosal injury by an outpouring of mucus, and (3) exudate (leukocytes) that originates from the site of inflammation.

▼ ***Key Point*** Abnormal fecal constituents such as fresh red blood, mucus, and leukocytes are localizing signs indicative of colonic disease.

  - Blood may coat the feces, streaks of blood may be mixed within the feces, or drops of blood may be passed at the end of defecation.
  - Excessive mucus may give the feces a glistening or jelly-like appearance.
  - Exudates are detected by the positive identification of fecal leukocytes using cytology stains.
- Because the principal function of the colon is absorption of water and electrolytes rather than digestion and absorption of nutrients, nutrient malabsorption and steatorrhea are absent in large bowel diarrhea. Thus, dramatic weight loss and wasting are unlikely if the animal is eating, and the daily fecal output (volume or weight of feces) usually is only minimally increased.
- Vomiting is a clinical sign in about 30% of patients with colitis.

DIAGNOSTIC APPROACH FOR DIARRHEA

Initial evaluations are aimed at diagnosis of dietary, parasitic, and infectious causes of diarrhea. This should include fecal examinations, therapeutic deworming trials (fenbendazole, 50 mg/kg PO daily for 3 days), and a 4-week dietary trial using a highly digestible commercial or homemade GI diet, either alone (for small bowel diarrhea) or with psyllium added as a fiber source (for dogs with large bowel diarrhea). If diarrhea persists and the cause is not apparent, additional diagnostic evaluations may include a complete blood count (CBC), serum chemistry profile, urinalysis, additional fecal exams for infectious agents (cytology, toxin assay, and cultures), abdominal imaging (radiography and ultrasonography), and enteropancreatic function tests. Finally, endoscopic examination and biopsy may be indicated.

History

The history is especially helpful for localizing the disease process to the small or large bowel. It also may indicate underlying non-intestinal causes of diarrhea (e.g., renal failure, liver disease, hypoadrenocorticism, or feline hyperthyroidism) and identify important predisposing factors such as breed, diet, environmental factors, current medications, and exposure to parasites, infectious agents, and toxins. The following historical aspects of the diarrhea may be diagnostically useful:

- Mode of onset (abrupt versus gradual)
- Duration (acute versus chronic)
- Clinical course (intermittent, continuous, or progressive)
- Fecal characteristics (small bowel versus large bowel; see previous section)
- Correlation with diet (food intolerances and dietary indiscretions)
- Correlation with medication usage (drug side effects)
- Correlation with stressful events (psychogenic, anxiety, or "irritability" factors)
- Response to previous treatments (prescribed diets, antibiotics, corticosteroids, or fenbendazole)
- Association with other signs (weight loss, vomiting, or polyuria-polydipsia)

▼ ***Key Point*** Consider extraintestinal causes of diarrhea, such as diseases of the pancreas (exocrine pancreatic insufficiency, pancreatitis), liver, kidneys (azotemia), endocrine system (e.g., hypoadrenocorticism and hyperthyroidism), cardiovascular system, and central nervous system (CNS).

Physical Examination

A complete physical examination may reveal important clues about the severity, nature, and cause of diarrhea (Table 69-2), although in many patients the findings are nonspecific.

- Identify physical findings that may indicate underlying systemic disease that could be a cause or consequence of diarrhea.
- Identify abnormalities on abdominal palpation of the intestinal loops and digital palpation of the rectum.

Table 69-2. PHYSICAL FINDINGS IN INTESTINAL DISEASE

Physical Finding	Potential Clinical Associations
General Physical Examination	
Dehydration	Diarrheal fluid loss
Depression/weakness	Electrolyte imbalance, severe debilitation
Emaciation/malnutrition	Chronic malabsorption, protein-losing enteropathy
Dull unthrifty haircoat	Malabsorption of fatty acids, protein, and vitamins
Fever	Infection, transmural inflammation, neoplasia
Edema, ascites, pleural effusion	Protein-losing enteropathy
Pallor (anemia)	Gastrointestinal blood loss, anemia of chronic inflammation
Intestinal Palpation	
Masses	Foreign body, neoplasia, granuloma
Thickened loops	Infiltration (inflammation, lymphoma)
"Sausage loop"	Intussusception
Aggregated loops	Linear intestinal foreign body, peritoneal adhesions
Pain	Inflammation, obstruction, ischemia, peritonitis
Gas or fluid distention	Obstruction, ileus, diarrhea
Mesenteric lymphadenopathy	Inflammation, infection, neoplasia
Rectal Palpation	
Masses	Polyp, granuloma, neoplasia
Circumferential narrowing	Stricture, spasm, neoplasia
Coarse mucosal texture	Colitis, neoplasia

Table 69-3. LABORATORY FINDINGS IN INTESTINAL DISEASE

Abnormal Laboratory Findings	Clinical Associations
Hematologic Findings	
Eosinophilia	Parasitism, eosinophilic enteritis, hypoadrenocorticism, mast cell tumor
Neutrophilia	Bowel inflammation, necrosis, or neoplasia
Neutropenia or "toxic" neutrophils	Parvovirus, FeLV, FIV, endotoxemia, or overwhelming sepsis (e.g., leakage peritonitis)
Monocytosis	Chronic or granulomatous inflammation (e.g., mycosis)
Lymphopenia	Loss of lymphocytes associated with intestinal lymphangiectasia
Anemia	GI blood loss, depressed erythropoiesis (chronic inflammation, neoplasia, malnutrition)
Elevated PCV	Hemoconcentration from GI fluid loss
RBC microcytosis	Iron deficiency (chronic GI blood loss), portosystemic shunt
RBC macrocytosis	RBC regeneration, feline hyperthyroidism, FeLV, nutritional deficiencies (rare)
Serum Biochemical Findings	
Panhypoproteinemia	Protein-losing enteropathy
Hyperglobulinemia	Chronic immune stimulation, basenji enteropathy
Azotemia	Dehydration (prerenal), primary renal failure
Hypokalemia	GI loss of fluid and electrolytes, anorexia
Hyperkalemia/hyponatremia	Hypoadrenocorticism, trichuriasis (rare)
Hypocalcemia	Hypoalbuminemia, lymphangiectasia, pancreatitis
Hypocholesterolemia	Lymphangiectasia, liver disease
Elevated liver enzymes or bile acids	Liver disease
Elevated amylase/lipase	Pancreatitis, enteritis, or azotemia
Elevated thyroxine (T4)	Feline hyperthyroidism

FeLV, feline leukemia virus; FIV, feline immunodeficiency virus; GI, gastrointestinal; PCV, packed cell volume; RBC, red blood cell.

- Inspect the fecal material obtained on the palpation glove for abrasive particles (such as bone chips), blood, and mucus. If indicated, examine the fecal material microscopically for parasites, microorganisms, and inflammatory cells or submit for culture.

Routine Laboratory Tests

- Evaluate a CBC for leukocyte responses and anemia that may be associated with intestinal disease (Table 69-3).
- Perform a serum biochemical profile and urinalysis to identify metabolic or systemic disorders that could cause or result from diarrhea (see Table 69-3).
- Measure serum thyroxin (T4) concentration in all cats over 5 years of age with diarrhea or weight loss to exclude hyperthyroidism as a cause (see Chapter 31).

Fecal Examinations

Fecal examinations are an important aspect of the diagnostic approach to diarrhea and should involve visual inspection (for blood, mucus, and foreign matter), parasite evaluation, and microscopic examinations. Specialized evaluations can include quantitative fecal collection and fat analysis, chemical determinations, cultures, toxin assays, virology, and nuclear scans, but these are used only in selective cases.

▼ ***Key Point*** Examination of feces for parasites should be part of the minimum database for all animals with diarrhea.

- In cases of chronic unresponsive diarrhea, expand the database to include microscopic examination of stained fecal smears for fat, starch, and leukocytes.
- If circumstances suggest infection, perform fecal culture for specific enteropathogenic bacteria *(Salmonella, Campylobacter)* or toxin assay for enterotoxigenic *Clostridium perfringens*.
- Diagnostic methods for intestinal parasites and infectious agents are listed in Table 69-4.

Fecal Examination for Parasites

Fecal examination for parasites can include fecal flotation, zinc sulfate centrifugation-flotation, direct wet smears, and immunoassays. Examine fresh feces within 1 hour of collection. Alternatively, refrigerate feces within 1 hour and examine within 3 days, or preserve feces in formalin for later examination.

Table 69-4. DIAGNOSIS OF INTESTINAL PATHOGENS OF DOGS AND CATS

Pathogen	Method of Diagnosis
Helminths	
Ascarids *(Toxocara, Toxascaris leonina)*	Routine fecal flotation for ova
Hookworms *(Ancylostoma)*	Routine fecal flotation for ova
Whipworms *(Trichuris vulpis)*	Routine fecal flotation for ova; fenbendazole trial
Tapeworms *(Taenia, Dipylidium caninum)*	Fecal proglottids or flotation for ova
Strongyloides	Fecal sediment or Baermann test for larvae
Others (flukes)	Fecal zinc sulfate centrifugation-flotation for ova
Protozoa	
Coccidia (Isospora)	Fecal flotation for oocysts
Cryptosporidium spp.	Microplate ELISA, direct immunofluorescence, PCR, Sheather's flotation
Giardia	Fecal zinc sulfate centrifugation-flotation for cysts; fecal ELISA or IFA; duodenal wash for trophozoites; fenbendazole trial
Tritrichomonas foetus	Fecal wet smear for trophozoites; InPouch TF culture; PCR
Entamoeba histolytica	Fecal wet smear for trophozoites
Balantidium coli	Fecal wet smear for trophozoites
Viruses	
Canine parvovirus	Fecal ELISA (SNAP-Parvo Test) for viral antigen (see Chapter 14)
Feline panleukopenia virus	Signs, leucopenia (see Chapter 14)
Canine coronavirus	Fecal EM, virus culture, PCR (see Chapter 14)
Feline enteric coronavirus and FIP	Signs, serology, fecal EM, PCR, biopsies (see Chapter 10)
Rotaviruses	Fecal EM, virus culture, PCR (see Chapter 14)
Astrovirus	Fecal EM, PCR (see Chapter 14)
Canine distemper virus	Signs (see Chapter 13)
Retroviruses (FeLV, FIV)	FeLV antigen test (ELISA, IFA); FIV antibody test (see Chapters 8, 9)
Rickettsia	
Salmon poisoning *(Neorickettsia helminthoeca)*	Operculated trematode eggs in feces; rickettsia in lymph node cytology (see Chapter 17)
Bacteria	
Salmonella	Fecal culture
Campylobacter jejuni	Fecal microscopy and culture
Yersinia enterocolitica, Y. pseudotuberculosis	Fecal culture
Bacillus piliformis (Tyzzer's disease)	Biopsy (gut, liver) for filamentous bacteria; mouse inoculation
Mycobacterium spp.	Acid-fast bacteria in cytology/biopsy; culture, PCR (see Chapter 19)
Clostridium perfringens, C. difficile	ELISA-based fecal enterotoxin assays; PCR
Enteropathogenic *Escherichia coli* (?)	Fecal culture and toxin assays
Fungi	
Histoplasma capsulatum	Fungi in biopsies/cytologies; serology (see Chapter 20)
Pythium, Zygomycetes	Pythium ELISA; poorly septate hyphae in biopsies (Chapters 20, 40)
Others (*Candida albicans, Aspergillus,* etc.)	Yeast or hyphae in biopsies; fungal culture (see Chapters 20, 40)
Algae *(Prototheca)*	Unicellular algae in cytology or biopsy; fecal culture (Sabouraud's)

ELISA, enzyme-linked immunosorbent assay; EM, electron microscopy; FeLV, feline leukemia virus; FIP, feline infectious peritonitis; FIV, feline immunodeficiency virus; IFA, immunofluorescent antibody; PCR, polymerase chain reaction test; Rx, therapeutic response.

- Use routine fecal flotation to identify nematode ova and coccidian oocysts other than *Cryptosporidium.*
- In warm, humid regions (e.g., southern United States) endemic for *Strongyloides* species, perform a direct wet smear, sedimentation, or Baermann procedure to identify larvae in the feces.
- For *Giardia,* use zinc sulfate centrifugation-flotation to identify cysts or an immunoassay to identify fecal antigen. Reliable fecal immunoassays are the point-of-care SNAP Giardia Test Kit (IDEXX), the microplate enzyme-linked immunosorbent assay (ELISA) (Remel), or an immunofluorescent antibody (IFA) test at a commercial lab. Evidence suggests the rapid ELISA test for human *Giardia* is not reliable in animals.
- Use a direct saline smear of fresh feces to detect motile trophozoites of protozoan parasites, including *Giardia, Tritrichomonas, Entamoeba histolytica,* and *Balantidium coli.* This is an insensitive method for diagnosis of *Giardia.* The distinguishing characteristics of each of these protozoa are discussed under "Protozoan Parasites."
- For diagnosis of *Tritrichomonas foetus* infection in cats, fecal culture using InPouch-TF and fecal polymerase chain reaction (PCR) assay are more sensitive than direct fecal smear microscopy.
- For *Cryptosporidium parvum,* a very small coccidian, use fecal antigen immunoassay (microplate ELISA or IFA), Sheather's sugar flotation for oocysts, or modi-

fied acid-fast staining. Evidence suggests the rapid ELISA test for human *Cryptosporidium* is not reliable in animals.
- Diagnosis of occult parasite infections (e.g., *Giardia* and most nematodes including whipworms) can be based on response to a therapeutic trial using fenbendazole (50 mg/kg PO q24h for 3–5 days).

▼ ***Key Point*** Intestinal parasitism can resemble many other small and large bowel disorders. Common examples are hookworms, whipworms, and *Giardia.*

Fecal Examination for Infectious Agents

The diagnosis of infectious diarrhea often depends on the detection of the offending viral, bacterial, or fungal organisms in the feces. Details of diagnosis of these various enteric infections are found in the respective sections of this chapter.

Viruses

Viral diarrhea is generally acute and is confirmed by detection of viral antigen in the feces (ELISA, PCR, etc.) or virus particles by electron microscopy (see Chapter 14).

Bacteria

The common enteropathogenic bacteria in dogs and cats are listed in Table 69-4.

- Specific enteropathogenic bacteria, such as *Salmonella* and *Campylobacter,* can be isolated from fresh feces using appropriate culture media. Cultures are particularly indicated when examination of fecal cytology preparations reveals the presence of numerous fecal leukocytes or *Campylobacter*-like bacteria or when there is an outbreak of diarrhea in groups of animals housed together.
- For diagnosis of *Clostridium perfringens* and *Clostridium difficile* enterotoxigenic diarrhea, use validated fecal ELISA (Techlab, Blacksburg, VA) and PCR assays to detect clostridial enterotoxins. The finding of numerous large gram-positive sporulating rods with a "safety pin" appearance in stained fecal smears is not a reliable indicator of toxin-producing *C. perfringens.* Nontoxigenic *C. perfringens* is part of the normal intestinal flora in dogs and cats; thus, cultures are not useful.

Fungi and Prototheca

The diagnosis of fungal *(Histoplasma, Aspergillus, Pythium, Candida)* and protothecal infections is usually based on identification of the organisms in feces or more often in rectal scrapings *(Histoplasma)*, tissue aspirates, or intestinal biopsies (see Chapters 20 and 40).

- Serodiagnostic tests for presumptive diagnosis of histoplasmosis and pythiosis also are available.
- Affected tissues can be cultured for systemic fungi and *Prototheca* (a rare cause of colitis), but culture growth takes weeks and the isolation rate is low.

Fecal Examination Using Special Stains

Feces can be examined microscopically for abnormal constituents using Sudan, Lugol iodine, Gram, and various other cytologic stains. In each test, one to two drops of fresh feces are stained on a microscope slide and examined. In general, these procedures are relatively insensitive and nonspecific and are affected by many factors, including diet.

Sudan and Iodine Stain

Fecal staining with Sudan for undigested fat and Lugol iodine for undigested starch may suggest exocrine pancreatic insufficiency (maldigestion); however, these evaluations are too insensitive, nonspecific, and diet dependent to be recommended. These procedures have been replaced by more reliable diagnostic tests for exocrine pancreatic insufficiency (see Chapter 73).

Cytology Stain

Routine cytology staining (e.g., new methylene blue, Wright, and Diff-Quik stains) identifies fecal leukocytes that are markers of exudative inflammatory colonic disease. Cytology may occasionally identify neoplastic cells or *Histoplasma* or *Prototheca* organisms. It is advisable to follow up with patients that are positive for fecal leukocytes with colonoscopy and fecal cultures for invasive bacteria such as *Campylobacter* and *Salmonella.*

Gram Stain

With gram staining, the experienced observer may identify large numbers of *C. perfringens* or *Campylobacter*-like spiral bacteria; however, microscopy is much less reliable than toxin assays for *Clostridium* and culture for *Campylobacter.*

Tests for Fecal Occult Blood

These include a simple, in-office qualitative screening test (Hemoccult test) and a more accurate, semiquantitative send-out test (HemoQuant, SmithKline). These tests are sensitive for detecting even very small amounts of GI hemorrhage. Because of this sensitivity, it is recommended that the owner exclude meat from the animal's diet for at least 3 days prior to testing to avoid false-positive results.

- The presence of fecal occult blood signifies a bleeding lesion of the GI tract, which suggests an ulcerative, inflammatory, or neoplastic condition, or a hemostatic abnormality.
- The fecal occult blood test is also indicated to document GI bleeding as a cause of blood loss anemia.

Quantitative Fecal Fat Analysis

This can be used as an intestinal function test to confirm steatorrhea, but it is rarely used because it is cumbersome and impractical to perform and does not differentiate pancreatic maldigestion from intestinal malabsorption. Feces must be collected for a 24- to 72-hour period while the animal is confined and fed a standard diet. The feces are weighed and sent to a commercial laboratory for analysis. Normally, less than 10% of ingested fat is excreted in the feces, or less than 0.3 g/kg/day in dogs and less than 0.4 g/kg/day in cats.

Fecal Proteolytic Activity

Fecal proteolytic activity can be assayed as an indicator of pancreatic secretion of proteases (trypsin) for the diagnosis of exocrine pancreatic insufficiency (EPI). The serum trypsin-like immunoreactivity (TLI) assay is more accurate and is now preferred for the diagnosis of exocrine pancreatic insufficiency in both dogs and cats (see Chapter 73).

Tests for Fecal Protein Loss

See under "Tests for Protein-Losing Enteropathy."

Enteropancreatic Function Tests

The following tests are designed to evaluate digestive and absorptive functions.

Tests for Exocrine Pancreatic Insufficiency

Tests for exocrine pancreatic insufficiency (pancreatic maldigestion), such as serum trypsin-like immunoreactivity and fecal assays for proteolytic activity, are described in Chapter 73.

Serum Folate and Cobalamin Assays

Serum concentrations of folate and cobalamin (vitamin B_{12}) are indicative exocrine pancreatic function (cobalamin), intestinal absorptive function, and the status of the intestinal bacterial flora.

Serum Folate

Folate, a water-soluble B vitamin, is plentiful in most commercial pet foods, and serum concentration depends primarily on the absorptive function of the proximal small intestine.

- Serum folate (normal, dog: 6.5–11.5 µg/L; cat: 9.7–21.6 µg/L) may be decreased in enteropathies that impair absorption in the proximal small intestine or in diffuse small intestinal disease. Widespread malignancy and sulfasalazine treatment also may decrease serum folate.
- Serum folate may be increased with overproliferation of the normal intestinal flora because many species of bacteria synthesize folic acid.
- Serum folate also may be increased by high dietary intake of folic acid, low intestinal pH, exocrine pancreatic insufficiency (32% of cases), and artifactually by hemolysis or heating of the blood specimen.

Serum Cobalamin

Cobalamin, a water-soluble B vitamin, is plentiful in most commercial pet foods, and serum concentration depends on the secretion of pancreatic intrinsic factor necessary for normal cobalamin absorption and on the absorptive function of the ileum.

- Serum cobalamin (normal, dog: 249–733 ng/L; cat: 290–1500 ng/L) is frequently decreased in exocrine pancreatic insufficiency (deficiency of intrinsic factor) and in enteropathies that impair absorption in the distal small intestine, including diffuse small intestinal disease. It also is decreased in presumed small intestinal bacterial overgrowth.
- Because cobalamin has a shorter half-life in cats, cats with chronic intestinal disease are particularly susceptible to developing cobalamin deficiency.
- Prolonged exposure of the blood specimen to bright light may artifactually decrease cobalamin.
- An isolated hereditary defect in cobalamin absorption has been recognized in some dog breeds (giant schnauzer, Border collie, Shar-Pei).

▼ ***Key Point*** In small intestinal bacterial overgrowth, serum folate may be increased due to synthesis of folate by the proliferated bacteria, whereas cobalamin may be decreased because bacteria can utilize or bind the vitamin, making it unavailable for absorption.

Breath Hydrogen Test

This assesses monosaccharide or disaccharide malabsorption or bacterial overgrowth, based on the principle that intestinal bacteria ferment intraluminal carbohydrate and produce hydrogen gas, some of which is absorbed into the blood and excreted by the lungs. This test is impractical for routine clinical use and is affected by diet, gastric emptying, intestinal transit, and the status of the intestinal flora.

Five-Sugar Absorption Tests for Intestinal Permeability

These oral sugar absorption tests are variations on the other carbohydrate absorption tests. A mixture of sugars is used as a noninvasive molecular probe of mucosal permeability and injury based on urine recovery (in a 6-hour urine sample) after oral administration. These sugar probes measure passive diffusion. Lactulose, cellobiose, and raffinose are probes of the large pores of the paracellular pathway, and urine recovery increases with mucosal epithelial damage. Mannitol and rhamnose are probes of the numerous small pores of

the transcellular pathway, and urine recovery decreases with loss of mucosal absorptive surface area (such as villous atrophy). An increase in the lactulose-to-rhamnose ratio is typical of intestinal disease with mucosal damage and increased permeability.

One variation on this procedure involves giving a mixture of lactulose, rhamnose, xylose, methylglucose, and sucrose, and the ratios are determined in 6-hour urine for lactose-to-rhamnose (permeability test), xylose-to-methylglucose (absorption test), and sucrose-to-methylglucose (mucosal digestion test).

In addition to reflecting absorptive function and permeability, results are also affected by gastric emptying, intestinal dilution and transit, systemic distribution, metabolism, and renal clearance. Results have not shown good correlation with clinical disease activity and histologic findings.

Unreliable Absorption Tests

In general, the reliability of oral absorption tests is affected by gastric emptying time, intestinal dilution and transit time, digestion and absorption, systemic distribution, metabolism, and renal excretion. Because of inconsistent results, the following absorption tests are not considered clinically useful in dogs and cats:

- Absorption of glucose substrates (glucose, lactose, starch)—Affected by insulin, etc.
- Xylose absorption—For detection of brush border monosaccharide malabsorption
- Quantitative fecal fat analysis—For detection of fat malabsorption (steatorrhea)
- Oral triglyceride absorption
- Vitamin A absorption
- Bentiromide para-aminobenzoic acid (BT-PABA) absorption

Tests for Protein-Losing Enteropathy

Excessive GI loss of plasma proteins can be documented using fecal assays that quantitate the intestinal loss of specific serum proteins, such as alpha-1-proteinase inhibitor, or an IV dose of ^{51}chromium-labeled albumin, a radiopharmaceutical.

- Alpha-1-proteinase inhibitor is a serum protein similar in molecular size to albumin. The intestinal loss of alpha-1-proteinase inhibitor in protein-losing enteropathy parallels the loss of albumin, except that it is not digested and is excreted intact in the feces. Thus, using a canine-specific assay, alpha-1-proteinase inhibitor can be measured in the feces as a marker for intestinal protein loss in dogs. This test is useful for evaluation of dogs with unexplained hypoproteinemia and for early detection of affected dogs in high-risk breeds, such as the soft-coated wheaten terrier.
- Normal fecal excretion of the alpha-1-proteinase inhibitor is <5.7 µg/g feces in dogs and <1.6 µg/g feces in cats. The assay requires submission of three fresh fecal specimens to the Gastrointestinal Laboratory, Department of Small Animal Medicine and Surgery, College of Veterinary Medicine, Texas A&M University, College Station, TX 77843-4474 (website: http://www.cvm.tamu.edu/gilab).

Tests for Bacterial Overgrowth

Direct evidence of small intestinal bacterial overgrowth is conventionally based on quantitative cultures of small intestinal juice; however, because of extensive overlap in the bacterial counts found in normal and diarrheic dogs and cats, the diagnostic criteria for small intestinal bacterial overgrowth in animal patients is uncertain. Indirect evidence of small intestinal bacterial overgrowth is indicated by the following:

- Increased serum folate and decreased serum cobalamin, reflecting increased bacterial metabolic activity
- Abnormal hydrogen breath test results, reflecting increased bacterial fermentation activity
- Increased serum unconjugated bile acids, reflecting increased bacterial deconjugation activity
- Idiopathic chronic small bowel diarrhea that is antibiotic responsive

Tests for Intestinal Motility

Tests for clinically assessing intestinal motility have limited clinical usefulness except for identifying obstruction to flow. These include intestinal transit time of barium, barium-impregnated spheres, or radiopharmaceuticals. The hydrogen breath indirectly reflects transit time of the proximal GI tract.

Radiography and Ultrasonography

Plain Abdominal Radiography

Plain radiography is indicated for detection of intestinal masses or abnormal gas-fluid patterns, especially when mechanical or obstructive disorders are suspected (e.g., intestinal mass, foreign body, or intussusception).

Gastrointestinal Barium Contrast Radiography

Upper GI barium radiography is indicated when other evaluations fail to determine the cause of small bowel diarrhea or when intestinal obstruction is suspected (see Chapter 4). This may help detect obstructive lesions, neoplastic masses, and inflammatory lesions that cause an irregular mucosal pattern or distortion of the bowel wall. In most cases, however, diarrhea involves microscopic and functional changes in the bowel that are not detected by barium radiography.

Barium Enema Contrast Radiography

Barium enema radiography is indicated in selected cases of large bowel diarrhea for evaluating the colon

and cecum for intussusceptions, neoplasms, polyps, strictures, inflammatory lesions, and colonic displacement or malformation. Colonoscopy is generally preferred over barium enema for evaluating the colon because it yields more definitive diagnostic information.

Abdominal Ultrasonography

Ultrasonography is indicated for assessing intestinal wall thickness and layering, for defining intestinal and other abdominal masses, and for evaluating other abdominal organs—e.g., lymph nodes, spleen, pancreas, liver, biliary tract, kidneys, adrenals, and prostate (see Chapter 4).

Endoscopy

▼ ***Key Point*** Endoscopic examination with mucosal biopsy is required for definitive diagnosis or accurate characterization of the disease in many cases of chronic intractable diarrhea in which non-intestinal, dietary, parasitic, and infectious causes have been excluded.

Gastrointestinal Endoscopy

Duodenoscopy with a flexible fiberoptic endoscope can be performed in the anesthetized animal for visual examination of the upper GI tract, including duodenum; for duodenal aspiration (for quantitative bacterial culture or detection of *Giardia* trophozoites); and for directed forceps biopsy of the intestinal mucosa (see Chapter 67 for a description of endoscopic equipment and discussion of gastroscopy).

- The normal duodenal mucosa appears pale pink with a uniformly granular villus pattern.
- Biliary and pancreatic duct papillae and Peyer lymphoid patches are normally seen.
- The mucosa is non-friable and should be free of excessive granularity, hemorrhages, erosions, ulcers, thickened folds, masses, or strictures. Villous lymphatics (lacteals) should not be prominent in the fasted animal.
- The lumen is easily and uniformly distensible with air.

Colonoscopy

Colonoscopy allows direct visualization of the lumen of the colon, sampling of luminal content for culture and exfoliative cytology, and directed forceps biopsy of the ileocolic mucosa.

- Suitable rigid colonoscopes are relatively inexpensive and easy to use. Because colonic diseases are often diffuse, examination and biopsy of the descending colon with a rigid instrument is sufficient for diagnosis in many patients.
- When lesions are located predominantly in the ascending or transverse colon, areas inaccessible with a rigid colonoscope, use a flexible fiberoptic or video colonoscope. A flexible colonoscope can be navigated through the ileocolic sphincter for examination and biopsy of the ileum in some animals.
- The normal colonic mucosa appears pale pink through the colonoscope and reflects light uniformly. It is non-friable, thin enough that the submucosal vessels are visible, and free of erosions, ulcers, thickened folds, masses, or strictures.

Intestinal Biopsy

The least invasive and, in many cases, preferred method for procurement of intestinal biopsies is endoscopy. If endoscopy is not available, or if endoscopic biopsies are inconclusive, consider full-thickness intestinal biopsy by laparotomy (see Chapter 70).

- Obtain multiple biopsies along the length of the gut even if no lesions are visible by gross inspection, which is often the case.
- Biopsy mesenteric lymph nodes and evaluate other abdominal organs, especially the pancreas, liver, and colon.
- Duodenal aspirates or duodenal mucosal impression smears may be examined for *Giardia* trophozoites or cultured quantitatively for aerobic and anaerobic bacterial overgrowth.

Therapeutic Trials

In some cases, the response to a dietary modification or therapeutic drug trial is used as an empirical diagnostic approach, when supported by adequate clinical information. Common therapeutic trials are given in the sections that follow.

Diet Modification

- Commercial GI diet for optimal digestability
- Novel protein diet—For dietary hypersensitivity or food allergy
- Fiber supplemented diet—For fiber-responsive large bowel diarrhea (dogs)

Fenbendazole

- For helminths (especially whipworms)
- For *Giardia*

Metronidazole

- For *Giardia*
- For enteropathogenic bacteria (especially *Clostridium*)
- To suppress flora in bacterial overgrowth
- To treat idiopathic inflammatory bowel disease (via flora effects or immune modulation)

NONSPECIFIC TREATMENT OF DIARRHEA

Dietary, supportive, and symptomatic therapy often is beneficial in diarrhea, especially acute diarrhea. In

severe acute diarrhea, fluid and electrolyte therapy can be lifesaving.

Dietary Management

Acute Diarrhea

- The initial goal is to physiologically "rest" the GI tract by restricting food intake for at least 24 hours.
- When resuming feeding, give bland, low-fat foods in small amounts at frequent intervals. Various commercial diets are available that have been specially formulated for animals with GI disease. Recipes for appropriate homemade diets are available as well. Examples of appropriate foods include boiled rice combined with turkey, boiled skinless chicken, yogurt, or low-fat cottage cheese as protein sources.
- Examples of commercial "intestinal diets" appropriate for nonspecific therapy of diarrhea include Eukanuba Low Residue (Iams), Prescription Diet i/d (Hill's), Low Fat (Waltham), and EN Formula (Purina). Other highly digestible diets can also be used.
- When the diarrhea has been resolved for 48 hours, gradually reintroduce the animal's regular diet.

Chronic Diarrhea

Divide daily food intake into three or four feedings, and use (1) commercial diets designed for GI disease with high digestibility and mild fat restriction (for all types of diarrhea); (2) novel protein diets (for dietary hypersensitivity and inflammatory bowel disease); or (3) fiber-enriched diets (for canine large bowel diarrhea).

Fluid Therapy

- In severe, acute diarrhea, such as occurs with parvoviral enteritis, fluid and electrolyte replacement is essential for management of intestinal fluid loss that may lead to serious dehydration, shock, and death (see Chapter 5).
- Parenteral methods of fluid therapy are preferred in most cases; however, over-the-counter oral glucose-electrolyte solutions (Pedialyte) are available for counterbalancing intestinal fluid losses in cases of mild diarrhea.

Antidiarrheal Drugs

Symptomatic treatment is based on drugs that modify motility, fluid secretion, and absorption or on drugs that act locally within the lumen as protectants or adsorbents.

- In most cases, these drugs are reserved for short-term use, usually for periods of 5 days or less. Some commonly used antidiarrheal drugs and their dosages are listed in Table 69-5.
- The purposes of antidiarrheal drugs are to provide short term relief from diarrhea, to provide relief from bowel discomfort ("crampiness"), and to control intestinal fluid losses.

Opiate and Opioid Narcotic Analgesics

▼ ***Key Point*** Opioid drugs such as loperamide are the most effective all-purpose antidiarrheal agents (see Table 69-5).

Table 69-5. DRUGS USED FOR SYMPTOMATIC TREATMENT OF DIARRHEA

Drug	Product (Manufacturer)	Preparation	Dosage	Frequency
*Narcotic Analgesics**				
Diphenoxylate	Generic	Tab: 2.5 mg Liq: 0.5 mg/ml	0.1–0.2 mg/kg PO	q6–8h
Loperamide	Imodium AD (McNeil)	Cap: 2 mg Liq: 0.2 mg/ml	0.1–0.2 mg/kg PO	q6–8h
Codeine	Many	Tab, Cap, Liq	0.25–0.5 mg/kg PO	q6–8h
Anticholinergics/Antispasmodics				
Aminopentamide	Centrine (Fort Dodge)	Tab: 0.2 mg Inj: 0.5 mg/ml	0.01–0.03 mg/kg SC, IM, PO	q8–12h
Dicyclomine	Generic	Tab: 20 mg Cap: 10 mg	0.2 mg/kg PO	q8–12h
Propantheline	Generic	Tab: 15 mg	0.25 mg/kg PO	q8–12h
Hyoscyamine	Levsin (Schwarz)	Tab: 0.125 mg Liq: 0.025, 0.125 mg/ml	0.003–0.006 mg/kg PO, SC	q8–12h
Antisecretory/Protectant				
Bismuth subsalicylate†	Pepto-Bismol (Procter & Gamble)	Liq: 9, 16 mg/ml	0.5–1.0 ml/kg PO	q6–8h

*Narcotic analgesics are not recommended in bacterial enteritis or liver disease.
†Avoid long-term (>3 days) use in cats because of low tolerance for salicylates.
Cap, capsules; Inj, injectable; Liq, elixir, suspension, or drops; Tab, tablets.

- Examples include loperamide (Imodium A-D), diphenoxylate (Lomotil), paregoric, morphine, and codeine.
- Opioids delay gastric emptying and slow bowel transit by stimulating non-propulsive contractions while decreasing propulsive motility (peristalsis), thereby allowing more contact time for absorption. This promotes fluid and electrolyte absorption.
- Opioids inhibit intestinal fluid loss through modification of mucosal fluid and electrolyte transport.
- Opioids increase anal tone and reduce the discomfort (i.e., crampiness) associated with acute diarrhea.
- Side effects are bloating, cramping, constipation, vomiting, and CNS depression. Use is not recommended with invasive bacterial enteritis.

Anticholinergic Drugs

- Examples include aminopentamide (Centrine), dicyclomine, and propantheline.
- They cause a generalized suppression of all gut motility, including beneficial non-propulsive motility, that may lead to unwanted ileus. The atropine-like antispasmodic action may be beneficial for controlling the urgency and discomfort of anorectal disease in some cases.
- They inhibit intestinal fluid loss, presumably through an antisecretory effect.
- Side effects are GI paralysis (ileus), worsening of diarrhea, constipation, tachycardia, xerostomia, urinary retention, ocular effects, and CNS stimulation.

Protectants and Adsorbents

- Examples include kaolin-pectin (Kaopectate), bismuth (Pepto-Bismol), aluminum and magnesium salts, activated charcoal, cholestyramine, and barium.
- These oral agents remain in the lumen, and they are proposed to adsorb or bind harmful bacteria and bacterial toxins and to provide a protective coating on inflamed mucosal surfaces.
- The efficacy of these drugs is controversial. There is little evidence that they diminish intestinal fluid losses. Large doses are often required, and they are difficult for owners to administer.

Anti-inflammatory Therapy

Non-infectious inflammatory bowel diseases are often treated with corticosteroids or nonsteroidal anti-inflammatory agents (NSAIDs).

Corticosteroids

- Examples include prednisone, prednisolone, dexamethasone, and budesonide.
- Corticosteroids have anti-inflammatory, antisecretory, and mucosal-stimulating properties. The primary indication is for inflammatory bowel disease.

Nonsteroidal Anti-inflammatory Drugs

- Bismuth subsalicylate (Pepto-Bismol) has a mild mucosal anti-inflammatory action in the lumen of the proximal GI tract. Efficacy for small animal diarrhea is infrequent.
- Preparations of 5-aminosalicylic acid (5-ASA) (mesalamine) are poorly absorbed in the proximal GI tract so that they reach the colon where colonic bacteria release the active drug to produce a mucosal anti-inflammatory action for treatment of chronic colitis. Examples include sulfasalazine (Azulfidine), olsalazine (Dipentum), encapsulated mesalamine (Asacol), polymer-coated mesalamine (Pentasa), and mesalamine enema (Rowasa).
- Avoid systemic nonsteroidal anti-inflammatory drugs (e.g., flunixin meglumine, ibuprofen, and aspirin) in dogs and cats with GI disease, or use them cautiously because they cause GI ulceration.

Antibiotic Therapy

Do not use antibiotics routinely as empirical therapy in cases of uncomplicated diarrhea of undetermined cause because of the adverse effects of antibiotics on the normal intestinal flora and the risk of promoting resistant strains of bacteria.

- Use well-chosen antibiotics when specific bacterial enteropathogens, such as *Salmonella, Campylobacter,* or enterotoxigenic *C. perfringens,* are suspected.
- Antibiotics are appropriate in conditions associated with severe mucosal damage and a high risk of secondary sepsis or endotoxemia, such as parvoviral enteritis and hemorrhagic gastroenteritis (HGE). Thus, indications for antibacterial therapy in animals with acute GI disease include bloody diarrhea, fever, leukocytosis, leukopenia, fecal leukocytes, and shock.
- Metronidazole is an antibiotic frequently used in animals with diarrhea. Its potential indications are as follows:
  - To treat *Giardia* (and various other protozoa)
  - To treat certain enteropathogenic bacteria, such as *Clostridium* species
  - To suppress overabundant enteric flora in small intestinal bacterial overgrowth
  - To modify normal enteric flora that may play a role in chronic inflammatory bowel disease
  - To immunomodulate in chronic inflammatory bowel disease

Fenbendazole-Responsive Diarrhea

Fenbendazole (50 mg/kg PO q24h for 3 days) is highly effective for treating common intestinal nematode and *Giardia* infections.

Cobalamin Therapy

Cobalamin (vitamin B_{12}) is vital for many cellular processes, and it is frequently depleted in patients with

chronic small intestinal disease or exocrine pancreatic insufficiency. Cobalamin deficiency can impair intestinal mucosal regeneration and cause villous atrophy and malabsorption, exacerbating diarrhea and contributing to anorexia and depression in patients with chronic GI disease.

- Treat with parenteral cobalamin (1000 µg/ml) when serum levels are decreased, especially if <200 ng/L. Give injections weekly for at least 6 weeks, then every other week for 6 weeks, and then monthly.
- For cats and small dogs: Give 250 µg SC, weekly
- For medium dogs: Give 500 µg SC, weekly
- For large dogs: Give up to 1000 µg SC, weekly

DIETARY DIARRHEA

Etiology

- Diarrhea as a result of indiscriminant eating and chewing behavior is particularly common in dogs. Dietary indiscretions include overeating, ingestion of spoiled garbage or decomposing carrion, and ingestion of abrasive or indigestible foreign material (e.g., bones, stones, hair, plants, wood, cloth, carpeting, foil, or plastic) that can traumatize the GI mucosa.
- Diarrhea may result from an abrupt change in diet. Any change in the composition of the diet should be made in gradual increments over a period of several days to allow adaptation.
- Animals may be intolerant of certain foods, such as lactose ingested as milk, fatty foods, spicy foods, and food additives found in certain commercial diets. Food hypersensitivity to specific protein sources is implicated as a cause of inflammatory bowel disease in dogs and cats.
- Fiber-responsive diarrhea is sometimes seen in dogs.

Diagnosis

Dietary causes of diarrhea usually are identified by careful history-taking and the response to a restricted diet.

- Carefully question the owner about all aspects of diet and environment, including recent changes in type and brand of food, all supplemental feeding practices using "people foods," patterns of chewing behavior involving non-food items (including toys, plants, and haircoat), likelihood of garbage ingestion, and potential for unobserved indiscretions in free-roaming animals.
- Examine the feces for abrasive particles.

Treatment

Dietary diarrhea is self-limiting with feeding of a restricted diet, elimination of identifiable offending substances from the diet, and prevention of indiscriminant eating or chewing behavior. Management of dietary hypersensitivity is discussed under "Chronic Inflammatory Bowel Disease" later in this chapter.

DRUG- AND TOXIN-INDUCED DIARRHEA

Etiology

- Diarrhea is a frequent adverse side effect of many medications, including nonsteroidal anti-inflammatory agents (e.g., aspirin, ibuprofen, indomethacin, phenylbutazone, and flunixin meglumine), digitalis and other cardiac drugs, dithiazanine (Dizan), magnesium-containing compounds, lactulose (for hepatic encephalopathy), some anthelmintics, most anticancer drugs, and many antibacterial drugs (partly from adverse effects on the flora).
- Dexamethasone has been associated with hemorrhagic gastroenterocolitis characterized by erosion, ulceration, necrosis, and sometimes fatal colonic perforation, especially in dogs treated for intervertebral disc disease.
- Many exogenous toxins cause diarrhea, including biologic toxins such as the enterotoxins that cause staphylococcal and clostridial food poisoning and various diarrheogenic chemical poisons, such as heavy metals (lead, arsenic, thallium), insecticides (organophosphate dips, flea treatments), lawn and garden products (insecticides, herbicides, fungicides), and some houseplants.
- Free-roaming animals may drink from stagnant or runoff water polluted or potentially contaminated with toxic industrial, petroleum, or agricultural chemicals.

Diagnosis

Suspect drug- and toxin-induced diarrhea on the basis of history of exposure (or opportunity for exposure), clinical signs, and exclusion of other causes of diarrhea.

- Many medications and most toxins that cause diarrhea also cause vomiting.
- Some toxicities are associated with various extraintestinal signs (e.g., neurologic manifestations of lead and organophosphate toxicity).

Treatment

- Drug-induced diarrhea usually resolves after discontinuation of the offending medication or a reduction in its dosage.
- Toxin-induced diarrhea resolves with symptomatic antidiarrheal therapy, prevention of further exposure to the toxin, and gradual elimination of the substance from the body. However, if the exact toxin is known, consult other sources of information for additional specific treatments and antidotes.

INTESTINAL PARASITES (HELMINTHS)

The majority of intestinal parasite infections are asymptomatic: when clinical signs do occur, diarrhea and weight loss are most common. Young growing animals generally are more frequently and severely parasitized, but never overlook endoparasitism as a possible cause of acute or chronic diarrhea of either small or large bowel type in dogs and cats of all ages. Other intestinal diseases, such as viral or bacterial enteritis, often are complicated by intestinal parasite infection.

The diagnosis of parasitism depends on the identification of eggs, cysts, larvae, trophozoites, or proglottids in the feces (see Table 69-4). Parasites that are notorious for evading detection include *Giardia* in dogs and cats with small bowel diarrhea and whipworms in dogs with large bowel diarrhea. In such cases, response to a therapeutic trial is an indirect method of diagnosis. Anthelmintics used to treat the common parasites are listed in Table 69-6.

Ascarids

Etiology

Ascarid nematodes are the most prevalent intestinal parasites of dogs and cats worldwide. The ascarids of the dog are *Toxocara canis* and the less common *Toxascaris leonina;* those in the cat are *Toxocara cati* and *Toxascaris leonina.*

Life Cycle

Ascarid infection occurs by four routes:

- Prenatal infection results from transplacental migration, which occurs only with *T. canis.* Many puppies are born infected with ascarids because of transplacental migration of the bitch's somatic *T. canis* larvae into the fetus (prenatal infection).
- Milk-borne infection results from transmammary migration, which occurs with both *T. canis* and *T. cati.* Milk-borne infection during nursing is the major source of ascariasis in kittens.
- Infection by ingestion of infective eggs occurs with all three ascarids *(T. canis, T. cati,* and *T. leonine).*
- Infection by ingestion of a paratenic (transport) host *(T. canis, T. cati)* or an intermediate host *(T. leonina).*

Three types of migration pattern occur when an animal is infected:

- Liver-lung migration *(T. canis, T. cati)*
- Migration within the wall of the GI tract (all three ascarids)
- Somatic tissue migration *(T. canis, T. cati)*

Clinical Signs

- Signs of ascariasis occur most often in young puppies and kittens, in which the adult worms in the small intestine may cause abdominal discomfort, whimpering and groaning, potbellied appearance, dull haircoat, unthriftiness, stunted growth, and

Table 69-6. ANTHELMINTICS FOR DOGS AND CATS

Drug	Product (Manufacturer)	Dosage	Efficacy			
			Ascarids	Hookworms	Whipworms	Tapeworms
Dichlorophene	Many products	Dog: Capsule size as directed	++	++	–	+
Diethylcarbamazine*	Many products	Dog: 6.6 mg/kg daily or 110 mg/kg once PO	++	–	–	–
Epsiprantel	Cestex (Pfizer)	Dog: 5.5 mg/kg PO Cat: 2.75 mg/ kg PO	–	–	–	+++
Febantel plus praziquantel and pyrantel	Drontal-Plus (Bayer)	15 mg/kg of febantel	+++	+++	+++	+++
Fenbendazole	Panacur (Intervet)	50 mg/kg PO for 3–5 days	+++	+++	+++	++†
Ivermectin*‡	Heartgard Plus (Merial)	Dog: 6 µg/kg PO monthly	++	++	–	–
Milbemycin oxime*	Interceptor, Sentinel (Novartis)	Dog: 0.5 mg/kg PO monthly	++	++	++	–
Piperazine	Many products	110 mg/kg PO	++	–	–	–
Praziquantel	Droncit (Bayer)	See label; PO, SC, IM	–	–	–	+++
Pyrantel pamoate	Nemex (Pfizer)	10 mg/kg PO if <2.5 kg, 5 mg/kg PO if >2.5 kg	+++	+++	–	–

+++, excellent efficacy; ++, good efficacy; +, minimal efficacy.
*Drugs used concomitantly as heartworm preventatives (see Chapter 152).
†Efficacious for *Taenia* species of tapeworms only; not effective against *Dipylidium caninum.*
‡Consult package insert because of special safety precautions or potential for serious side effects.

diarrhea. Worms frequently are passed in vomitus or diarrhea.
- Rarely, large, tangled masses of worms occlude the lumen in young pups and cause death from intestinal obstruction, intussusception, or intestinal perforation.
- In the neonatal pup, the migration of large numbers of *T. canis* larvae through the lungs can cause severe damage and fatal pneumonia.
- In young animals with light infections and in adults, infection is most commonly asymptomatic or is evidenced merely by a loss of body condition.

Diagnosis

- The diagnosis of ascariasis is readily established by the identification of ascarid eggs in routine fecal flotation.
- Most pups begin passing large numbers of eggs in their feces around 3 weeks of age and continue to shed eggs for most of early puppyhood (4–6 months) until treated.

Treatment

- Numerous effective anthelmintics for ascarids are available (see Table 69-6). Pyrantel pamoate is especially well tolerated and effective in puppies and kittens; it also is effective in controlling hookworms.
- Because many pups are born infected with *T. canis,* treatment is recommended at 2 weeks of age, before eggs are first passed in the feces, and repeated at 4, 6, and 8 weeks to kill all worms derived from prenatal, milk-borne, and ingestion routes of infection.
- Toxocaral visceral larva migrans (VLM) is a serious disease of humans (especially children) produced by the invasion of visceral tissues by migrating *T. canis;* thus, infected pups are considered public health hazards.

Hookworms

Etiology

- *Ancylostoma caninum,* the most common hookworm in the dog, is a voracious bloodsucker.
- *Ancylostoma tubaeforme,* the common hookworm in the cat, is more of a tissue feeder than a bloodsucker and is far less pathogenic than *A. caninum* in dogs.
- *Ancylostoma braziliense* (southern United States) and *Uncinaria stenocephala* (Canada) affect both dogs and cats but are less common than *A. caninum* and *A. tubaeforme* and are only mildly pathogenic.

Life Cycle

Hookworm infection can occur by five routes: prenatal, milk-borne, ingestion of infective larvae (L3), skin penetration by infective larvae, and ingestion of paratenic hosts. Ingestion and cutaneous migration probably are the most common routes of infection. With all routes of infection, eggs are passed in feces after 2 to 3 weeks.

Clinical Signs

Pathogenicity is directly related to the hookworm's bloodsucking activity and capacity for causing intestinal blood loss. Hookworms embed their mouthparts in the mucosa to suck blood and tissue fluid, leaving bleeding, punctiform ulcers as they "graze." Hence, an important consequence of severe hookworm infection is blood loss anemia.

- The clinical signs of ancylostomiasis include tarry (melena) or bloody diarrhea accompanied by pallor, weakness, emaciation, and dehydration.
- Rapidly progressive blood loss anemia may result in acute death of neonates. In other animals, chronic blood loss may cause iron deficiency anemia characterized by erythrocytes that show hypochromasia and microcytosis.
- Acute, pruritic dermatitis occasionally is associated with the active penetration of skin by hookworm larvae.
- Hookworm infections in mature animals often are asymptomatic.

Diagnosis

Young dogs are most often affected, and the diagnosis usually is readily established by identification of the characteristic *Strongyloides* hookworm ova by routine fecal flotation. Ancylostomiasis often is associated with eosinophilia on the CBC.

Treatment

Anthelmintics effective for eradicating hookworms include pyrantel pamoate (safest for young animals), fenbendazole, and febantel (see Table 69-6 for product names and dosages).

- In areas in which *A. caninum* is a frequent problem, routinely treat bitches and pups. Because of prenatal and milk-borne infection, initiate treatment of pups at 2 weeks of age, along with treatment for *T. canis.*

▼ ***Key Point*** Pyrantel pamoate suspension is an excellent anthelmintic for nursing pups because it is safe and is active against both hookworms and ascarids.

- Severely anemic animals should receive whole blood transfusions, iron supplementation, and supportive therapy as needed.

Prevention

- Parasite control is aided by good sanitation and impervious flooring in kennels and dog runs.

- Various commercial products have a combined effect as preventive agents against both heartworms and hookworms (e.g., milbemycin) (see Table 69-6).

Whipworms

Etiology

The canine whipworm, *Trichuris vulpis,* is a common cause of large bowel diarrhea in dogs in many areas. The adult nematode has a predilection for the proximal colon and cecum, where its distinctive threadlike head end, or "whip," firmly embeds deep within the mucosa to feed on blood and tissue fluids, thereby causing colitis and typhlitis.

The feline whipworms, *Trichuris campanula* and *Trichuris serrata,* are rare and usually are not associated with clinical signs.

Life Cycle

- Whipworm infections occur by ingestion of infective ova, and the life cycle is direct.
- The prepatent period is approximately 3 months. Ova may survive and remain infectious in the environment for 4 to 5 years; hence, contaminated ground is probably the major reservoir of infection.

Clinical Signs

- Whipworms infect dogs of all ages. Although there may be minimal clinical signs in light infestations, trichuriasis frequently causes acute, chronic, or intermittent signs of mucoid large bowel-type diarrhea with urgency and sometimes hematochezia.
- Pseudohypoadrenocorticism, characterized by hyperkalemia and hyponatremia in the presence of normal adrenal function, has been associated with severe whipworm diarrhea in several dogs.

Diagnosis

- Definitive diagnosis of whipworm infection requires identification of the characteristic brown, bipolar-operculated, football-shaped ova by routine fecal flotation.
- Repeated fecal examinations may be necessary to identify ova because of the unusually long prepatent period and because it is not uncommon for active infection to be characterized by prolonged periods when ova are not shed in the feces.
- Alternative means of diagnosis of ova-negative, or so-called occult, infections, include the following:
  - Colonoscopic observation of adult whipworms in the bowel lumen
  - Resolution of signs in response to a therapeutic trial of fenbendazole or febantel

Treatment

- Give fenbendazole or febantel for 3 days (see Table 69-6). In refractory cases, a 5-day course is recommended. Routinely repeat treatment at 3 weeks and 3 months, because whipworms are difficult to eradicate.
- Rarely, trichuriasis has been associated with severe transmural granulomatous typhlitis that may be palpable as a tender right-midabdominal mass. This lesion may be refractory to anthelmintics and require typhlectomy.

Prevention

- Because it is virtually impossible to eradicate the parasite from infected ground, frequent reinfection is a common problem. For this reason, collect and properly dispose of feces whenever possible.
- In dogs with frequent access to ground that has been heavily contaminated with whipworm ova (a common situation in many public parks and backyards), reinfection is so frequent that retreatment every 2 to 3 months may be necessary.
- Disinfect concrete runs with dilute sodium hypochlorite bleach.

Strongyloides

Etiology

Strongyloides are tiny (2 mm) rhabdoid nematodes found in warm, humid tropical regions such as the southern Gulf states of the United States.

- In dogs, strongyloidiasis is caused by *Strongyloides stercoralis,* a parasite that burrows in the mucosa of the proximal small bowel.
- In cats, strongyloidiasis is caused by *Strongyloides tumefaciens,* a parasite that burrows within the mucosa of the large intestine.

Life Cycle

- Infection with third-stage larvae is by the oral or cutaneous route, and adult worms develop in the small intestine following migration in the circulation and lung.
- Parthenogenetic female adults produce eggs that hatch within the gut lumen so that first-stage (rhabdoid) larvae are passed in the feces. These larvae may develop into infectious third-stage (filariform) larvae or free-living adults.

Clinical Signs

- *S. stercoralis* is mainly a problem in pups, in which it causes acute hemorrhagic enteritis that is often fatal.
- *S. tumefaciens* infection in cats is usually asymptomatic, but in some cats the parasite causes peculiar tumor-

like, white, nodular (2–3 mm) proliferations in the colonic mucosa and submucosa that are associated with chronic diarrhea and debilitation.

Diagnosis

- Ova containing first-stage *Strongyloides* larvae can be identified in feces by flotation techniques. Free larvae (0.8 to 1.6 mm long × 30 to 80 µm) may be identified by direct microscopic examination of fresh feces or by the Baermann technique.
- In cats, the diagnosis of *S. tumefaciens* also can be established by colonoscopic observation and biopsy of mucosal nodules filled with adult worms.

Treatment

Treat with fenbendazole (50 mg/kg/day PO for 5 days), diethylcarbamazine (100 mg/kg PO once), or pyrantel pamoate (20 mg/kg/day PO for 5 days).

Tapeworms

Etiology

- The most common tapeworm (cestode) of dogs and cats is *Dipylidium caninum.* Fleas and lice are intermediate hosts.
- Several species of *Taenia* can be acquired by dogs and cats (most commonly *Taenia pisiformis* in the dog and *Taenia taeniaeformis* in the cat) from ingestion of cysticercus-infected tissues from intermediate hosts (e.g., rabbits, rodents, sheep, and ungulates).
- Other cestodes that are less common include *Echinococcus, Multiceps, Mesocestoides,* and *Spirometra.*

Clinical Signs

- Tapeworms that parasitize the small bowel of dogs and cats are relatively harmless, rarely causing more than a subtle decline in body condition.
- The proglottids of *D. caninum* are highly motile and may cause anal pruritus as they crawl on the perineum; crawling proglottids are often detected by observant owners in the animal's stool or on the perineum.

Diagnosis

- Tapeworms are diagnosed by the identification of proglottids or ova in the feces.
- *D. caninum* proglottids are distinguished from *Taenia* spp. by their barrel shape and double genital pore. Also, a proglottid can be squashed in a drop of water between a slide and a cover slip to identify the characteristic *D. caninum* egg capsules that contain up to 20 eggs.

Treatment

- Praziquantel and epsiquantel are the most effective all-around drugs for treatment of cestodiasis (see Table 69-6).
- Fenbendazole is effective against *Taenia* species but not *D. caninum.*
- Flea and lice control is important for preventing *D. caninum* reinfection. Control of predation and scavenging helps prevent infection with other cestodes.

PROTOZOAN PARASITES

Coccidia

Etiology

Canine and feline intestinal *Coccidia* are protozoan parasites that belong to the genera *Isospora, Besnoitia, Hammondia, Sarcocystis, Neospora, Toxoplasma,* and *Cryptosporidium.* Most enteric coccidial infections of dogs and cats are commensal and nonpathogenic.

- Primary enteric disease in small animals has been described only with *Isospora* and *Cryptosporidium.*
- *Toxoplasma gondii* and *Neospora caninum* are multisystemic infections discussed in Chapter 21.
- *Isospora* spp. that infect dogs include *I. canis, I. ohioensis, I. burrowsi,* and *I. neorivolta; I. felis* and *I. rivolta* infect cats.

Life Cycle

- Intestinal coccidiosis occurs most commonly by ingestion of infective (sporulated) oocysts from a feces-contaminated environment. *Cryptosporidium* infection is often water borne.
- Infection occurs occasionally from ingestion of infective cyst-containing tissues of paratenic (transport) hosts such as rodents and other prey and ingestion of uncooked meat of herbivores.

Clinical Signs

- Coccidiosis in most animals is an asymptomatic, incidental infection.
- *Coccidia* are opportunists. Clinical disease is usually related to massive oocyst ingestion in newborn animals and is associated with overcrowded, unsanitary, high-stress conditions in settings such as pet shops, kennels, shelters, catteries, and laboratory colonies. Concurrent disease, malnutrition, and immunosuppression are predisposing factors.
- Cryptosporidiosis has complicated canine distemper, feline leukemia virus, feline immunodeficiency virus, and advanced neoplasia.

- Clinical disease usually is characterized by diarrhea that varies from soft to fluid and is occasionally mucoid or bloody. Other signs can include vomiting, lethargy, weight loss, and dehydration. Coccidia have been associated with chronic malabsorption.

Diagnosis

Isospora Coccidia

- Coccidiosis is diagnosed by the identification of oocysts in fresh feces.
- Because many normal dogs and cats harbor intestinal coccidia and these protozoa are generally regarded as minimally pathogenic, the clinical significance of finding coccidial oocysts often is questionable.

Cryptosporidium

- Fecal immunoassay is the preferred method for diagnosis of *Cryptosporidium*. The direct immunofluorescence test (Merifluor, Meridian) and microplate ELISA (ProSpecT, Remel) are most reliable; however, false-negative reactions may occur with some strains.
- Fecal PCR is also used but is not widely available.
- *Cryptosporidium* oocysts can be isolated for identification from feces using concentration techniques, such as Sheather's sugar flotation or formaldehyde-ether sedimentation, or by staining feces with Kinyoun carbol fuchsin stain or modified acid fast stain. Cryptosporidia oocysts are so small (as little as one-tenth the size of common *Isospora* oocysts) that careful examination of slides under oil immersion is necessary to visualize these tiny structures.
- Histologic or electron microscopic identification of *Cryptosporidium* in intestinal biopsies is another means of diagnosis.

Treatment

Identification of oocysts in a healthy animal with normal feces indicates a self-limiting commensal infection and does not necessarily warrant treatment, although treatment may help reduce environmental contamination with oocysts.

Treatment for Isospora

If clinical signs are attributed to coccidiosis, as in young puppies and kittens with diarrhea, treat with one of the following coccidiostats:

- Sulfadimethoxine—50 to 60 mg/kg/day PO for 1 to 3 weeks
- Trimethoprim-sulfa—15 to 30 mg/kg q12–24h PO for 1 week
- Furazolidone—8 to 20 mg/kg/day PO for 1 week
- Amprolium (unapproved for use in dogs but often recommended for treating animals in kennels or other groups of dogs)—20% powder in gelatin capsules, 100 mg q24h for small-breed pups or 200 mg q24h for larger-breed pups, PO for 7 to 12 days; alternatively, 1/4 tsp of 20% powder per four pups mixed with puppy ration or 1 ounce (30 ml) of 9.6% solution per gallon of free-choice water

Treatment for Cryptosporidiosis

Cryptosporidiosis is generally self-limiting in immunocompetent hosts. The infection may be persistent in severely immunocompromised animals or humans.

- The drug of choice for treating *Cryptosporidium* is azithromycin (Zithromax, 7–15 mg/kg PO q12h for 5–7 days).
- Other suggested antibiotics include clindamycin and tylosin, but efficacy is questionable. Nitazoxamide has been used but causes severe vomiting. Paromomycin has been used but causes acute renal failure and deafness.
- Because *Cryptosporidium* are not species specific, zoonotic transmission between animals and humans can occur, sometimes with fatal consequences in the presence of severe immunosuppression. Case studies have implicated pets as a source of human infection.

Giardia

Giardia are pear-shaped, binucleated, flagellated protozoa that infect the small intestine, where they may interfere with mucosal absorption, and sometimes produce diarrhea. There are two forms: motile trophozoites that inhabit the intestinal tract and non-motile infective cysts that are passed through the feces into the environment.

Motile trophozoites attach to the brush border surface of the mucosal epithelium by means of ventral cup-shaped suction discs or float free within the adjacent mucus layer. They are mainly found in the duodenum in the dog and in the jejunum and ileum in the cat.

Life Cycle

The life cycle of *Giardia* is direct, and the usual source of infection is the ingestion of food or water contaminated with cysts. Wild animals are potential reservoirs. The prevalence is highest in young animals and animals confined together in groups.

Clinical Signs

- The majority of *Giardia* infections are subclinical, especially in mature animals.
- Clinically apparent giardiasis occurs most frequently in young dogs and cats and is characterized by intestinal malabsorption with large volumes of foul-smelling, light-colored, watery or cow patty–like diarrhea, steatorrhea, and weight loss. Diarrhea may be acute or chronic, intermittent or continuous, and self-limiting or persistent.

- The severity of giardiasis is enhanced by concomitant viral, bacterial, or helminth infections.

Diagnosis

- Fecal immunoassays for *Giardia* antigen are accurate and convenient. Reliable immunoassays include the point-of-care SNAP Giardia Test Kit (IDEXX), the microplate ELISA (Alexon Trend), or a direct immunofluorescence test available at commercial labs. Evidence suggests that the rapid ELISA test intended for humans is not reliable in animals.
- Microscopic diagnosis of giardiasis depends on identification of cysts (oval, 8 to 12 µm × 7 to 10 µm) by zinc sulfate centrifugation-flotation of feces or of motile flagellated trophozoites (pear-shaped, 9 to 21 µm × 5 to 15 µm × 2 to 4 µm) in fresh diarrheic feces suspended in saline or in duodenal specimens (aspirates, brushings, or impression smears of mucosal biopsies).

▼ ***Key Point*** *Giardia* cysts are identified in feces much more frequently than trophozoites. Negative fecal examinations do not exclude a diagnosis of giardiasis.

- Consider a therapeutic trial of fenbendazole or metronidazole when diagnostics are negative and "occult" giardiasis is suspected.

Treatment

Drugs that are effective for treating giardiasis include metronidazole, fenbendazole, albendazole, febantel, quinacrine, and furazolidone.

▼ ***Key Point*** Fenbendazole is the initial treatment of choice for giardiasis.

- Fenbendazole (Panacur) (50 mg/kg PO q24h for 3 days) is very safe and effective for treating *Giardia* in dogs and probably cats.
- Febantel (Drontal Plus, 15 mg/kg q24h for three doses or a single dose of 30 mg/kg PO) appears to be effective but needs further study.
- Metronidazole (25–30 mg/kg PO q12h for 5–10 days) is usually effective, although up to one-third of infections may be metronidazole resistant. Side effects include anorexia, vomiting, and reversible CNS toxicity (weakness, ataxia, disorientation, seizures, and blindness).
- Albendazole (Valbazen) (25 mg/kg PO q12h for 5 days in cats and 2 days in dogs) is effective but has been associated with severe bone marrow toxicity. For this reason, fenbendazole is preferred.
- Furazolidone (Furoxone, SmithKline) (4 mg/kg PO q12h for 5 days) is effective and convenient for cats, as it is available in a suspension form.

Prevention

Failure to respond to treatment is often the result of repeat exposure and recurrence of infection, especially in groups of animals confined together.

- Decontaminate the environment with quaternary ammonia.
- Bathe animals to remove cysts from the haircoat.
- Treat all animals that are confined together.
- *Giardia* vaccine is available but is not recommended. It does not prevent infection. It may reduce cyst shedding, but this is inconsistent.

Tritrichomonas foetus in Cats

Tritrichomonas foetus is a frequent cause of mild to severe lymphoplasmacytic colitis and chronic large intestinal diarrhea in young cats, especially cats confined in crowded cattery conditions.

Clinical Signs

The diarrhea may wax and wane and is semiformed or "cow pie" in consistency and malodorous. It may contain blood or mucus. The diarrhea often improves transiently in response to antibiotics. Affected cats generally remain otherwise healthy and in good body condition. Diarrhea is often exacerbated by concurrent enteric infections or parasites, especially *Giardia* and *Cryptosporidium*.

Diagnosis

The diagnosis can be confirmed by direct fecal microscopy, fecal culture, or PCR assay.

- Motile trophozoites of *Tritrichomonas foetus* can be identified in fresh fecal wet smears taken directly from the rectum in about 14% of cases. The likelihood of detecting trophozoites is lower in formed feces, desiccated feces, or in cats recently treated with antibiotics.
- Fecal culture is more sensitive for diagnosis than microscopy. Culture requires 0.05 g of freshly voided feces inoculated in special media (InPouch TF, BioMed Diagnostics). The instructions on using this culture system are found at the website below.
- Fecal PCR assay is the most accurate test (high sensitivity and specificity) for detecting *T. foetus*, and information on submitting samples is found at http://www.cvm.ncsu.edu/mbs/gookin_jody.htm.
- Trichomonads may be observed in the superficial mucus and crypts in colonic biopsies.

Treatment

T. foetus is virtually impossible to eradicate with antibiotics. Numerous antibiotic agents have been evaluated without success. Treatment can reduce the number of organisms and improve clinical signs, but it usually does not eliminate the infection.

- Diarrhea often improves with antibiotics but relapses when antibiotics are stopped.
- Other measures include reducing housing density, reducing stress, improving diet, and treating concurrent infections such as *Giardia* and *Cryptosporidium.*
- The long-term prognosis is good based on findings that most infected cats resolve the clinical signs of *T. foetus* infection within 2 years (median, 9 months). However, many of these cats remain subclinically infected for several years. Clinical disease may be prolonged in cats living under dense housing conditions, possibly attributable to stress.

Entamoeba

E. histolytica, primarily a human pathogen, rarely may cause amebic colitis (bloody-mucoid diarrhea) in dogs and cats that drink polluted water.

Diagnosis

Diagnosis is based on identification of ameboid trophozoites with pseudopodial movement in saline smears of fresh diarrheic feces, amebic cysts in zinc sulfate flotation of formed feces, or trophozoites in colon biopsies.

Treatment

Optimal treatment for amebic colitis in dogs and cats is unknown, but response has been seen with metronidazole (25–30 mg/kg PO q12h for 5–10 days) or furazolidone (2.2 mg/kg PO q8h for 7 days).

Balantidium

B. coli, a ciliated protozoan that primarily infects swine, is a rare cause of chronic ulcerative colitis in dogs.

Diagnosis

Diagnosis is based on identification of large (40 to 80 µm × 25 to 45 µm), oval, brown, rapidly swimming ciliated trophozoites with prominent macronuclei in saline suspensions of fresh feces or identification of protozoal cysts in zinc sulfate or sedimentation preparations of feces.

Treatment

Optimal treatment is unknown, but metronidazole (25–30 mg/kg PO q12h for 5–10 days) appears to be effective.

VIRAL INFECTIONS OF THE INTESTINES

Canine Intestinal Viruses

- Canine parvovirus, coronavirus, and rotavirus cause viral enteritis and diarrhea in dogs. Canine parvovirus is an acute, severe, highly contagious enteritis that is prevalent worldwide. Coronavirus and rotavirus are less prevalent and cause relatively mild clinical signs except in neonates. For details concerning intestinal viruses, see Chapter 14.
- Because of its epitheliotropism, canine distemper virus also causes diarrhea (see Chapter 13).

Feline Intestinal Viruses

- The most clinically important primary enteric virus is feline panleukopenia virus (FPV), a parvovirus. Other feline intestinal viruses include enteric coronavirus, rotavirus, and astrovirus (see Chapter 14).
- The intestine may be involved as part of generalized viral infections such as feline leukemia virus (see Chapter 8), feline immunodeficiency virus (see Chapter 9), and feline infectious peritonitis, a coronavirus (see Chapter 10).

BACTERIAL INFECTIONS OF THE INTESTINES

Most enteropathogenic bacteria produce intestinal disease by invading the epithelium (invasive bacteria) or by liberating diarrheogenic enterotoxins (noninvasive or enterotoxigenic bacteria).

Enteropathogenic bacteria of clinical importance include *Salmonella* species, *Campylobacter jejuni, C. perfringens,* and *C. difficile. Yersinia* species and *Bacillus piliformis* are rare and are not discussed here. *Salmonella* and *Campylobacter* are primarily invasive, causing mucosal damage that leads to inflammation, exudation, mucus secretion, and bleeding. Bacterial enterotoxins may also play a role in the pathogenesis of these agents. *C. perfringens* and *C. difficile* are noninvasive and cause diarrhea by an enterotoxigenic mechanism.

▼ ***Key Point*** Because *Salmonella, Campylobacter,* and *Yersinia* also are potentially zoonotic pathogens, pets occasionally are reservoirs for human infection.

Salmonella

Etiology

- Salmonellosis is caused by gram-negative bacilli belonging to the genus *Salmonella* of the family *Enterobacteriaceae. Salmonella* frequently are isolated from the feces of normal dogs and cats, but clinical signs of salmonellosis are uncommon, indicating a prevalent asymptomatic carrier state.
- *Salmonella* infection is transmitted by the fecal-oral route, mainly through ingestion of contaminated food or water. The organisms can survive in the environment for long periods outside the host; thus, fomite transmission also can occur.
- Infected migratory birds have been a source of fatal infections in cats, and raw meat, bone, and raw food

diets have recently been implicated in canine infections.
- Infection risk depends on infectivity of the strain, size of the inoculum, competition from the established flora, age of the host, and host defense factors. Infection rates are greatest in young animals and in group confinement situations with overcrowding and poor sanitation.

Clinical Signs

Manifestations of *Salmonella* infection may be categorized into three syndromes: subclinical carrier state, enterocolitis, and enterocolitis with bacteremia. Virulence of the bacterial strain and host susceptibility play roles in the severity of infection.

- Clinical salmonellosis is relatively uncommon compared with the prevalence of the subclinical carrier state.
- *Salmonella* enterocolitis is characterized by acute watery or mucoid diarrhea (containing blood in severe cases), vomiting, tenesmus, fever, anorexia, lethargy, abdominal pain, and dehydration. Most animals recover in 3 to 4 weeks, although shedding of organisms often persists up to 6 weeks and sometimes persists longer.
- *Salmonella* can cause chronic or intermittent diarrhea in some animals.
- Rarely, *Salmonella* enterocolitis progresses to a potentially fatal bacteremia or endotoxemia with signs of systemic inflammatory response syndrome, shock, and disseminated intravascular coagulation (DIC).

Diagnosis

Suspect salmonellosis in animals that develop acute diarrhea and have identifiable risk factors, such as known or probable exposure, young age, immune deficiency, debilitating illness, or housing in overcrowded or unsanitary conditions.

- Nosocomial outbreaks with high morbidity and mortality have been recorded in hospitalized animals, the greatest risk occurring in the following animals:
  - With severe illness
  - Undergoing major surgery
  - Hospitalized for 5 or more days
  - Receiving glucocorticosteroids, anticancer chemotherapy, or oral antibiotics (especially ampicillin) that upset the normal flora
- Routine diagnostic tests usually are noncontributory, except that a degenerative neutropenia may be found in severe cases with bacteremia and endotoxemia. Feces may contain leukocytes.
- Confirmation of the diagnosis depends on isolation of *Salmonella* spp. from properly cultured fecal specimens or from blood cultures in bacteremic animals.

Treatment

The use of antibiotics in the treatment of salmonellosis is controversial. *Salmonella* invasion that is confined locally to the mucosa produces enterocolitis that is self-limiting and is not likely to be affected by antibiotics.

▼ ***Key Point*** Antibacterial therapy, especially oral, non-absorbable antibiotics that alter the flora, may actually prolong shedding of *Salmonella* organisms and encourage development of a prolonged convalescent carrier state.

Antibiotics are indicated when *Salmonella* invasion becomes severe or complicated by bacteremia and endotoxemia—as indicated by signs such as shock, dehydration, high fever or hypothermia, and extreme depression—or by laboratory findings such as azotemia, electrolyte imbalances, neutropenia, hypoglycemia, hypoproteinemia, or coagulopathy. Peracute onset and severe hematochezia may also be an indication of impending systemic invasion and should prompt antibiotic therapy.

- Base antibiotic selection on culture and sensitivity testing. Most isolates are susceptible to enrofloxacin (Baytril, Bayer) (dog: 5 mg/kg PO q12h; cat: 2.5 mg/kg PO q12h), trimethoprim-sulfa (15 mg/kg PO q12h), or chloramphenicol. Administer antibiotics for 7 to 10 days and reculture feces 1 and 4 weeks after treatment.
- In addition to antibiotics, fluid and electrolyte replacement and identification and correction of underlying predisposing conditions are important aspects of therapy.
- Proper hygiene in handling of infected animals is necessary to prevent fecal-oral or fomite transmission of infection to other animals or to humans.

Prognosis

- The prognosis for most animals with salmonellosis is good, although the mortality rate can be high in outbreaks in extremely susceptible populations (e.g., hospital patients and neonates).
- Prognosis is guarded to poor for animals with extremely bloody diarrhea, fever > 104°F or hypothermia, neutropenia with a left shift, and indications of sepsis with multiorgan failure (DIC, hypoglycemia, azotemia, jaundice).

Campylobacter

C. jejuni organisms are fastidious, microaerophilic, gram-negative, motile, slender, and curved bacteria that are important pathogens of animals and humans worldwide.

Etiology

Many clinically normal dogs and cats shed *Campylobacter* in their feces. Isolation rates vary widely, from less than 1% in confined pet populations to 50% or more in some animal shelters. Thus, conditions of close confinement and poor sanitation apparently provide the greatest opportunity for exposure. The majority of *Campylobacter*-positive dogs are clinically normal carriers.

Clinical Signs

Because it is difficult to produce enteritis with *Campylobacter* experimentally in dogs and cats and because many of the animals that harbor these organisms are asymptomatic, it has been debated whether *Campylobacter* by itself causes diarrhea in dogs and cats unless superimposed on other enteropathogenic infections with viruses, other bacteria, *Giardia,* or helminths.

- Clinical signs associated with *Campylobacter* infection in dogs and cats have been attributed to superficial erosive enterocolitis or enterotoxin-mediated secretory diarrhea. Clinical signs are characterized by watery-mucoid diarrhea, with or without blood and fecal leukocytes, lasting 5 to 15 days and may be accompanied by vomiting or tenesmus.
- Fever is usually mild or absent.
- In some animals the diarrhea appears to be chronic or intermittent.

Diagnosis

- *Presumptive* diagnosis of campylobacteriosis can be made by fecal microscopy; however, this requires an experienced examiner, because spirochetes and other motile bacteria that are part of the normal flora may be mistaken for *Campylobacter*. The presence of fecal leukocytes may also be noted.
  - *Campylobacter*-like organisms are identified as slender, curved, gram-negative rods that are characteristically W-shaped in stained fecal smears and as highly motile, darting, spiral, or S-shaped bacteria in fresh saline fecal smears examined by dark-field or phase-contrast microscopy.
- *Definitive* diagnosis requires isolation of *Campylobacter* from fresh feces using special selective media. Since *Campylobacter* organisms are microaerophilic and difficult to isolate, obtain fecal specimens for culture directly from the rectum and place them in anaerobic transport media immediately after collection.

Treatment and Prognosis

- Effective antibiotics include erythromycin (10–15 mg/kg PO q8h for 7 days; vomiting is a frequent side effect), enrofloxacin (for dogs, Baytril at 5 mg/kg PO q12h for 7 days), or azithromycin (Zithromax at a dosage of 7–15 mg/kg PO q12h for 5–7 days).
- Antibiotics may not eliminate fecal shedding of the organisms, which can persist up to 4 months. Repeat fecal cultures 1 and 4 weeks after treatment.
- Because contact with feces from infected animals is a potential source of infection for humans as well as for other animals, advise owners of infected pets to take standard precautions such as proper disposal of potentially infectious feces, hand washing after handling infected animals, and separating infected animals from infants and small children until post-treatment cultures confirm that infection has been eliminated.
- The prognosis is considered good, although rare fatalities in dogs and cats have been reported.

Clostridium perfringens

Etiology

Enterotoxigenic *C. perfringens* is an important cause of acute and chronic diarrhea in dogs and cats. *C. perfringens* is a large, anaerobic, gram-positive bacillus that normally exists in the intestinal tract of most dogs and cats. Enterotoxin-producing strains of *C. perfringens* can be associated with nonspecific episodes of diarrhea, acute hemorrhagic diarrhea, chronic or recurrent diarrhea, and outbreaks of diarrhea in animal groups.

These bacteria normally reside in the bowel in the vegetative form, but they can release their toxin during sporulation endogenously within the bowel or exogenously in contaminated food. The *cpe* gene that regulates production of *C. perfringens* enterotoxin (CPE) is up-regulated by factors that activate sporulation; thus, the presence of clostridial endospores in feces or food has been suggested as an indirect marker for the presence of CPE. Whether derived endogenously or ingested, CPE causes diarrhea by binding to intestinal epithelium and causing increased permeability, hypersecretion, and cell damage (cytotoxicity).

Endogenous sporulation and the production of CPE can be associated with alteration of the intraluminal environment caused by sudden changes in diet, antibiotic administration, alkaline conditions, immunosuppression, inflammatory bowel disease, or concurrent intestinal infections.

Clinical Signs

Enterotoxigenic *C. perfringens* infection is associated with diarrhea that varies from watery to soft and may contain mucus or blood. Increased frequency is common, and tenesmus may be seen.

- In dogs, enterotoxigenic *C. perfringens* has also been associated with a syndrome of acute hemorrhagic gastroenteritis accompanied by severe hemoconcentration.
- Infection can also cause diarrhea in groups of animals confined together and nosocomial outbreaks in hospitalized animals.

- Clostridial diarrhea is usually self-limiting after a few days, but in some animals diarrhea can persist chronically for weeks to months. Some animals have recurrent episodes of diarrhea.

Diagnosis

Routine hematologic and serum chemistry evaluations are usually normal in animals with clostridial diarrhea. Colonoscopy is not routinely necessary in these cases, but endoscopic findings are usually nonspecific (diffuse hyperemia, increased friability, fresh bleeding, and increased mucus). Biopsies range from minimal abnormalities to catarrhal, lymphoplasmacytic, or suppurative colitis.

A definitive diagnostic test for *C. perfringens*-induced diarrhea is lacking. Further work is needed to determine the role of CPE in canine and feline diarrhea and to define the optimal diagnostic parameters for clostridial diarrhea. Fecal spore counts in stained fecal smears are commonly used for routine cage-side screening; however, studies have not shown a correlation between spore counts and positive assays for CPE or a correlation between either of these diagnostic procedures and the presence or absence of diarrhea. In people, fecal assays for CPE are considered more accurate than spore counts; however, the commercially available CPE assays used in people need to be validated for dogs and cats. In principle, CPE assays should be valid across species.

- The identification of more than five clostridial endospores per oil immersion field (identified by their "safety pin" appearance with Diff-Quik or Wright staining) is considered by many to be presumptive evidence for a diagnosis of enterotoxigenic diarrhea caused by *C. perfringens*. Clostridial spores are generally larger than other bacilli found in feces. Malachite green can be used as a special stain for endospores. Fecal leukocytes also may be present. Unfortunately, the appearance or absence of clostridial spores in the feces does not correlate well with CPE assays or signs; thus, it might be advisable to take into account spore counts, CPE assays, and clinical information before making a diagnosis of clostridial diarrhea.

▼ ***Key Point*** Fecal ELISA assay for CPE is generally more reliable and specific than fecal spore counts.

- Commercial fecal assays for CPE are available in kit form for testing humans. The ELISA test (C. perfringens Enterotoxin Test; Techlab, Blacksburg, VA) appears to be the most reliable in dogs. Another commercial test, reverse passive latex agglutination (RPLA Kit, Oxoid), is insensitive and nonspecific in dogs and thus is not recommended. Use fresh feces only and transport without delay to the laboratory in prechilled diluent at 4°C (freezing should be avoided), because the fecal toxin breaks down after 24 hours.
- Cultures are not useful because non-toxigenic *C. perfringens* is part of the flora in normal dogs and cats and cultures do not reliably distinguish toxigenic and non-toxigenic strains.
- Assays using molecular probes and PCR are being evaluated as improved diagnostic procedures for enterotoxigenic *C. perfringens*.

Treatment

Diarrhea caused by enterotoxigenic *C. perfringens* can be effectively treated with ampicillin (20 mg/kg PO q8h), amoxicillin-clavulanate (12–25 mg/kg PO q12h), tylosin (20–40 mg/kg PO q12h), or clindamycin (5–10 mg/kg PO q12h) for 5 to 7 days. Metronidazole (10–20 mg/kg PO q12h) can also be effective but seems to work less consistently.

- Clostridial diarrhea is usually self-limiting or responsive to antibiotics in 2 to 3 days; however, chronic or recurrent clostridial diarrhea may require long-term antibiotics (e.g., tylosin once daily or every other day) and a fiber-supplemented diet to prevent relapses.
- Commercial fiber-containing diets or regular diets supplemented with psyllium (Metamucil at a dosage of 1–2 tbsp/day for dogs) may help reduce bacterial proliferation and sporulation because fiber is fermented to short-chain fatty acids that acidify bowel contents. Alkaline rather than acid conditions are most favorable for *C. perfringens*. In addition, short-chain fatty acids nourish colonic epithelium and protect against injury.

Clostridium difficile

C. difficile is an anaerobic, gram-positive, spore-forming bacillus. Toxigenic *C. difficile* and its toxin have been isolated from normal dogs and cats and occasionally from animals with mild diarrhea or acute hemorrhagic diarrhea; however, this organism does not appear to be a frequent enteropathogen in dogs and cats. Pseudomembranous colitis as seen in people is not seen in dogs and cats.

Diagnosis

C. difficile can be cultured using selective medium; however, the organism is isolated from normal dogs as well, and culture alone does not confirm the production of diarrheogenic toxins.

Commercial ELISA kits that detect both toxins A and B in feces are recommended, but validation in dogs and cats is needed.

Treatment

Use metronidazole for treatment of suspected or confirmed *C. difficile* infections.

FUNGAL INFECTIONS OF THE INTESTINES

Mycotic infections of the bowel are uncommon; however, fungi are opportunists that capitalize on predisposing factors such as lowered host resistance, malnutrition, antecedent debilitating illness, and prolonged therapy with antimicrobials or corticosteroids. Fungi may cause acute, dysentery-like diarrhea or chronic diarrhea accompanied by emaciation.

Causes of mycotic intestinal disease include *Histoplasma capsulatum, Pythium* spp., *Aspergillus* spp., *Candida albicans,* and other saprophytes. Histoplasmosis is a multisystemic mycotic infection and is discussed in Chapter 20. Intestinal aspergillosis and candidiasis are rare and discussed briefly in Chapter 20.

Intestinal Pythiosis and Zygomycosis

Various poorly septate saprophytic molds and fungi that include *Pythium insidiosum* (pythiosis) and several genera of *Zygomycetes* (zygomycosis) can deeply invade the tissues of the GI tract. These infections were formerly misnamed phycomycosis.

Pythiosis is most common and is seen in young, large-breed dogs that live in the southern Gulf states of the United States. Rare feline cases are characterized by ulcerative gastroenteritis.

Clinical Signs

Pythium and *Zygomycetes* can infect any part of the digestive tract, but lesions most commonly involve the stomach, small intestine, mesentery, and mesenteric lymph nodes, resulting in an extensive granulomatous tissue reaction.

- Signs include chronic intractable diarrhea and vomiting, anorexia, depression, and progressive weight loss.
- Bowel necrosis and ulceration may cause bloody diarrhea in some cases.
- Regions of extensive granulomatous inflammation may produce palpable enteromesenteric masses.
- The infection may disseminate beyond the GI tract to other abdominal viscera.

Diagnosis

- Physical examination may reveal an abdominal mass or marked regional thickening of the bowel.
- The CBC may reveal mild to moderate nonregenerative anemia and mild neutrophilia, with or without a left shift.
- Routine abdominal radiography frequently demonstrates an abdominal mass. Ultrasonography and barium contrast GI radiography often delineate a thickened, stenosed segment of bowel.
- A sensitive and specific ELISA test for presumptive diagnosis of pythiosis is available.
- Confirmation depends on histologic identification of broad, non-septate or sparsely septate hyphae in biopsies of the stomach, intestine, or abdominal lymph nodes. The organisms stain with Gridley or methenamine silver stains and are found mostly within the necrotic regions of granulomas in the submucosa and muscularis mucosa.
- Differentiate intestinal pythiosis from other granulomatous and neoplastic proliferations of the GI tract, including histoplasmosis, lymphoma, and regional (granulomatous) enteritis.
- The extensive tissue reaction can easily be mistaken for neoplasia at laparotomy (or necropsy); thus, careful histologic evaluation including use of fungal stains is essential for accurate diagnosis.

Treatment

Because these fungi are resistant to standard antifungal drugs, the most effective treatment is radical surgical excision of the severely involved segments of bowel (for surgical technique, see Chapter 70). Some animals with pythiosis have been treated successfully with itraconazole and terbinafine in combination or with lipid-complexed amphotericin B as described in Chapter 20. The prognosis is guarded to poor.

INTESTINAL PROTOTHECOSIS

Etiology

Prototheca spp. are ubiquitous unicellular algae that may rarely colonize the lamina propria and submucosa of the intestinal tract of dogs and cause severe necrotizing or ulcerating enterocolitis.

Clinical Signs

- The algae appear to have a predilection for initially invading the colon, resulting in signs of chronic large bowel diarrhea with hematochezia.
- The organisms typically disseminate widely throughout the body and most frequently involve other visceral organs, the eyes, and the CNS.
- Only a cutaneous form has been described in cats.

Diagnosis

- Colonoscopy reveals thickened, corrugated mucosal folds that may be friable or ulcerated.
- Organisms can be identified in feces, cytology preparations (Wright or Gram stain), and biopsies (Gomori or periodic acid-Schiff stain) as clusters of endosporulated, ovoid structures (5–16 µm in length).
- *Prototheca* can also be cultured on Sabouraud's cycloheximide-free dextrose media.

Treatment

Successful treatment of systemic protothecosis in animals is rare. A combination of IV lipid-complexed amphotericin B with itraconazole is suggested (see Chapter 20 for pharmacology and dosages).

CHRONIC INFLAMMATORY BOWEL DISEASE

The term *inflammatory bowel disease* (IBD) refers to a diverse group of chronic enteropathies characterized by idiopathic infiltration of the GI tract mucosa and (sometimes) submucosa with inflammatory cells. The infiltration may involve the stomach, small intestine, colon, or a combination of these and is classified on the basis of the predominant cell type as lymphocytic-plasmacytic, eosinophilic, neutrophilic, granulomatous, or histiocytic. A mixture of inflammatory cells in some lesions makes classification difficult.

Lymphocytic-Plasmacytic Inflammatory Bowel Disease

Etiology

- Lymphocytic-plasmacytic IBD is by far the most common form of IBD in both dogs and cats. The etiology is not determined in most cases; however, genetic, dietary, bacterial, immunologic, and mucosal permeability factors have been implicated.
- The pathogenesis of lymphocytic-plasmacytic IBD may involve a mucosal hypersensitivity reaction to antigens from food, intestinal bacteria, or the intestinal tract itself. This may result from a primary disorder of the intestinal immune system and its regulation or from immune events that occur secondary to mucosal injury and permeability. Chronic inflammation of the bowel may become self-perpetuating when loss of mucosal integrity allows bacterial or dietary proteins to enter the lamina propria, where they incite further immune reaction and inflammation.
- Genetic factors appear to be involved in predisposing certain breeds to lymphocytic-plasmacytic IBD (e.g., German shepherd, basenji, soft-coated wheaten terrier, and Shar-Pei). Basenjis develop a severe form of IBD (also called immunoproliferative enteropathy) that is thought to be related to a genetic disorder of immune regulation, is progressive in nature, and is exacerbated by stress.

Clinical Signs

The most common signs of IBD are vomiting, diarrhea, and weight loss. The signs vary with the region of the GI tract affected and the severity of the mucosal disease. The clinical course is typically waxing and waning and can go on for months to years. Dogs and cats of all ages are affected.

- *Lymphocytic-plasmacytic enteritis* causes chronic diarrhea and weight loss. Vomiting occurs more frequently in cats with IBD.
- *Lymphocytic-plasmacytic colitis* causes chronic large bowel diarrhea characterized by increased frequency of defecation, urgency, tenesmus, increased fecal mucus, and hematochezia. Fecal consistency varies. Intermittent hematochezia may be the only sign of IBD in some cats.
- Signs may be intermittent or persistent. In severely affected dogs, protein-losing enteropathy (ascites, hydrothorax, edema) can occur.
- Some animals with a biopsy diagnosis of lymphocytic-plasmacytic enteritis that fail to respond to treatment or that later relapse and deteriorate rapidly are found to have diffuse intestinal lymphoma.

Diagnosis

Precise criteria for the diagnosis of IBD have not been established. In general, the clinical criteria for diagnosis are (1) chronic signs of GI disease, (2) characteristic mucosal lesions of IBD in endoscopic biopsies, (3) failure to respond to dietary trials, and (4) exclusion of known causes of chronic inflammation of the intestinal tract based on thorough diagnostic evaluation. This last criterion emphasizes that IBD is a diagnosis of exclusion and not a catch-all label to be used as a substitute for diagnostic evaluation. Because lymphocytic-plasmacytic inflammation is a nonspecific lesion, only a thorough diagnostic workup can establish that it is truly idiopathic and not merely an inflammatory response to an undiagnosed condition.

- In the diagnostic evaluation, exclude parasitic (*Giardia, Tritrichomonas,* canine whipworms), infectious *(Campylobacter, Salmonella, Histoplasma)* and other causes of chronic intestinal inflammation.
- The differential diagnosis of lymphocytic-plasmacytic IBD includes dietary hypersensitivity, small intestinal bacterial overgrowth, intestinal lymphoma, intestinal lymphangiectasia, and the other histologic types of chronic IBD.

Laboratory Findings

- Routine hematologic and biochemical parameters typically are unremarkable except for occasional nonspecific findings such as a stress leukogram, hypoproteinemia, hypokalemia, and mildly elevated serum liver enzymes. Basenji enteropathy is associated with hypoalbuminemia and hyperglobulinemia, whereas affected soft-coated wheaten terriers may have hypoalbuminemia with concurrent protein-losing glomerulonephropathy. Cats with IBD may have concurrent cholangitis, pancreatitis, or both.
- Serum vitamin levels (cobalamin, folate, vitamin K) can be decreased from malabsorption. Bleeding and abnormal hemostasis have been associated with vitamin K deficiency in some cats with IBD. Markedly

decreased serum cobalamin is common, especially in cats and Shar-Peis with IBD.

Radiography and Ultrasonography

In most cases, radiographic and ultrasonographic findings are unremarkable and do not aid diagnosis. Some animals have a nonspecific finding of fluid- and gas-distended bowel loops on plain abdominal radiography. Barium contrast radiography occasionally demonstrates diffuse mucosal irregularity and ultrasonography may reveal intestinal thickening, but these are nonspecific findings that merely suggest an infiltrative lesion. In selected cases, contrast radiography and ultrasonography can be helpful nonetheless, because they may discover an unexpected diagnosis other than IBD—for example, pancreatitis, hepatobiliary disease, or intestinal tumors, polyps, granulomas, or malformations (e.g., diverticulum or short colon).

Endoscopic Examination

In animals with GI disease, the spectrum of clinical signs usually suggests the most appropriate region of the GI tract for endoscopic examination. In IBD, however, signs do not always correlate with the region of greatest cellular infiltration, especially in cats. It is not uncommon to find significant involvement of the colon in cats that present with vomiting. Conversely, cats with hematochezia or other colonic signs may have unexpected gastroduodenal lesions. Therefore, it may be advisable in many cases to obtain biopsies from the stomach, duodenum, jejunum (if possible), colon, and ileum (if the ileocolic sphincter can be navigated during colonoscopy).

Endoscopically, the mucosa in IBD may appear to be normal or it may have any of the following abnormalities: erythema, petechiae, increased mucus, increased friability, increased surface granularity, decreased visibility of the colonic submucosal vessels, thickened or increased folds, erosions or ulcers, or decreased distensibility. The mucosal lesions may only be apparent microscopically; thus, a normal endoscopic appearance does not rule out IBD and multiple biopsies should be taken even if there are no endoscopically visible abnormalities.

Mucosal Histopathology

The histopathologic lesion of lymphocytic-plasmacytic IBD is characterized by diffuse infiltration of the lamina propria with mature lymphocytes and plasma cells in association with mucosal damage. For definitive diagnosis of lymphocytic-plasmacytic IBD, there must be abnormal infiltration of lymphocytes and plasma cells, as well as evidence of mucosal damage.

- Pathologists may differ in their interpretation of endoscopic biopsies and in their definition of how many lymphocytes and plasma cells within the lamina propria are too many. Infiltrates assessed to be minimal or mild by an inexperienced pathologist may not be truly abnormal. Various grading systems have been proposed, but these have not correlated well with clinical disease activity.
- In some cases the inflammation is mostly lymphocytic; in others the infiltrate also contains a mixture of other types of inflammatory cells (neutrophils, eosinophils, macrophages). The cellular infiltrate is usually confined to the mucosa but occasionally may extend to the submucosa.
- Additional findings indicative of mucosal damage include architectural distortion (e.g., atrophic or fused villi), fibrosis, and epithelial abnormalities (hyperplasia, degeneration, necrosis, erosion, ulceration, glandular dilation, loss of goblet cells).
- A severe infiltration of lymphocytes that extends beyond the mucosa into the submucosa and muscularis should raise the suspicion of early lymphoma mimicking IBD, and further diagnostics should be recommended.

Evaluation for Dietary Hypersensitivity

Dietary hypersensitivity or food allergy is an immunologically mediated adverse reaction to a protein component in food. A well-controlled dietary trial using a protein elimination diet is the basis for diagnosis of dietary hypersensitivity as a cause of IBD (for additional information on diagnostic food trials, see Chapter 47). The diet is changed to a well-defined, additive-free, highly digestible diet that contains a single source of protein not found in the animal's normal diet. Intake of all other foods or sources of antigen must be eliminated throughout the feeding trial, including table scraps, treats, and flavored medications such as vitamin supplements. The goal is to feed a single protein source to which the animal is not yet sensitized. Although many commercial hypoallergenic diets are available (see the next section), home-prepared single-protein diets are preferred for diagnostic testing purposes. Examples of novel protein sources not likely found in the animal's regular diet might include turkey, duck, lamb, rabbit, venison, fish, or soybeans (tofu). Once dietary hypersensitivity is confirmed with a home-prepared diet, commercial hypoallergenic diets can be substituted for more convenient long-term management.

A cooperative and patient owner is required for a successful elimination diet trial. A minimum of 3 to 4 weeks should be allowed for initial response to an elimination diet. If no improvement has occurred during this time, then dietary hypersensitivity is unlikely and medical therapy should be instituted. If some improvement has been observed, then the trial should continue as it may require 6 weeks or more before improvement is complete.

If there is a substantial improvement with the elimination diet, then the animal can be rechallenged with

its original diet. Recurrence of clinical signs confirms dietary intolerance or hypersensitivity. In addition, once remission is restored with the controlled diet, the animal can then be challenged sequentially with individual dietary components to identify the specific offenders. To do this, individual components of the original diet are added one at a time to the controlled diet while the animal is in remission. With each challenge the animal is monitored for recurrence of signs for 7 to 10 days. If signs recur, then that substance is implicated as an offender.

After several weeks to months of remission on the controlled diet, some animals can be returned to their original diet and remain asymptomatic, but in most cases, specially formulated or novel protein diets may need to be continued indefinitely to prevent relapse. If there is no response to dietary management within 4 to 6 weeks, the animal can be fed a digestible commercial GI diet or returned to its original diet and medical therapy can be instituted.

Treatment

Well-controlled therapeutic trials for chronic IBD in animals are lacking; thus, treatment is largely empirical and based on clinical experience. Because dietary hypersensitivity, parasites (see previous section), and bacterial enteropathogens (see previous section) may cause lymphocytic-plasmacytic IBD, it is appropriate to first consider evaluation and treatment for these possibilities.

In most cases of lymphocytic-plasmacytic IBD, an underlying cause cannot be identified and the most effective treatment is an anti-inflammatory regimen of either corticosteroids or mesalamine (5-ASA derivative) combined with dietary modification (e.g., novel protein diet, hydrolyzed diet, or fiber-enriched diet). If diet and anti-inflammatory drugs fail to control the disease, metronidazole is added for its antibacterial and immunomodulatory properties. Metronidazole can also be used as a single drug to induce or maintain remission in less severe cases. For refractory cases, a cytotoxic immunosuppressive agent such as azathioprine or chlorambucil can be added to the corticosteroid regimen. Cyclosporine may also be beneficial in steroid-refractory cases. Various drugs used to treat IBD and their suggested dosages are indicated in Table 69-7.

Dietary Therapy

Various strategies for dietary modification have been used for treatment of chronic IBD, including novel protein diets, hydrolyzed diets, fiber-enriched diets, diets with adjusted omega-6 and omega-3 fatty acid levels and diets with prebiotics and probiotics. In some animals with IBD, dietary modification produces complete or partial resolution of the signs and sometimes regression of the lesions. Potential explanations for a beneficial response to dietary modification include the effects of the diet on bowel motility, composition of the microflora, mucosal morphology and function, and exposure to food-borne antigens or additives.

- The treatment of IBD associated with dietary hypersensitivity is based on the controlled feeding of a well-defined, additive-free, highly digestible diet that contains a single source of protein not found in the animal's normal diet (i.e., a novel protein to which the animal is not yet sensitized). Home-prepared diets (turkey, duck, lamb, rabbit, venison, white fish, or tofu) are most suitable for diagnostic testing purposes (see previous "Diagnosis" section); however, if the home-prepared diet suggests diet-responsive disease, then a commercial "hypoallergenic" novel protein diet can be substituted and is more convenient and balanced for long-term feeding. Many commercial diets that contain novel protein sources are now marketed for dietary hypersensitivity. A relapse rate of approximately 15% to 20% is to be expected when switching from a home-prepared to a commercial hypoallergenic diet. For long-term feeding of a home-prepared diet, recipes for balanced diets containing novel protein sources can found in veterinary nutrition text books or various reliable websites under supervision of Diplomates of the American College of Veterinary Nutrition.
- An alternative approach is to use a diet containing hydrolyzed proteins (oligopeptides) that may be less antigenic (e.g., Prescription Diet z/d, Hills; or HA Diet, Purina).
- In cases in which hypoallergenic novel protein diets have not been effective, other dietary adjustments may be beneficial as an adjunct to medical therapy for IBD. This includes fiber supplementation (psyllium, bran, canned pumpkin) of the regular diet or switching to a commercial diet enriched with fermentable fiber (e.g., beet pulp) marketed for improving colonic function and ameliorating diarrhea in animals with colitis. Fiber has many beneficial effects on colonic function and helps keep enteropathogens in check. Colonic bacteria metabolize fermentable fiber to short-chain fatty acids that nourish colonic epithelium and protect against mucosal injury.
- Modification of the intestinal bacterial flora is the aim of probiotics (orally administered live bacterial cultures such as *Lactobacillus*) and prebiotics (beneficial dietary carbohydrate substrates such as lactulose and fructo-oligo-saccharides).
- Adjustment of the levels of omega-6 and omega-3 fatty acids in the diet has been proposed to manage bowel inflammation through decreasing inflammatory mediators, although evidence for this is lacking.

Cobalamin Therapy

Cobalamin (vitamin B_{12}) is frequently depleted in patients with chronic IBD, especially cats, and cobalamin deficiency can impair intestinal mucosal

Table 69-7. TREATMENT OF INFLAMMATORY BOWEL DISEASE

Drug	Product (Manufacturer)	Preparations	Dosage
Anti-inflammatory Drugs/Immunosuppressives			
Prednisone*	Many	Tab: 5, 10, 20, 50 mg	Dog: 1–2 mg/kg PO q24h Cat: 2–3 mg/kg PO q24h
Budesonide	Entocort (AstraZeneca)	Cap: 3 mg	Dog: 1–3 mg PO q24h Cat: 1 mg PO q24h
Methylprednisolone acetate	Depo-Medrol (Upjohn)	Inj: 40 mg/ml	Cat: 20 mg IM q2–4wk
Azathioprine†	Imuran; Azasan (Salix)	Tab: 25, 50, 75 mg	Dog: 1–2 mg/kg PO q24–48h Cat: 0.3–0.5 mg/kg PO q24–48h
Chlorambucil	Leukeran (Glaxo)	Tab: 2 mg	0.1–0.2 mg/kg PO q24–48h, or 2–3 mg/m^2 PO q24–48h, or 15–20 mg/m^2 PO once every 3 weeks (cats)
Cyclosporine	Atopica (Novartis)	Cap: 10, 25, 50, 100 mg	5 mg/kg PO q24h
Colonic Anti-inflammatory Drugs			
Sulfasalazine‡	Generic	Tab: 500 mg	Dog: 10–30 mg/kg PO q8–12h Cat: 10–20 mg/kg PO q12–24h
Olsalazine	Dipentum (Celltech)	Cap: 250 mg	Dog: 10–20 mg/kg PO q12h
Mesalamine	Asacol (Procter & Gamble)	Tab: 400 mg	Dog: 10–20 mg/kg PO q8–12h
	Pentasa (Shire)	Tab: 250 mg	
Anti-inflammatory Retention Enemas§			
5-Aminosalicylate	Rowasa (Solvay)	Enema: 4 g/60 ml	To be determined
Hydrocortisone	Cortenema (Reid-Rowell)	Enema: 100 mg/60 ml	20–60 ml rectally q24h
Antibiotics			
Metronidazole	Flagyl (Searle) or generic	Tab: 250 mg, 500 mg	10–20 mg/kg PO q8–12h
Tylosin tartrate¶	Tylan Soluble (Elanco)	Powder: 2270 mg/tsp	Dog: 20–40 mg/kg PO q12h Cat: 10–20 mg/kg PO q12h
Opioid Motility/Secretory Modifier			
Loperamide	Imodium AD	Tab: 2 mg Liq: 0.2 mg/ml	Dog: 0.1–0.2 mg/kg PO q8–12h Cat: 0.1–0.3 mg/kg PO q12–24h
Adjunct Therapy			
Cobalamin	Generic	Inj: 1000 µg/ml	Dog: 250–1000 µg weekly Cat: 250 µg weekly
Psyllium	Metamucil (Procter & Gamble)	Powder	Dog: 1–3 tbsp/day with food Cat: 1–3 tsp/day with food

*In some cats with severe colitis, prednisone dosage may need to be increased to 5 mg/kg/day, divided bid. In dogs, if steroidal side effects become a problem, decrease dosage and combine with azathioprine, metronidazole, or both.
†May cause myelotoxicity, so monitor the complete blood count; formulate as an oral suspension for accurate dosing of cats.
‡Dosage may need to be increased to 25–50 mg/kg q8h to achieve effect in some dogs; may cause keratoconjunctivitis sicca in dogs and salicylate toxicosis in cats.
§Retention enemas for topical therapy of the distal colon may relieve signs of tenesmus and urgency in some animals with proctitis.
¶Tylan Soluble can be mixed with dextrose or cornstarch. Tylosin powder is bitter-tasting and thus best tolerated when mixed with food.
Cap, capsules; Inj, injectable; Liq, elixir, suspension, or drops; Tab, tablets.

regeneration and cause mucosal atrophy, exacerbating diarrhea and making the patient refractory to the usual anti-inflammatory therapy. Thus, evaluate serum cobalamin and treat with parenteral cobalamin (1000 µg/ml) when serum levels are decreased, especially if <100 ng/L. Give injections weekly for at least 6 weeks, then every other week for 6 weeks, and then monthly.

- For cats and small dogs: Give 250 µg SC, weekly
- For medium dogs: Give 500 µg SC, weekly
- For large dogs: Give up to 1000 µg SC, weekly

Corticosteroids

Oral prednisone or prednisolone is the most consistently effective medical therapy (1–2 mg/kg/day for dogs and 2–4 mg/kg/day or a 5-mg total dose q12h for cats) for initial treatment of lymphocytic-plasmacytic IBD. Clinical improvement using this dosage should be noted within 1 to 2 weeks. After 2 weeks of remission, the dosage is tapered in 2- to 4-week increments to the lowest effective alternate-day dosage.

- In some cases dexamethasone seems to be more effective than prednisolone with fewer side effects.
- In cats that are too difficult to medicate orally, periodic injections of methylprednisolone acetate (20 mg IM or SC q2–4wk) may be substituted for oral treatment.
- Budesonide (0.5–1-mg total dose/cat and 0.5–3-mg total dose/dog, PO q24–48h) is an alternative corticosteroid for refractory cases. Budesonide has high

receptor-binding affinity in the mucosa and undergoes extensive first-pass metabolism in the liver. It achieves particularly high mucosal anti-inflammatory activity with less systemic side effects. It may be cost prohibitive for some owners.
- Corticosteroid therapy may be discontinued on a trial basis after 6 to 12 weeks of remission; however, continuous alternate-day therapy is often required to prevent relapse.
- In refractory cases, metronidazole or mesalamine (see the next sections) should be added to the prednisolone regimen. If this fails to control the disease, then the combination of azathioprine in dogs or chlorambucil in cats (see a later section) with prednisolone may be more effective for achieving remission of the disease.

5-Aminosalicylic Acid (Mesalamine)

These drugs exert an anti-inflammatory effect targeted at the colon through local inhibition of mucosal leukotrienes and prostaglandins. In dogs with IBD, 5-ASA drugs are the initial drugs of choice when the colon alone is involved. Orally administered 5-ASA derivatives are designed to be minimally absorbed during passage through the small intestine so that they reach the colon. These drugs should be used cautiously in cats as some salicylate absorption occurs and cats metabolize salicylates very slowly.

Sulfasalazine

In this drug, 5-ASA is combined with sulfapyridine by an azo bond that prevents significant absorption of the drug so that 75% of it reaches the colon, where bacteria split the bond and release the 5-ASA for its local effect in the colon (see Table 69-7 for dosages).

- The most common adverse side effect of sulfasalazine is keratoconjunctivitis sicca. When it occurs, the decline in tear production is often irreversible. For this reason, it is recommended that a baseline Schirmer tear test be performed at the start of therapy and monitored subsequently at monthly intervals if treatment is long term.
- Less common side effects include allergic dermatitis, nausea and vomiting, and cholestatic jaundice. Rarely, cats may develop anemia.
- Because up to 30% of the salicylate is absorbed and cats metabolize salicylates very slowly, use caution when treating cats with this drug to avoid salicylate toxicity.

Olsalazine (Dipentum)

This newer derivative, consisting of two molecules of azo-bonded 5-ASA, is poorly absorbed so that more than 90% reaches the colon, where the two 5-ASA molecules are then released by the action of colonic bacteria on the azo bond (see Table 69-7 for dosages).

- The advantages of olsalazine over sulfasalazine are that olsalazine contains only 5-ASA (without sulfa) so that side effects are fewer and that a greater percentage of the drug reaches the colon.
- Unfortunately, olsalazine is currently available only in 250-mg capsules, an inconvenient size for dosing most animals.

Polymer-Coated Mesalamine (Asacol)

A pH-sensitive coating prevents release of 5-ASA until the drug reaches the site of inflammation in the colon.

Pentasa

Encapsulation prevents release of 5-ASA until the drug reaches the site of inflammation in the colon.

Mesalamine Suspension Enema

This form of 5-ASA (Rowasa, Reid-Rowell) is available for direct instillation into the rectum. In animals, enema administration of 5-ASA is probably not as effective as the oral route except when proctitis is the principal manifestation.

Metronidazole and Other Antibiotics

Low-dose metronidazole therapy (Flagyl at a dosage of 10–20 mg/kg q12h) is often beneficial either alone or in combination with prednisolone to treat IBD.

- The beneficial effects of metronidazole in any animal with diarrhea might be attributable to an antibacterial effect on enteropathogens (e.g., enterotoxigenic *C. perfringens*), an antiprotozoal effect (e.g., *Giardia*), a reduction of bacterial-derived antigens that could be involved in the immunopathogenesis of IBD, or the immunomodulating effect of the drug on cell-mediated immunity and neutrophil chemotaxis.
- Metronidazole tablets have an unpleasant taste and provoke salivation in most cats and sometimes vomiting. For ease of administration and accurate dosing, a liquid suspension can be formulated on request by many pharmacists or the tablets can be split and placed in gel capsules.
- Dosages of metronidazole exceeding 50 mg/kg/day for prolonged periods (weeks) occasionally cause signs of reversible CNS toxicity (ataxia, weakness, seizures).
- Other antibiotics that might be helpful to control intestinal microflora include tylosin (Tylan) or doxycycline (see Table 69-7).

Azathioprine and Chlorambucil

- In IBD patients refractory to 5-ASA drugs, prednisone, and metronidazole, the combination of azathioprine (Imuran) or chlorambucil (Leukeran) with prednisone may be a more effective immunosuppressive regimen for producing remission of the

disease (see Table 69-7). Besides treating refractory IBD, the addition of azathioprine enables use of a lower dose of corticosteroid to control the disease and thereby minimizes steroidal side effects.

- Azathioprine usually is given as a daily treatment until remission occurs and then decreased to an alternate-day treatment (alternating with every-other-day prednisone) for maintenance. Because of its myelosuppressive toxicity (leukopenia), periodically monitor the CBC of azathioprine-treated animals, especially in the first 2 months, and use lower dosages in cats (see Table 69-7). In cats, formulate azathioprine as an oral suspension to facilitate accurate and safe dosing.
- Chlorambucil (0.1–0.2 mg/kg PO, or 2.0 mg/m^2 PO, q24–48h; alternatively, 15–20 mg/m^2 PO, once every 3 weeks) is an effective alternative to azathioprine that is well tolerated by most cats.

Cyclosporine

Cyclosporine (Atopica, Novartis) (5 mg/kg PO q24h) is useful for treating corticosteroid-refractory IBD. Cyclosporine is a potent immunosuppressive drug that inhibits interleukin-2 and T cell recruitment. Transient anorexia and vomiting are common side effects at the start of treatment but these resolve within 2 weeks.

Motility-Modifying Antidiarrheal Drugs

Adjunctive use of motility-modifying drugs may provide some symptomatic relief for animals with IBD (see Table 69-5 for dosages).

- Opioid drugs such as loperamide (Imodium) and diphenoxylate (Lomotil) may aid control of diarrhea by acting on intestinal smooth muscle to inhibit propulsive movements and by inhibiting mucosal efflux of water and electrolytes.
- Anticholinergic antispasmodics such as dicyclomine (Bentyl) may be beneficial in colitis patients with severe tenesmus and urgency associated with rectocolonic spasm.

Prognosis

- Monitor clinical response using a canine IBD activity index and sequential evaluation of C-reactive protein as a serum marker of inflammation.
- Inform the owner that persistence or recurrence of IBD is likely despite therapy; thus, a realistic expectation is the maintenance of remission or control of relapses rather than a permanent cure.
- The clinical course in basenjis, soft-coated wheaten terriers, and Shar-Peis is often progressive despite treatment.

Eosinophilic Gastroenteritis

Eosinophilic gastroenteritis (EGE) is a relatively uncommon form of IBD that is characterized by diffuse or segmental infiltration of some portion of the GI tract with mature eosinophils, often accompanied by a peripheral eosinophilia.

Etiology

Food allergy and parasitism (e.g., visceral larva migrans) have been proposed as causes, but in most patients evidence for these is lacking and the disease must be considered idiopathic.

Clinical Signs

- One or more layers of the stomach, small intestine, or colon may be affected, resulting in clinical syndromes of chronic vomiting (eosinophilic gastritis) (see Chapter 67), chronic small bowel-type diarrhea (eosinophilic enteritis), chronic large bowel-type diarrhea (eosinophilic colitis), or any combination of these. Weight loss is frequent.
- Diffuse infiltration of the intestinal tract with eosinophils may result in malabsorption (watery diarrhea and weight loss) or protein-losing enteropathy.
- Diarrhea or vomitus may contain blood from mucosal erosions or ulcers.
- Eosinophilic granulomas of the deeper layers of the bowel wall occasionally produce segmental tumor-like thickenings that can cause partial intestinal obstruction.

Diagnosis

- The history may indicate dramatic responsiveness to prior glucocorticoid therapy.
- Palpation may reveal diffusely thickened intestinal loops or a tumor-like intestinal mass (eosinophilic granuloma).
- Laboratory evaluation may reveal peripheral eosinophilia (although not present in all cases), hypoproteinemia, or impaired absorptive function tests.
- Routine fecal flotation is indicated because parasitism can also cause eosinophilic inflammation; it is important to exclude occult whipworm or hookworm infection in dogs by response to a therapeutic trial of an anthelmintic such as fenbendazole (see Table 69-6).
- Barium GI radiography and abdominal ultrasonography may be normal, may indicate thickening and irregularity (mucosal filling defects) of bowel loops, or may delineate sites of partial luminal obstruction caused by eosinophilic granulomas.
- The diagnosis is based on demonstration of eosinophilic inflammation in intestinal biopsies. The endoscopic appearance is similar to that described for lymphocytic-plasmacytic IBD except that mucosal ulceration is more common in EGE. Occasionally, lesions are deep in the submucosa and found only by full-thickness biopsy.

Treatment

- Consider a trial of fenbendazole (Panacur), given at 50 mg/kg daily for 3 days, to rule out GI parasitism.
- Because food allergy is a potential cause of EGE in some animals, a feeding trial using an elimination or novel protein diet (as described for lymphocytic-plasmacytic IBD) can be considered initially; however, dietary therapy alone is seldom effective.
- Oral prednisone usually is the most effective treatment for EGE at an initial dosage of 1 to 2 mg/kg/day for dogs and 2 to 3 mg/kg/day for cats. Clinical signs typically improve rapidly, especially when infiltration is limited to the mucosa. When remission has been maintained for 2 weeks, gradually taper the dosage over an additional 2 to 4 weeks to the lowest effective maintenance dose.
- In some animals the treatment can eventually be discontinued, but in others alternate-day maintenance therapy is required.
- In some patients it may be necessary to add azathioprine to the corticosteroid regimen (as described for lymphocytic-plasmacytic IBD) to facilitate reduction of corticosteroid dosage and side effects or to provide more effective control of the disease.
- Obstructing transmural eosinophilic granulomas involving a localized segment of bowel wall occasionally require surgical excision followed by corticosteroid therapy.

Feline Hypereosinophilic Syndrome

Feline hypereosinophilic syndrome, a rare disease of cats, is characterized by severe eosinophilic GI infiltration accompanied by widespread infiltration of various other organs (liver, spleen, lymph nodes, bone marrow, lung, pancreas, adrenals, skin).

Etiology

The aggressive course and high mortality associated with this syndrome are consistent with malignant neoplasia involving eosinophils (see Chapter 22); thus, it is very distinct from the benign EGE that is confined to the GI tract.

Clinical Signs

- Vomiting, diarrhea (sometimes bloody), anorexia, and weight loss are the most consistent clinical signs.
- Clinical deterioration is rapidly progressive and the disease is eventually fatal.

Diagnosis

- Abdominal palpation may reveal intestinal thickening, hepatosplenomegaly, or mesenteric lymphadenopathy because of the disseminated visceral infiltration of eosinophils.
- Persistent, severe eosinophilia is a consistent CBC finding in affected cats.
- The diagnosis depends on histopathologic confirmation of tissue infiltration and effacement by eosinophils in biopsies of affected organs.

Treatment

- Use high-dose prednisolone (4–6 mg/kg/day for 2–4 weeks) to induce remission, followed by half this dose for 2 to 4 weeks and then by 1 to 2 mg/kg daily or on alternate days for maintenance. Add chlorambucil (see Table 69-7) or other cancer chemotherapeutics in refractory patients.

Prognosis

Unlike EGE confined to the GI tract, feline hypereosinophilic syndrome has a poor prognosis despite treatment.

Regional Granulomatous Enterocolitis

Regional granulomatous enterocolitis (RGE) is an uncommon form of IBD characterized by transmural granulomatous inflammation that results in a stenosing, mass-like thickening of a region of the bowel wall. The ileocolic junction is most often involved, and the mass may incorporate adjacent lymph nodes and mesentery. In some dogs the granulomatous lesions also contain numerous eosinophils (eosinophilic granuloma).

Clinical Signs

The principal clinical sign of RGE is chronic large bowel diarrhea containing mucus and fresh blood, sometimes accompanied by tenesmus and abdominal pain. Additional signs may include weight loss, anorexia, and depression.

Diagnosis

- The diseased segment of bowel may be palpable as a firm mass in the mid-abdomen. The adjacent intestinal loops and mesentery may also be thickened and regional lymph nodes may be enlarged.
- A routine CBC may reveal eosinophilia, neutrophilia, or monocytosis. Panhypoproteinemia due to excessive enteric loss of protein may be found in some animals.
- Barium contrast radiography of the ileum and colon may delineate a thickened or stenosed segment of bowel and ultrasonography may identify an intestinal mass.
- Definitive diagnosis of RGE requires biopsy by colonoscopy or laparotomy. The key feature is transmural granulomatous inflammation. Fibrosis and aggregates of epithelioid cells, giant cells, and eosinophils often are found deep in the lesion. Deep ulceration is common.
- Differentiate RGE from intestinal neoplasia and infectious causes of granulomatous bowel lesions,

such as histoplasmosis (Chapter 20), pythiosis, and mycobacteriosis (Chapter 19). Examine granulomatous lesions by special stains to detect fungi and acid-fast organisms. In cats, feline immunodeficiency virus (Chapter 9) and feline infectious peritonitis (Chapter 10) occasionally are associated with pyogranulomatous IBD.

Treatment

- Medical treatment of regional granulomatous colitis is based on the use of anti-inflammatory and immunosuppressive agents such as olsalazine or sulfasalazine, prednisone, azathioprine, and metronidazole, as described for treatment of lymphocytic-plasmacytic IBD (see Table 69-7).
- If the degree of thickening and cicatrization of the affected segment of bowel produces severe stenosis and obliteration of the lumen, surgical excision of the lesion may be necessary, followed by medical therapy for 6 to 8 weeks or longer to prevent recurrence of the lesion at the surgical site. Always submit the excised lesion for histopathological evaluation.

Histiocytic Ulcerative Colitis

- Histiocytic ulcerative colitis is a chronic idiopathic IBD of young boxer dogs characterized by infiltration of the lamina propria and submucosa of the colon by distinctive histiocytes engorged with deposits that stain positive with periodic acid-Schiff (PAS) stain.
- In addition to boxers, there have been isolated case reports of histiocytic colitis in a cat and a French bulldog, but it is not known if this is the same disease that occurs in boxers.

Clinical Signs

- Affected boxers generally develop severe, unresponsive, bloody-mucoid large bowel diarrhea before 2 years of age.
- Severe weight loss and debilitation occur in dogs with long-standing disease.

Diagnosis

The diagnosis is based on the known breed predisposition and the presence of numerous PAS–positive histiocytes in a colonoscopic biopsy. A mixture of other types of inflammatory cells is also found in the lesion, and usually there is severe mucosal ulceration.

Treatment

- The treatment of choice is enrofloxacin (Baytril at 5 mg/kg PO q12h) alone or in combination with metronidazole, based on evidence that bacteria play a pivotal role in this disease. The optimal duration of therapy is not known, but clinical signs are resolved in most dogs within 3 to 4 weeks of starting enrofloxacin, and recovery has persisted more than 3 years after stopping the antibiotic.
- Anti-inflammatory and immunosuppressive therapy (e.g., olsalazine or sulfasalazine, prednisone, azathioprine, and metronidazole) in single-agent or combination regimens, as described for lymphocytic-plasmacytic colitis, generally only provides temporary palliation of the disease.
- In general, these dogs seem to have less diarrhea on a highly digestible diet than on a high-fiber diet.

Neutrophilic (Suppurative) Enterocolitis

Etiology

- Bacterial enterocolitis (see under "Bacterial Infections of the Intestines")
- Idiopathic (i.e., neutrophilic IBD in the absence of an identifiable infectious cause)

Clinical Signs

- Large bowel diarrhea that can be either acute or chronic.

Diagnosis

- Colonoscopic biopsy shows infiltration of predominantly neutrophils, with variable mucosal ulceration, necrosis, or crypt abscesses.
- Diagnosis is based on tests to exclude bacterial enteropathogens (see under "Bacterial Infections of the Intestines").

Treatment

Give antibiotics (e.g., enrofloxacin, trimethoprim-sulfa, or tylosin) or regimens consisting of sulfasalazine, metronidazole, or anti-inflammatory or immunosuppressive drugs, as described for lymphocytic-plasmacytic IBD (see Table 69-7).

FIBER RESPONSIVE DIARRHEA (IRRITABLE BOWEL SYNDROME)

Etiology

Fiber-responsive diarrhea is characterized by chronic, non-inflammatory, mucoid large bowel diarrhea. The condition has resemblances to irritable bowel syndrome (IBS) seen in people.

Clinical Signs

- Signs associated with myoelectrical dysfunction in humans with IBS are alternating patterns of diarrhea, constipation, and abdominal cramping.
- Evidence for the existence of IBS in animals is circumstantial, but psychomotor diarrhea due to colonic motility dysfunction or neurogenic hyperre-

activity may be a consideration in animals that have intermittent mucoid diarrhea but lack evidence of organic disease.
- Hematochezia is usually absent.
- Large breeds, especially those used as working dogs (e.g., police dogs, Seeing Eye dogs, and sled dogs), and temperamental or excitable dogs seem to be predisposed.

Diagnosis

The diagnosis is based on the complete absence of abnormal findings on diagnostic evaluation, minimal abnormalities on colonoscopic biopsy, and remission of clinical signs in response to modification of diet, particularly supplementation of fiber.

- By definition, IBS is a functional disorder. The diagnosis can be established only by normal colonoscopic biopsy and diligent exclusion of the other known causes of colonic disease, such as dietary, parasitic, infectious, and chronic colitis (IBD).
- At colonoscopy, the colon may appear to be hypermotile or spastic. The mucosa appears normal except for increased intraluminal mucus and an erythematous response to insufflation.

Treatment

Dietary Modification

Supplement a digestible GI diet with added dietary fiber in the form of psyllium (Metamucil) (1–5 tbsp/meal). This is sufficient to produce remission in many cases. Fiber may normalize colonic myoelectrical function and have beneficial effects on fecal consistency, water content, and bulk. In addition, fermentable soluble fiber is fermented by colonic bacteria to short-chain fatty acids that provide an energy source for colonic epithelium, protect against mucosal injury, and acidify bowel contents, which may alter the bacterial flora.

Medical Therapy

- If dietary fiber supplementation is unsuccessful, consider medication to alter motility such as opioid drugs such as loperamide (see Table 69-5 for dosages).
- Consider amitriptylin (Elavil) at 1 to 2 mg/kg PO q12h.
- Light sedation during stressful times may be beneficial in excessively nervous or excitable animals.

PROTEIN-LOSING ENTEROPATHY

GI loss accounts for approximately 40% of the normal daily turnover of plasma proteins. The term *protein-losing enteropathy* refers to a variety of intestinal diseases that are associated with hypoproteinemia caused by an accelerated loss of plasma proteins into the gut. Mechanisms of excessive enteric loss of protein include the following:

- Impaired intestinal lymphatic drainage (e.g., lymphangiectasia) that results in extravasation of protein-rich lymph into the lumen
- Disruption of the mucosal barrier (e.g., inflammation) that results in protein leakage from sites of exudation, bleeding, or increased permeability

Etiology

Severe protein-losing enteropathy occurs most frequently in association with chronic enteropathies, such as the following:

- Idiopathic canine intestinal lymphangiectasia
- Chronic inflammatory small bowel diseases (lymphocytic-plasmacytic enteritis, granulomatous enteritis, eosinophilic enteritis, immunoproliferative enteropathy of basenjis)
- Intestinal histoplasmosis
- Intestinal lymphoma

Intestinal Lymphangiectasia

Lymphangiectasia is a chronic protein-losing enteropathy in dogs, characterized by marked dilation and dysfunction of the intestinal lymphatic network. Impaired intestinal lymph drainage is presumably caused by obstruction to the normal lymphaticovenous flow. It leads to stasis of chyle within dilated lacteals and lymphatics of the bowel wall and mesentery. Overdistended lacteals release intestinal lymph into the gut lumen by rupture or extravasation, causing loss of the constituents of chyle, including plasma proteins, lymphocytes, and lipid (chylomicrons).

Clinical Signs

- The presenting signs of lymphangiectasia usually are attributable to protein-losing enteropathy and include dependent pitting edema of subcutis and limbs, fluid distention of the abdomen (ascites), and respiratory distress (hydrothorax). These manifestations of fluid transudation are the result of hypoalbuminemia and reduced plasma colloidal osmotic pressure.
- Chronic intermittent or persistent diarrhea with a watery or semisolid consistency often is observed, but not all patients have diarrhea.
- Progressive weight loss is common. Clinical signs often develop insidiously.

Diagnosis

▼ ***Key Point*** Typical laboratory findings in intestinal lymphangiectasia include hypoalbuminemia, hypoglobulinemia, lymphocytopenia, hypocholesterolemia, and hypocalcemia.

- Differentiate protein-losing enteropathy from non-enteric causes of hypoproteinemia, such as liver failure (impaired hepatic synthesis of albumin) and renal disease (protein-losing glomerulonephropathy), through liver function testing (Chapter 71) and urine protein determinations (Chapter 77), respectively.
- Radiography can detect or confirm ascites and pleural effusion.
- Fluid analysis of body cavity effusions may be helpful. The effusion associated with lymphangiectasia is usually a transudate. Chylous ascites and chylothorax are found occasionally.
- Cardiac evaluations can exclude right-sided congestive heart failure, which is a rare cause of lymphangiectasia.
- Definitive diagnosis of lymphangiectasia is based on identification of the characteristic lymphatic lesions in biopsies obtained via laparotomy, or less invasively by endoscopy. Laparotomy may reveal the mesentery and serosa to have a prominent, weblike network of distended, milky-white lymphatics along with small, yellow-white nodules and foamy granular deposits (lipogranulomas) adjacent to lymphatics.

Treatment

The major goal in treating intestinal lymphangiectasia is to decrease the enteric loss of plasma proteins so that normal plasma protein levels can be restored and edema and effusions can be controlled. This is accomplished with dietary manipulation and anti-inflammatory therapy as described under "Inflammatory Bowel Disease."

- The plasma protein loss and diarrhea of lymphangiectasia often benefit from anti-inflammatory doses of corticosteroids (prednisone at a dosage 2–3 mg/kg/day PO). When remission has been achieved, adjust the dosage to the lowest effective maintenance level. The addition of metronidazole and azathioprine is helpful in some cases (see Table 69-7).
- Because absorption of dietary long-chain triglycerides (LCTs) is a major stimulus of intestinal lymph flow, restriction of dietary intake of fat may reduce lymph flow, lymphatic distention, and protein loss in lymphangiectasia. Supplement diets with fat-soluble vitamins.

Prognosis

The prognosis and response to therapy is unpredictable. Many patients achieve remission of months to years with combined dietary and anti-inflammatory therapy. However, some animals fail to respond and many eventually relapse to finally succumb to severe protein-calorie depletion, incapacitating effusions, or intractable diarrhea.

VILLOUS ATROPHY

Etiology

Villous atrophy is a lesion of the small intestine characterized by short, blunted mucosal villi and is associated with intestinal malabsorption and chronic diarrhea. The forms of villous atrophy may be categorized as primary or secondary.

Primary Forms

- Gluten-sensitive enteropathy of Irish setters resembles gluten enteropathy of humans (celiac disease, non-tropical sprue). This is inherited as an autosomal recessive trait, mostly in Irish setters in Great Britain and is characterized by partial villous atrophy, deficiency or delayed development of specific microvillus enzymes, and dietary sensitivity to wheat.
- Idiopathic canine villous atrophy is recognized most often in German shepherds.

Secondary Forms

- Sequelae of diffuse infiltrative diseases of the intestines, such as chronic IBD and lymphoma
- Sequelae of enteric infections, such as viruses (coronavirus, rotavirus), bacteria (small intestinal bacterial overgrowth syndrome), and parasites *(Giardia)*

Clinical Signs

Villous atrophy generally causes chronic small bowel-type diarrhea and weight loss. The severity of signs depends on the degree of disruption of the villous absorptive surface area.

Diagnosis

Histologic examination usually is adequate for documentation of villous atrophy. However, because this can be a nonspecific secondary lesion found in various enteropathies, the diagnosis is mainly based on the following:

- Breed predilection (German shepherds, Irish setters in Great Britain)
- Response to withdrawal of wheat from the diet
- Tests or procedures to identify enteric infections (e.g., *Giardia*) or bacterial overgrowth
- Characterization of morphologic and biochemical abnormalities in jejunal biopsies

In some cases, infiltration of lymphocytes and plasma cells and fibrosis make it difficult to determine if the lesion should be categorized as a primary idiopathic villous atrophy or as chronic IBD (lymphocytic-plasmacytic enteritis) with secondary villous atrophy (see under "Lymphocytic-Plasmacytic Inflammatory Bowel Disease").

Treatment

Gluten-Sensitive Enteropathy

In gluten-sensitive Irish setters, the signs and lesions of villous atrophy promptly resolve with complete elimination of wheat and other gluten-containing cereal grains (barley and rye) from the diet. Most commercial dog foods contain gluten; however, diets that are based on rice or corn rather than wheat or gluten-containing grains are commercially available. Wheat restriction must continue for life, and breeding of affected animals is discouraged.

Idiopathic Villous Atrophy

- Dietary management with a gluten-restricted hypoallergenic diet (e.g., Hill's Prescription Diet d/d) is sometimes beneficial.
- Vitamin therapy with folate (5 mg daily PO) and cobalamin (250–1000 µg SC weekly for 6 weeks, then every 2–4 weeks, for 6 months) is indicated if serum levels of these are low.
- Antibiotic therapy is sometimes beneficial, using antibiotics such as oxytetracycline, tylosin, or metronidazole to empirically treat bacterial overgrowth (see under "Small Intestinal Bacterial Overgrowth").
- Prednisone as used for treatment of IBD (1–3 mg/kg/day PO for 4 weeks, followed by tapering to lowest effective alternate-day dosage) may produce clinical improvement in dogs with idiopathic villous atrophy that fail to respond to dietary modification, vitamins, or antibiotics.

Prognosis

The prognosis is guarded, as diarrhea and weight loss often persist despite treatment.

SMALL INTESTINAL BACTERIAL OVERGROWTH

Bacterial overgrowth syndrome is an overproliferation of microflora within the proximal small intestine that results in malabsorption and diarrhea. Human criteria that define bacterial overgrowth as a fasting bacterial count in duodenal juice of greater than 10^5 organisms per milliliter of intestinal contents do not appear to be valid in dogs and cats; thus, definitive evidence of this syndrome in animals is lacking. For this reason, some veterinary gastroenterologists prefer to call this syndrome *antibiotic-responsive diarrhea.*

Etiology

The normal small intestinal microflora is a stable population of aerobic and facultative anaerobic bacteria whose growth is regulated and influenced by a combination of host factors, bacterial interactions, and dietary composition. Mechanical self-cleansing action of normal intestinal motility and continuous downstream flow of ingesta are especially important for preventing bacterial overgrowth.

Because documentation of bacterial overgrowth is difficult, the syndrome may occur more frequently in dogs and cats than is generally recognized. Development of an abnormal small bowel flora should be considered a potential secondary complication in the following situations:

- Intestinal surgery
- Stasis-producing mechanical obstructions such as chronic intestinal foreign bodies and stenosing neoplastic or inflammatory lesions of the gut
- Destructive lesions of the ileocecocolonic junction that allow colono-enteric reflux
- Motility disorders such as idiopathic intestinal pseudo-obstruction
- Immune deficiency states with lack of immunoglobulin A (proposed as the explanation for an apparent breed predilection for overgrowth in German shepherds, basenjis, and Shar-Peis)
- Conditions associated with hyposecretion of gastric acid
- Exocrine pancreatic insufficiency

Clinical Signs

- Bacterial overgrowth typically causes chronic, foul-smelling watery diarrhea, steatorrhea, and weight loss; however, additional presenting clinical signs can depend somewhat on the underlying cause of the abnormal proliferation of flora.
- Diarrhea caused by overgrowth usually does not contain blood or mucus.
- Bacterial overgrowth may be responsible for failure of some dogs with exocrine pancreatic insufficiency to respond adequately to enzyme supplementation.

Diagnosis

Definitive diagnosis of small intestinal bacterial overgrowth requires quantitative aerobic and anaerobic cultures of duodenal juice. Duodenal culture specimens are taken by endoscopy, intestinal intubation, or laparotomy after an 18-hour fast. This is impractical for routine clinical application.

Indirect evidence of bacterial overgrowth in animals with unexplained small bowel diarrhea and malabsorption includes the following observations:

- Responsiveness to antibiotics (e.g., tetracyclines, tylosin, or metronidazole)
- Delayed intestinal transit of barium on radiographs (suggestive of obstruction or poor motility)
- Idiopathic pseudo-obstruction manifested by a dilated, hypomotile segment of gut
- Elevated serum folate and decreased serum cobalamin (because bacteria may synthesize folate and bind with or utilize cobalamin)

- Minimal morphologic abnormalities in intestinal biopsies
- Unlike many other enteropathies, mucosal morphology in bacterial overgrowth may be normal or characterized by mild atrophy of villi and minimal increase in mononuclear cells in the lamina propria
- Failure to obtain the expected treatment response in other intestinal disorders known to be conducive to bacterial overgrowth (such as exocrine pancreatic insufficiency)

Treatment

- Identify and treat underlying disorders or predisposing factors. In animals with stasis caused by anatomic abnormalities, this may include surgery.
- Antibiotic therapy:
  - Oral broad-spectrum antimicrobials and those with activity against anaerobes are recommended, such as tetracycline, oxytetracycline, doxycycline, metronidazole, ampicillin, chloramphenicol, tylosin, and erythromycin.
  - Continue treatment for at least 10 to 14 days and repeat as necessary. Some animals need continuous treatment; others may remain in remission for months after one course of antibiotics.
  - Clinical signs and abnormal function tests usually resolve within the first week of therapy, which in itself is good indirect evidence in support of the diagnosis.
- Treatment with *Lactobacillus* or live yogurt culture usually is not effective for altering the enteric microflora.

INTESTINAL NEOPLASIA

Benign tumors of the intestinal tract include adenomatous polyps, adenomas, and leiomyomas. In dogs these occur most commonly in the rectum and terminal colon. The most common malignant neoplasms of the intestinal tract are adenocarcinoma and lymphoma. Less common malignancies include carcinoid tumors, leiomyosarcoma, fibrosarcoma, mastocytoma, hemangiosarcoma, and anaplastic sarcoma.

Etiology

Adenocarcinoma

- Adenocarcinomas are locally invasive and slow growing and are usually seen in older animals. The most common sites in dogs are the duodenum and colon; in cats, the ileum and distal jejunum are the most common locations.
- Morphologically there are three forms of adenocarcinoma:
  - *Infiltrative*—Thickened stenotic region of the bowel that obstructs the lumen
  - *Ulcerative*—Deep indurated mucosal ulcer with raised edges
  - *Proliferative*—Lobulated expanding intestinal mass
- Mucosal ulceration is frequent, sometimes resulting in melena and blood loss anemia.
- Local invasion of the mesentery, omentum, and regional lymph nodes is common. More widespread metastasis also may occur.

Lymphoma

- GI lymphoma arises from lymphocytes of the gut-associated lymphoid tissue (GALT) and is the most common extranodal lymphoma in dogs and cats (see Chapter 27).
- In cats, intestinal lymphoma occurs mostly over 8 years of age and can be caused by feline leukemia virus (see Chapter 8), although as few as 30% are viremic.
- Morphologically there are two types of intestinal lymphoma:
  - *Diffuse lymphoma*—Diffuse infiltration of the lamina propria and submucosa with neoplastic lymphocytes, causing malabsorption and occasionally deep ulceration; this is difficult to distinguish from IBD
  - *Nodular lymphoma*—Expanding intestinal mass, most often in the ileocecocolic region, causing progressive luminal obstruction
- Metastasis to regional lymph nodes and other organs is common.

Clinical Signs

- Small intestinal neoplasia typically develops insidiously with initial vague signs of anorexia and lethargy, progressing to diarrhea and intermittent vomiting. Weight loss develops and progresses in severity in parallel with tumor growth. Melena, hematemesis, anemia, fever, icterus, and abdominal effusion may also occur.
- Colonic polyps and tumors cause hematochezia, dyschezia, and tenesmus, sometimes with mucoid diarrhea; thus, they are easily confused with inflammatory diseases of the colon and anorectal disease.
- Multifocal GI lymphoma may invade the stomach, small intestine, or colon, in any combination, thereby varying the clinical presentation. Furthermore, signs of extraintestinal involvement of organs such as the liver, spleen, or kidney may add to the clinical signs and physical findings.

Diagnosis

- Abdominal palpation often detects intestinal neoplasia as a firm midabdominal mass, thickened intestinal loops, or mesenteric lymphadenopathy.
- Rectal palpation detects stenosing or polypoid rectal masses. Most adenomatous rectal polyps can be exposed at the anus by everting the rectal mucosa

with gentle traction. Polyps usually appear dark red and lobulated, are extremely friable, and bleed easily.
- Laboratory evaluation may reveal blood loss anemia, neutrophilic leukocytosis with left shift, hypoproteinemia, or elevated serum hepatic enzyme concentrations.
- Radiography, particularly barium contrast, can be helpful for delineating regions of mucosal irregularity, luminal narrowing, and intramural infiltration, thickening, or nodularity. Thoracic radiography is indicated for detection of metastasis.
- Abdominal ultrasonography may be used to detect and define intestinal mass lesions.
- Surgical excision or biopsy of the affected segment of the bowel provides a definitive diagnosis.
- Gastric, duodenal, or colonic lesions are accessible to endoscopic biopsy.
- Percutaneous fine-needle aspiration can be used to make a cytologic diagnosis in selected cases in which the neoplastic intestinal mass or loop can be well delineated by palpation or ultrasonography.

Treatment

- Surgical resection is the treatment of choice for benign tumors such as polyps and, when feasible, for adenocarcinomas and other non-lymphomatous tumors. Unfortunately, many malignant tumors of the intestinal tract are too advanced for successful resection by the time they are recognized clinically. Always submit excised tissue for thorough histopathologic examination, including evaluation of surgical margins.
- Intestinal lymphoma can be treated with anticancer chemotherapy (see Chapters 26 and 27). Long-term remissions are possible in cats with low-grade or lymphocytic ("small cell") lymphoma of the small intestine.
- Treatment strategy and prognosis may be affected by complications such as malabsorption, protein-losing enteropathy, intestinal blood loss anemia, intestinal obstruction, intussusception, intestinal perforation and peritonitis, and metastasis to the liver or kidneys.

INTESTINAL OBSTRUCTION

Etiology

Intestinal obstruction in dogs and cats may be caused by intraluminal objects, intramural thickening or stenosis, and extramural compression. Specific causes include the following:

- Foreign bodies (e.g., bones, toys, cloth, metallic objects, stones, peach pits, acorns, rubber nipples, rubber balls, and linear objects such as string and thread)
- Intussusception
- Intestinal volvulus
- Intestinal torsion
- Incarceration of bowel in a hernia (includes abdominal hernias of all types, diaphragmatic hernia, and internal herniation of gut loops through a tear in the mesentery)
- Adhesions or stricture (post-trauma or post-surgery)
- Intramural abscess, granuloma, or hematoma
- Congenital malformation (stenosis or atresia)
- Intestinal neoplasia

Pathophysiology

Proximal versus Distal Obstruction

The more proximal and complete the obstruction, the more acute and severe the signs and the greater the likelihood of dehydration, electrolyte imbalance, and shock.

- *Proximal obstructions* cause gastric outlet occlusion, leading to persistent vomiting, loss of gastric secretions (hydrochloric acid), and metabolic alkalosis.
- *Distal obstructions* cause varying degrees of metabolic acidosis. Distal and incomplete obstructions can be insidious, with vague, intermittent signs of chronic anorexia and occasional vomiting that span several days or even weeks, leading to progressive starvation.

Simple versus Strangulated Obstruction

Vascular compromise of the obstructed bowel worsens the severity of the condition.

- *Simple obstructions* occlude the lumen without compromising vascular integrity.
- *Strangulated obstructions* cause vascular compromise of the obstructed bowel segment. This occurs most often with intussusception, volvulus, and incarcerated hernia. The sequence of events following strangulation are edema and engorgement of the affected loop, tissue hypoxia and infarction of the bowel wall, accumulation of gut bacteria and toxins in the peritoneal fluid, and rapidly progressive toxemia and shock, culminating in death.

Clinical Signs

The clinical manifestations and consequences of obstruction depend on its location, completeness, and duration, as well as the vascular integrity of the affected bowel segment.

- Acute onset of vomiting, anorexia, and depression are the most consistent clinical signs.
- Other signs may include abdominal distention, diarrhea (watery, hemorrhagic, or melenic), abdominal pain (restlessness, panting, or abnormal body posture), and shock (acute collapse).

Diagnosis

- Abdominal palpation may identify intestinal foreign bodies, intussusceptions ("sausage loop"), or gas- and fluid-distended loops of bowel proximal to the obstruction.
- Radiography often confirms the presence of obstruction and delineates the cause, especially when contrast studies are used.
- Radiographic findings suggesting obstruction include gas or fluid distention (mechanical ileus) of the bowel, delayed transit of contrast material, fixation or displacement of gut loops, luminal filling defects, and foreign objects within the lumen.
- Cats commonly ingest radiolucent linear intestinal foreign bodies (e.g., thread, string, cloth, fishing line, dental floss, and decorative tinsel) that cause aggregation and plication of the bowel and have a distinctive radiographic pattern.
- Laboratory findings often reflect fluid, electrolyte, and acid-base derangements; these vary with location, completeness, and duration of obstruction.
- Leukocytosis with a left shift or degenerative leukopenia accompanied by septic abdominal effusion indicates intestinal ischemia or perforation with peritonitis (see Chapter 76).

Treatment

- Intestinal obstructions are treated surgically. Give close attention to supportive care, especially maintenance of fluid, electrolyte, and acid-base homeostasis before, during, and after surgery (for further information on intestinal surgery, see Chapter 70).
- Treatment includes management of complications such as necrosis or perforation of the bowel, peritonitis (see Chapter 76), and septic shock (see Chapter 156).

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Chapter

70 Surgery of the Intestines

Ronald M. Bright

Surgical therapy is indicated for structural disease of the bowel. Most animals that require surgery of the small bowel are physiologically compromised. When obstruction of the small bowel is proximal in location (high obstruction), serious electrolyte and water abnormalities can place these patients at high risk.

Prophylactic antibiotics administered perioperatively are indicated in small bowel surgery.

- Before surgery of the upper and middle small bowel, give a first-generation cephalosporin such as cefazolin (20 mg/kg) intravenously (IV) initially; repeat IV 3 hours later.
- Before surgery of the distal small bowel and large intestine, give a second-generation cephalosporin such as cefmetazole (15 mg/kg) IV or cefoxitin (30 mg/kg) IV; repeat IV 3 hours later.

ANATOMY

- The small intestine extends from the pylorus to the cecum.
- The duodenocolic ligament restricts the movement of the distal duodenum.
- The jejunum is the major portion of the small bowel and is a very mobile structure.
- The major blood supply is from the cranial mesenteric artery.
- A portion of the proximal duodenum is supplied by the celiac artery and shares a source of blood with the right lobe of the pancreas via the pancreaticoduodenal artery.
- The tunica of the small intestine includes the mucosa, submucosa, muscularis, and serosa.
- The submucosal layer provides blood vessels, lymphatics, and nerves. It is also the support or "holding" layer for sutures.

ENTEROTOMY

Preoperative Considerations

- Give perioperative antibiotics, as previously described.
- Attempt to correct electrolyte and water abnormalities before surgery.
- Several factors may contribute to intestinal leakage following resection and anastomosis. Dogs are at higher risk for leakage when there are two or more of the following factors: hypoalbuminemia (<2.5 g/dl), intestinal foreign body, peritonitis.

Surgical Procedure

Objectives

- Gain access to the lumen of the small bowel to remove a foreign body.
- Help define a disease by acquiring a full-thickness biopsy.
- Avoid contamination of the peritoneal cavity.

Equipment

- General surgical pack
- Babcock forceps
- Laparotomy sponges
- Doyen non-crushing intestinal clamps
- #11 Bard-Parker blade
- Fine-tip needle holders
- Ewald thumb forceps

Technique

1. Make a midline abdominal incision to allow access to the small bowel.
2. Isolate the segment of bowel to be entered with moistened laparotomy sponges.
3. Place a 3-0 stay suture at both ends of the proposed enterotomy incision (Babcock forceps may be substituted).
4. Milk bowel contents away from the proposed enterotomy site; place non-crushing intestinal forceps (or an assistant's fingers) across the bowel to minimize spillage.
5. Make a full-thickness stab incision into the lumen, using a #11 Bard-Parker scalpel blade. Place a suction tip in the bowel lumen and remove its contents. Enlarge the incision as needed with Metzenbaum scissors.

6. If removing a foreign body, perform the enterotomy over healthy bowel distal to the foreign body.
7. If a biopsy is needed, excise a 2- to 3-mm strip of bowel parallel to the enterotomy incision.
8. Trim any everted mucosa with scissors.
9. Close the enterotomy incision with 3-0 or 4-0 synthetic absorbable or monofilament non-absorbable suture material on a swaged-on taper-point or taper-cut needle. A full-thickness, simple interrupted or continuous appositional suture pattern is preferred.

▼ ***Key Point*** To minimize tissue trauma, avoid repeatedly grabbing the intestinal wall with thumb forceps.

10. Rinse the enterotomy site thoroughly with warm saline.
11. Use omentum or a jejunal onlay patch to reinforce the suture line. I prefer to use omentum, even in relatively healthy tissue.
12. Some severely debilitated animals may benefit from placement of a jejunostomy tube for postoperative enteral nutritional support. (See Chapter 3 for nutritional support of critical patients.)
13. Perform routine closure of the abdomen.

Postoperative Care and Complications

Short Term

- Monitor for signs of leakage peritonitis by abdominal palpation, body temperature measurements, and a complete blood count (CBC).
- Give food and water the day after surgery.
- Gradually taper off fluid and electrolyte therapy as the animal returns to normal eating and drinking.

Long Term

- Strictures are rare unless an excessive amount of tissue was removed for biopsy and the lumen diameter was compromised.
- Slow leakage from an enterotomy site may become walled off and later be manifested as an abscess.

Prognosis

- The prognosis is fair to good if the enterotomy was done for a foreign body.
- If biopsy indicates neoplasia, the prognosis is poor.
- If biopsy reveals a protein-losing enteropathy due to benign infiltrative disease, the prognosis is poor to guarded (see Chapter 69).

INTESTINAL RESECTION AND ANASTOMOSIS

Indications for intestinal resection and anastomosis include the following:

- Diseases causing bowel necrosis (e.g., foreign body, volvulus, trauma)
- Neoplasia
- Intussusception
- Severe, focal infiltrative bowel disease (e.g., phycomycosis pythiosis, zygomycosis)

Preoperative Considerations

- Administer perioperative antibiotics starting 20 to 40 minutes before surgery, as described previously.
- Although controversy surrounds the choice of suture pattern for intestinal anastomosis, any of several techniques probably is acceptable in the hands of a competent surgeon who follows sound intestinal surgery principles.
- It is probably best to use synthetic monofilament absorbable sutures. Polypropylene used in a continuous pattern has been associated with attaching to foreign bodies after being extruded into the lumen of the bowel and was the cause of pyloric outflow obstruction in a dog following the formation of a granuloma around the suture.
- I prefer the simple interrupted appositional (SIA) suture pattern for intestinal (large or small) anastomoses. This non-crushing technique causes little compromise of the blood supply of the intestinal segments. (Disruption of vascularity is the most common biologic cause of failure of an anastomosis.)

▼ ***Key Point*** Accurate and atraumatic placement of sutures and gentle handling of the bowel gives the best results. Failure of an anastomosis usually is due to poor surgical technique or a combination of the risk factors previously mentioned.

- Assess bowel viability before determining the amount of bowel to be resected. Standard clinical criteria include color, peristalsis, and arterial pulsations.
- In the rare case in which standard criteria are not adequate to determine bowel viability, an intravenous fluorescein dye technique can be used.
- Inject 2 ml of 5% fluorescein dye IV; in a darkened surgery room, evaluate the pattern of fluorescence using #3600 ultraviolet illumination (Wood's lamp).
- A smooth, uniform green-gold color or a finely mottled pattern with no areas of non-fluorescence greater than 3 mm denotes acceptable bowel viability.

Surgical Procedure

Objectives

- Remove the diseased or non-viable segment of bowel and restore bowel continuity with an end-to-end anastomosis.
- Preserve lumen diameter and tissue blood supply.
- Avoid spillage of bowel contents.

Equipment

- General surgical pack
- Doyen non-crushing clamps
- Laparotomy pads
- Abdominal retractors

Technique

1. Make a midline abdominal incision long enough to accommodate a thorough abdominal exploratory procedure.
2. Isolate the affected bowel segment with saline-moistened laparotomy sponges.
3. Isolate and ligate the mesenteric vessels to the affected area. Ligate the arcadial vessels within the mesenteric fat similarly.
4. Place crushing clamps across the bowel at a 60 degree angle to the long axis of the bowel and just inside the arcadial vessels.
5. Milk the ingesta away from the crushing clamps. Place a non-crushing clamp across the viable segments of bowel to be anastomosed, or have an assistant gently hold the bowel segments during the anastomosis.
6. Excise the diseased bowel by incising between the crushing clamp and the arcadial vessel ligation.
7. The mucosal collar may evert around the ends of the transected bowel. This can be trimmed with scissors.
8. Atropine given in a mesenteric vessel at a dose of 0.04 mg/kg has been shown to decrease the amount of mucosal eversion of jejunal segments.
9. Correct lumen disparity by cutting the small lumen at a more acute angle, longitudinally incising the antimesenteric edge of the small end, or oversewing the larger end.
10. Use a 3-0 or 4-0 suture on a small taper-point needle to place the sutures. All knots are extraluminal.
11. Carefully place the first suture at the mesenteric border. The second suture apposes the antimesenteric border. Place sutures approximately 2 to 3 mm apart along the "near" side of the anastomosis. Include the entire thickness of the bowel. Pull down the sutures slowly so as to gently appose the edges of the bowel (SIA pattern). Alternatively, close the bowel in a simple continuous suture pattern (see study by Weisman et al for details).
12. Appose the "far" side or back wall similarly.
13. Gently flush warm sterile saline over the anastomotic site and adjacent lengths of bowel.

▼ ***Key Point*** Do not flush the entire abdominal cavity unless there is gross contamination from the surgery or preexisting peritonitis.

14. Wrap a piece of omentum around the line of anastomosis and gently tack it to the bowel above and below the anastomosis.
15. Close the defect in the mesentery with a continuous suture.
16. If nutritional support is necessary, place a jejunostomy tube before closure of the abdomen.

Postoperative Care and Complications

- Maintain intravenous fluid and electrolyte supplementation until the animal is drinking water.
- Withhold food and fluids for 12 to 24 hours, after which the regular diet can be fed.
- Discontinue antibiotics over the next 4 to 12 hours unless peritonitis was present. In this case, continue empirical antibiotic therapy and modify if necessary based on culture and sensitivity results.
- Monitor for signs of depression, high fever, excessive abdominal tenderness, vomiting, and ileus, which may indicate leakage peritonitis. If warranted, initiate appropriate diagnostic (e.g., abdominocentesis) and therapeutic measures (see Chapter 76).

ENTEROENTEROPEXY/ENTEROPEXY (COLOPEXY)

- Enteroenteropexy, or plication of loops of bowel, is done to prevent recurrence of intussusception and is usually performed at the time of definitive surgical repair of the intussusception.
- Enteropexy, or fixation of bowel to the abdominal wall, is done as part of a tube jejunostomy placement procedure, as a colopexy for treatment of rectal prolapse, or as an adjunctive procedure for correcting rectal sacculation related to a perineal hernia (see Chapter 75).
- These procedures have limited use in dogs and cats.

Surgical Procedures

Objectives

- Prevent recurrent telescoping of bowel following surgical repair of intussusception.
- Diminish likelihood of leakage around a jejunostomy tube as it exits the bowel and enters the abdominal wall.
- Prevent caudal movement of the colon and rectum (colopexy) to correct anorectal prolapse.

Equipment

- General surgical pack
- Balfour abdominal retractor

Technique

Enteroenteropexy

1. Place loops of small bowel side by side to form a series of gentle loops. Suture loops to each other by engaging the seromuscular layers with monofilament

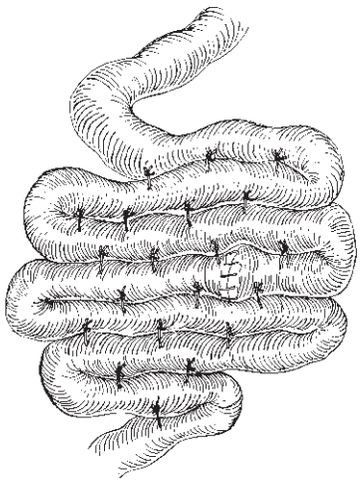

Figure 70-1. Jejunal enteroenteropexy to prevent intussusception via a ventral midline abdominal approach.

non-absorbable suture (Fig. 70-1). Place sutures approximately 6 to 10 cm apart.
2. The amount of bowel to include in the "pexy" procedure is controversial. Some surgeons include the entire small bowel, starting at the descending duodenum and finishing at the ileocecocolic junction. Others include only two or three loops of bowel above and below the point of intussusception. Another option is to include only the distal jejunum and ileum, because most intussusceptions involve the distal small bowel.

Colopexy

1. Reduce the rectal prolapse by placing gentle traction on the descending colon, pulling it cranially.
2. Scarify an 8- to 10-cm portion of the descending colon with a surgical blade along the antimesenteric border.
3. Alternatively, make a longitudinal seromuscular incision along the antimesenteric border. This may result in a more consistent colopexy. Avoid entering the lumen.
4. Make an incision into the peritoneum and underlying musculature in the abdominal wall opposite the segment of prepared colon.
5. Preplace four to six horizontal mattress sutures between the colon and the exposed surface of the abdominal wall (Fig. 70-2). Monofilament non-absorbable suture is preferred.
6. Tie the sutures to securely appose the fresh bleeding surfaces of the colon and abdominal wall (see Fig. 70-2).

Postoperative Care and Complications

- No special feeding limitations are necessary.
- Recurrence of intussusception (following enteroenteropexy) or rectal prolapse (following colopexy) suggests that the pexy site has broken down.

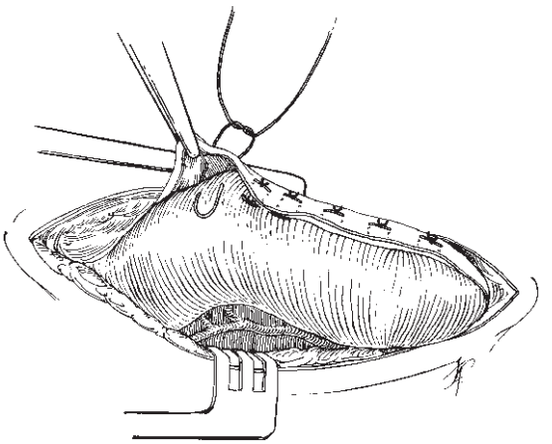

Figure 70-2. Technique for colopexy to prevent recurrence of rectal prolapse.

COLOTOMY

The most common indication for a colotomy is a full-thickness biopsy when diagnosis has eluded other diagnostic procedures. Whenever possible, colonoscopic methods of biopsy are preferred (see Chapter 69). Rarely, a colotomy is done to remove a foreign body.

Preoperative Considerations

- Surgical procedures involving the colon are more likely to be associated with dehiscence than those involving other portions of the gastrointestinal tract.

▼ ***Key Point*** Gentle handling of the colon and the prevention of excessive tension across the suture line will help preserve a good blood supply and promote ideal wound healing.

- The risk of a serious abdominal infection is considerable with colonic surgery.
- To reduce the risk of postoperative sepsis, administer perioperative antibiotics for gram-negative aerobes and anaerobes. Give cefmetazole (15 mg/kg) IV q1.5h for 2 or 3 doses, starting 20 to 30 minutes before surgery. Cefoxitin (30 mg/kg) may be substituted.
- Preoperative mechanical cleansing of the colon via multiple enemas may be indicated. This can be especially helpful to improve exposure of colonic polyps or neoplasms during resection.

Surgical Procedure

Objectives

- Collect tissue for biopsy.
- Remove foreign body in cases of low bowel obstruction.
- Prevent spillage of colonic contents.

Equipment

- General surgery pack
- Babcock forceps
- Laparotomy sponges
- Doyen non-crushing intestinal clamps
- #11 Bard-Parker blade

Technique

1. Make a caudal midline abdominal incision for access to the colon.
2. Pack off the colon with laparotomy sponges at the proposed incision site.
3. Place stay sutures at both ends of the proposed colotomy incision (Babcock forceps can be substituted).
4. Milk the colonic contents away from the incision site and cross-clamp the bowel segment with Doyen clamps.
5. Using a #11 Bard-Parker surgical blade, stab into the lumen of the colon. Remove a full-thickness elliptical piece of tissue with Metzenbaum scissors.
6. Close the colotomy incision side-to-side with 3-0 or 4-0 synthetic absorbable suture (e.g., polydioxanone, PDS) in a simple interrupted appositional pattern. A non-absorbable suture (e.g., polypropylene) may be substituted.
7. Gently irrigate the bowel immediately adjacent to the colotomy incision with warm saline before removing the laparotomy pad. Do not allow irrigation fluid to enter the peritoneal cavity.
8. Cover the colotomy incision line with omentum.
9. Perform routine closure of the abdomen.

Postoperative Care and Complications

Short Term

- Monitor closely for signs of leakage peritonitis for 48 hours.
- Abdominal pain, an unusually high fever, and a neutrophilia with a left shift suggest a need for further diagnostic tests such as radiography and diagnostic peritoneal lavage.

Long Term

- Strictures occur rarely.
- Slow-leakage peritonitis may be masked by antibiotics, or the infected area may be walled off, only to be manifested later as an abscess.

Prognosis

- The prognosis is good if the colotomy is done to remove a foreign body.
- If the biopsy suggests a non-neoplastic process, the prognosis depends on the underlying disease (see Chapter 69).

SUBTOTAL COLECTOMY

The primary indication for subtotal (90–95%) removal of the colon is for palliation of severe or recurrent constipation (obstipation related to megacolon). Idiopathic megacolon in the cat (see Chapter 69) is the most common disease for which surgery is indicated.

▼ ***Key Point*** Meticulous handling and careful apposition of tissue and a tension-free anastomosis are critical for the success of subtotal colectomy.

Preoperative Considerations

- In cats, the ileocolic valve can be resected with few postoperative problems. Reestablishing bowel continuity with an ileocolostomy versus a colocolostomy (when the ileocolic valve is preserved) is technically easier. However, it is preferable to preserve the ileocolic valve. The postoperative convalescent period is shorter and the likelihood of intractable diarrhea secondary to small bowel bacterial overgrowth is diminished.
- Administer prophylactic antibiotics, as described previously.
- Preoperative enemas are not necessary and, in fact, can complicate the surgery because of potential leakage of fluid from the colon.

Surgical Procedure

Objectives

- Palliate signs of constipation or obstipation that are associated with megacolon.
- Remove most of the colon with restoration of continuity by ileocolostomy or colocolostomy.
- Promote movement of bowel contents from the small bowel to the rectum.
- Prevent spillage of colonic contents.

Equipment

- General surgery pack
- Balfour abdominal retractors
- Laparotomy sponges
- Doyen non-crushing straight intestinal clamps
- Carmalt crushing forceps

Technique

1. Make a ventral midline abdominal incision, starting from midway between the xiphoid and umbilicus and coursing caudally to the brim of the pelvis.
2. Exteriorize and carefully isolate the colon and distal small bowel from the rest of the abdominal viscera outside the abdominal cavity.

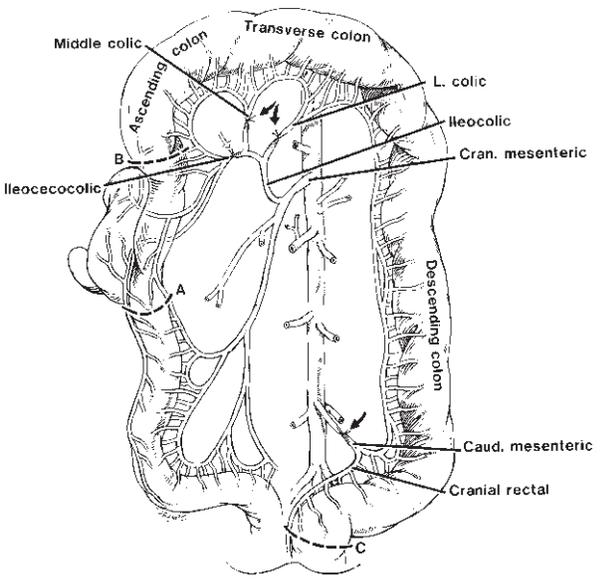

Figure 70-3. Subtotal colectomy. Sites of ligation of colic blood vessels before anastomosis and resection. Colonic resection can either include resection of the ileocecocolic valve (incision at *A*) or preserve the ileocecocolic area (incision at *B*). Distal incision *(C)* made in the colon.

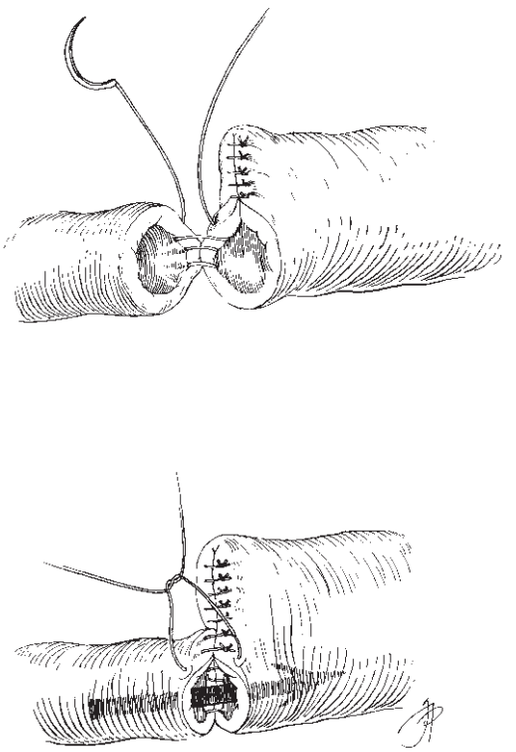

Figure 70-4. Subtotal colectomy. Correction of luminal disparity of the bowel by partial closure of larger segment before anastomosis.

3. Isolate the appropriate colic vessels approximately 1 to 2 cm from the mesenteric side of the colon. Ligate and divide these (Fig. 70-3).
4. If the ileocolic valve is being removed, ligate an additional set of vessels (ileocecocolic artery and vein) (see Fig. 70-3).
5. Caudally, ligate the caudal mesenteric artery and vein.
6. Milk the fecal contents toward the center of the segment of colon to be removed.
7. Place a non-crushing intestinal clamp across the distal colon approximately 1 cm cranial to the brim of the pelvis; if the ileocolic valve is being preserved, place another clamp across the short 1-cm segment of proximal colon remaining below the ileocolic valve.
8. If the ileocolic valve is being resected, place a non-crushing clamp across the ileum just proximal to the ileocolic valve.
9. Use crushing forceps to clamp the colon approximately 1 cm to the inside of the previously placed non-crushing clamps. Transect the colon next to the crushing forceps and the segment of bowel being removed (i.e., the crushing forceps come out with the resected bowel segment).
10. Perform an end-to-end anastomosis using 4-0 polypropylene or a monofilament synthetic absorbable suture in a simple interrupted, full-thickness, appositional suture pattern.
11. Correct any lumen disparity by longitudinally incising the antimesenteric side of the bowel with the smaller lumen. Lumen disparity can also be corrected by partial closure of the larger colonic segment, using the same suture and pattern (Fig. 70-4).
12. Be careful to incorporate the serosa and to ensure accurate and gentle placement of all sutures. Place the sutures at 2- to 3-mm intervals.
13. Gently irrigate the anastomotic site and adjacent 4 to 5 cm of bowel with warm saline. Do not allow fluid to enter the peritoneal cavity.
14. Place an omental patch over the site of anastomosis and gently tack it with one or two sutures below the line of anastomosis.
15. Remove the laparotomy sponges and replace the bowel in the abdominal cavity.
16. Use new gloves and a sterile set of instruments for closure of the midline incision.

Postoperative Care and Complications

Short Term

- Withhold food and liquids for 24 hours.
- Monitor closely for signs of leakage from the anastomosis for 48 to 72 hours.
- Some animals continue to have some tenesmus for 7 to 10 days after surgery.
- Loose stools and increased frequency of defecation occur but usually improve somewhat over a period of weeks to months.
- Continue intravenous fluids for 36 to 48 hours.

Long Term

- The frequency of defecation generally increases by 30% to 50%.
- The stools remain soft indefinitely but often become less fluid and more semiformed within a few weeks.
- Cats do not need a special diet.
- It may be necessary to keep animals on a diet low in volume and high in caloric density for 10 to 14 days. Thereafter, feed a diet that minimizes diarrhea and results in solidly formed stools.

▼ ***Key Point*** Cats seem to adapt well to subtotal colectomy, whereas dogs may have persistent diarrhea postoperatively.

TYPHLECTOMY

Indications for typhlectomy, or surgical removal of the cecum, include the following:

- Typhlitis (cecal inflammation) caused by chronic whipworm infection
- Cecal inversion
- Cecal neoplasia

Preoperative Considerations

- If possible, evert the inverted cecum before its amputation.
- If manual reduction of cecal inversion is not possible because of adhesions, reduction may need to be done through a colotomy incision.
- The cecum is attached to the terminal ileum by the ileocecal fold, which consists of fascia and peritoneum.

Surgical Procedure

Objective

- Remove the cecum without interfering with ileocolic anatomy and function.

Equipment

- General surgery pack
- Doyen non-crushing straight intestinal forceps
- Abdominal retractor

Technique

1. Bluntly dissect the ileocecal fold to free the cecum from its attachments to the ileum.
2. Preserve the ileocecal vessels while ligating and dividing the cecal branches.
3. Carefully incise the remaining attachments of the cecum to the proximal colon.
4. When the cecum is isolated from its attachments and blood supply, double-clamp the base of the cecum with straight intestinal forceps.
5. Amputate the cecum between the two forceps.
6. Oversew the forceps remaining on the base of the cecum with 2-0 or 3-0 synthetic absorbable suture using a Parker-Kerr suture pattern.
7. Place a second layer of a continuous Lembert inverting suture.

Postoperative Care and Complications

Short Term

- Give food and liquids the day after surgery.

Long Term

- Complications are rare.

Prognosis

- The prognosis is good.

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Chapter

71 Diseases of the Liver and Biliary Tract

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DIAGNOSTIC STRATEGY FOR LIVER DISEASE

The liver has many diverse functions related to hepatic blood flow; protein, carbohydrate, and fat metabolism; detoxification and excretion of drugs and toxins; and formation and elimination of bile. Consequently, the clinical and laboratory abnormalities associated with liver failure are diverse.

Overview of the Diagnostic Strategy

- Clinical, laboratory, and imaging studies to identify the presence of liver disease
- Characterization of the functional aspects of the hepatic disease
- Determination of an etiologic or histologic diagnosis, which usually requires a liver biopsy

Acute versus Chronic Disease

The clinical approach and management of patients with hepatic disease is dictated largely by the acute versus chronic nature of the hepatic disorder. Historical, physical, laboratory, and radiographic findings may suggest whether the hepatic disease is acute or chronic, but hepatic biopsy often is required for definitive evaluation. Classifying a disorder as acute or chronic has diagnostic, therapeutic, and prognostic implications.

- In acute hepatic failure, toxic or infectious causes are common, and intensive supportive care is warranted to allow time for hepatic regeneration. The long-term prognosis for recovery is favorable if the animal survives the initial stages.
- Chronic hepatic disorders are more likely to be accompanied by irreversible changes (cirrhosis); thus, the long-term prognosis may not be favorable.

Clinical Signs

Clinical signs of liver disease include those typically associated with hepatic dysfunction, such as jaundice, hepatic encephalopathy (HE), ascites, and excessive bleeding, and nonspecific signs such as vomiting, diarrhea, anorexia, lethargy, and weight loss, which overlap with signs of other body system disorders.

Nonspecific Signs

- *Vomiting* is a common sign of liver disease. Hematemesis suggests gastroduodenal ulceration, a recognized complication of hepatobiliary disease.
- *Diarrhea* occurs less frequently than vomiting and is characteristically small-bowel diarrhea.
- *Anorexia* is a common but nonspecific sign of hepatobiliary disease.
- *Weight loss and stunted growth* are nonspecific signs that suggest chronic rather than acute hepatic disease.

Polyuria and Polydipsia

- Polyuria and polydipsia (PU/PD) may be important presenting clinical signs in dogs with liver disease. The mechanism is multifactorial and includes psychogenic polydipsia, hypercortisolism, and renal concentrating defects.

Signs of Abnormal Bilirubin Excretion

- *Pigmented urine* (bilirubinuria) and *jaundice* (icterus) of the sclera, oral mucous membranes, and skin are classic signs of cholestatic liver disease. However, these findings are not specific for hepatobiliary disease and can also be caused by hemolytic disorders.
- *Acholic (gray) feces* occur secondary to severe cholestasis (usually from common bile duct obstruction), which prevents bilirubin in the bile from entering the intestinal tract and imparting the normal brown color to the feces.

Coagulopathy

- Excessive bleeding (i.e., hemorrhages of the skin and mucous membranes, melena, and hematuria) occasionally is associated with liver disease, especially if hepatic damage is severe or is associated with common bile duct obstruction.
- Subclinical clotting abnormalities may become clinically apparent after liver biopsy, surgery, and development of gastroduodenal ulcers.
- Potential mechanisms for bleeding include primary failure of the hepatocytes to synthesize clotting factors, vitamin K deficiency, and disseminated intravascular coagulation (DIC) (see Chapter 23).

Hepatic Encephalopathy

- HE is a metabolic encephalopathy that occurs secondary to severe liver disease or portosystemic shunting of blood.
- Clinical signs include depression, hypersalivation, behavioral changes, altered consciousness, motor disturbances, seizures, and coma. As with other metabolic encephalopathies, signs typically wax and wane and are interspersed with normal periods.
- Ammonia, mercaptans, short-chain fatty acids, gamma-aminobutyric acid (GABA), and endogenous benzodiazepines are potential encephalopathic toxins that are produced in the colon by bacterial action on various substrates. Because the liver normally detoxifies these substances, systemic concentrations are low. With severe liver disease or portosystemic shunting, these potential toxins reach high concentrations in the systemic circulation and the central nervous system (CNS), resulting in clinical signs.
- Exacerbation of encephalopathy occurs after eating a meal high in protein because protein is a substrate for toxins such as ammonia and mercaptans.
- HE must be differentiated from other metabolic encephalopathies and primary CNS disorders.

Ascites

- Ascites is a common feature of severe chronic liver disease. Mechanisms of ascites and edema formation in liver disease include hypoalbuminemia, portal hypertension, and sodium and water retention.
- Rupture of the biliary tract causing bile peritonitis also is associated with abdominal fluid accumulation.

Signalment and History

- The signalment often provides important clinical information, because breed predilections for specific liver diseases have been recognized, and young animals are more likely to be presented for congenital hepatic disorders such as portosystemic shunt.
- The history is helpful to characterize the clinical course of liver disease as acute or chronic. Recent onset of signs in an animal that was previously healthy suggests acute hepatic failure. However, because of the large functional reserve capacity of the liver, in occult chronic liver disease the clinical signs may be vague and may not be recognized by the owner until the final phase of hepatic decompensation.

▼ ***Key Point*** Chronic hepatic disease can be associated with recent onset of clinical signs and can initially seem to be an acute disease. However, persisting signs of weight loss and ascites and diagnostic findings of hypoalbuminemia and microhepatica are indicative of chronic hepatic disease.

- The history may provide important information regarding the potential for exposure to known causes of hepatic injury such as drug therapy, surgical and anesthetic procedures, and toxins or infectious agents.
- Determine if the animal has a history of intolerance to drugs normally metabolized by the liver, such as sedatives, tranquilizers, anticonvulsants, and anesthetics.
- Determine the current vaccination status and exposure potential for infectious agents known to affect the liver, such as leptospirosis, infectious canine hepatitis, and feline infectious peritonitis (FIP).

Physical Examination

Skin and Mucous Membranes

- Evaluate the sclera, oral mucous membranes, and skin for jaundice. Jaundice is not clinically detectable until serum bilirubin concentrations are >2.5 to 3.0 g/dl. In cats, subtle jaundice often is best detected on the palatine mucosa.
- Evaluate the skin and mucous membranes for evidence of bleeding. Pallor may be detected with blood loss anemia.

Abdominal Palpation

Palpate the abdomen carefully. The normal liver can be difficult to palpate in dogs and cats, and the edges are normally sharp, not rounded.

- Hepatomegaly is caused by passive venous congestion, diffuse inflammation, nodular hyperplasia, cysts, bile engorgement, marked biliary hyperplasia (cats), and infiltration by fat, glycogen, and neoplastic cells.
- Pain on palpation of the liver (hepatodynia) usually indicates acute liver disease. The pain is caused by stretching of the liver capsule and must be differentiated from pain arising in the pancreas, stomach, or spleen.
- Moderate to severe abdominal effusion may be detected.

Neurologic Exam

Perform a neurologic examination in animals with a history of neurologic signs. With HE, the neurologic examination may be normal or suggestive of diffuse cerebral disease (e.g., depression and dementia, disorientation, pacing, circling, head pressing, hypersalivation, seizures, or coma).

Rectal Exam

Perform a rectal examination and obtain a fecal sample to evaluate for melena (indicative of GI bleeding) and acholic feces.

Routine Laboratory Evaluations

Because clinical findings in hepatobiliary disease often are vague, hepatic disease may not be suspected until

biochemical tests identify elevated liver enzyme activity or other evidence of hepatic dysfunction (e.g., hyperbilirubinemia or hypoalbuminemia). Liver function studies such as serum bile acid (SBA) concentrations are used to achieve the following:

- Identify occult liver disease
- Assess liver function when there is increased liver enzyme activity but normal serum bilirubin concentrations
- Determine whether significant hepatic dysfunction is present to warrant performing a liver biopsy
- Monitor response to therapy

Findings consistent with liver disease on routine laboratory tests are described below.

Complete Blood Count

- *Mild to moderate anemia* may occur secondary to liver disease because of blood loss (e.g., gastroduodenal ulceration or coagulopathy) or may be associated with normocytic-normochromic anemia of chronic disease.
- *Erythrocytic microcytosis* is a common finding in dogs and cats with portosystemic shunts. Decreased serum iron concentration, normal to increased serum ferritin concentration, and accumulation of stainable iron in the liver suggests that microcytosis is associated with abnormal iron metabolism (impaired iron transport or sequestration of iron) rather than absolute iron deficiency. Decreased availability of iron for hemoglobin synthesis appears to occur despite adequate tissue iron stores.
- *Target cells and poikilocytosis* (acanthocytes and elliptocytes) may occur in dogs and cats with various types of hepatic disease, due to altered red blood cell (RBC) membranes.

Urinalysis

- *Urine specific gravity* may be isosthenuric or hyposthenuric if liver disease is associated with PU/PD.
- *Bilirubinuria* is a sensitive indicator of abnormal bilirubin metabolism, and this finding precedes hyperbilirubinemia and jaundice. Bilirubinuria imparts a yellow-orange color to the urine. Bilirubin crystals may form in the presence of bilirubinuria.
  - Trace amounts of bilirubin may be found in concentrated urine of normal dogs (especially males).
  - Bilirubinuria is always abnormal in cats and suggests underlying hemolytic or hepatobiliary disease.
- *Urine urobilinogen* is a colorless product of enteric bacterial degradation of bilirubin that is absorbed from the gut. A small portion of urobilinogen escapes the enterohepatic circulation and is excreted in the urine. The finding of urobilinogenuria indicates an intact enterohepatic circulation of bilirubin pigments. The absence of urobilinogenuria in a jaundiced animal suggests common bile duct obstruction. However, this test is not reliable in a clinical setting because many non-hepatic factors affect urine urobilinogen concentration, including altered intestinal flora, GI bleeding, intestinal absorption, renal excretion, urine pH, urine volume, and urine storage.
- *Ammonium biurate crystals* are commonly detected in animals with portosystemic shunts.

▼ ***Key Point*** Suspect liver disease in any cat or dog with ammonium biurate crystalluria (except in dalmatians and bulldogs).

Liver Enzymes

Evaluation of serum liver enzyme activity is used as a screening test to detect liver disease. Increases in liver enzyme activity are not specific for the underlying hepatic disorder. However, liver enzymes can be used to categorize the underlying pathophysiologic mechanism. Increases in liver enzyme activity may occur secondary to hepatocellular injury and leakage (Fig. 71-1), or due to increased production stimulated by bile retention (cholestasis) or drug induction (Fig. 71-2).

Many systemic diseases can secondarily affect the liver (reactive hepatopathy), causing increased liver enzyme activity, but these are not necessarily associated with clinical liver disease. For example, feline hyperthyroidism is commonly associated with increased liver enzyme activity without significant hepatic dysfunction.

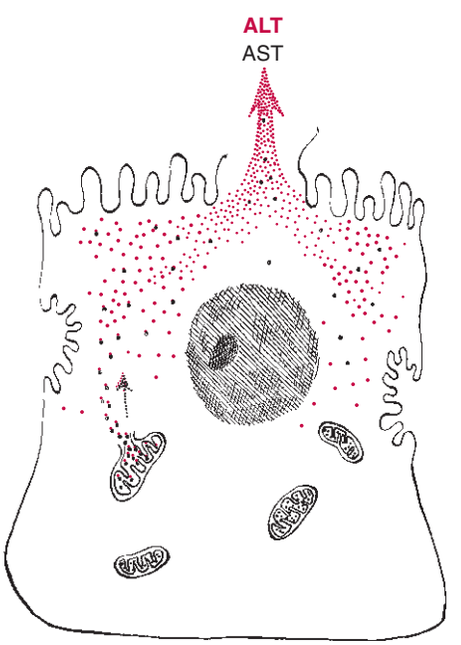

Figure 71-1. With hepatocyte injury, leakage of alanine aminotransferase (ALT) from the cytoplasm results in increased serum activity. Aspartate aminotransferase (AST) is primarily associated with mitochondria but is also present in the cytoplasm. Release of AST from the mitochondria requires a severe insult. Thus, with hepatocyte injury, ALT is more readily released and its activity level will usually be higher than that of serum AST.

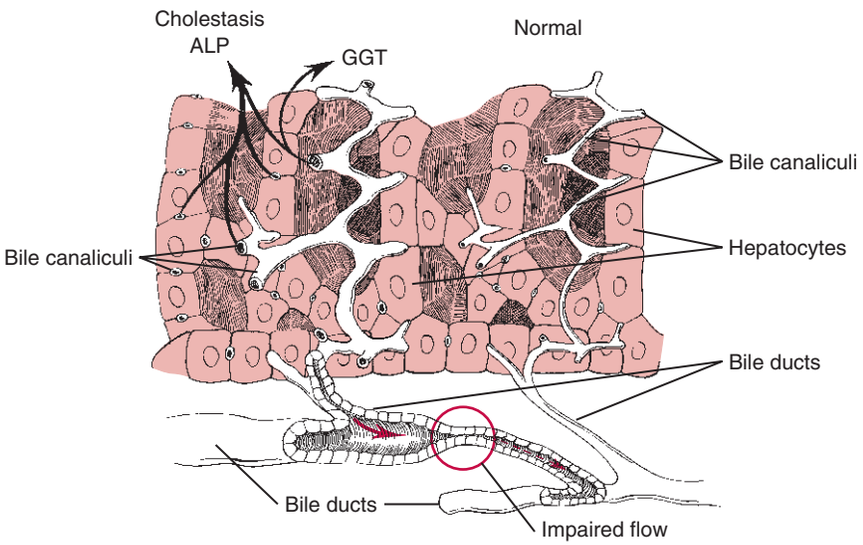

Figure 71-2. Impaired bile flow (cholestasis) causes increased synthesis of alkaline phosphatase (ALP) and gamma-glutamyltransferase (GGT). ALP is a sensitive indicator of cholestasis in dogs but is less sensitive in cats (see text). With cholestatic disorders, increased ALP activity precedes hyperbilirubinemia. ALP and GGT lack specificity in differentiating between intrahepatic and extrahepatic cholestasis.

▼ ***Key Point*** Liver enzymes do not evaluate liver function. Thus, severe hepatic dysfunction may coexist with normal liver enzyme activity; conversely, increased liver enzyme activity may be detected in animals without significant hepatic dysfunction.

Alanine Aminotransferase

Increased alanine aminotransferase (ALT) activity indicates hepatocyte injury with leakage of enzyme from the cytoplasm of the hepatocyte (see Fig. 71-1). The magnitude of ALT increase generally correlates with the number of injured hepatocytes.

- The largest increases in ALT activity occur with hepatocellular necrosis and inflammation (up to 100 times normal). Increases also occur with increased hepatocyte membrane permeability, such as that caused by hypoxia. Severe cholestasis can also cause secondary hepatocyte injury, with increases in ALT up to 20 to 40 times normal. Increased production of ALT by regenerating hepatocytes may account for persisting increases in enzyme activity after resolution of the initial injury.
- Anticonvulsant drug therapy (primidone, phenytoin, and phenobarbital) in dogs can be associated with mild increases in ALT activity (2 times normal) in the absence of obvious hepatocellular injury.
- Corticosteroid therapy or hyperadrenocorticism is associated with mild to moderate (2–10 times normal) increases in ALT activity.
- Small amounts of ALT are present in canine skeletal muscle; it has been shown that severe skeletal muscle degeneration or necrosis (canine muscular dystrophy, necrotizing myopathy, polymyositis) may be associated with increases in ALT activity of 5 to 25 times normal. When increased ALT activity is caused by muscle injury, creatine kinase (CK) and AST activity are also markedly increased. Whether ALT is liver specific in cats remains to be determined.

Aspartate Aminotransferase

Hepatocyte injury is associated with increased AST activity secondary to leakage from mitochondria and cytoplasm of hepatocytes (see Fig. 71-1).

- AST is not liver specific in dogs and cats; it is present in significant quantities in hepatocytes and skeletal muscle tissue.
- Comparison of activities of ALT, AST, and CK, a muscle enzyme, can indicate whether AST activity is increased due to hepatic or muscle injury.

▼ ***Key Point*** Increased AST activity associated with hepatic injury generally parallels but is less than the increase in ALT activity, and CK is normal. Increased AST activity due to skeletal muscle injury is associated with increased CK activity and normal or mildly increased ALT activity.

- In some cats with liver disease, AST may be more sensitive than ALT in detecting hepatic disease.

Alkaline Phosphatase

Increases in serum alkaline phosphatase (ALP) activity are due to accelerated production of this enzyme, stimulated by cholestasis or drug induction (see Fig. 71-2). ALP is a membrane-associated enzyme present in many tissues; however, only liver, bone, and corticosteroid-induced isoenzymes contribute to serum ALP activity. Serum ALP activity in normal dogs and cats is usually due to the liver isoenzyme. An increase in this type of ALP activity indicates intrahepatic or extrahepatic cholestasis.

- Young growing animals or animals with severe bone disease may have mild increases in ALP activity due to the bone isoenzyme.
- Cats generally have smaller increases in serum ALP activity with hepatobiliary disease than do dogs owing to a limited capacity for ALP production and a shorter serum half-life (6 hours in cats versus 72 hours in dogs). Therefore, even small increases in serum ALP activity (2–3 times normal) in cats suggest significant cholestasis.
- Exogenous or endogenous glucocorticoids are associated with hepatic production of a novel isoenzyme of ALP, corticosteroid-induced ALP (CIALP), in dogs but not in cats. The CIALP isoenzyme can be distinguished from the liver isoenzyme (LALP) by levamisole inhibition using an automated analyzer. Increased CIALP activity is a consistent finding in dogs with spontaneous hyperadrenocorticism and absence of this isoenzyme is uncommon in this disorder.

▼ ***Key Point*** Hypercortisolism caused by glucocorticoid therapy or hyperadrenocorticism (Cushing's disease) is the most common pathologic cause of increased serum ALP activity in dogs; it is usually attributed to an increase in CIALP.

- Increase in ALP activity associated with corticosteroid therapy varies considerably with the individual dog and the drug, dose, and duration of therapy. In the first 7 to 10 days of oral or parenteral glucocorticoid therapy, increases in ALP are primarily due to LALP activity. By 7 days, CIALP activity begins to increase, and it predominates in the serum after a month of therapy. Chronic treatment with otic, ophthalmic, and topical preparations is also capable of inducing ALP activity. Increases in CIALP activity do not necessarily imply the presence of iatrogenic hyperadrenocorticism, a suppressed pituitary-adrenal axis, or corticosteroid-induced hepatopathy, nor does it indicate that corticosteroid therapy must be discontinued.
- Increased CIALP activity is a sensitive but not a specific test for exposure to excess glucocorticoids (iatrogenic or endogenous). Increases in CIALP activity may be detected with diabetes mellitus, anticonvulsant drug therapy, primary hepatic disorders including neoplasia, hypothyroidism, and chronic illnesses (associated with disease-related stress and increased endogenous cortisol secretion). In this setting, a mixed pattern of increased CIALP and LALP activity is seen.
- Increased CIALP activity associated with exogenous or endogenous glucocorticoids may be accompanied by mild to moderate (2–10 times normal) increases in ALT activity that typically are of lesser magnitude than increases in ALP activity.
- Anticonvulsant drug therapy is associated with enzyme induction of the liver isoenzyme of ALP in dogs (but not in cats) in the absence of obvious hepatocellular injury. CIALP activity also may be increased in some dogs. Reported maximal increases for induced serum ALP activity include those caused by phenobarbital (30 times normal), primidone (5 times normal), and diphenylhydantoin (3 times normal).

Gamma-Glutamyltransferase

This membrane-associated enzyme is present in many tissues. Increased serum gamma-glutamyltransferase (GGT) activity usually reflects cholestasis and increased production by hepatocytes (see Fig. 71-2).

- Increased GGT activity parallels increased ALP activity in dogs, including increases associated with excess corticosteroids.
- Anticonvulsant therapy causes mild (2–3 times normal) increases in serum GGT activity in dogs.
- In cats, serum GGT is more sensitive for detecting hepatobiliary disease than ALP. Serum GGT activity exceeds serum ALP activity in most hepatobiliary diseases; an exception is hepatic lipidosis, in which GGT activity may be normal or mildly increased despite a moderate to severe elevation of serum ALP.

Other Biochemical Tests

Numerous biochemical tests can be altered by liver disease, including serum bilirubin, albumin, globulin, urea nitrogen, glucose, and cholesterol. Many of these parameters reflect some aspect of liver function; however, they lack sensitivity or specificity for liver disease.

Bilirubin

Increased serum bilirubin concentration occurs secondary to hemolysis or cholestasis. Evaluate for underlying hemolytic disorders by performing a complete blood count (CBC) to detect anemia.

- Fractionation of the total serum bilirubin into conjugated and unconjugated components (van den Bergh test) to distinguish the mechanism of hyperbilirubinemia is of little diagnostic value because there is considerable overlap in hemolytic, hepatocellular, and extrahepatic biliary disorders.
- Lipemia falsely elevates serum bilirubin concentration; the absence of concurrent bilirubinuria suggests pseudohyperbilirubinemia.

Albumin

Albumin is synthesized exclusively by the liver. Because of a large reserve capacity for albumin production, hypoalbuminemia does not occur until the functional hepatic mass is reduced 70% to 80%.

▼ ***Key Point*** Hypoalbuminemia associated with hepatic disease implies chronicity because of the long half-life of albumin.

- With chronic liver disease, fluid retention and dilution of existing serum albumin may also contribute to hypoalbuminemia.
- When the serum albumin is <1.5 g/dl, hypoalbuminemia contributes to the development of ascites and edema.
- Hypoalbuminemia is not specific for liver disease, and other causes of hypoalbuminemia such as urinary and gastrointestinal (GI) loss must be excluded.
- Inappropriate dietary protein restriction should be avoided since it can worsen hypoalbuminemia.

Globulin

- Hyperglobulinemia due to increased gamma globulins occurs in some dogs and cats with chronic liver disease. The most likely mechanism is a systemic response to antigens that escape from the GI tract because of impaired hepatic mononuclear phagocyte system function or portosystemic shunting.
- Significant hypoglobulinemia does not usually occur with liver disease despite the liver's role in the synthesis of alpha and beta globulins.

Blood Urea Nitrogen

Blood urea nitrogen (BUN) concentration may be decreased secondary to liver disease because the liver is responsible for converting ammonia to urea. However, many non-hepatic factors (e.g., PU/PD, fluid diuresis, and low-protein diet) can also decrease BUN levels.

Glucose

Hypoglycemia may occur secondary to hepatic dysfunction because of impaired hepatic gluconeogenesis, decreased hepatic glycogen stores, and decreased hepatic insulin degradation. However, because <30% of liver function is sufficient to maintain euglycemia, hypoglycemia is an insensitive indicator of hepatic function.

- Because it indicates severe liver dysfunction, liver-associated hypoglycemia is a poor prognostic factor, except in dogs and cats with congenital portosystemic shunts.
- Some hepatic neoplasms such as hepatocellular carcinoma and adenoma, leiomyosarcoma, and hemangiosarcoma have been associated with profound hypoglycemia.
- Also consider non-hepatic causes of hypoglycemia such as sepsis, hypoadrenocorticism, and insulinoma (see Chapters 33 and 35).

Cholesterol

- Hypercholesterolemia occurs with acute cholestatic disorders because of increased synthesis of cholesterol and decreased incorporation of cholesterol into bile acids; however, there are many non-hepatic causes of hypercholesterolemia.
- Although cholesterol is synthesized in the liver, hypocholesterolemia secondary to liver disease is uncommon; it has been noted with congenital portosystemic shunts and phenobarbital-induced hepatic disease.

Electrolytes

Serum electrolyte changes secondary to liver disease are variable.

- In acute liver failure, serum electrolyte concentrations are usually normal.
- With chronic liver disease, total body potassium depletion and sodium and water retention are common, and the serum sodium concentration is usually normal or decreased.

Liver Function Tests

Liver function tests can document clinically significant hepatic dysfunction when liver disease is suspected, based on historical, clinical, laboratory, and radiographic findings. SBA determinations have largely replaced the use of organic anion dyes such as sulfobromophthalein (Bromsulphalein) and indocyanine green (ICG). Blood ammonia concentration and ammonia tolerance tests can specifically evaluate the portal circulation (for portosystemic shunts) and detect HE.

▼ ***Key Point*** The test of choice for clinical evaluation of liver function is the combined fasting and 2-hour postprandial SBA test.

Serum and Urine Bile Acids

The normal physiology of bile acid metabolism is shown in Figure 71-3*A*. In health, bile acids are confined to the enterohepatic circulation, and systemic concentrations are low. SBA concentrations increase in the systemic circulation with all types of liver disease (Fig. 71-3*B*). Because the liver has a large reserve capacity for synthesis of bile acids, even severe hepatic dysfunction does not cause decreased SBA concentrations.

Fasting Serum Bile Acid Concentration

A fasting serum bile acid (FSBA) concentration obtained after a 12-hour fast is a sensitive, specific measure of hepatobiliary function in dogs and cats. Normal FSBA values in dogs and cats are <20 µmol/L. When concentrations exceed 30 µmol/L, a liver biopsy may be warranted to evaluate the underlying liver disease.

- Increased concentrations occur with hepatocellular and cholestatic disorders that interfere with hepatic uptake or secretion of bile acids and with portosys-

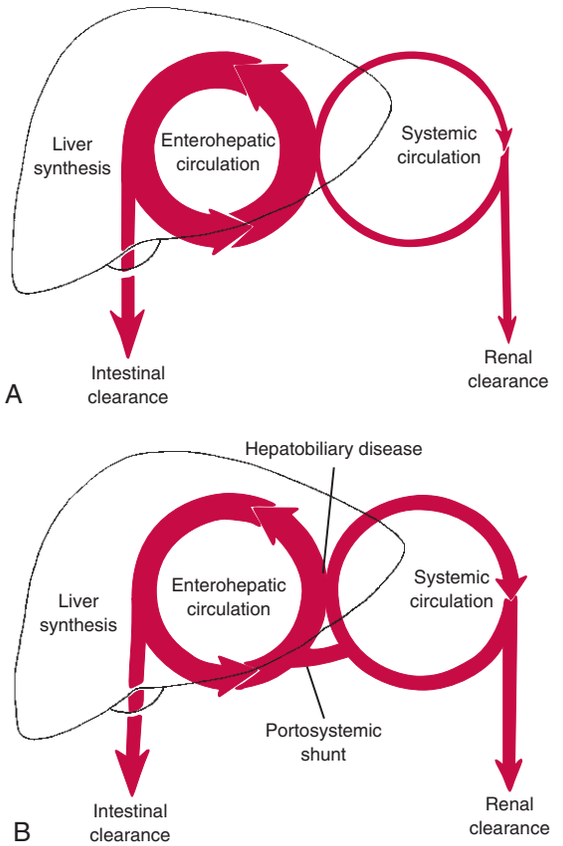

Figure 71-3. *A,* Bile acids are synthesized in the liver, secreted into the biliary system, and stored in the gallbladder during fasting. With ingestion of a meal, cholecystokinin release stimulates gallbladder contraction and entry of bile acids into the intestinal tract. Bile acids are efficiently reabsorbed in the distal ileum and carried in the portal blood back to the liver, thus completing the enterohepatic circulation. In the healthy animal, the liver removes 90% to 95% of bile acids from the portal circulation during the first pass of the enterohepatic circulation. This allows only small amounts of bile acids to escape to the systemic circulation. Normal serum concentrations are therefore low (fasting < 15 µmol/L, postprandial < 25 µmol/L). *B,* Hepatocellular dysfunction or cholestasis interferes with hepatic uptake, storage, and secretion of bile acids. Thus, impaired extraction of bile acids from the portal blood results in increased serum bile acid concentrations. With portosystemic shunting, bile acids in the portal blood are diverted directly into the systemic circulation.

temic shunting, in which bile acids are diverted directly into the systemic circulation (see Fig. 71-3*B*).

- Serial evaluation of SBA concentration to monitor liver function may not have merit unless the SBA concentration returns to normal. This is because there are wide fluctuations in SBA concentration in a given patient with liver disease within a 24-hour period (although all values are abnormal).
- Dogs and cats receiving the oral synthetic bile acid, ursodiol, may have an increase in SBA concentration because of the absorption of the drug and reflection of its presence in the serum.
- Interference in bile acid measurement can occur with hemolysis or lipemia.
- In dogs with unexplained increases in SBA, consider the possibility of small intestinal bacterial overgrowth causing increases in unconjugated bile acids.
- Healthy Maltese dogs were reported to have significantly higher SBA (mean 70 µmol/L ± 50; range 1–362 µmol/L) as measured by the enzymatic spectrophotometric method than as measured by high-performance liquid chromatography, suggesting the presence of additional reacting substances or unusual bile acids in their serum. However, a methodological problem related to lipemia or hemolysis cannot be excluded. It is also possible that these dogs had underlying hepatic microvascular dysplasia.
- When hepatic disease causes hyperbilirubinemia, measurement of SBA concentrations does not provide any additional diagnostic information. SBA concentrations are most helpful diagnostically in dogs and cats with anicteric liver disease.

Postprandial Serum Bile Acid Concentration

Postprandial serum bile acid (PPSBA) concentration is an endogenous challenge test of liver function. Whether PPSBA concentration is a more useful diagnostic test than FSBA concentration remains unclear. In dogs, similar information is provided by either test in most hepatobiliary disorders. Notable exceptions include dogs with portosystemic shunts or cirrhosis, because with these disorders, FSBA can be in the normal range. In cats, the diagnostic efficacy of PPSBA exceeds that of FSBA for all hepatic disorders, including portosystemic shunts. For best diagnostic utility, paired FSBA and 2-hour PPSBA is recommended. To perform the PPSBA concentration test, take the following steps:

- Obtain a serum sample for FSBA concentration, and then feed at least 2 teaspoons of food to small dogs and cats (<5 kg) and at least 2 tablespoons to larger patients.
- To ensure gallbladder contraction, feed a diet high in fat (e.g., Hill's Pet Prescription Diet p/d and Hill's Pet Prescription Diet c/d for cats). For encephalopathic animals in which a high-protein diet is contraindicated, substitute a protein-restricted diet and add a few milliliters of corn oil per feeding.
- Obtain a second serum sample 2 hours after feeding.
- *Results:* In normal dogs and cats, PPSBA concentrations are <25 µmol/L and peak 2 hours after a meal. A liver biopsy may be indicated when concentrations are >30 µmol/L.
- On occasion, FSBA is higher than PPSBA. This probably occurs because of sporadic gallbladder contraction during fasting, which releases bile into the intestinal tract, resulting in increased SBAs.

Urine Bile Acids

Recently, urine bile acids (UBAs) have been investigated as a diagnostic tool in dogs and cats. Normally only small amounts of bile acids are present in the

urine. Liver disease and increased SBA result in increased excretion of bile acids in the urine. Potential advantages of UBA over a random FSBA are that UBA may reflect an average value over time, ease of sample collection, and lack of interference from oral ursodiol administration.

- UBAs are normalized with urine creatinine (Cr), and values are expressed as UBA/Cr (μmol/mg) × 100. Values greater than 7.3 are abnormal in dogs. Values greater than 4.4 are abnormal in cats.
- Timing of urine collection to the 4- to 8-hour postprandial period may improve diagnostic performance, particularly in dogs with congenital portosystemic shunting where sensitivity of UBA (taken 4 to 8 hours after eating) was 100% compared with 84% for FSBA and 98% for PPSBA.
- The role of UBA in the evaluation of hepatobiliary function awaits further clinical evaluation.

Blood Ammonia Concentration

Ammonia is metabolized by the liver, and normal plasma concentrations are low. Measurement of ammonia is technically difficult, and appropriate sample handling requires heparinized blood samples to be stored immediately on ice, cold-centrifuged, and assayed as soon as possible.

- Measurement of blood ammonia concentration primarily is indicated to document HE. However, normal values do not exclude this diagnosis, because other toxins can contribute to the encephalopathy.
- Portosystemic shunting (congenital or acquired) is the most common mechanism of hyperammonemia, but severe, diffuse hepatic disease (especially acute hepatic necrosis) also increases blood ammonia concentrations.
- Blood ammonia values have poor sensitivity in detecting other types of hepatobiliary disease without portosystemic shunting.
- Blood ammonia concentration is not a suitable screening test for congenital portosystemic shunt in young Irish wolfhounds since a transient metabolic hyperammonemia unassociated with liver disease occurs in this breed.
- Congenital urea cycle enzyme deficiency is a rare cause of hyperammonemia.

Ammonia Tolerance Test

This is a more sensitive test than blood ammonia concentration for documenting portosystemic shunting. However, the ammonia tolerance test (ATT) is contraindicated if resting ammonia levels are already increased, because no further diagnostic information will be obtained and performing an ATT can cause signs of HE. *Note:* The ATT is not recommended for use in cats.

- The test is performed in a fasted dog by giving 100 mg/kg of ammonium chloride (do not exceed a total dose of 3 g), either as a dilute solution by stomach tube or as a powder in a gelatin capsule.
- Take a heparinized blood sample before and 30 minutes (stomach tube method) or 45 minutes (capsule method) after administering the ammonium chloride. Vomiting may occur but does not invalidate the test.
- In normal dogs, there is no increase in blood ammonia concentration or a mild increase (<2 times greater than baseline). In dogs with portosystemic shunting, results are consistently abnormal (up to 10 times baseline values).
- The ATT and paired FSBA and PPSBA tests have equal sensitivity in detecting portosystemic shunting. Consequently, the SBA testing has largely replaced blood ammonia and ATT. Paired FSBA and PPSBA provide a better screening test because it detects a broader range of hepatobiliary disorders, and bile acids are stable, permitting routine laboratory analysis.

Protein C

Protein C, an anticoagulant protein synthesized in the liver, has been investigated as a clinical marker of liver disease. Preliminary results show decreased protein C concentrations in 100% of dogs with liver failure, 98% of dogs with portosystemic shunt, and 30% of dogs with hepatic microvascular dysplasia. The role of protein C in the detection of liver disease awaits further clinical studies.

Parameters of Hemostasis

The liver plays a central role in the coagulation and fibrinolytic systems. The liver is responsible for synthesis of all coagulation factors except factor 8, von Willebrand factor. Fibrinogen, antithrombin, and protein C are all synthesized in the liver and can be decreased with hepatic dysfunction. Activated coagulation factors and fibrinolytic enzymes are also cleared by the liver.

- Mechanisms of excessive bleeding associated with hepatobiliary disease include primary failure of hepatocytes to synthesize clotting factors, DIC, and vitamin K deficiency. Vitamin K deficiency in hepatobiliary disease is usually caused by malabsorption of vitamin K secondary to complete bile duct obstruction. However, a vitamin K–responsive coagulopathy may sometimes be detected in dogs and cats with severe hepatic insufficiency, possibly due to marked intrahepatic cholestasis causing vitamin K malabsorption or the inability of the liver to reactivate vitamin K from its inactive (epoxide) form.
- Clinical evidence of bleeding secondary to hepatobiliary disease is uncommon; however, the frequency of abnormal coagulation tests is much higher.

Coagulation Tests

- Measure prothrombin time (PT) to evaluate the extrinsic coagulation system and activated partial

thromboplastin time (APTT) to evaluate the intrinsic coagulation system. These tests can be abnormal in the presence of liver disease. Activated coagulation time also can be used as a rapid screening test for abnormalities of the intrinsic coagulation system. For further discussion of these tests, see Chapter 23.

- The PIVKA (proteins induced by vitamin K absence) clotting time is a more sensitive test than PT or APTT to detect bleeding tendencies in dogs and cats with liver disease. Normalization of PIVKA clotting time may occur after treatment with vitamin K_1.
- The combination of prolonged PT and APTT, low plasma fibrinogen, increased fibrin degradation products, fragmented RBCs, and thrombocytopenia suggests DIC (see Chapter 23).

Thrombocytopenia and Platelet Dysfunction

- Thrombocytopenia may occur secondary to splenic sequestration of platelets associated with portal hypertension or consumption of platelets from DIC.
- Platelet function defects also have been documented in dogs with liver disease, which may account for clinical bleeding tendencies in the presence of normal coagulation tests and platelet numbers. Use mucosal bleeding time to detect platelet function abnormalities.

Blood Gas Analysis

Various acid-base imbalances may occur secondary to liver disease, including respiratory alkalosis, metabolic alkalosis, metabolic acidosis, and mixed acid-base disturbances.

Abdominal Fluid Analysis

- Ascitic fluid that accumulates secondary to liver disease and hypoalbuminemia is usually a transudate. With hepatic venous congestion from vena caval obstruction or cardiac causes, the fluid typically is a modified transudate with protein concentration > 2.5 g/dl.
- Rupture of the biliary tract is associated with bile peritonitis. Grossly, the abdominal fluid appears yellow or green. Chemical tests for bilirubin are positive, and concentrations of bilirubin are higher in abdominal fluid than in serum. Cytologic examination reveals a mixed inflammatory infiltrate and bile-laden macrophages. Bacteria may be seen if bile peritonitis is complicated by sepsis.

Diagnostic Imaging

Survey Radiography

Abdominal radiographs are useful to evaluate for the following:

- Changes in liver size (hepatomegaly, microhepatica)
- Altered tissue characteristics such as mineralized hepatic densities (choleliths) and radiolucencies (abscesses)
- Presence of abdominal effusion

If hepatic neoplasia is suspected, take thoracic films to evaluate for pulmonary metastases.

Ultrasonography

Ultrasonography can be used to image the liver noninvasively, especially when abdominal effusion precludes survey radiographic evaluation. A normal ultrasonographic appearance of the liver does not eliminate the possibility of significant hepatic pathology; however, ultrasonography is diagnostically useful to achieve the following:

- Detect focal parenchymal abnormalities such as masses, abscesses, cysts, and regenerative nodules. The ultrasonographic appearance of these focal lesions often is similar, and biopsy is required for differentiation.
- Document that a palpable mass is associated with the liver.
- Investigate disorders of the biliary tract and gallbladder, such as biliary obstruction, cholelithiasis, or gallbladder mucocele.
- Detect vascular lesions such as portosystemic shunts, hepatic arteriovenous fistulas, and hepatic venous congestion.
- Obtain percutaneous liver biopsies (see below).
- Identify abnormalities in other abdominal organs that may be a cause or effect of liver disease (e.g., pancreas, spleen, kidneys, bladder, GI tract, adrenal glands, and lymph nodes). For example, urate or uric acid urolithiasis may be detected in animals with portosystemic shunts, the primary tumor may be identified in animals with hepatic metastases, and identification of adrenal gland enlargement may aid the diagnosis of steroid hepatopathy.

Angiography

Angiography is useful to diagnose vascular disorders involving the liver, such as congenital and acquired portosystemic shunts, hepatic arteriovenous fistulas, and vena caval obstruction causing hepatic venous obstruction (see under "Congenital Portosystemic Shunt").

Liver Cytology

Fine-needle aspiration (FNA) of the liver for cytology is commonly performed because it is easy and safe, does not require sedation or anesthesia, and provides rapid preliminary information. However, the diagnostic accuracy of cytology versus histopathology of the liver is controversial. Studies suggest a lack of correlation exists as much as 50% of the time. Cytology of impression smears of liver biopsy tissue correlates better than samples obtained by fine-needle aspirate.

- Cytology of the liver is most useful if the pathologic process is diffuse and architectural relationships (which can be obtained only by histopathology) are not essential to the diagnosis. Examples include vacuolar hepatopathies such as feline hepatic lipidosis,

diffuse hepatic neoplasia, and liver disease associated with infectious agents such as histoplasmosis.
- In cats, primary liver diseases such as lymphoma and cholangitis may be accompanied by hepatic vacuolar changes. These cats may be misdiagnosed as idiopathic hepatic lipidosis if cytology only reflects the vacuolated hepatocytes.
- For focal lesions, accuracy is improved when the fine-needle aspirate is guided by ultrasound.
- Poor correlation of cytology with histopathology occurs in primary inflammatory liver diseases, although it may be better for detection of suppurative inflammation than for lymphocytic-plasmacytic inflammation.

Liver Biopsy

Liver biopsy often is required to definitively characterize the nature and severity of hepatic disease, to differentiate acute from chronic disorders, and to assess response to therapy. Selection of the best procedure for obtaining a liver biopsy depends on numerous factors, including liver size, presence of coagulopathy, diffuse versus focal hepatic lesions, presence of biliary tract obstruction, presence of other intra-abdominal abnormalities, likelihood of surgical resection of a mass, tolerance of general anesthesia, available equipment, and expertise of the clinician.

▼ ***Key Point*** Perform a hemostasis screen prior to liver biopsy to detect coagulopathy. After the biopsy is performed, monitor for bleeding from the biopsy site.

Biopsy Methods

Ultrasound-Guided Needle Biopsy

This technique is the most common percutaneous method used for liver biopsy. However, it is dependent on the availability of equipment and clinician expertise.

- With ultrasound-guided biopsy, it is possible to obtain tissue from focal lesions (whether superficial or deep within the hepatic parenchyma), avoid structures adjacent to the liver, and monitor post-biopsy bleeding.
- Ultrasound-guided biopsy may be difficult if the liver is small or the ultrasonographer lacks experience.
- Because needle biopsy specimens are smaller than wedge biopsies, they may not be representative of underlying liver pathology. In one study, the morphologic diagnosis made by needle biopsy correlated with the definitive diagnosis obtained by wedge biopsy in only 48% of dogs and cats.

Laparoscopy

Laparoscopy provides direct visualization of the liver and adjacent structures such as the pancreas and extrahepatic biliary tract. Biopsies also are obtained under direct visualization.

- Laparoscopy is a useful alternative to ultrasound-guided needle biopsy when the liver is small.
- It is preferable to ultrasound-guided biopsy when excess bleeding is anticipated and to laparotomy when delayed wound healing (hypoalbuminemia) is anticipated.
- Laparoscopy requires heavy sedation or anesthesia and is subject to equipment availability and clinician expertise.

Laparotomy

Laparotomy is indicated for liver biopsy when a surgically correctable disease is suspected, such as extrahepatic biliary tract obstruction or a single, large hepatic mass (see Chapter 72 for a description of the procedure for surgical biopsy).

- Laparotomy makes it possible to obtain large samples of liver tissue and monitor for post-biopsy bleeding.
- Disadvantages include the need for general anesthesia, the relatively high risk of complications, and the risk of delayed wound healing in hypoalbuminemic patients.

Biopsy Analysis

- To prepare biopsy tissue for histopathology, place samples in 10% buffered formalin and allow them to fix for 24 hours. The volume of fixative should be 20 times the volume of biopsy tissue.
- To prepare needle biopsy samples, gently remove liver tissue from the biopsy needle and place it on tissue paper; fold the paper and place it in a formalin jar.
- Perform routine light microscopy on liver tissue stained with hematoxylin and eosin (H&E).
- Additional stains may be requested, including trichrome for fibrous connective tissue, periodic acid-Schiff (PAS) for glycogen, rhodanine or rubeanic acid for copper, Prussian blue for iron, Congo red for amyloid, oil red O for fat, and silver or acid-fast stains for infectious organisms.
- Submit fresh liver tissue for bacterial and fungal culture as indicated.
- Perform quantitative copper analysis on fresh hepatic tissue.
- Place samples for electron microscopy in chilled, buffered 2.5% glutaraldehyde.

PRINCIPLES OF TREATMENT FOR LIVER DISEASE

Objectives

- Whenever possible, identify and eliminate the inciting or predisposing causes of liver disease. Identifi-

cation of the underlying cause of hepatobiliary disease can provide insight into specific therapy, the likelihood and nature of potential complications, and the prognosis for recovery. (Therapy for individual hepatobiliary disorders is discussed later under specific diseases.)
- Prevent or manage complications of liver failure, including HE, ascites, GI ulceration, coagulopathy, infection, and endotoxemia.
- In patients in which hepatic regeneration and recovery are possible, supportive care allows time for this to occur. In other cases, clinical manifestations of hepatic failure may be minimized for variable periods.

Consider Drug Metabolism

The liver is a major site of drug metabolism, and liver disease may alter drug metabolism. In many cases, hepatic disease is associated with decreased hepatic clearance of a drug, with subsequent potential toxicity.

▼ ***Key Point*** Prior to administering any drug to a patient with hepatic disease, consider whether the drug is metabolized or excreted by the liver, is potentially hepatotoxic, or may exacerbate signs of liver failure.

Avoid drugs that fit the following descriptions:
- Are known to depend primarily on the liver for inactivation or excretion
- Are potential hepatotoxins, such as phenobarbital
- May worsen signs of hepatic failure, such as methionine-containing products, tranquilizers, sedatives, and diuretics (may exacerbate HE) and nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids (may cause GI bleeding and exacerbate HE)

Supportive Therapy for Liver Disease

Supportive measures for patients with liver disease are summarized in Table 71-1.

Restore Fluid, Electrolyte, and Acid-Base Balance

- Maintain normal fluid balance to support hepatic blood flow and microcirculation and prevent complications such as HE, DIC, shock, and renal failure. The composition of the fluid to be given is influenced by the patient's electrolyte and acid-base status and the presence or potential for hypoglycemia (see Table 71-1 for guidelines; also see Chapter 5).
- Avoid alkalinizing agents (e.g., lactate in lactated Ringer's solution and sodium bicarbonate) when HE

Table 71-1. GENERAL THERAPY OF HEPATOBILIARY DISEASE

Therapeutic Goals	Therapeutic Regimen
Fluid Therapy	
Maintain hydration	Use a balanced polyionic solution such as lactated Ringer's solution or Plasma-Lyte 148 IV.[a] Use 0.45% NaCl in patients with ascites or edema.
Prevent hypokalemia	Add 20–30 mEq KCl to each liter of maintenance fluid. Monitor serum potassium daily and adjust as necessary.
Maintain acid-base balance	Avoid alkalosis in HE by using 0.45% or 0.90% saline for IV fluid therapy. Give $NaHCO_3$ or acetate-containing fluids (Plasma-Lyte) rather than lactated fluids for treatment of severe metabolic acidosis. Avoid lactate-containing fluids in cats with severe hepatic lipidosis.
Prevent or control hypoglycemia	To treat hypoglycemia, give 50% dextrose (0.5–1 ml/kg) IV to effect. To maintain normoglycemia, add dextrose to fluids to achieve a 2.5–5.0% solution.
Nutritional Support	
Maintain caloric intake	Provide 40–60 kcal/kg/day of good-quality diet.
Provide adequate vitamins and minerals	Add B vitamins to fluids of anorexic cats. For long-term therapy, give an oral vitamin-mineral (especially B vitamin) supplement. Give vitamin K_1 (0.5–1.5 mg/kg IM or SC q12h for three treatments, then weekly as needed) in biliary obstruction or severe cholestatic liver disease (dogs and cats).
Modify diet to control complications	See specific complications (e.g., HE and ascites).
Control HE	
Modify diet	Give NPO in initial stages of HE. For long-term management, provide a reduced-protein (dairy or vegetable source protein preferred; avoid red meat protein), easily digested, high-carbohydrate diet. Recommend moderate protein restriction of 15–20% dry matter (dogs) or 30–35% dry matter (cats). Increase dietary soluble fiber (psyllium 1–3 tsp/day).
Prevent formation and absorption of enteric toxins	In hepatic coma, give a warm-water cleansing enema initially (10–20 ml/kg) until fluid is clear, followed by retention enema (5–10 ml/kg q8–12h) containing lactulose (30% lactulose with 70% water) and neomycin solution (22 mg/kg) and held for 20–30 minutes or povidone iodine solution (diluted 1:10 with water, 50–200 ml total) and flushed out within 10 minutes. For follow-up oral therapy, give neomycin[b] (22 mg/kg q8–12h PO), metronidazole (7.5 mg/kg q12h PO), or amoxicillin (22 mg/kg q12h PO) combined with lactulose[c] (0.25–0.5 ml/kg q8–12h PO) or lactitol (0.5–0.75 g/kg q12h PO) to achieve two or three soft stools per day; if diarrhea occurs, reduce dose.
Control gastrointestinal hemorrhage	Correct coagulopathy. Treat GI parasites and treat gastric ulcer (famotidine or nizatidine or omeprazole[d] combined with sucralfate[e]). Avoid drugs that exacerbate GI hemorrhage (e.g., aspirin and other NSAIDs or glucocorticoids).

Table continued on following page

Table 71-1. GENERAL THERAPY OF HEPATOBILIARY DISEASE—cont'd

Therapeutic Goals	Therapeutic Regimen
Correct metabolic imbalances (e.g., dehydration, azotemia, hypokalemia, alkalosis, and hypoglycemia)	See fluid therapy above.
Avoid drugs or therapies that exacerbate HE	When possible, avoid sedatives, tranquilizers, anticonvulsants, analgesics, anesthetics, methionine-containing products, diuretics, or stored blood transfusion.
Control seizures	For refractory seizures in dogs, use loading dosages of sodium bromide IV (3% NaBr 600–800 mg/kg over 24 hours) or potassium bromide orally (KBr 100–200 mg/kg q6h for 24 hours), followed by KBr at a dosage of 15–30 mg/kg q12h PO[f] or IV phenobarbital[g] at reduced doses in dogs and cats (monitor serum concentrations to adjust the dose). Avoid benzodiazepines. For status epilepticus, consider general anesthesia with propofol to control seizures. Intubate and use mechanical respirator to maintain pO_2 and pCO_2. Give mannitol (0.5–1 g/kg by IV bolus over 20 minutes) for suspected cerebral edema. For chronic, stable seizure management or long-term therapy in dogs, give potassium bromide (15–30 mg/kg q12h PO in food). For maintenance therapy in cats, consider topiramate (3.125 mg q12h PO initially, then 6.25 mg q12h PO). For short-term perioperative anticonvulsant therapy for congenital PSS, consider felbamate (15–20 mg/kg q8h PO), levetiracetam (20–30 mg/kg q12h), or topiramate[h] (5–10 mg/kg q12h PO) in dogs or topiramate (3.125 mg q12h PO initially, then 6.25 mg q12h PO) in cats.
Control infection	Give systemic antibiotics (see below).
Control ascites and edema	Give a low-sodium diet; combine furosemide (1–2 mg/kg q12h PO)[i] and spironolactone (1–2 mg/kg q12h PO)[g], or spironolactone and hydrochlorothiazide (Aldactazide,[j] 2 mg/kg q12h PO). Use paracentesis for relief of dyspnea or extreme abdominal distention, synthetic colloids such as hetastarch (10–20 ml/kg/day IV in dogs and 10–15 ml/kg/day IV in cats) or human albumin 25% (2 ml/kg in dogs), or plasma transfusion for albumin replacement (25–45 ml/kg).
Control coagulopathy and anemia	Give vitamin K_1 (0.5–1.5 mg/kg q12h, IM or SC for three treatments, then weekly as needed for dogs and cats); fresh plasma or fresh-frozen plasma (10 ml/kg); or a fresh blood transfusion (10–15 ml/kg). For DIC, give heparin (75–100 IU/kg q8–12h SC). For dogs with vWD and liver failure, give DDAVP once (1 µg/kg diluted in 10–20 ml of saline and given IV slowly over 10 minutes or undiluted SC) (effective for 4–6 hours).
Control gastrointestinal ulceration	Give famotidine (0.5–1.0 mg/kg q12–24h PO or IV), nizatidine (2.5–5.0 mg/kg q24h PO), or omeprazole[d] (0.5–1.0 mg/kg q24h PO) and sucralfate[e] (1-g tablet/25 kg q8h PO).
Control infection and endotoxemia	Give systemic antibiotics (e.g., amoxicillin, ampicillin, cephalosporins, aminoglycosides, and metronidazole[k]).

[a] May be given SC if animal is mildly dehydrated and is not vomiting.
[b] Neomycin has been associated with rare ototoxicity and nephrotoxicity; its use should be restricted to acute management of HE.
[c] Crystalline lactulose (powder) is also available commercially (Kristalose, Bertek Pharmaceuticals) as 10- or 20-g packets (syrup concentration is 10 g/15 ml).
[d] Partially metabolized by the liver; use a reduced dose in animals with liver failure. Inhibits hepatic P-450 enzymes.
[e] Beware of drug-associated constipation, which may worsen HE.
[f] Avoid bromide in cats due to cough and asthma-like side effects.
[g] Can be used in dogs and cats with congenital PSS, but avoid in animals with acquired liver disease.
[h] Start at the low end of the dose range due to impaired hepatic metabolism.
[i] Dose may be doubled if there is no effect in 4–7 days.
[j] GD Searle & Co., Chicago, IL.
[k] Partially metabolized by liver. Use a reduced dosage (7.5 mg/kg q12h PO) in animals with liver failure.
DDAVP, desmopressin acetate; DIC, disseminated intravascular coagulation; GI, gastrointestinal; HE, hepatic encephalopathy; NPO, nothing per os; NSAIDs, nonsteroidal anti-inflammatory drugs; vWD, von Willebrand disease.
Adapted from Johnson SE: Liver and biliary tract. In Anderson NV (ed): Veterinary Gastroenterology, 2nd ed. Philadelphia: Lea & Febiger, 1992, p 504.

is present or impending, because alkalosis augments the entry of ammonia into the CNS and can exacerbate signs of HE.

Give Nutritional Support

Nutritional support is important for promoting hepatic regeneration and maintenance of body weight.

- Modify the diet as needed to control complications of hepatic disease, such as HE, hypoproteinemia, and ascites (see Table 71-1).
- Supply the bulk of the calories by carbohydrates, which provide an easily assimilated source of nonprotein calories.
- Avoid high-protein diets that may exacerbate signs of HE. Indiscriminate protein restriction is discouraged, however, because adequate protein intake is important for normal hepatic regeneration and to counteract hypoproteinemia.
- When voluntary food intake is lacking, provide other methods of nutritional support, such as feeding through a gastrostomy tube (see Chapter 3).

Control Complications

Hepatic Encephalopathy

Goals for treatment of HE are summarized in Table 71-1. Restrict dietary protein intake. Increase dietary soluble fiber (see Table 71-1). Prevent formation and absorption of enteric toxins.

- Give antibiotics (e.g., neomycin, amoxicillin, or metronidazole) to alter the urease-producing bacterial population in the colon, thus decreasing conversion of urea to ammonia (see Table 71-1).
- Lactulose, a synthetic disaccharide, often is effective in controlling signs of HE and decreasing arterial blood ammonia concentrations through its actions as a cathartic and colonic acidifier (see Table 71-1). It usually is given in combination with antibiotics.

▼ ***Key Point*** Detect and control GI hemorrhage, which could provide enteric bacteria with a source of protein for toxin production. Give fresh rather than stored blood if a transfusion is required, because stored blood contains substantial amounts of ammonia.

Ascites and Edema

Ascites in liver disease usually is associated with hypoalbuminemia, portal hypertension, and renal retention of sodium and water.

- For treatment of ascites, restrict dietary sodium and use diuretics to promote urinary sodium and water excretion (see Table 71-1).
- For temporary support of plasma colloid osmotic pressure in hypoproteinemic animals, consider plasma transfusion to supply albumin or colloid administration such as hetastarch (see Table 71-1 and Chapter 5).
- Avoid using abdominocentesis to treat ascites except when required for relieving respiratory distress.

Coagulopathy and Anemia

Hemostatic defects associated with hepatobiliary disease can be attributed to primary failure of hepatocytes to synthesize clotting factors, vitamin K deficiency, or DIC.

- Parenteral administration of vitamin K_1 corrects coagulopathy caused by vitamin K deficiency within 24 to 72 hours, but no response is seen when bleeding is caused by hepatocyte failure or DIC (see Table 71-1).
- For treatment of DIC and other coagulopathies, see Chapter 23.

Gastrointestinal Ulceration

Dogs and cats with hepatobiliary disease are at increased risk for GI ulceration. Possible mechanisms include gastric acid hypersecretion, impaired gastric mucosal blood flow secondary to portal hypertension, and decreased gastric epithelial cell turnover.

- GI bleeding is deleterious in patients with HE because blood is a substrate for ammonia production.
- Manage GI ulceration with an H_2 blocker for control of acid secretion and with sucralfate for mucosal cytoprotection, as described in Chapter 67. Famotidine and nizatidine are preferable to cimetidine and ranitidine as H_2 blockers in animals with liver disease, because they do not inhibit hepatic microsomal enzymes.

▼ ***Key Point*** The proton pump inhibitor, omeprazole, inhibits hepatic microsomal enzymes and undergoes hepatic metabolism, making it less predictable for use in animals with liver disease.

Infection and Endotoxemia

An increased incidence of infection may be seen in animals with hepatic disease as enteric bacteria and endotoxins gain access to the systemic circulation as a result of impaired hepatic mononuclear phagocyte system function or portosystemic shunting. Septicemia and endotoxemia may, in turn, perpetuate liver injury.

- Give systemic antibiotics to control extrahepatic infections or sepsis. Penicillins, cephalosporins, or aminoglycosides are good choices because they are eliminated primarily by renal mechanisms.

Renal Failure

Renal dysfunction and azotemia may complicate liver disease, especially chronic liver dysfunction, and can be pre-renal, primary renal, or both.

- Pre-renal mechanisms that decrease effective circulating volume and renal perfusion include dehydration (including that induced by diuretics), hypoalbuminemia, ascites, and overzealous abdominal paracentesis. Appropriate fluid therapy is essential to avoid pre-renal azotemia.
- Primary renal failure may occur with pre-existing renal disease or may result from infectious or toxic agents (e.g., leptospirosis) that affect the liver and kidneys concurrently or secondary to advanced liver disease.

Hepatoprotectants

Consider ancillary treatment with the hepatoprotectants listed in Table 71-2. These do not appear to be toxic when used as described.

- Hepatoprotectants include a varied group of compounds (prescription drugs, nutraceuticals, vitamins) that may protect the liver from injury caused by free radicals, bile salts, drugs, environmental toxins, or other insults.
- Nutraceuticals are products that have characteristics of both a nutrient and a pharmaceutical. They are readily available through health food stores or Inter-

Table 71-2. HEPATOPROTECTANTS

Product	Preparation	Dosage	Mechanism of Action	Comments
S-adenosylmethionine (SAMe)	Denosyl SD4 (Nutramax Labs): 90 and 225 mg tab	20 mg/kg PO q24h (D&C)	Intermediary metabolite: indirect glutathione precursor (antioxidant), choleretic (cats), detoxification. Supports membrane function.	Don't break enteric-coated tablets. Use only foil-wrapped products. Food decreases absorption. No side effects are noted. Can be used in acetaminophen toxicity. Expensive.
Acetylcysteine	10% or 20% solution	Dilute at least 1 : 4 with saline. Give 140 mg/kg IV through 0.25-µm filter over 20–30 min, then 70 mg/kg PO or IV q6h for seven treatments (D&C)	Glutathione precursor.	Antidote for acetaminophen toxicity. May have protective effects for other drug-induced (carprofen, potentiated sulfas, methimazole, diazepam) or toxin-induced liver injury. Safe. May cause nausea and vomiting when given orally.
Milk thistle (Silybin)	Marin (Nutramax Labs: silybin, vitamin E, zinc)* 9-, 24-, or 70-mg tab; Sil-phos (Indea Labs)	6–100 mg total dose PO q24h per package insert (D); 9–18 mg total dose PO q24h (C)	Antioxidant, anti-inflammatory, antifibrotic. Protects against *Amanita* mushroom toxicity (experimental) in dogs.	Silybin has low bioavailability; improved when complexed with phosphatidylcholine (Marin, Sil-phos). Other products have variable potency and absorption.
Vitamin E (alpha-tocopherol)	Many available	50–400 IU PO q24h (D&C)	Membrane-associated antioxidant. Protects liver against oxidative injury.	Natural Vitamin E (d-α tocopherol) has greater bioavailability than synthetic (d,l) form. In severe cholestasis, use water-soluble form.
Ursodiol	Actigall (Ciba): 300-mg caps	15 mg/kg PO q24h (D&C)	Hydrophilic bile acid. Shifts bile acid pool to less toxic hydrophilic bile acids. Choleretic in dogs (cats unknown). Protects hepatocyte membranes. Modulates immune response.	Used in cholestatic disorders; contraindicated in biliary obstruction. Side effects are rare (vomiting). Expensive.
L-carnitine	Many available	250 mg PO q24h (C)	Essential cofactor for transport of fatty acids into mitochondria for oxidation.	May improve fatty acid oxidation in obese cats undergoing weight loss but will not prevent hepatic lipidosis. Used in ancillary treatment of hepatic lipidosis.
Zinc	Zinc acetate: Galzin (Gate Pharmaceuticals); many others available	To decrease Cu absorption: 100-mg elemental zinc PO q12h for 2–3 months, then 50 mg PO q12h (D). For zinc supplementation in chronic liver disease: 1–2 mg/kg PO q12h (D)	Induces intestinal metallothionein, which preferentially binds Cu and decreases absorption. Zinc has antioxidant and antifibrotic effects; supports cell membrane function and immune response.	Many zinc products are available (acetate, sulfate, gluconate). Avoid zinc methionine if impending HE. Calculate dose on elemental zinc content. Monitor blood zinc levels: Ideal = 200–400 µg/dl; avoid >800 µg/dl (hemolysis). Do not give concurrently with Cu chelator (will be chelated). Nausea, vomiting, decreased appetite (less with zinc acetate).
Vitamin C (ascorbic acid)	Many available	100–500 mg PO q24h (D&C)	Free radical scavenger; functions in converting vitamin E back to active form. Acts as pro-oxidant in the presence of high iron, Cu levels.	Avoid in Cu-associated hepatopathy.

C, cats; Cu, copper; D, dogs; HE, hepatic encephalopathy.
*No zinc in the 9 mg tab for cats.

net mail-order sites, yet for many of these products there is a lack of safety and efficacy data.
- Lack of a regulatory mechanism for nutraceuticals is not justification for ignoring the potential therapeutic benefits of some of these products. However, most of these drugs have not been studied adequately in spontaneous hepatobiliary diseases of dogs and cats to prove efficacy.

ACUTE HEPATIC FAILURE

Acute hepatic failure occurs when a sudden severe insult to the liver compromises at least 70% to 80% of functional hepatic tissue. The clinical manifestations and laboratory findings associated with acute hepatic failure reflect general liver failure and are not specific for the underlying cause of injury.

Etiology

Causes of acute hepatic injury in dogs and cats include hepatotoxins, infectious or parasitic agents, systemic or metabolic disorders, or miscellaneous causes of liver injury (Table 71-3). In many cases, a specific cause cannot be identified.

Toxin-Induced Injury

- Hepatic injury may occur after exposure to a wide variety of industrial chemicals, organic solvents, pesticides, heavy metals, and biologic toxins (see Table 71-3). Exposure can be unobserved in a free-roaming animal that drinks from a contaminated water source.
- When hepatic necrosis is severe and widespread, rapid deterioration and death in 3 to 4 days often occur. With less extensive damage, complete recovery is possible.

Drug-Induced Injury

Drug-induced injury is a recognized cause of acute hepatic failure in dogs and cats. The incidence of drug-induced hepatic disease is unknown but is probably underestimated. Hepatic drug reactions are categorized as *dose dependent* or *idiosyncratic*.

Dose-Dependent Hepatotoxins

These hepatotoxins predictably damage the liver in an exposed population. The effect is dose-related and reproducible experimentally. All members of a species are affected at high doses. Toxicity is due to the parent drug or a consistently generated toxic metabolite.

- If a hepatotoxic reaction occurs, lowering the dose, rather than stopping the drug, can be tried.
- Examples of dose-related hepatotoxins include acetaminophen, tetracycline, stanozolol (cats only), and possibly phenobarbital (dogs only).

Idiosyncratic Hepatotoxins

These hepatotoxins cause hepatic injury at therapeutic doses in only a few individuals in the exposed population. These reactions are unpredictable and infrequent; most individuals treated with the drug do not have a reaction, even at high doses. Affected individuals appear to be unusually susceptible, possibly because they generate a unique toxic intermediate metabolite. An immunologic response may or may not be involved. Within susceptible individuals, toxicity may be more pronounced at higher doses. Because of the unpredictable nature of the reaction, they can be difficult to recognize clinically.

- If an idiosyncratic reaction occurs, the drug must be discontinued or it could result in the death of the patient.
- Examples include halothane and methoxyflurane, carprofen and other NSAIDs, lomustine, mebendazole, oxibendazole, potentiated sulfonamides, and methimazole.
- Drugs that have been incriminated as potential hepatotoxins include analgesics, anticonvulsants, and antimicrobials (see Table 71-3). Specific clinical details regarding known drug reactions in dogs and cats are summarized in Table 71-4.

▼ ***Key Point*** Dose-dependent hepatotoxic drugs cause predictable liver injury in all animals of a species, especially at high or excessive doses, whereas idiosyncratic hepatotoxic drugs affect only certain uniquely susceptible animals, even at low or therapeutic doses.

Infectious Agents

Infectious causes of acute hepatic injury (see Table 71-3) include leptospirosis (see Chapter 19), toxoplasmosis (see Chapter 21), histoplasmosis (see Chapter 20), FIP virus (see Chapter 10), and infectious canine hepatitis virus (see Chapter 16).

Miscellaneous Systemic Diseases

Hepatic injury can occur secondary to various systemic conditions, including those discussed below.

Hemolytic Anemia

Hemolysis, especially immune-mediated hemolytic anemia in dogs, can be complicated by centrilobular necrosis attributed to acute hepatocellular hypoxia or DIC-induced sinusoidal thrombosis. The hepatic injury generally resolves with resolution of the anemic crisis.

Anesthesia, Surgical Hypotension, Hypoxia, and Shock

Conditions that decrease liver blood flow can lead to hypoxia and hepatic damage. In the postoperative

Table 71-3. CAUSES OF ACUTE HEPATIC INJURY IN DOGS AND CATS

Hepatotoxins

Drugs and Anesthetics

Acetaminophen	(D&C)
Amiodarone	(D)
Aspirin	(D&C)
Anticonvulsants	
Phenobarbital*	(D)
Phenytoin*	(D)
Primidone*	(D)
Valproic acid*	(D)
Diazepam	(C)
Aprindine	(D)
Azathiaprine	(D)
Carprofen	(D)
Danazol	(D)
Glipizide	(C)
Griseofulvin	(C)
Halothane	(D)
Itraconazole	(D&C)
Ketoconazole	(D&C)
Lomustine (CCNU)*	(D)
Macrodantin	(D)
Mebendazole	(D)
Megestrol acetate	(C)
Methimazole	(C)
Methotrexate	(D)
Methoxyflurane	(D)
Mibolerone	(D)
Mithramycin	(D)
Mitotane	(D)
Oxibendazole	(D)
Phenazopyridine	(C)
Potentiated sulfonamides	(D)
Stanozolol	(C)
Tetracycline	(D&C)
Thiacetarsamide	(D)
Tolbutamide	(D)

Biologic Substances

Aflatoxin (contaminated dog food)
Amanita mushrooms
Blue-green algae
Sago palms
Hymenoptera toxins (hornet sting)
Indigofera sp. (toxic plant)
Pennyroyal oil

Chemicals

Carbon tetrachloride
Dimethylnitrosamine
Galactosamine
Metals (copper, iron, zinc, phosphorus)
Organochloride pesticides
Salt poisoning
Many others

Infectious or Parasitic Agents

Viral

Infectious canine hepatitis (adenovirus I)
Canine herpesvirus
Feline infectious peritonitis (coronavirus)
Feline calicivirus (virulent strains)

Bacterial

Cholangiohepatitis
Leptospirosis
Liver abscess
Bacillus piliformis (Tyzzer's Disease)
Salmonella spp.
Francisella tularensis (Tularemia)

Fungal

Histoplasma
Coccidioides
Blastomyces
Others

Protozoal and Parasitic

Toxoplasma
Babesia
Cytauxzoon felis
Dirofilaria (Postcaval syndrome)

Rickettsial

Ehrlichia canis
Rickettsia rickettsii

Systemic or Metabolic Disorders

Acute pancreatitis
Acute hemolytic anemia
Extraheptic infection, septicemia and endotoxemia
Idopathic feline hepatic lipidosis
Inflammatory bowel disease

Traumatic, Thermal, or Hypoxic Injury

Abdominal trauma
Diaphragmatic hernia with liver entrapment
Heat stroke
Liver lobe torsion
Shock
Surgical hypotension and hypoxia

*Usually causes chronic rather than acute hepatic disease.
D, dog; C, cat.

Table 71-4. SELECTED HEPATOTOXIC DRUG REACTIONS IN DOGS AND CATS

Drug	Species	Onset of Signs and Key Features	Hepatic Lesions	Suggested Mechanism	Comments
Analgesics					
Acetaminophen (Tylenol, McNeil)	Canine and feline	Initial toxicity is cyanosis and methemoglobinemia. Acute hepatic failure[a] occurs in dogs but is less likely in cats.	Centrilobular necrosis and congestion, vacuolar hepatopathy and bile stasis	Dose-related	Dose-related injury (doses exceeding 200 mg/kg in dogs and 120 mg/kg in cats). Treatment: N-acetylcysteine (140 mg/kg IV or PO initially, then 70 mg/kg IV or PO q6h for 36 hours) and ascorbic acid (30 mg/kg q6h for 36 hours). SAMe (20 mg/kg PO q24h) can also serve as a glutathione source. Cimetidine (5–10 mg/kg IV q8–12h for at least 3 days) inhibits hepatic P-450 enzymes and prevents further conversion of acetaminophen to toxic product.
Carprofen (Rimadyl, Pfizer)	Canine	Acute hepatic failure[a] within 5–30 days after starting drug. Labrador retrievers may be at increased risk.	Hepatocellular necrosis, ballooning degeneration, cholestasis	Idiosyncratic	Evaluate liver and kidney function prior to starting treatment. Concurrent renal tubular necrosis and glucosuria may occur. Rapid recovery in Labradors after stopping drug and giving supportive care. A 50% mortality rate in non-Labrador breeds. Whether dogs with carprofen hepatotoxicity can be safely switched to another NSAID without experiencing a hepatic reaction is unknown.
Anticonvulsants					
Phenobarbital	Canine	Chronic liver disease and cirrhosis. Anorexia, lethargy, weight loss, sedation, PU/PD, icterus, ascites, encephalopathy. ↑ ALP, ↑ ALT, ↑ GGT, ↑ total bilirubin, ↑ SBA, hypoalbuminemia, hypocholesterolemia, coagulopathy.	Hepatocellular hypertrophy and vacuolar hepatopathy (early); bridging portal fibrosis, nodular regeneration, biliary hyperplasia, mild inflammatory infiltrates	Dose- related?	Phenobarbital causes chronic hepatic disease and cirrhosis when given at high doses (serum concentrations >40 µg/ml) or for long periods (months to years). Dogs with phenobarbital hepatotoxicity may improve when dosage is decreased to therapeutic range as determined by serum phenobarbital levels or when potassium bromide therapy is substituted for phenobarbital. Incidence of chronic hepatic disease from long-term anticonvulsant therapy is approximately 6–14%. Hepatocutaneous syndrome has also been described in dogs on long-term phenobarbital therapy.
Diazepam	Feline	Acute hepatic failure[a] within 4–13 days of starting oral drug administration.	Diffuse hepatic necrosis	Idiosyncratic	Most cats with hepatotoxicity die within 15 days of initial administration of drug. In cats treated with oral diazepam, monitor baseline liver enzymes before and within 5 days after starting therapy; if enzymes are increased, discontinue drug and give supportive therapy.
Antimicrobials					
Ketoconazole (Nizoral, Janssen Pharmaceuticals)	Canine and feline	Asymptomatic with ↑ ALT, ↑ ALP, or rarely acute hepatic failure.[a]	Not characterized	Idiosyncratic[b]	May be dose-related phenomenon: >40 mg/kg/day in dogs. In humans, asymptomatic serum enzyme elevations are considered harmless and enzymes usually return to normal despite continued therapy. Therapy should be discontinued if ↑ ALT >3 times normal or if clinical signs or jaundice occur. Recovery is usually uneventful.
Itraconazole (Sporanox, Janssen Pharmaceuticals)	Canine and feline	Asymptomatic with ↑ ALT or anorexia.	Not characterized	Dose- related?	Hepatotoxicity most likely at higher doses. Therapy should be stopped if ↑ ALT >3 times normal or if anorexia occurs. When appetite returns, can reinstitute itraconazole at half the original dose.

Table continued on following page

Table 71-4. SELECTED HEPATOTOXIC DRUG REACTIONS IN DOGS AND CATS—cont'd

Drug	Species	Onset of Signs and Key Features	Hepatic Lesions	Suggested Mechanism	Comments
Tetracycline	Canine and feline	Not characterized.	Vacuolar hepatopathy	Dose-related	Experimental hepatic injury induced by high doses given IV. Avoid in animals with PSS. Unlikely to be clinically important as a hepatotoxin. Not clear whether doxycycline has same effect on liver.
Potentiated sulfonamides[c]	Canine	Acute hepatic failure[a] 5–36 days after starting therapy.	Diffuse necrosis or periportal hepatitis and intrahepatic cholestasis	Idiosyncratic	Multiple exposures may predispose to reaction, but previous exposure to sulfonamides is not required. Dogs with intrahepatic cholestasis recover rapidly after drug withdrawal. High mortality with diffuse hepatic necrosis. Consider treatment with N-acetylcysteine and vitamin C or SAMe to promote detoxification of toxic intermediate, nitroso-SMX.
Steroids					
Glucocorticoids (various types)	Canine	Chronic hepatopathy, but hepatic failure rare. Signs indicative of hypercortisolism (e.g., PU/PD, polyphagia, hepatomegaly, and lethargy). ↑ ALP, usually with induction of steroid isoenzyme of ALP. Mild ↑ ALT; normal total bilirubin. SBA within normal limits or mildly ↑ (<60 µmol/L).	Centrilobular vacuolization due to glycogen accumulation	Dose-related but considerable individual variation	Lesions reversible after treatment is discontinued. Does not occur in cats.
Stanozolol (Winstrol-V, Pharmacia and Upjohn)	Feline	Increased ALT and hyperbilirubinemia; anorexia.	Hepatic lipidosis	Dose-related	Most cats recover after discontinuing stanozolol and after supportive care.
Miscellaneous					
Methimazole (Tapazole, Lilly)	Feline	Acute hepatic failure[a] within 2 months of starting therapy.	Necrosis and cholestasis	Idiosyncratic	Clinical signs resolve within 7 days of stopping therapy. Biochemical resolution by 45 days.
Lomustine (CCNU) (CeeNu, Bristol-Meyers Squibb)	Canine	Chronic liver disease with decreased appetite, weight loss, PU/PD, vomiting, ascites and ↑ ALT, ↑ ALP, hypoalbuminemia.	Hepatocellular vacuolization, mild to moderate periportal inflammation, fibrosis, hemosiderin-laden Kupffer cells	Idiosyncratic	Median time to detection of hepatic disease from last dose of CCNU was 11 weeks (range of 2–49 weeks). Cumulative drug doses and number of doses tends to be higher in dogs that develop hepatotoxicity than in those that do not. Majority of affected dogs die of progressive chronic liver disease.

[a] Typical manifestations of acute hepatic failure include anorexia, depression, vomiting, and jaundice accompanied by ↑ ALT, ↑ ALP, and ↑ serum bilirubin.
[b] For drug reaction accompanied by clinical signs and hyperbilirubinemia.
[c] Includes trimethoprim-sulfadiazine, trimethoprim-sulfamethoxazole, and ormetoprim-sulfadimethoxine.
ALP, alkaline phosphatase; ALT, alanine aminotransferase; GGT, gamma-glutamyltransferase; NSAID, nonsteroidal anti-inflammatory drug; PSS, portosystemic shunt; PU/PD, polyuria/polydipsia; SAMe, S-adenosylmethionine; SBA, serum bile acid.

period it is difficult to differentiate hepatic damage or jaundice caused by the hypoxic effects of anesthesia and surgery from other potential causes, such as toxic injury induced by anesthetic agents (e.g., halothane or methoxyflurane) and other drugs, postoperative infections, endotoxemia, or a combination of these factors.

Acute Pancreatitis

Pancreatitis in dogs and cats often is characterized by increased serum concentrations of liver enzymes resulting from secondary hepatic injury from released enzymes and inflammatory cytokines (see Chapter 73). Hepatic lesions usually resolve with resolution of the pancreatitis and require no special treatment. Less commonly, jaundice results from partial to complete obstruction of the common bile duct associated with peripancreatic inflammation, pancreatic abscess, or pancreatic healing by fibrosis. Surgical intervention to relieve biliary obstruction is indicated in animals with pancreatic abscess or if jaundice persists after resolution of acute pancreatitis, which usually indicates pancreatic fibrosis as a cause of biliary obstruction (see Chapter 73).

Extrahepatic Bacterial Infections

Septicemia and endotoxemia associated with infections such as pneumonia, pyometra, peritonitis, and abscesses can cause jaundice, mild to moderate increases in liver enzyme activity (especially ALP), and increased SBA concentration. Liver biopsy reveals intrahepatic cholestasis without significant necrosis or inflammation. The hepatic injury resolves when the infection is controlled.

Clinical Signs

Clinical signs of acute hepatic failure often are nonspecific and overlap signs of disorders of other body systems. Clinical signs reflect general hepatic dysfunction rather than the specific underlying cause. Signs of extrahepatic or multisystemic disease often provide important diagnostic clues when hepatic injury occurs secondary to acute pancreatitis, hemolytic disease, septicemia or endotoxemia, and many infectious diseases.

- Acute onset of anorexia, lethargy, vomiting, and diarrhea are the most common presenting signs of acute hepatic failure.
- Other potential findings include PU/PD, jaundice, excessive bleeding, and HE.

Diagnosis

- When acute hepatic failure is diagnosed, attempt to identify the underlying cause with a complete history, ancillary diagnostic testing, and if indicated, a liver biopsy. In many cases, a specific cause cannot be identified.
- When acute hepatic failure is accompanied by jaundice, consider diseases of the extrahepatic biliary tract, such as biliary obstruction and rupture. Surgical intervention may provide both diagnostic and therapeutic benefit.

History

Attempt to document recent or potential exposure to any drug, toxin, or infectious disease, especially those listed in Table 71-3.

- Suspect a drug- or toxin-induced cause of acute hepatic failure when clinical and biochemical evidence of acute hepatic dysfunction is associated with recent exposure to a potential hepatotoxin.
- Consider toxin-induced injury even in the absence of known exposure to toxins, because potential hepatotoxins can be present in contaminated dog food (aflatoxins), pond water (cyanobacteria, or "blue-green algae"), and many other unobserved sources.
- Although numerous drugs have been incriminated (see Tables 71-3 and 71-4), remember that an idiosyncratic reaction can occur with *any* drug. With most drug- and toxin-induced disorders, the diagnosis is presumptive and cannot be proved.
- To confirm the diagnosis, discontinue the drug and observe for clinical improvement, which usually occurs within several weeks, even after chronic drug administration. Recurrence of hepatic damage after a challenge dose of the same drug (or inadvertent reexposure) supports the diagnosis of drug-induced hepatotoxicity. *Note:* This is not recommended as a diagnostic procedure because it is potentially dangerous, especially with a drug that causes hepatic necrosis.
- Determine if there is a history of recent surgical or anesthetic procedures that may be associated with drug- or hypoxia-related hepatic damage.
- Evaluate the animal's vaccination status for infectious diseases that can involve the liver, such as leptospirosis and infectious canine hepatitis.
- Determine if there are any subtle chronic signs of illness that suggest that the underlying liver disease may be chronic rather than acute and that the current illness may be exacerbation or decompensation of chronic liver disease.

Physical Examination

Physical findings often reflect general hepatic dysfunction rather than the specific etiology (see previous discussion of physical examination findings under "Diagnostic Strategy for Liver Disease").

- Hepatodynia may occur with any cause of acute hepatic injury that results in swelling and stretching of the liver capsule.
- Findings of weight loss and ascites are indicative of a chronic rather than an acute process.
- Signs of extrahepatic or multisystemic disease may be important clues when liver injury occurs secondary to systemic disorders.
  - For example, fever may be present with infectious causes of hepatic injury such as leptospirosis, infec-

tious canine hepatitis, bacterial cholangitis, liver abscess, systemic mycoses, and extrahepatic infections that secondarily involve the liver.
- Fever and acute abdominal pain are presenting signs of acute pancreatitis but can also occur with cholangitis and hepatic abscess.
- When jaundice is accompanied by pallor, consider immune hemolytic anemia.

Laboratory Evaluation

Acute hepatotoxicity frequently is associated with abnormal serum biochemical analyses, liver function tests, and urinalysis.

- Because diffuse hepatic necrosis is the most common lesion associated with acute hepatic failure, increased ALT activity is the most consistent finding, and values are often markedly increased. Increased ALP activity may also occur.
- Other potential findings include hyperbilirubinemia, increased SBA concentrations, hypoglycemia, hyperammonemia, and coagulopathy. Hypoalbuminemia usually suggests chronic rather than acute liver disease.
- Some hepatotoxins (e.g., carprofen) and infectious agents (e.g., leptospirosis) may concurrently damage the kidneys; thus, biochemical evidence of concomitant renal failure may be present.
- An inflammatory CBC suggests possible acute pancreatitis or underlying infectious disease. Evaluate serum amylase and lipase (dogs) and pancreatic lipase immunoreactivity (PLI) (dogs and cats) to diagnose acute pancreatitis.

Abdominal Imaging

- Liver size on abdominal radiographs usually is normal to increased unless massive hepatic necrosis causes parenchymal collapse and microhepatica.

▼ ***Key Point*** A small liver generally suggests chronic rather than acute hepatic disease.

- Additional radiographic and ultrasonographic findings may be noted, depending on the underlying disorder (Table 71-5).

Liver Biopsy

Perform a liver biopsy when the cause of acute hepatic failure is not suggested by preliminary laboratory evaluation.

- Histopathologic examination of hepatic tissue can help establish the cause and distinguish between acute and chronic liver disease. Diffuse hepatic necrosis is the histologic lesion most consistently associated with acute hepatic failure.
- If overt bleeding is present, liver biopsy may be contraindicated.

Ancillary Diagnostic Procedures

Perform ancillary diagnostic procedures (see Table 71-5) to diagnose underlying causes of acute hepatic failure.

Treatment

- Management of the patient with acute hepatic failure is first directed toward supportive therapy (see Table 71-1). In many cases, even though the cause remains unidentified or specific therapy is unavailable, supportive care alone may allow adequate time for hepatic regeneration to occur.
- Maintenance of fluid, electrolyte, and acid-base balance is the cornerstone of supportive therapy (see Chapter 5).
- Prevent or control complications such as hypoglycemia, HE, coagulopathy, and endotoxemia (see "Principles of Treatment for Liver Disease").
- Whenever possible, institute specific treatment for the underlying cause; for example, administer injectable penicillin or amoxicillin for treatment of possible leptospirosis. Discontinue use of a suspect drug to prevent further hepatic injury and observe for clinical improvement.
- With the exception of acetylcysteine for acetaminophen toxicity and milk thistle (silybin) for Amanita mushroom poisoning, no specific antidotes are available for drug- or toxin-induced hepatic injury. However, hepatoprotectants (Table 71-2) may be helpful in treating hepatotoxicity but have not been adequately evaluated.

INFECTIOUS AND PARASITIC HEPATIC DISEASE

The liver can be involved in many systemic infections (Table 71-6). In some disorders, such as leptospirosis and infectious canine hepatitis, the liver is a target organ, and evidence of liver failure dominates the clinical presentation. In other infections, such as many of the systemic protozoal infections, the liver is involved as a result of widespread invasion of organs with a large mononuclear phagocyte population, such as the spleen, lymph nodes, and bone marrow (see Table 71-6). Signs of hepatic dysfunction may or may not be present and may be overshadowed by more obvious extrahepatic involvement. Liver cytology and biopsy can be diagnostically useful for identification of these organisms.

Systemic infections are covered in detail elsewhere in this book. Infections localized to the hepatobiliary tract are covered in greater detail here.

Infectious Causes of Liver Disease

Several specific infectious diseases that involve the liver are listed in Table 71-6 and are discussed elsewhere in

Table 71-5. ANCILLARY DIAGNOSTIC EVALUATIONS FOR HEPATOBILIARY DISEASE

Diagnostic Evaluation	Intended Diagnosis (Rule Out)
Bacterial cultures	
Liver, gallbladder, bile	Bacterial cholangiohepatitis, cholecystitis, hepatic abscess
Blood, urine, infected tissues	Extrahepatic infections and sepsis
Serologic tests (antibody titers)	Leptospirosis
	Mycoses (histoplasmosis, coccidioidomycosis, blastomycosis)
	Toxoplasmosis
	Feline infectious peritonitis
	Bartonellosis
	Other infectious diseases
Microfilaria exam	Heartworm disease
Heartworm antigen or antibody tests	Heartworm disease
Fecal sedimentation (formalin-ether technique)	Liver fluke infection
Serum amylase and lipase	Acute pancreatitis in dogs
Serum pancreatic lipase immunoreactivity	Pancreatitis in cats and dogs
Serum T_4	Feline hyperthyroidism
Coombs' test	Immune hemolytic anemia
Lymph node aspiration cytology	Mycoses
	Lymphoma
Hepatic fine-needle aspiration cytology	Infectious agents (e.g., mycoses)
	Neoplasia (e.g., lymphoma)
	Feline hepatic lipidosis
	Hepatic abscess (ultrasound guided)
Abdominocentesis	Ruptured biliary tract
	Feline infectious peritonitis
	Neoplasia
Thoracic radiography	Mycoses
	Toxoplasmosis
	Heartworm disease
	Metastatic neoplasia
	Diaphragmatic hernia
Abdominal radiography	Hepatic abscesses
	Emphysematous cholecystitis
	Cholelithiasis
	Pancreatitis
Abdominal ultrasonography	Focal and diffuse hepatic parenchymal abnormalities
	Biliary or gallbladder disease
	Portosystemic shunt(s)
	Hepatic arteriovenous fistulas
	Pancreatic disease
	Diaphragmatic hernia
Angiography	
Portogram	Portosystemic shunt(s)
	Portal vein obstruction
Hepatic venography	Obstruction of caudal vena cava and hepatic veins
Celiac arteriography	Hepatic arteriovenous fistulas
Nuclear imaging	
Portal scintigraphy	Portosystemic shunting

Modified from Johnson SE: Diseases of the liver. In Ettinger SJ, Feldman EC (eds): Textbook of Veterinary Internal Medicine, vol. 2, 4th ed. Philadelphia: WB Saunders, 1995, p 1316.

this book, including leptospirosis (see Chapter 19), ehrlichiosis and rickettsial diseases (Chapter 17), toxoplasmosis (see Chapter 21), systemic mycoses (see Chapter 20), FIP virus (see Chapter 10), and infectious canine hepatitis virus (see Chapter 16).

Hepatic Abscess

Hepatic abscesses from bacterial infection of the liver occur uncommonly in dogs and cats. Abscesses may form as a solitary large mass, multiple small masses scattered throughout the liver, or microabscesses that are only detected histologically.

Etiology

- Potential sources of bacteria include hematogenous spread, translocation of intestinal bacteria into the portal blood, ascension via bile ducts, penetrating abdominal and caudal thoracic wounds, and direct extension from local suppurative diseases. Umbilical infections are the most common cause of hepatic

Table 71-6. INFECTIOUS DISEASES WITH POTENTIAL HEPATOBILIARY INVOLVEMENT*

Disease	Agent	Refer To
Viral		
Infectious canine hepatitis	Canine adenovirus I	Chapter 16
Systemic neonatal herpesvirus	Canine herpesvirus	Chapter 16
Canine acidophil cell hepatitis	Unknown	Chapter 16
Feline infectious peritonitis	Feline coronavirus	Chapter 10
Feline systemic hemorrhagic-like febrile disease	Feline calicivirus (virulent strains)	Chapter 11
Bacterial		
Leptospirosis	*Leptospira interrogans sensu strictu*	Chapter 19
Acute hepatic failure	Serovars *icterohaemorrhagiae, canicola, autumnalis, pomona, bratislava, bataviae, hardjo,* and *Leptospira kirshneri* serovar *grippotyphosa*	
Chronic hepatitis	Serovars *grippotyphosa* and *australis*	
Tyzzer's disease	*Bacillus piliformis*	Chapter 69
Nocardiosis	*Nocardia* species	Chapter 19
Actinomycosis	*Actinomyces* species	Chapter 19
Tuberculosis	*Mycobacterium tuberculosis, M. bovis, M. avium*	Chapter 19
Salmonellosis	*Salmonella typhimurium*	Chapter 69
Brucellosis	*Brucella canis*	Chapter 19
Bartonellosis (dogs)	*Bartonella henselae, B. clarridgeiae*	Chapter 19
Hepatic abscess	Gram-negative bacteria (especially *Escherichia coli*), anaerobes, mixed infections common, *Staphylococcus* species (puppies)	
Cholangitis/cholangiohepatitis	Gram-negative bacteria (especially *Escherichia coli*), anaerobes	
Cholecystitis	Gram-negative bacteria (especially *Escherichia coli*), *Campylobacter jejuni, Clostridium* species	
Yersiniosis	*Yersinia pestis*	Chapter 19
Tularemia	*Francisella tularensis*	Chapter 19
Fungal		
Histoplasmosis	*Histoplasma capsulatum*	Chapter 20
Blastomycosis	*Blastomyces dermatitidis*	Chapter 20
Coccidioidomycosis	*Coccidioides immitis*	Chapter 20
Aspergillosis	*Aspergillus terreus*	Chapter 20
Others		
Protozoal		
Toxoplasmosis	*Toxoplasma gondii*	Chapter 21
Babesiosis	*Babesia canis, B. gibsoni*	Chapters 21 & 22
Cytauxzoonosis	*Cytauxzoon felis*	Chapters 21 & 22
Hepatozoonosis	*Hepatozoon canis*	Chapter 21
Leishmaniasis	*Leishmania* species	Chapter 21
Encephalitozoonosis	*Encephalitozoon cuniculi*	Chapter 21
Rickettsial		
Ehrlichiosis	*Ehrlichia* species	Chapter 17
Rocky Mountain spotted fever	*Rickettsia rickettsii*	Chapter 17
Algal		
Protothecosis	*Prototheca* species	Chapter 69
Parasitic		
Canine schistosomiasis	*Heterobilharzia americana*	
Visceral larval migrans	*Toxocara canis*	
Liver flukes	*Platynosomum concinnum* (feline) *Amphimerus pseudofelineus* (feline)	
Canine hepatic capillariasis	*Capillaria hepatica*	
Canine hepatic alveolar echinococcosis	*Echinococcus multilocularis*	

*Not necessarily associated with clinical hepatobiliary disease.

abscesses in puppies *(Staphylococcus)* and kittens *(Streptococcus).*

- *Escherichia coli* and anaerobic bacteria are most commonly identified; mixed bacterial infections are common.
- Hypoxia of hepatic tissue caused by hepatic neoplasia, liver lobe torsion, or trauma may predispose the patient to abscess formation, because small numbers of anaerobes (e.g., *Clostridium* spp.) normally are present in the liver and can proliferate under these conditions.
- Systemic diseases that are associated with immunosuppression (e.g., feline leukemia virus and feline immunodeficiency virus) or that predispose the

patient to infection (e.g., diabetes mellitus) may predispose the patient to hepatic abscesses.
- Systemic infections (urinary tract infection, pneumonia), pancreatitis, gallbladder rupture, and previous surgical liver biopsy have also been associated with hepatic abscesses.

Clinical Signs

- Signs are attributed to sepsis, inflammation, and hepatic dysfunction and include anorexia, lethargy, fever, vomiting, and diarrhea.
- Rupture of a hepatic abscess leads rapidly to peritonitis, septic shock, and death.

Diagnosis

- Physical examination findings are often vague but may include depression, fever, hepatomegaly, abdominal tenderness, and abdominal effusion.
- Potential laboratory findings include neutrophilia with a left shift (or neutropenia and degenerative left shift if rupture occurs), thrombocytopenia, markedly increased ALT and ALP activity (although they may be in the normal range), hyperglobulinemia, hyperbilirubinemia, hypoglycemia, and septic suppurative abdominal effusion. Increased ALT and ALP activity occur in less than 50% of cats with hepatic abscesses.
- Radiolucent areas may be seen on abdominal radiographs when gas-producing organisms are involved. Ultrasonography may reveal one or more parenchymal abscess cavities. They appear as poorly echogenic lesions that may be round, oval, or irregular in shape. Ultrasound-guided FNA for cytology and culture may be diagnostic.
- Diagnosis often is established at exploratory laparotomy to determine the cause of septic peritonitis.
- Perform aerobic and anaerobic cultures of abdominal effusion, blood, and hepatic tissue.

Treatment

- Treatment of large, unifocal hepatic abscesses requires surgical excision of the affected liver lobe (see Chapter 72).
- Ultrasound-guided percutaneous abscess drainage has been advocated for medical management of single lesions. No complications were observed in one series of cases.
- Initiate broad-spectrum antibiotics such as intravenous penicillin combined with an aminoglycoside (e.g., gentamicin or amikacin) while awaiting culture results. Monitor renal function during aminoglycoside therapy, and base further therapy on results of sensitivity testing. Give long-term antibiotic therapy (but not aminoglycosides) for at least 6 to 8 weeks.
- The mortality rate was high (79%) in a recent series of cats with hepatic abscesses as compared with dogs (50%).

Liver Fluke Infection

Liver fluke infection is uncommon in cats and rare in dogs. Infection usually is asymptomatic but may cause clinical biliary tract disease when associated with marked biliary fibrosis, cholangitis, cholangiohepatitis, or extrahepatic bile duct obstruction. Cholangiocarcinoma has been reported in cats chronically infected with *Platynosomum concinnum.*

Etiology

- *P. concinnum (Platynosomum fastosum)* is the most important liver fluke in cats and is found in tropical and subtropical geographic areas, including Hawaii, Florida, and the Caribbean. In endemic areas, the prevalence of infection is high.
- Other liver flukes that have been identified in cats include *Amphimerus pseudofelineus (Opisthorchis pseudofelineus), Opisthorchis tenuicollis, Opisthorchis sinensis,* and *Metorchis conjunctus (Metorchis complexus).*
- Liver flukes require two intermediate hosts for their life cycle. Adult flukes reside in the gallbladder and bile ducts. Embryonated eggs are shed in the feces and ingested by a snail, the first intermediate host for all liver flukes. The house gecko, skink, lizard, and Bufo toad are second intermediate hosts for *P. concinnum;* fish are second intermediate hosts for the other species of flukes.

Clinical Signs

- Most infected cats are asymptomatic for liver fluke infection.
- Liver fluke infection occasionally is associated with anorexia, weight loss, diarrhea, vomiting, jaundice, hepatomegaly, abdominal distention, and death.

Diagnosis

- Operculated fluke eggs can be identified in feces by a formalin-ether technique (a sedimentation procedure). Routine methods for flotation do not consistently identify eggs. With complete bile duct obstruction, no eggs will be passed in the feces. Eggs may be identified on cytologic examination of the bile.
- Other laboratory findings are inconsistent and often unremarkable. Eosinophilia, hyperbilirubinemia, and increased serum ALP and ALT activity are sometimes detected.
- A possible relationship between positive feline immunodeficiency virus status and infection with *A. pseudofelineus* has been suggested.
- At laparotomy or necropsy, the bile ducts and gallbladder may be distended and thick walled and may contain inspissated bile and small (<12 mm long) adult flukes. The liver frequently is enlarged. In many cases, no visible abnormalities are present.

Treatment

Minimal information is available about treatment of liver flukes.

- Praziquantel (Droncit), 40 mg/kg, given orally or parenterally once a day for 3 consecutive days, or fenbendazole (Panacur) 50 mg/kg PO q24 for 10 to 14 days, has been suggested.
- Drugs used unsuccessfully include mebendazole, levamisole, thiabendazole, diamphenethide, and rafoxanide. At least one follow-up fecal examination by formalin-ether sedimentation should be performed 30 days following treatment.
- Manage complications such as biliary obstruction and secondary bacterial cholangitis or cholangiohepatitis as described elsewhere in this chapter.

FELINE HEPATIC LIPIDOSIS

Hepatic lipidosis is an excessive accumulation of triglyceride in the liver that occurs when there is an imbalance between the rate of deposition and the rate of mobilization of fat from the liver. It is the most common liver disease in cats and is associated with severe intrahepatic cholestasis and hepatic failure. Mortality is high if the disorder is untreated.

Etiology

General mechanisms of hepatic lipidosis include nutritional, metabolic, hormonal, toxic, and hypoxic liver injury. Diabetes mellitus is a well-recognized and easily diagnosed cause of hepatic lipidosis. Drug- (tetracycline, stanozolol) or toxin-induced injury can also cause histologic lesions of lipidosis. Hepatic lipidosis often occurs secondary to other systemic disorders associated with anorexia and a catabolic state, especially cholangitis, pancreatitis, inflammatory bowel disease (IBD), and systemic neoplasia. The term *idiopathic hepatic lipidosis* is used when no other underlying causative disease is identified.

The following mechanisms may be important in the development of idiopathic hepatic lipidosis:

- Cats have higher nutritional requirements for protein, essential amino acids, and essential fatty acids than dogs.
- Systemically ill cats have a propensity for accumulating fat in their hepatocytes.
- Profound anorexia and stress may be associated with hormonal (catecholamines, other) alterations that influence fat metabolism and predispose the patient to peripheral fat mobilization and hepatic fat uptake.
- Obese cats do not seem to be able to adapt to metabolism of fat for energy during periods of starvation.

▼ ***Key Point*** Persistent anorexia and rapid weight loss are hallmarks of severe hepatic lipidosis. It most commonly develops in overweight cats that experience prolonged (usually >2 weeks) inappetence, sometimes triggered by a stressful event.

- The exact mechanism or biochemical aberration in cats with hepatic lipidosis is unknown. However, there appears to be an imbalance in the mobilization of peripheral fat, the hepatic use of fatty acids for energy, and the hepatic dispersal of triglycerides.

Clinical Signs

- Hepatic lipidosis is a disease of middle-aged or older cats without breed or gender predilection. Many affected cats are obese prior to the onset of disease.
- Prolonged anorexia, often several weeks in duration, is the most consistent clinical sign.
- Other findings include lethargy, vomiting, constipation or diarrhea, and weight loss. Weight loss can be dramatic and may exceed 25% of the previous weight.
- Overt signs of HE (hypersalivation, severe depression, stupor) are uncommon.
- Overt bleeding occurs in 20% of cases.

Diagnosis

Clinical findings and laboratory evaluation in cats with hepatic lipidosis suggest hepatic disease, but liver biopsy is required to distinguish hepatic lipidosis from other causes of hepatic disease such as cholangitis, FIP, and neoplasia. When hepatic lipidosis occurs secondary to another disorder, additional testing is required to identify the primary disease (e.g., pancreatic lipase immunoreactivity for pancreatitis or GI endoscopy and biopsy for IBD).

History

The history may reveal precipitating causes of anorexia such as stressful events (e.g., boarding, surgery, or change in living arrangements), a diet change for weight reduction, or non-hepatic diseases associated with anorexia.

Physical Examination

- Findings include hepatomegaly, jaundice, muscle wasting, seborrhea, and pallor.
- Ventroflexion of the head and neck occurs in some cats and may represent muscle weakness associated with electrolyte imbalances (hypokalemia, hypophosphatemia) or thiamine deficiency.

Laboratory Evaluation

- Hematologic findings are nonspecific and include a nonregenerative, normocytic, normochromic anemia with poikilocytosis and mature neutrophilia and lymphopenia (stress response). Hemolysis may occur secondary to hypophosphatemia or Heinz bodies.

- Serum ALP, ALT, and AST activities; FSBA and PPSBA concentrations; and total serum bilirubin concentration usually are increased. Increases in liver enzymes precede increases in total bilirubin and bile acids.

▼ ***Key Point*** Serum ALP activity is generally higher in cats with lipidosis than with other hepatic diseases. Serum GGT activity, which usually parallels or exceeds serum ALP activity in most feline hepatic diseases, is normal or only mildly increased in hepatic lipidosis.

- Other potential findings include hypokalemia, hyperammonemia, hypoalbuminemia, and decreased BUN. Many affected cats have abnormal coagulation tests, especially PIVKA values and hypofibrinogenemia. In one study, PIVKA values improved in 50% of the cats treated with vitamin K_1, suggesting acquired vitamin K deficiency.
- Consider serum pancreatic lipase immunoreactivity to evaluate for concurrent pancreatitis.
- Consider serum cobalamin (B_{12}) levels if an underlying intestinal disorder suspected.

Radiography and Ultrasonography

- Radiographically, the liver is normal to increased in size.
- Ultrasonographic findings include hepatomegaly and diffuse hyperechogenicity of the liver. Ascites is rare. Evaluate for concurrent pancreatitis or other disorders causing secondary hepatic lipidosis.

Fine-Needle Aspiration Cytology

- FNA cytology is a less invasive alternative to liver biopsy that can provide similar information. Results of FNA cytology occasionally can be misleading because the small sample size may not be representative of the pathologic process in the liver.
- Correct coagulopathy with vitamin K_1 prior to performing liver aspirate or liver biopsy.
- On cytologic evaluation, hepatocytes are foamy and vacuolated, and inflammatory cells are absent.

Liver Biopsy

Liver biopsy is required for definitive diagnosis but is not routinely performed unless there is failure to respond to appropriate therapy or a high level of suspicion of another primary hepatic disorder.

- Grossly, the liver is enlarged, yellow, greasy, and friable with rounded edges. Biopsy specimens usually float in formalin.
- On routine H&E staining, there is severe vacuolization of hepatocytes (>50% of acinar unit involved).
- Oil red O stain performed on formalin-fixed (non–paraffin-embedded) frozen tissue can confirm excess fat in the vacuoles.
- Inflammation or necrosis usually is absent.

Treatment

Because of lack of information regarding the underlying cause, treatment is primarily supportive. The greatest success has been with aggressive nutritional support. During initial stabilization, correct dehydration, electrolyte imbalances, coagulopathies and any complications of liver failure. A nasogastric tube can be placed for short-term nutritional support. CliniCare (Abbott Veterinary Diets) can be used initially through the nasogastric tube while stabilizing the patient prior to anesthesia for a longer-term feeding tube (gastrostomy or esophagostomy tube).

Initial Fluid Therapy

- Use intravenous fluid therapy with a balanced electrolyte solution supplemented with potassium chloride in the initial stages of treatment (see Table 71-1). Hepatic lactate metabolism may be impaired in cats with hepatic lipidosis; thus, avoid lactated Ringer's solution.
- If hypokalemia persists despite supplementation, evaluate serum magnesium concentration to see if hypomagnesemia is the cause of refractory hypokalemia.

▼ ***Key Point*** Avoid dextrose supplementation unless hypoglycemia is documented, because glucose may promote hepatic lipid accumulation if caloric needs are not being adequately met.

- Monitor serum phosphorus concentration and treat with IV potassium phosphate if levels decline to <2 mg/dl (see Chapter 5). Hemolysis may occur secondary to severe hypophosphatemia.
- Abnormal blood coagulation test results and excess bleeding occasionally respond to vitamin K_1 therapy, suggesting severe cholestasis and vitamin K malabsorption (see Table 71-1). Consider fresh blood transfusion as needed for management of anemia.
- Treat HE as described in Table 71-1, using a low-protein diet, lactulose, and amoxicillin, neomycin, or metronidazole.
- Consider antibiotic therapy with amoxicillin to prevent infection secondary to compromised hepatic clearance of enteric organisms. Avoid tetracycline because it can predispose the patient to hepatic lipid accumulation.

Nutritional Therapy

- Provide the daily caloric requirement (40–60 kcal/kg of body weight per day) via nasogastric, esophagostomy, or gastrostomy tube. An endoscopically placed gastrostomy tube is preferable because long-term nutritional therapy (at least 3–6 weeks) is necessary in most cases. Nasogastric tubes are adequate for

short-term management and are preferable to force-feeding. Techniques for placement of indwelling feeding tubes are described in Chapter 3.

- Feed Maximum Calorie (Iams), Prescription Diet a/d (Hill's Pet Nutrition), or other complete and balanced feline diet that can be delivered through a tube in small feedings.
- Initially, give one-fourth to one-half of the daily dietary caloric requirement through the tube, divided into 4 to 6 feedings per day. Gradually increase the total amount fed over 3 to 4 days until maintenance requirements are achieved.
- Use a restricted-protein diet only if hyperammonemia or overt signs of HE occur.

▼ ***Key Point*** Do not rely on appetite stimulant medications, because they rarely achieve the consistent caloric intake required for effective reversal of lipidosis. Avoid diazepam, in particular, because it has been associated with idiosyncratic hepatic necrosis in cats.

- If vomiting or delayed gastric emptying is a problem, give metoclopramide (0.4 mg/kg SC q8h, 30 minutes before feeding), or feed a liquid enteral diet by constant rate infusion into the feeding tube. Dilution of the diet with water may also improve tolerance.

Dietary Supplements

Numerous vitamins and supplements have been empirically recommended in the treatment of idiopathic hepatic lipidosis, but further controlled studies are needed to determine clinical usefulness. Consider each of the following:

- ***B complex vitamins*** added to the fluids (1–2 ml).
- ***Cobalamin*** **(B_{12})**, 250 µg SC initially while awaiting serum cobalamin levels. If decreased serum cobalamin is documented (usually indicating primary intestinal disease), continue it long term (see Chapter 69).
- ***Thiamine*** (if severe ventroflexion of neck), at a dosage of 50 to 100 mg PO q24h, for 1 week (or added to IV fluids).
- ***L-Carnitine,*** 250 to 500 mg PO q24h, as an essential cofactor for fatty acid oxidation (for relative carnitine deficiency).
- ***Taurine,*** at a dosage of 250 to 500 mg PO q24h, for the initial 7 to 10 days. Plasma taurine is decreased in many cats with hepatic lipidosis, and taurine is required for bile acid conjugation.
- ***Vitamin E*** (water-soluble form), 50 to 100 units total dose per cat PO q24h, as an antioxidant.
- ***S-adenosylmethionine (SAMe)*** (Denosyl SD, Nutramax Labs), 20 to 40 mg PO q24h, as a glutathione source, because decreased hepatic glutathione levels occur in hepatic lipidosis.

Response to Treatment and Prognosis

- With aggressive nutritional and supportive care, approximately 60% to 85% of cats with lipidosis respond within 3 to 6 weeks. Biochemical improvement (decreases in bilirubin, ALP, and ALT) is usually seen within 1 to 2 weeks of initiating tube feeding. Normalization may take several weeks. Do not remove the tube until the cat is eating on its own for at least a week.
- Recurrence is rare and there is no evidence of residual hepatic damage.
- The earlier treatment is initiated, the better the prognosis.

▼ ***Key Point*** Monitor serum liver enzymes and institute nutritional support early in obese cats that become inappetent or undergo rapid weight loss secondary to other disease processes.

- Consider the potential for lipidosis in any obese cat placed on a reducing diet. Monitor liver enzymes to evaluate for onset of lipidosis. Consider l-carnitine supplementation (250 mg/cat/day) in obese cats undergoing dietary weight reduction.

CANINE VACUOLAR HEPATOPATHIES

The term *vacuolar hepatopathy* is used to describe the cytologic or histologic appearance of hepatocytes, which contain either discrete cytoplasmic vacuoles (usually fat) or *cytoplasmic rarefaction,* a term used to describe ballooned cells with less cytoplasmic density but devoid of distinct vacuoles.

- Cytoplasmic rarefaction is seen with either hepatocellular hydropic degeneration (increased cellular water) or *steroid hepatopathy* (increased glycogen) and cannot be differentiated without special stains. Glycogen is PAS positive.
- Vacuoles containing lipid (fat) can be confirmed by oil red O staining of formalin-fixed, non-paraffin embedded frozen tissue.
- Vacuolar hepatopathy is a common histologic diagnosis in dogs. Clinical associations are numerous and are listed in Table 71-7.

Glucocorticoid Hepatopathy (Steroid Hepatopathy)

Glucocorticoid hepatopathy, or steroid hepatopathy, is a commonly recognized sequela of glucocorticoid administration in dogs. Glucocorticoids cause hepatic glycogen accumulation and hepatomegaly (see Table 71-4). Steroid hepatopathy is a benign, reversible hepatic lesion that, with rare exceptions, is not associated with clinical liver dysfunction. The most important

Table 71-7. DIFFERENTIAL DIAGNOSES FOR CANINE VACUOLAR HEPATOPATHY

Glucocorticoid therapy
Including oral, parenteral, topical (eye, ear, skin)
Hyperadrenocorticism
Pituitary or adrenal origin
Atypical form (normal cortisol but increased adrenal steroid hormones, especially 17-OH progesterone)
Idiopathic vacuolar hepatopathy
Scottish terriers (progesterone?)
Others
Reactive hepatopathy
Common lesion in dogs with other systemic illnesses
Chronic (>4 weeks) illness (increased endogenous corticosteroids?)
Hepatic nodular regeneration
Hyperlipidemia
Diabetes mellitus
Idiopathic hyperlipidemia (miniature schnauzers, Shetland sheepdog, others?)
Hypothyroidism (severe)
Hepatocutaneous syndrome
Tetracycline administration
Glycogen and lysosomal storage disorders

clinical significance of this disorder is that it can easily be mistaken for a more serious hepatic disease.

▼ ***Key Point*** To avoid unnecessary diagnostic and therapeutic measures, remember that increased serum ALP activity and hepatomegaly are commonly caused by glucocorticoid therapy in dogs.

- Recognition of steroid hepatopathy often alerts the clinician to the presence of previously unsuspected spontaneous hyperadrenocorticism in dogs without a history of glucocorticoid therapy (see Chapter 33).
- Cats are resistant to the hepatic effects of glucocorticoids, and development of steroid hepatopathy is rare.

Etiology

- Glucocorticoid hepatopathy has been associated with numerous glucocorticoids including cortisone, prednisone, prednisolone, dexamethasone, and triamcinolone. Lesions of steroid hepatopathy can develop within 7 to 14 days of corticosteroid administration.
- Endogenous production of excess glucocorticoids caused by spontaneous hyperadrenocorticism also results in steroid hepatopathy. Hepatic lesions are identical to those seen with exogenous administration of glucocorticoids.
- Dogs with atypical hyperadrenocorticism can also develop lesions of steroid hepatopathy. These dogs present with clinical signs and laboratory findings typical for hyperadrenocorticism, but cortisol levels in response to adrenocorticotropic hormone (ACTH) or after low-dose dexamethasone are normal. Excess production of sex hormones, especially 17-hydroxyprogesterone, has been described (see Chapter 33).
- Individual variation in susceptibility to steroid hepatopathy also appears to play a role.
- Dogs that are chronically stressed (>4 weeks) due to other systemic illnesses (e.g., severe dental disease, chronic inflammation or infection, or neoplasia) may also develop this hepatic lesion, presumably due to stress-induced endogenous glucocorticoid release.

Clinical Signs

- Clinical signs reflect the systemic effects of hypercortisolism rather than hepatic disease and include PU/PD and polyphagia in an otherwise healthy dog.
- Dogs with other chronic illnesses do not typically have PU/PD but may show signs pertaining to their underlying disorder.

Diagnosis

Suspect steroid hepatopathy in any dog with hepatomegaly and increased serum ALP activity that has a history of recent glucocorticoid therapy and/or clinical signs of hyperadrenocorticism.

▼ ***Key Point*** Significant amounts of glucocorticoid can be absorbed from topical and ocular medications as well as from oral and injectable preparations.

History and Physical Examination

- Evaluate for previous glucocorticoid therapy within the past 3 months.
- Hepatomegaly, which may be quite massive, frequently is detected.
- Other findings in dogs with hyperadrenocorticism or exogenous glucocorticoid administration include abdominal distention and thinning of the skin and haircoat.

Laboratory Evaluation

- Increased serum ALP activity is the most consistent biochemical abnormality detected in dogs with this hepatic lesion. After glucocorticoid administration, the initial increase in ALP activity is attributed to the liver isoenzyme rather than the corticosteroid-induced isoenzyme (CIALP; see previous discussion). This increase can occur within 2 to 3 days of glucocorticoid therapy and often is as high as 150 times normal. After 7 to 10 days the ALP elevation becomes progressively more attributable to increased CIALP. The increase in CIALP can persist several months after exposure to corticosteroids.
- Increased CIALP activity is a consistent finding in dogs with spontaneous hyperadrenocorticism,

and absence of this isoenzyme is uncommon in this disorder.
- In contrast, ALT activity is normal or only mildly increased.
- SBA concentrations are normal or mildly increased (<60 µmol/L).
- Total serum bilirubin, serum albumin, blood ammonia concentration, and hemostatic tests typically are normal.
- Other findings characteristic of hypercortisolism include mature neutrophilia, lymphopenia, eosinopenia, monocytosis, and hypercholesterolemia.

Radiography and Ultrasonography

- Hepatomegaly usually is detected on abdominal radiographs.
- Ultrasonography reveals hepatomegaly and diffuse or multifocal increase in liver echogenicity. Adrenomegaly may be detected in dogs with underlying spontaneous hyperadrenocorticism.

Liver Biopsy

- Grossly, the liver is enlarged, smooth, pale, and friable. Microscopically, hepatic lesions are characterized by cytoplasmic rarefaction in a patchy distribution.
- PAS staining reveals that hepatocytes contain glycogen.
- When hepatic biopsy suggests steroid hepatopathy and a history of glucocorticoid administration is lacking, perform diagnostic tests for endogenous hyperadrenocorticism including the atypical form (see Chapter 33). If tests for hyperadrenocorticism are negative, evaluate for other disorders associated with vacuolar hepatopathy (Table 71-7).

Treatment

▼ ***Key Point*** Steroid hepatopathy does not require any specific therapy for the liver.

- Steroid hepatopathy is reversible after withdrawal of exogenous glucocorticoids or treatment of spontaneous hyperadrenocorticism.
- The length of time required for complete resolution is unpredictable, varying from weeks to months.

Vacuolar Hepatopathy in Scottish Terriers

Scottish terriers with diffuse vacuolar hepatopathy similar to steroid hepatopathy have been recently described. Increased levels of adrenal steroids (especially progesterone and 17-OH progesterone) have been documented. Progesterones, which are precursors of glucocorticoids, have intrinsic glucocorticoid activity and can promote hepatic glycogen accumulation.

Clinical Signs

Most dogs are asymptomatic although a few dogs may have mild PU/PD. Some dogs eventually develop typical signs of spontaneous hyperadrenocorticism.

Diagnosis

- Laboratory features include marked elevations in ALP activity (predominantly CIALP) with normal GGT and ALT activity. Total bilirubin concentrations are normal. SBA concentrations are normal or mildly increased.
- On abdominal ultrasonography, the liver is enlarged and hyperechoic. Adrenal glands appear normal. Liver biopsy reveals diffuse vacuolar hepatopathy, and PAS stains are positive for glycogen.
- Evaluation for spontaneous hyperadrenocorticism reveals normal ACTH stimulation and low-dose dexamethasone suppression tests. However, testing for adrenal sex hormones before and after ACTH reveals increased progesterone, 17-OH progesterone or other adrenal steroid hormones with normal cortisol levels (Clinical Endocrinology Service, College of Veterinary Medicine, University of Tennessee, 2407 River Drive, Room A105, Knoxville, TN 37996; telephone: 865-974-5638).

Treatment

- Although treatment with ketoconazole or mitotane will decrease ALP levels, no treatment is recommended if dogs are asymptomatic. Preliminary results suggest this is a benign disorder with a favorable long-term prognosis.
- If clinical signs of hyperadrenocorticism develop, these dogs respond to standard treatment (see Chapter 33).

Vacuolar Hepatopathy in Hyperlipidemic Miniature Schnauzers

Idiopathic hyperlipoproteinemia in miniature schnauzers is an inborn error of lipoprotein metabolism characterized by fasting hypertriglyceridemia and hypercholesterolemia. A partial decrease in lipoprotein lipase activity has been described in lipemic compared with non-lipemic miniature schnauzers. Other breeds (such as Shetland sheepdogs) may also be affected.

- Affected dogs typically develop a marked vacuolar hepatopathy. Vacuoles contain both fat and glycogen.
- Rarely, they may develop a nodular liver with stromal collapse and clinical evidence of hepatic insufficiency or severe sludging of bile and cholelithiasis.

Clinical Signs

Clinical findings in hyperlipidemic miniature schnauzers are referable to the lipemia and not hepatic dysfunction.

- Signs include lethargy, abdominal pain, decreased appetite, hepatomegaly, and seizures.
- Recurrent acute pancreatitis is common and many dogs will eventually develop diabetes mellitus.

Diagnosis

- Laboratory findings include moderate to marked increases in ALP and GGT activity. The corticosteroid-induced isoenzyme of ALP typically predominates. Increased ALT activity is variable. SBAs are typically normal or mildly increased. Associations with increased urine protein-to-creatinine ratio and microalbuminuria have also recently been described.
- Abdominal ultrasonography of the liver reveals hepatomegaly and diffuse increase in echogenicity.
- Cytology and biopsy are consistent with vacuolar hepatopathy.

Treatment

Manage hyperlipidemia with a low-fat, high-fiber diet and possibly lipid-lowering drugs. General liver support with hepatoprotectants such as antioxidants and ursodiol may be warranted (see Table 71-2). Avoid the use of corticosteroids.

Superficial Necrolytic Dermatitis (Hepatocutaneous Syndrome)

Superficial necrolytic dermatitis (SND), also called hepatocutaneous syndrome, necrolytic migratory erythema, or metabolic epidermal necrosis, is a crusting, ulcerative dermatopathy that appears to be a complication of hepatic or endocrine pancreatic disease in dogs and cats.

Etiology

The etiology and pathogenesis of this syndrome are poorly understood. In dogs it is most commonly associated with hepatopathy but has also been described with glucagon-producing pancreatic endocrine tumors or glucagon-producing hepatic tumors. The syndrome has also been reported in one cat with a pancreatic carcinoma and two cats with hepatopathy. Many dogs with SND develop diabetes mellitus in the late stages of the disease.

The hepatopathy is usually of unknown origin, although liver disease associated with anticonvulsant therapy and potential exposure to mycotoxins has been suggested. In a recent report, chronic phenobarbital therapy was associated with SND in 44% of cases. Biochemical evaluation, liver function testing, ultrasonographic appearance of the liver, and hepatic biopsy indicate that the hepatopathy of dogs with phenobarbital-related SND is distinctly different from the typical hepatic dysfunction and cirrhosis seen in dogs with phenobarbital hepatotoxicity (see under "Phenobarbital-Associated Hepatic Disease").

Pathogenesis

The dermatologic lesions are similar to necrolytic migratory erythema in humans, which is usually associated with hyperglucagonemia and hypoaminoacidemia secondary to a glucagon-secreting pancreatic tumor. Hyperglucagonemia is believed to cause severe hypoaminoacidemia by stimulating hepatic utilization of amino acids during gluconeogenesis, resulting in a metabolic or nutritional imbalance affecting the skin. Intravenous amino acid infusions can reverse the skin lesions in humans.

- Plasma glucagon levels are increased and most plasma amino acids are decreased in dogs with SND that have an underlying pancreatic endocrine tumor. Dermatologic signs resolve if the tumor can be completely resected.
- Plasma glucagon levels are reported to be normal or only mildly increased in dogs with SND and hepatopathy. However, most of these dogs have severe hypoaminoacidemia and some have responded to dietary supplementation with egg yolks, which are a rich source of amino acids. The plasma amino acid levels in dogs with SND and hepatopathy are significantly lower than in normal dogs or dogs with acute or chronic liver disease, suggesting that the pathogenesis is not simply related to hepatic dysfunction. Hyperglucagonemia may still play a central role in dogs with hepatopathy because glucagon exists in numerous immunoreactive fractions and the assay for this hormone may be insensitive to some glucagon species.
- Alternatively, up-regulation of hepatic amino acid utilization in a hypercatabolic state has also been hypothesized in dogs with SND and hepatopathy. Contributing factors may include hormonal imbalances (glucocorticoids, thyroid supplementation, increased adrenergic stimulation), phenobarbital therapy causing chronic hepatic microsomal enzyme induction, and age-related changes in hepatocellular membrane stability (increased hepatocyte responsiveness to adrenergic stimulation and enhanced amino acid utilization for gluconeogenesis). Aging has also been associated with alterations in hepatic sensitivity to glucagon.
- Other nutritional deficiencies such as zinc, biotin, or essential fatty acids have also been proposed.

Signalment and Clinical Signs

- SND is a disease of older dogs (mean age of 10 years), especially males. Shetland sheepdogs, West Highland white terriers, cocker spaniels, Scottish terriers may be at increased risk.

- Dogs are usually presented for dermatologic signs and lethargy and inappetence. Overt signs of liver failure are unusual.
- SND is characterized by bilaterally symmetrical crusting or erosive lesions of the pads, mucocutaneous junctions, and pressure points (hocks and elbows). The dermatologic manifestations are described in Chapter 49.

Diagnosis

Laboratory Evaluation

- Abnormalities may include nonregenerative anemia, abnormal red cell morphology (poikilocytes and target cells), mild to moderate increases in serum liver enzymes (ALP, ALT, and AST), hyperglycemia, and mild to moderate increases in SBA concentrations. Hypoalbuminemia and hyperbilirubinemia are less consistent findings.
- Other potential features include hypoaminoacidemia, hyperglucagonemia, and elevated insulin levels.

Ultrasonography

- Ultrasound examination of the liver may identify a unique "honeycomb" or "Swiss cheese–like" lesion consisting of 0.5- to 1.5-cm diameter hypoechoic regions surrounded by highly echogenic borders. Dogs with SND related to glucagonoma do not have these characteristic hepatic lesions on ultrasound.
- The pancreas should be evaluated for nodules consistent with neoplasia, although most glucagonomas in the pancreas have not been visualized on ultrasonographic examination.

Liver and Skin Biopsy

- Dermatohistopathology is pathognomonic for SND (see Chapter 49). Lesions consist of parakeratotic hyperkeratosis, intercellular or intracellular edema, and epidermal hyperplasia. Bacteria, dermatophytes, and yeast can be secondary contaminants.
- The liver is usually normal to increased in size and has a striking nodular appearance that grossly mimics cirrhosis. However, the hepatic lesion is not true cirrhosis because microscopically, the fibrous tissue is actually condensed stroma secondary to parenchymal collapse and not due to increased collagen production. Areas of severe parenchymal collapse contain hepatocytes with marked vacuolization (predominantly glycogen accumulation but also some lipid deposition). Regions of collapse surround sharply demarcated nodules of normal hepatic parenchyma. The hepatic lesion is most likely a reflection of underlying nutritional, hormonal, or toxic abnormalities.

Treatment

If a glucagon-producing pancreatic tumor is diagnosed (only 10% of cases), it should be surgically resected. When a toxic or metabolic cause of hepatic injury is identified (e.g., phenobarbital therapy), there is the potential for resolution of the disorder if the cause can be removed. However, most dogs with phenobarbital-associated SND do not improve after discontinuing phenobarbital.

Nutritional Considerations

▼ ***Key Point*** The most effective treatment is IV administration of amino acids.

- Give 10% amino acid solution (Aminosyn, Abbott Labs) at a dosage of 250 to 500 ml per dog (or 25 ml/kg) slowly IV over an 8- to 12-hour period. Repeat this treatment every 7 to 10 days as needed to control the dermatologic lesions. Some dogs show marked improvement after the first treatment. If a patient has not responded after four treatments, it probably won't.
- Despite underlying evidence for hepatic disease, do not restrict protein intake unless overt HE occurs. Feed a diet high in good-quality protein.
- Consider oral protein supplementation with three to six egg yolks q24h or an amino acid supplement (Pro-Mod, Ross Labs) 10 g per 7 kg of body weight (up to a maximum of 40 g) q24h.
- Give an oral multivitamin supplement (including vitamin E).
- Give elemental zinc, 1 mg/kg PO q12h, for possible zinc deficiency.
- Consider essential fatty acid supplementation.

Other Therapy

- Refer to Chapter 49 for recommendations for treating the cutaneous lesions and secondary cutaneous bacterial and fungal infections.
- Manage diabetes mellitus with insulin therapy and a high-fiber diet.
- Consider a long-acting somatostatin analogue (Octreotide, Sandostatin) to inhibit glucagon release.
- Parenteral corticosteroids are contraindicated because of the diabetic or prediabetic state. Topical triamcinolone ointment q12h can be used on a short-term basis to decrease pain and inflammation associated with deep fissures.

Prognosis

The prognosis is poor except in the small percentage of cases in which a glucagon-producing pancreatic tumor is identified and removed. Most dogs die or are euthanized within 5 months of onset of the skin lesions.

HEPATIC AMYLOIDOSIS

Amyloidosis is a progressive systemic disease associated with extracellular deposition of insoluble fibrillar proteins, which results in organ dysfunction. Amyloidosis in dogs and cats is reactive and may occur secondary to chronic inflammatory, infectious, or neoplastic disorders.

- Amyloidosis is a familial disorder in the Chinese Shar-Pei dog and in Abyssinian cats. Although concurrent amyloid deposition occurs in the liver, kidneys, spleen, and adrenal glands, clinical manifestations of renal failure are most common.
- Clinically significant hepatic involvement has been described in Chinese Shar-Pei dogs and Siamese, Oriental shorthair, Devon Rex, Burmese, and domestic shorthaired cats. Diffuse hepatic involvement predisposes patients to spontaneous hepatic rupture because of hepatic vascular fragility and coexistent coagulopathy.

Signalment and Clinical Signs

- Shar-Pei dogs and young cats are at increased risk.
- Clinical signs include anorexia, PU/PD, vomiting, and jaundice.
- Spontaneous rupture of the friable liver may cause acute hemoabdomen with signs of lethargy, hypovolemic shock, or sudden death.

Diagnosis

Physical Examination

Physical examination reveals hepatomegaly. With spontaneous rupture, findings include pale mucous membranes, hypothermia, and abdominal effusion.

Laboratory Evaluation

- Potential laboratory findings include increased ALT activity, hyperbilirubinemia, and increased SBAs.
- Regenerative anemia may occur secondary to hepatic rupture and hemorrhage. Thrombocytopenia and abnormally prolonged clotting times (which may be vitamin K responsive) have been described in some cats.
- Abdominocentesis reveals hemorrhagic abdominal effusion.
- Concurrent renal amyloidosis may cause azotemia and proteinuria (see Chapter 77).

Radiography and Ultrasonography

- Findings on abdominal radiographs may include hepatomegaly and possible abdominal effusion.
- Abdominal ultrasound may reveal a diffusely heterogenous liver with hypoechoic foci.

Liver Cytology and Biopsy

- Diagnosis of hepatic amyloidosis requires liver biopsy with special stains (Congo red) to confirm its presence. However, caution is advised since FNA for cytology or liver biopsy can be complicated by severe hemorrhage.
- Hepatic cytology may suggest amyloid based on the identification of pink amorphous material adjacent to hepatocytes (with a modified Wright-Giemsa stain).
- Grossly, the liver is pale, large, and friable with hemorrhages, hematomas, and capsular tears.
- Histologically, amyloid in the liver appears as a homogenous, amorphous, eosinophilic material within the space of Disse and vessel walls.

Treatment

- Use fluid therapy and blood transfusion to treat acute liver hemorrhage.
- Give vitamin K_1 for the coagulopathy (see Table 71-1).
- Consider colchicine therapy (0.03 mg/kg PO q24–48h), which may be beneficial in Chinese Shar-Pei dogs with hepatic amyloid.
- The long-term prognosis in cats with hepatic amyloidosis is poor.

CANINE CHRONIC HEPATITIS

Chronic hepatitis is a heterogeneous group of necrotizing inflammatory diseases of the liver. The clinical signs of chronic hepatitis initially are vague, such as anorexia, weight loss, and depression; however, as hepatitis becomes advanced, signs of liver failure develop, including jaundice, ascites, coagulopathy, or HE.

With few exceptions, the cause, pathogenesis, natural history, and optimal treatment of these disorders in dogs is unknown. Because the laboratory and histopathologic features often fail to determine the definitive etiology, combined clinical and histologic criteria rather than etiologic classifications generally are used to categorize patients with chronic hepatitis.

Idiopathic Chronic Hepatitis

Idiopathic chronic hepatitis is characterized by clinical signs and persistent laboratory indicators of hepatic disease in association with chronic portal inflammation, piecemeal hepatic necrosis, and fibrosis that frequently progresses to cirrhosis and liver failure.

Etiology

The disease must be considered idiopathic in most dogs; however, it is probable that after an initial inciting hepatocyte injury, immune mechanisms are involved in perpetuating the inflammation.

Signalment and Clinical Signs

- The incidence of idiopathic chronic hepatitis appears to be highest in female dogs.
- The mean age of onset is 5 to 6 years, but adult dogs of any age or breed can be affected.
- Common signs include anorexia, depression, weakness, PU/PD, ascites, jaundice, weight loss, and vomiting.

Diagnosis

The diagnosis is suggested by the clinical signs in conjunction with elevation of serum liver enzyme activity. The diagnosis can be confirmed only by liver biopsy. Historical and physical findings are consistent with chronic liver disease.

Laboratory Evaluation

- Serum ALT activity usually is >10 times normal, reflecting ongoing hepatic injury (inflammation). Serum ALP activity is usually >5 times normal, reflecting intrahepatic cholestasis. Hyperbilirubinemia and bilirubinuria also are common.
- Liver function tests such as SBA concentrations frequently are abnormal, reflecting the degree of liver dysfunction.
- Less consistent findings include hypoalbuminemia, hyperglobulinemia, mild nonregenerative anemia, and abnormal hemostasis. Ascitic fluid, when present, typically is a transudate or modified transudate.

Radiography and Ultrasonography

- Radiographically the liver may appear small, and on ultrasonography nonspecific changes in echogenicity may be detected.

Liver Biopsy

Liver biopsy and histopathology confirm the diagnosis.

- The liver often is small and nodular because of the fibrosis and nodular regeneration of cirrhosis.
- The primary lesion is portal inflammation consisting primarily of lymphocytes and plasma cells and occasional neutrophils and macrophages. The inflammation extends into the hepatic lobule, causing piecemeal necrosis of hepatocytes. These lesions are essential defining criteria for categorization as idiopathic chronic hepatitis.
- Fibrosis usually is present.

▼ ***Key Point*** Perform a quantitative copper analysis and special stains for copper to determine if increased hepatic copper content could be playing a role in chronic hepatitis.

Differential Diagnosis

When chronic hepatitis has been confirmed histologically, look for potential inciting or perpetuating factors. Recognized types of chronic hepatitis are listed in Table 71-8. If none are found, then idiopathic chronic hepatitis is the diagnosis.

Treatment

Treatment includes drug therapy, discussed below, and supportive measures, previously described under "Principles of Treatment for Liver Disease" (see Table 71-1). Treatment recommendations for idiopathic chronic hepatitis in dogs are empirical and clinical studies are lacking.

Glucocorticoids

Glucocorticoid therapy is the cornerstone of treatment for canine chronic hepatitis, yet efficacy has not been well documented. It is not clear whether immunosuppressive doses (as used for immune-mediated disorders) or anti-inflammatory doses are optimal. One retrospective study of dogs with chronic hepatitis suggested that immunosuppressive doses were associated with prolonged survival. Anti-inflammatory doses may nonspecifically decrease hepatic inflammation and release of local cytokines, which contribute to hepatic necrosis and fibrosis.

- Consider glucocorticoid therapy when infectious diseases have been ruled out and characteristic inflammatory infiltrates are detected on liver biopsy.
- Give prednisolone, 1 to 2 mg/kg PO q24h, until clinical remission occurs; then taper gradually to

Table 71-8. CANINE CHRONIC HEPATITIS

Familial predisposition
Bedlington terrier
Cocker spaniel (American and English)
Dalmatian
Doberman pinscher
Skye terrier
West Highland white terrier
Labrador retriever?

Infectious Hepatitis
Infectious canine hepatitis (experimental)
Acidophil cell hepatitis
Leptospirosis (serovars *grippotyphosa* and *australis*)

Drug- and Toxin-Induced Hepatitis
Anticonvulsants (phenobarbital, primidone)
Oxibendazole?
Carprofen?
Aflatoxin?

Lobular Dissecting Hepatitis
Idiopathic Chronic Hepatitis

0.5 mg/kg or the lowest effective dose for alternate-day maintenance.
- Although prednisone must be converted by the liver to its active metabolite, prednisolone, either drug can probably be used, based on the observation that humans with liver disease can still rapidly convert prednisone to prednisolone.
- Potential side effects of glucocorticoid therapy include sodium and water retention (exacerbation of ascites), GI bleeding and catabolic effects (exacerbation of HE), iatrogenic Cushing's disease, and secondary infections.
- Monitor serum biochemistries every 1 to 2 weeks in the initial stages of treatment.
- Consider a follow-up liver biopsy, 2 to 3 months after starting therapy, to confirm remission of the disease.

Azathioprine

Azathioprine is an antimetabolite with anti-inflammatory and immune-modulating effects. When prednisolone alone is ineffective or side effects become objectionable, consider combination therapy using azathioprine and prednisolone (at a lower dose if side effects are a problem).

- Give azathioprine (Imuran, Burroughs Wellcome) at a dosage of 1 to 2 mg/kg PO q24h for induction therapy. For maintenance, give the same dose once every other day while giving prednisolone on the alternate days.
- Because azathioprine may cause bone marrow suppression (neutropenia and thrombocytopenia), monitor periodically with a CBC. Other less common side effects include GI toxicity, pancreatitis, and hepatotoxicity.

Ursodiol

Ursodiol (Actigall) is a synthetic bile acid that has been useful in the treatment of humans with chronic hepatitis. Its use in conjunction with anti-inflammatory therapy in dogs with chronic hepatitis appears promising.

- Ursodiol, a hydrophilic bile acid, is believed to be beneficial by expanding the bile acid pool and displacing potentially hepatotoxic hydrophobic bile acids that may accumulate in cholestasis. It also has membrane-stabilizing, cytoprotective, and immunomodulatory effects on liver cells and promotes choleresis (see Table 71-2).
- Ursodiol appears to be well tolerated in dogs when used at a dosage of 15 mg/kg PO q24h.

Antioxidants

- Free radicals may be generated in chronic hepatitis, and they may contribute to hepatic injury. Antioxidants, such as vitamin E, are important to scavenge free radicals and prevent oxidative injury.
- Give vitamin E at a dosage of 50 to 400 IU PO q24h. Absorption of fat-soluble vitamins may be decreased in chronic cholestatic hepatobiliary disorders. In this setting, a water-soluble form of vitamin E may be preferable.

Prognosis

The response to treatment of idiopathic chronic hepatitis is variable, which is expected because it probably represents a heterogeneous group of diseases.

- Some dogs eventually can be taken off medication and remain in remission, but more often therapy must be continued indefinitely.
- Other dogs fail to respond, especially those that have advanced disease and cirrhosis (the treatment of cirrhosis and its complications is discussed elsewhere in this chapter).

Hepatic Copper Accumulation and Chronic Hepatitis

Copper accumulation in the liver can be associated with significant hepatic injury resulting in acute hepatitis, chronic hepatitis, and cirrhosis. It is one of the few well-documented causes of chronic hepatitis in the dog. The severity of hepatic injury is related to the amount of accumulated copper. Hepatic copper concentration in normal dogs is less than 400 µg/g (ppm) dry weight.

- An inherited metabolic defect in biliary copper excretion causes chronic hepatitis in Bedlington terriers. Copper concentrations range from 850 to 12,000 µg/g dry weight in affected Bedlingtons.
- Hepatic damage in Bedlington terriers does not consistently occur until the copper concentration exceeds 2000 µg/g dry weight. The concentration at which abnormal hepatic copper contributes to hepatic damage in other breeds is unknown and may vary among breeds.
- Copper accumulation in the liver may be a cause or an effect of chronic hepatitis. Because copper normally is excreted in the bile, hepatic copper accumulation can also occur secondary to any cholestatic hepatobiliary disorder (such as idiopathic chronic hepatitis) that impairs bile flow.
- Whether secondary copper accumulation can further contribute to hepatic injury is unclear, but this is an important question with therapeutic implications.
- Other breeds of dogs occasionally are diagnosed with chronic hepatitis and cirrhosis accompanied by increased hepatic copper concentrations. At this advanced stage of disease, it is difficult to know whether copper accumulation is a cause or an effect of the chronic hepatitis. As a general rule, the higher the copper content, the more likely it is to be a primary problem.

Copper-Associated Hepatitis in Bedlington Terriers

Bedlington terriers have a high incidence of an inherited (autosomal recessive) metabolic defect in biliary copper excretion that leads to progressive intrahepatic copper accumulation and chronic liver disease. Because of extensive inbreeding, the prevalence within the breed is quite high (25% affected, 50% carriers).

Etiology

- Hepatic copper content increases with age as a result of defective biliary copper excretion.
- Excess copper is bound to hepatic metallothionein and stored in hepatic lysosomes. When hepatic copper accumulation is >2000 µg/g dry weight, progressive hepatic injury occurs, including focal hepatic necrosis, chronic hepatitis, and eventually cirrhosis. This disease is similar but not identical to Wilson's disease in humans.
- Hepatic injury associated with copper accumulation involves free radical damage to hepatic mitochondria.

Clinical Signs

Clinical signs and presentation vary widely, depending on the stage of disease.

- Most affected dogs are presented as young or middle-aged adults of either sex with signs of hepatic failure of varying severity, including lethargy, depression, weight loss, vomiting, and jaundice. Acute fulminant hepatic failure with rapid deterioration and death occurs in rare instances.
- Some middle-aged and older dogs are presented initially with end-stage liver disease and cirrhosis. In these animals there is a more chronic, insidious clinical course with similar but less severe signs. In the advanced stages of disease, cachexia, jaundice, ascites, and HE can occur.
- Affected dogs may be asymptomatic, especially young dogs in which copper is accumulating but has not yet reached toxic hepatic concentrations.

Diagnosis

Suspect copper-associated hepatitis in any Bedlington terrier with historical, physical, or biochemical evidence of hepatic disease or with vague, unexplained illness. Asymptomatic dogs can be identified only by routine biochemical screening or liver biopsy. Definitive diagnosis requires liver biopsy.

History

- Acute, recurrent episodes of illness are common in many affected dogs. Stressful events such as whelping, showing, shipping, or a change in environment can precipitate these episodes.
- Dogs initially presenting with end-stage cirrhosis often have no history of previous episodes of hepatitis.

Physical Examination

- Findings in dogs with acute hepatitis include depression, lethargy, and dehydration. Hepatomegaly may occur. Jaundice may be detected within 48 hours of onset. Acute copper-induced hemolytic anemia may be a contributing factor.
- With advanced disease, dehydration, emaciation, ascites, HE, and jaundice may be detected. The liver is small and not palpable.
- Asymptomatic dogs are normal on physical examination.

Laboratory Evaluation

- Biochemical findings vary with the stage of disease. Increased serum ALT activity is the most sensitive laboratory indicator of this disease, although up to a third of affected dogs will have normal ALT values. These are mostly younger dogs that are in the early stages of the disease.
- Other serum biochemical abnormalities typical of hepatic dysfunction eventually develop, such as hyperbilirubinemia, bilirubinuria, hypoalbuminemia, increased SBA levels, and prolonged PT and APTT.
- Serum copper levels are not helpful for the diagnosis.
- Acute release of copper from necrotic hepatocytes occasionally causes hemolytic anemia. Laboratory findings include low packed cell volume (PCV), hemoglobinemia, and hemoglobinuria.

Radiography and Ultrasonography

- Abdominal radiographs are unremarkable except when advanced stages of disease are accompanied by microhepatica or ascites.
- Ultrasonography of the liver may be normal in the early stages. As the disease progresses, findings are indicative of diffuse liver disease or microhepatica and cirrhosis.

Liver Biopsy

Liver biopsy is indicated for definitive diagnosis and staging of the disease. Perform liver biopsies in all Bedlingtons being considered for breeding. Dogs should be older than 1 year because unaffected carrier dogs may have transient increases in hepatic copper that return to normal by 1 year of age. The spectrum of gross and microscopic features in the liver parallels the variable expression of the disease.

- The liver can be grossly normal or swollen and smooth with accentuation of the lobules. As cirrhosis

develops, the liver decreases in size and there is a mixture of fine and coarse nodules.
- Histologically, H&E-stained hepatic tissue reveals dark granules in hepatocyte cytoplasm. In the early stages, centrilobular hepatocytes are most affected, but later the distribution is diffuse.
- Histochemical stains for copper, such as rhodanine and rubeanic acid, are positive. These stains correlate well with quantitative copper analysis when values exceed 850 µg/g dry weight.
- Associated histologic hepatic damage is variable. In the most mildly affected animals, only centrilobular copper granules are detected. This progresses to focal hepatitis, lesions of chronic hepatitis, and eventually cirrhosis.

Hepatic Copper Analysis

Perform quantitative copper analysis on fresh hepatic tissue. Copper analyses are available to veterinarians through the veterinary diagnostic laboratories of Michigan State University and Colorado State University. Affected dogs have hepatic copper concentrations of 850 to 12,000 µg/g dry weight.

DNA Testing

- DNA testing is available (www.vetgen.com) that identifies a linked marker located in the chromosome close to the as-yet-unidentified causative gene.
- Carrier, affected, or unaffected dogs can be characterized with 90% accuracy.
- DNA-screened carriers or normal dogs should have annual liver enzyme evaluations. Increases in liver enzyme activity should merit further evaluation of the liver.

Treatment

Specific measures to control hepatic copper accumulation are summarized in Table 71-9. Base the choice of therapy for an individual patient on the severity of existing hepatic damage.

▼ ***Key Point*** Lifelong therapy is necessary because copper reaccumulates if treatment is stopped.

Management of the acute hepatic crisis also involves symptomatic and supportive care to control electrolyte, acid-base, and fluid imbalances and HE (see Table 71-1). Treatment of hemolytic anemia may require a blood transfusion.

Chelator Therapy

- Treat affected dogs with copper accumulation (>1500 µg/g dry weight) and chronic hepatitis with a copper chelator such as penicillamine or trientine hydrochloride, which promotes urinary copper excretion (see Table 71-9).
- For treating an acute hemolytic crisis, trientine hydrochloride (but not penicillamine) may be effective in chelating copper in the circulation.
- There may be other protective effects of penicillamine besides depletion of hepatic copper, because many Bedlington terriers on long-term therapy do not develop hepatic failure despite continued elevated copper levels and ongoing hepatic damage. Penicillamine may induce hepatic metallothionein, which binds and sequesters copper in a non-toxic form. Additional effects that may be beneficial include anti-inflammatory, antifibrotic activity, and immunomodulating effects.

Zinc Therapy

Use oral zinc therapy when hepatic copper concentrations are >400, but <1500 µg/g dry weight to prevent intestinal copper absorption and hepatic copper accumulation. Preliminary information in Bedlington terriers and West Highland white terriers suggests it may also deplete hepatic copper concentrations (see Table 71-9).

Dietary Therapy

Low copper diets are of little value once hepatic copper accumulation has occurred (see Table 71-9) but may be helpful in the early stages to decrease intestinal copper absorption.

Vitamin E Therapy

Administer vitamin E to all dogs with hepatic copper accumulation (see Table 71-9). Hepatic injury associated with hepatic copper overload in Bedlington terriers appears to involve free radical damage to hepatic mitochondria. Vitamin E therapy protects against copper-induced hepatic damage experimentally.

Prognosis

- Dogs with mild to moderate acute hepatic failure usually respond to supportive care.
- If this disease is detected before severe hepatic failure occurs, many dogs can live out their lives with penicillamine therapy.
- The prognosis is poor if there is fulminant hepatic failure or chronic end-stage cirrhosis and failure.

Prevention

- Treatment of affected dogs with minimal hepatic injury is recommended in the hope of preventing acute hepatitis or progression to cirrhosis.
- Zinc therapy is a promising and less expensive alternative to penicillamine in this setting.
- Bedlington terriers used in breeding programs can be certified free of disease through either the Canine Liver Registry at Purdue University or the Liver Registry of the Orthopedic Foundation for Animals in Columbia, Missouri.

Table 71-9. TREATMENT OF HEPATIC COPPER ACCUMULATION

Product	Formulation	Dosage	Side Effects	Comments
Chelate Systemic Cu				
Penicillamine (Cuprimine, MSD; Depen, Wallace)	Cuprimine: 125- and 250-mg caps Depen: 250-mg tabs	15 mg/kg q12h PO given on an empty stomach to improve absorption; do not give concurrently with any medication, including Zinc[a] or vitamin and mineral supplements.	Anorexia and vomiting[b] are common; dermatologic drug eruption or autoimmune-like excretion. Indicated when vesicular lesions of mucocutaneous junctions;[c] reversible renal disease.[c]	Causes systemic Cu chelation and urinary excretion. Indicated when hepatic Cu >1500 µg/g. Takes months to years to produce significant decrease in hepatic Cu concentration (900 µg/g/year)[d], but may produce subjective clinical improvement after a few weeks. May have protective effect in liver beyond chelation: induces hepatic metallothionein, which binds and sequesters Cu in non-toxic form? Not effective for treatment of Cu-associated hemolysis.
Trientine dihydrochloride[e] (Syprine, MSD)	250-mg caps	15 mg/kg q12h PO. Give 1 hour before meals; do not give concurrently with any medication, including zinc[a] or vitamin/mineral supplement.	None noted as yet.	Use as an alternative to penicillamine if vomiting occurs. May be useful for treatment of hemolysis by chelating Cu in blood. More expensive than penicillamine.
Decrease Intestinal Cu Absorption				
Zinc acetate, sulfate, or gluconate to obtain therapeutic zinc	Many available	100-mg elemental zinc PO q12h for 2–3 months, then 50 mg PO q12h for maintenance. Separate administration from meals by >1 hour.	Vomiting,[f] zinc-induced hemolysis at plasma levels >800 µg/dl.	Induces intestinal metallothionein, which preferentially binds Cu and decreases absorption. Takes 3–6 months. Monitor plasma zinc every 2–3 months. Ideal level is 200–400 µg/dl. Do not give concurrently with Cu chelators. Use when hepatic Cu is increased but is <1500 µg/g dry weight.
Decrease Cu Intake				
Cu-restricted diet	Prescription Diet l/d (Hill's) Homemade diets			Low Cu diet may slow further Cu accumulation but won't decopper the liver. Most commercial diets have abundant Cu. Avoid mineral supplements, liver, shell fish, organ meats, chocolate, nuts, mushrooms, cereals.
Antioxidant Therapy[g]				
Vitamin E	Many available	100–400 IU/day, PO.	None noted as yet.	Oxidative damage occurs in Cu-associated liver disease. Vitamin E protects the liver against oxidant damage.

[a] Penicillamine and trientine will chelate zinc (and decrease its absorption) when given concurrently.
[b] Often resolves after several weeks; start at a reduced dose and increase to maintenance after a few days. Giving with food will decrease absorption, but a small amount of milk, cheese, or bread given concurrently may decrease vomiting.
[c] Rare complications; renal compromise more likely with Depen?
[d] In Bedlington terriers; more rapid response in Doberman pinschers and other breeds.
[e] Availability limited; may require a special order direct from manufacturer.
[f] Zinc acetate may be less irritating to the stomach than other formulations. To minimize vomiting, open capsule and mix contents with small amount of tuna or hamburger.
[g] Although vitamin C has antioxidant effects, it should be avoided in dogs with Cu accumulation because it increases Cu's oxidative damage to the liver.
Cu, copper.

Chronic Hepatitis in West Highland White Terriers

West Highland white terriers (WHWTs) have increased risk for developing chronic hepatitis and cirrhosis. Hepatic copper accumulation is found in many WHWTs with chronic hepatitis. Hepatic copper accumulation in WHWTs is a familial trait, but the mode of inheritance has not been established.

Etiology

The etiopathogenesis is unknown. The notable differences between the copper retention in WHWTs and the disease in Bedlington terriers are that WHWTs do not accumulate copper continuously throughout life, the peak hepatic copper concentration in WHWTs occurs by 6 months of age and may even decrease after 1 year of age, and the magnitude of the copper increase is generally lower in WHWTs than in Bedlingtons.

- Many WHWTs have hepatic copper concentrations that range from 200 to 1500 µg/g dry weight, but rarely does the value exceed 2000 µg/g dry weight and clinical illness associated with excess hepatic copper accumulation is uncommon. Some dogs have high hepatic copper (usually <3500 µg/g dry weight) but no evidence of hepatic disease.
- In WHWTs with chronic hepatitis, increased hepatic copper concentration (>2000 µg/g dry weight) appears to be a factor in some but not most affected dogs. When hepatic copper concentrations are <2000 µg/g dry weight, the copper may not be contributing to hepatic injury. These dogs may have idiopathic chronic hepatitis.
- Chronic hepatitis in WHWTs may also occur without increases in hepatic copper.

Clinical Signs

- Affected animals in the early stages of copper accumulation or those with focal hepatitis are usually asymptomatic.
- When widespread necrosis occurs, nonspecific signs of liver disease include anorexia, vomiting, diarrhea, lethargy, and jaundice.
- With advanced disease, jaundice and ascites are common.

Diagnosis

Episodes of hepatic necrosis may be precipitated by stressful events such as whelping or showing.

- The earliest biochemical abnormality associated with hepatic necrosis is increased ALT activity.
- With advanced disease, laboratory findings include increased liver enzyme activity, hyperbilirubinemia, increased SBA levels, hyperammonemia, and hypoalbuminemia. Copper-associated hemolytic anemia has not been documented.
- Liver biopsy for histopathology and quantitative copper analysis are required for definitive diagnosis. Histologic features include copper granules (which are initially centrilobular but become diffusely distributed with time), multifocal hepatitis, subacute bridging necrosis, massive necrosis, and cirrhosis.

Treatment

If chronic hepatitis and cirrhosis are associated with increased hepatic copper (>1500 µg/g dry weight) in a WHWT, initiate treatment for hepatic copper accumulation as described for Bedlingtons (see previous section) and in Table 71-9.

- Preliminary evidence suggests that both penicillamine and zinc acetate can decrease hepatic copper concentrations in WHWTs when given on a long-term basis (see Table 71-9).
- Because hepatic copper accumulation is not continuous throughout life, mature dogs with chronic hepatitis and hepatic copper concentrations <1500 µg/g dry weight may not require chelator therapy. Consider glucocorticoid therapy as described previously for idiopathic chronic hepatitis.

Chronic Hepatitis in Doberman Pinschers

Doberman pinschers are at increased risk to develop chronic hepatitis and cirrhosis. Hepatic copper concentrations are increased in most affected dogs.

Etiology

- The underlying etiopathogenic mechanisms are unknown, but a genetic basis is suggested by the high incidence in this breed. Middle-aged (5–7 years old) female dogs are at increased risk.
- Hepatic copper concentrations are increased (650–4000 µg/g dry weight) in most affected dogs but not to the same magnitude as seen with Bedlington terriers, suggesting a different disease mechanism. The significance of the increased hepatic copper concentration is still under debate.
- Evaluation of Doberman pinschers with subclinical disease has recently provided further information on the role of copper in this disorder. Screening of 106 clinically healthy 3-year-old Doberman pinschers in the Netherlands (for liver enzyme elevations, increased SBA, or copper granules on FNA cytology of liver) with follow-up liver biopsy (including quantitative copper) revealed subclinical hepatitis in 21% of the screened dogs. Affected dogs were followed over 2 to 4 years with repeated liver biopsy and quantitative copper analysis. Persistent hepatitis was only documented in dogs (5 females, 1 male) with initial and final hepatic copper concentrations > 400 µg/g dry weight (939 +/− 299 µg/g dry weight). Those dogs with repeatedly normal hepatic copper levels (<400 µg/g dry weight) did not have persistent

hepatitis on liver biopsy (probably due to other reversible causes). These findings suggest that there is a relationship among copper storage, hepatocellular damage and hepatitis in Doberman pinschers.
- An immune-mediated mechanism of disease in affected Dobermans is supported by the finding of up-regulation of major histocompatibility complex class II antigens in hepatocytes.

Signalment and Clinical Signs

- Middle-aged females are predominantly affected.
- Clinical signs may be mild or absent when the disease is fortuitously diagnosed in the early stages. However, most dogs are diagnosed in the advanced stages of hepatic failure.
- Signs include anorexia, weight loss, lethargy, PU/PD, vomiting, diarrhea, ascites, and jaundice.
- Evidence of excessive bleeding (gingival bleeding, epistaxis, and melena) may be found.
- Signs of HE often predominate in the terminal stages.

Diagnosis

Suspect chronic hepatitis in any Doberman pinscher (especially female) with clinical and biochemical evidence of hepatic disease. Definitive diagnosis requires liver biopsy.

- Common physical examination findings include ascites, jaundice, weight loss, and encephalopathy. Splenomegaly (associated with portal hypertension) is common. The liver is small and not palpable.
- Laboratory findings frequently include increased ALP and ALT activity, hyperbilirubinemia, bilirubinuria, hypoalbuminemia, increased SBA levels, and hyperammonemia. Coagulopathy and thrombocytopenia are common in the advanced stages. Consider concurrent von Willebrand disease in affected dogs with a bleeding disorder, because of its prevalence in this breed (see Chapter 23).
- Radiographic and ultrasonographic findings of microhepatica and ascites are consistent with chronic liver disease and cirrhosis.

Liver Biopsy and Copper Analysis

- Liver biopsy and histopathologic evaluation are necessary to confirm the diagnosis.
- Grossly, the liver is small with micronodular or macronodular cirrhosis.
- Histologically, the earliest lesion is inflammation and fibrosis around the small hepatic vein branches. As the disease progresses, fibrous tissue septa radiate from hepatic vein branches to the portal areas. In the late stage of the disease, lymphoplasmacytic inflammation occurs around larger hepatic veins and portal tracts. Fibrosis and architectural distortion consistent with cirrhosis are present.
- Rhodanine and rubeanic acid stains usually are positive for copper, especially in centrilobular regions. Stains for hepatic iron also are usually positive.
- Quantitative copper analysis reveals mild to moderate copper accumulation (650–4000 µg/g dry weight).

Treatment

Optimal treatment has not been established.

- Institute, as needed, symptomatic and supportive therapy for complications of hepatic failure, including correction of fluid, electrolyte, and acid-base balance and treatment of ascites, HE, and coagulopathies (see Table 71-1 and "Principles of Treatment for Liver Disease").
- Therapy with anti-inflammatory or immunosuppressive drugs such as prednisolone with or without azathioprine may be given, as described previously for idiopathic chronic hepatitis. The efficacy of this treatment remains to be determined, but generally the response is poor, possibly because most dogs are presented in advanced stages of liver failure. Doberman pinschers with subclinical hepatitis treated with low doses of prednisolone (0.1–0.5 mg/kg/day) did not show any significant improvement.
- Consider penicillamine therapy, especially when subclinical hepatitis is diagnosed. Five female Doberman pinschers with persistent subclinical hepatitis and increased hepatic copper concentrations were treated with penicillamine (200 mg PO q12h for 4 months). Mean liver copper concentrations decreased from 1036 to 407 µg/g dry weight and improvement in liver histopathology was noted. Whether histopathologic improvement was related to copper-chelating or anti-inflammatory effects of penicillamine could not be ascertained.
- Consider ursodiol therapy in this cholestatic disorder (see Table 71-2). Vitamin E may also provide a beneficial antioxidant effect.

Prognosis

- When Doberman hepatitis is diagnosed in the advanced stages, treatment usually is unsuccessful. Most dogs die within weeks to months.
- The prognosis may be more favorable if the disease is detected in the subclinical stage, but the optimal therapeutic regimen remains to be determined.

Copper-Associated Hepatitis in Dalmatians

Chronic hepatitis and cirrhosis associated with hepatic copper accumulation has been reported in dalmatians. Cholestasis is not a prominent biochemical or histologic feature until later in the disease, suggesting that hepatic copper accumulation is more likely to be caused by a familial metabolic disorder than to be secondary to

altered hepatic biliary copper excretion. Two of the dogs were related.

Clinical Signs

Most dogs presented initially with acute GI signs (anorexia, vomiting, diarrhea).

Diagnosis

- Biochemical findings revealed markedly increased ALT activity (average 10.8 times above normal range) and moderately increased ALP activity (average 5.5 times above normal range).
- Hyperbilirubinemia and hypoalbuminemia were seen with advanced disease. Glucosuria (in the absence of hyperglycemia) and proteinuria were identified in some dogs.
- Liver biopsy revealed hepatocellular degeneration, necrosis, and inflammation (predominantly lymphocytes or neutrophils). The mean hepatic copper concentration was 3197 µg/g dry weight (range of 754–8390 µg/g dry weight).

Treatment and Prognosis

- Rapid progression of the disease was characteristic.
- Copper chelator therapy may be beneficial if diagnosed before advanced liver disease occurs (see Table 71-9).

Copper-Associated Hepatitis in Skye Terriers

Chronic hepatitis and cirrhosis associated with hepatic copper accumulation (range of 358–2257 µg/g dry weight) has been described in genetically related Skye terriers.

- In the early stages, copper accumulation is absent, and biopsy findings indicate hepatocellular degeneration with cholestasis and mild inflammation.
- Chronic lesions are associated with intracanalicular cholestasis, chronic hepatitis, and cirrhosis.
- Skye terrier hepatitis is speculated to be a result of disturbed bile secretion with secondary accumulation of copper.

Chronic Hepatitis in Cocker Spaniels

American and English cocker spaniels have an increased incidence of chronic hepatitis. The cause is unknown. Hepatic copper accumulation does not appear to be a consistent feature. Accumulation of alpha-1-antitrypsin in hepatocytes, a well-recognized cause of cirrhosis in man, may be important in the pathogenesis.

Clinical Signs

- Male cocker spaniels (average age 5 years) are at increased risk. Despite the chronicity and severity of the underlying hepatic lesions, most affected dogs have a short duration of clinical illness prior to presentation of usually 2 weeks or less.
- Ascites is the most consistent presenting complaint. Other nonspecific signs of liver disease include depression, mild jaundice, melena, dehydration, subcutaneous edema, and coma.

Diagnosis

▼ ***Key Point*** Ascites and profound hypoalbuminemia (mean of 1.7 g/dl) are consistent findings.

- Laboratory findings include mild anemia and mild to moderate increases in serum liver enzyme activity (although some dogs have normal values).
- The total serum bilirubin concentration is normal or mildly increased, suggesting that cholestasis is not a key feature of the disorder. FSBA and PPSBA concentrations are increased.
- Ascitic fluid analysis is consistent with a transudate or modified transudate.
- Radiographic findings include microhepatica and ascites. Ultrasonography often shows a diffuse increase in echogenicity, although some dogs have a normal-appearing liver.
- Liver biopsy reveals chronic periportal hepatitis (lymphocytes, plasma cells, and lesser numbers of neutrophils), portal fibrosis, and micronodular or macronodular cirrhosis.
- Hepatic copper accumulation is not a consistent feature (200–550 µg/g dry weight).

Treatment

Treatment for cocker spaniels with chronic hepatitis consists of general supportive therapy for the complications of liver failure (see "Principles of Treatment for Liver Disease" and Table 71-1).

- Corticosteroid therapy may be beneficial.
- The prognosis is poor and most dogs die within a month of diagnosis. Early diagnosis appears to be the key to long-term survival.

Lobular Dissecting Hepatitis

Lobular dissecting hepatitis is a distinctive histologic form of chronic hepatitis that occurs in young dogs. The median age of 21 affected dogs was 11 months, with 54% of dogs being 7 months or younger. It has been suggested that this is a specific reaction pattern of the liver in neonatal and juvenile dogs to a wide variety of hepatic insults. Standard poodles may be at increased risk for this form of chronic hepatitis.

Clinical Signs

Clinical features are those of advanced hepatic failure and portal hypertension. The most consistent clinical finding is ascites.

Diagnosis

An attempt should be made to identify other causes of chronic hepatic disease (see Table 71-8). Diagnosis requires liver biopsy.

- Liver enzymes are typically increased.
- Hypoalbuminemia and increased SBA concentrations are common.
- The lesion is characterized histologically by lobular hepatitis; inflammation (lymphocytes, plasma cells, macrophages, and neutrophils) is scattered throughout the hepatic lobule rather than concentrated in periportal regions. Bands of collagen and reticulin fibers dissect around single or small groups of hepatocytes and disrupt hepatic lobular architecture. Copper stains are negative or moderately positive, consistent with secondary copper accumulation. The liver is shrunken, pale to tan, with an almost smooth surface and occasional hyperplastic nodules. Multiple acquired portosystemic shunts are present.

Treatment

Optimal treatment has not been determined, but general measures for management of chronic liver failure are appropriate (see Table 71-1).

Acidophil Cell Hepatitis

Acidophil cell hepatitis has been described in Great Britain and is caused by an unidentified transmissible agent that is probably viral but distinct from canine adenovirus type 1 (see Chapter 16).

- It is characterized by acute or chronic hepatitis with slow progression to cirrhosis. Acidophils, which are a consistent histologic feature of the disease, represent dying hepatocytes.
- Signs usually are typical of chronic liver failure.
- Specific treatment has not been described, but general measures for management of chronic liver failure are appropriate.

PHENOBARBITAL-ASSOCIATED HEPATIC DISEASE

Long-term phenobarbital therapy for control of seizures has been associated with chronic hepatic disease and cirrhosis in dogs (see Table 71-4). Most dogs have been treated with phenobarbital for months to years before the liver disease is apparent. Chronic phenobarbital therapy also is rarely associated with SND (hepatocutaneous syndrome) in dogs (see previous discussion in this chapter), which is distinct from the characteristic phenobarbital-associated chronic hepatic disease and cirrhosis described in this section.

Etiology

- The mechanism of phenobarbital-induced injury is not known, but higher doses, higher blood levels (>40 µg/ml), and long duration appear to be important factors.
- Prior therapy with phenytoin or primidone may increase the risk of hepatotoxicity.
- Hepatotoxicity has not been described in association with short-term injectable (IV or IM) doses.

Clinical Signs

- Clinical signs are those of chronic hepatic disease and include anorexia, lethargy, weight loss, weakness, PU/PD, coagulopathy, and jaundice. Signs of overdosage (sedation and ataxia) are consistent findings in dogs with phenobarbital hepatotoxicity. Ascites and HE are most likely with advanced hepatic disease.
- When impaired hepatic inactivation of phenobarbital causes increased blood levels, seizure frequency may decrease.
- An increased frequency of seizures may be related to the development of HE.

Diagnosis

Suspect phenobarbital-induced hepatopathy in any dog with a history of chronic phenobarbital therapy and clinical and biochemical evidence of hepatic injury.

Laboratory Evaluation

▼ ***Key Point*** To detect early evidence of hepatic damage, routinely monitor liver enzymes (serum ALP and ALT), total serum bilirubin, cholesterol, albumin, and phenobarbital levels at least every 6 months in all dogs on chronic phenobarbital therapy.

- Mild reversible increases in serum ALP and ALT activity (usually <5 times upper normal limit) are common in dogs treated with phenobarbital related to microsomal enzyme induction rather than hepatocyte injury. The increased ALP is usually attributable to induction of the liver isoenzyme, but sometimes it results from increased CIALP.
- Elevations in ALT and ALP activity greater than 5 times the upper limit of normal or any elevation in AST may be an indicator of hepatotoxicity.
- Increased SBA, hyperbilirubinemia, hypoalbuminemia, and hypocholesterolemia are better indicators of significant hepatic damage.

Radiography and Ultrasonography

▼ ***Key Point*** Dogs on phenobarbital without hepatic injury often have an incidental finding of hepatomegaly.

With phenobarbital-induced chronic hepatic disease, radiographic findings may suggest microhepatica due to cirrhosis. Ultrasonography is useful to further characterize liver changes and to evaluate for other hepatic disorders.

Liver Biopsy

Perform a liver biopsy in dogs on phenobarbital when hepatic function tests are abnormal, liver enzyme activities are greatly increased, clinical signs of hepatic dysfunction are present, or ultrasonographic hepatic abnormalities are detected.

- The most consistent histologic finding in dogs on phenobarbital therapy is hepatocellular hypertrophy with a ground-glass appearance of the cytoplasm. Hypertrophy is due to hyperplasia of smooth endoplasmic reticulum. This finding is commonly identified in dogs without clinical or biochemical evidence of hepatic dysfunction and does not warrant a change in drug therapy.
- Chronic hepatic disease associated with phenobarbital therapy is characterized histologically by biliary hyperplasia, nodular hyperplasia, fibrosis, and cirrhosis. A mild inflammatory infiltrate (neutrophils, lymphocytes, plasma cells) is often present. These lesions are by no means specific for phenobarbital-induced hepatic damage; however, in the absence of other known causes of hepatic damage, circumstantial evidence would support drug therapy as a likely cause.

Treatment

- If possible, discontinue phenobarbital (gradual taper) in dogs with biochemical and histologic evidence of hepatic disease (see Chapter 127).
- Consider replacing phenobarbital with potassium bromide (15–30 mg/kg PO q12h with food) as an anticonvulsant in dogs with phenobarbital-associated hepatotoxicity because of its lack of hepatic metabolism or hepatotoxicity (see Chapter 127).
- Clinical, biochemical, and histologic improvement can occur if phenobarbital is discontinued or used at a reduced dosage prior to severe, end-stage liver disease. Clinical signs improve within days to weeks of decreasing serum phenobarbital levels.
- Additional supportive measures are important in managing dogs with phenobarbital-induced hepatic disease. Control complications such as ascites and HE, as discussed previously (see Table 71-1).
- Consider hepatoprotectants such as ursodiol, SAMe, or vitamin E (see Table 71-2). Corticosteroids are not indicated unless a significant inflammatory component is documented histologically.

Prevention

Despite evidence for hepatotoxicity, phenobarbital is still the drug of choice for long-term control of seizures in dogs.

▼ ***Key Point*** To decrease the likelihood of hepatotoxicity in dogs treated with phenobarbital, monitor serum levels and adjust the dosage so that serum phenobarbital concentrations do not exceed 35 µg/ml.

HEPATIC CIRRHOSIS AND FIBROSIS

Cirrhosis is characterized by diffuse fibrosis and replacement of liver tissue with structurally abnormal regenerative nodules.

Etiology

- Cirrhosis is the irreversible end stage of chronic hepatic injury caused by infection, hepatotoxins (e.g., copper or phenobarbital), immunologic injury (chronic hepatitis), chronic cholestasis (chronic cholangitis in cats), or hypoxia. The common denominator is hepatocyte death, which leads to repair by fibrosis and nodular regeneration.
- When cirrhosis is fully developed, the histologic features of the original inciting injury often are obscured by the cirrhotic changes.

▼ ***Key Point*** Fibrosis, regenerative nodule formation, and structural disruption further compromise adjacent normal hepatocytes, intrahepatic blood flow, and intrahepatic bile flow; thus, cirrhosis eventually reaches a point at which it is self-perpetuating.

Clinical Signs

Cirrhosis causes generalized hepatic dysfunction; thus, the clinical signs are those of chronic hepatic failure. A combination of jaundice, ascites, and HE is highly suggestive of cirrhosis.

Diagnosis

Laboratory Evaluation

Laboratory evidence of liver disease usually precedes the development of cirrhosis but may go undetected because signs at that stage may be insidious and vague.

- Serum liver enzymes usually are increased, although more modestly than during the active injury stage of liver disease.
- Circulating bilirubin, ammonia, and bile acids usually are increased, whereas serum albumin usually is decreased. Hyperglobulinemia is sometimes seen.

- Hemostatic abnormalities may reflect DIC, impaired hepatic synthesis of coagulation factors, or vitamin K deficiency due to cholestasis (least likely).

Radiography and Ultrasonography

▼ ***Key Point*** Microhepatica is common in dogs with cirrhosis, whereas most cats with biliary cirrhosis have hepatomegaly due to marked biliary hyperplasia.

Ultrasonography findings include microhepatica, irregular hepatic margins, focal lesions representing regenerative nodules, and increased parenchymal echogenicity associated with increased fibrous tissue. Splenomegaly and secondary acquired portosystemic shunts also may be detected.

Liver Biopsy

Definitive diagnosis of cirrhosis requires liver biopsy.

- Laparotomy or laparoscopy provides a better appreciation for the gross nodularity of the liver than can be ascertained from blind percutaneous needle biopsy.
- Microscopic features include fibrosis, regenerative nodules, and disruption of normal hepatic architecture.
- Concurrent inflammation may be detected, especially when the inciting cause of cirrhosis is chronic inflammation.

Treatment

Because cirrhosis is essentially irreversible, treatment is mainly supportive, emphasizing measures that control the various complications of severe generalized liver failure, such as ascites, encephalopathy, gastric ulcers, coagulopathies, and infection (see Table 71-1 and "Principles of Treatment for Liver Disease").

If a probable cause or category of injury can be determined, specific treatment directed at preventing further injury may slow progression of cirrhosis. If an underlying cause can be determined (or is suspected), refer to the appropriate section of this chapter for specific details regarding treatment. For example, adjust the drug regimen of dogs receiving phenobarbital (see under "Phenobarbital-Associated Hepatic Disease").

Penicillamine

Use a chelating agent such as penicillamine to treat dogs with copper-positive biopsies (see Table 71-9). Penicillamine also has antifibrotic properties.

Anti-inflammatory Therapy

Treat dogs with histologic features of chronic hepatitis with anti-inflammatory drugs (see under "Idiopathic Chronic Hepatitis"). Prednisolone has antifibrotic properties as well as anti-inflammatory activity; however, weigh the benefits of corticosteroids with the risks of potential adverse effects, such as GI ulceration and bleeding, increased body catabolism that may exacerbate HE, and sodium retention that may exacerbate ascites and edema.

Colchicine

Colchicine (0.025–0.03 mg/kg PO q24h) is an antifibrotic drug used to treat humans with cirrhosis. It acts as a microtubule inhibitor, stimulant of collagenase activity, and inhibitor of collagen deposition. Its benefit in dogs with cirrhosis is unproven. The major side effects in dogs are nausea, vomiting, and diarrhea. In humans, other side effects include bone marrow toxicity and myoneuropathy.

CONGENITAL PORTOSYSTEMIC SHUNTS

Portosystemic shunts (PSSs) are vascular communications between the portal and the systemic venous systems that allow portal blood to access the systemic circulation without first passing through the liver. Clinical signs of HE result from inadequate hepatic clearance of enterically derived toxins such as ammonia, mercaptans, short-chain fatty acids, GABA, and endogenous benzodiazepines. Decreased hepatic blood flow and lack of hepatotrophic factors result in hepatic atrophy.

Etiology

PSS in dogs and cats can be a congenital malformation or develop secondary to portal hypertension.

Single Congenital Portosystemic Shunts

Single PSSs are most common and occur as a congenital developmental malformation. Single shunts are not associated with portal hypertension. Single PSSs can be further categorized as intrahepatic or extrahepatic.

Single Intrahepatic Shunts

- Single intrahepatic shunts provide a communication between the portal vein and the caudal vena cava, often via the left hepatic vein. This results from failure of the fetal ductus venosus to close.
- This type of shunt is most frequent in large-breed dogs.

Single Extrahepatic Shunts

- Single extrahepatic shunts usually connect the portal vein or one of its tributaries (left gastric or splenic vein) with the caudal vena cava cranial to the phrenicoabdominal veins. Less frequently, the anomalous vessel will enter the azygous vein.
- This type of shunt is most frequent in small-breed dogs and cats.

Table 71-10. DISORDERS ASSOCIATED WITH PORTAL HYPERTENSION AND MULTIPLE EXTRAHEPATIC PORTOSYSTEMIC SHUNTS

Chronic hepatitis and cirrhosis
Lobular dissecting hepatitis
Congenital hepatic arteriovenous fistula
Portal vein hypoplasia, including hepatoportal fibrosis variant
Postoperative complication of congenital portosystemic shunt ligation
Chronic biliary obstruction
Portal vein obstruction (thrombosis, neoplasia, extraluminal compression)
Caudal vena cava or main hepatic vein obstruction (kinking, thrombosis, neoplasia)

Multiple Extrahepatic Portosystemic Shunts

Multiple extrahepatic PSSs are collateral vessels that develop as a compensatory response to sustained portal hypertension. These shunts are rudimentary, nonfunctional, microvascular communications between the portal and the systemic veins that are present in normal dogs and cats. With sustained portal hypertension, these vessels enlarge and function to shunt blood into the lower-pressure systemic circulation, thus decreasing portal pressure.

- Multiple extrahepatic PSSs occur secondary to disorders causing portal hypertension (Table 71-10).
- These shunts usually appear as a tortuous plexus of vessels that communicate with the caudal vena cava in the area of the kidneys.
- Diagnosis and therapy are directed toward the underlying liver or portal vascular disorder.

Clinical Signs

The following discussion focuses on single congenital PSS. Clinical signs of congenital PSS are usually referable to the CNS, GI system, or urinary tract (see also under "Signalment," "History," and "Physical Examination" in this section).

Central Nervous System Signs

- Signs of HE often predominate, including episodic weakness, ataxia, head pressing, disorientation, circling, pacing, behavioral changes, amaurotic blindness, seizures, and coma.
- Hypersalivation, seizures, and blindness are more common in cats with PSS than in dogs.
- Clinical signs of encephalopathy tend to wax and wane and are often interspersed with normal periods, reflecting the variable production and absorption of neurotoxic enteric products.

Gastrointestinal Signs

- GI signs of intermittent anorexia, vomiting, and diarrhea are common and are not necessarily accompanied by overt signs of HE.
- Stunted growth, weight loss, failure to gain weight, and unthriftiness are common.

Urinary Signs

▼ ***Key Point*** Urate urolithiasis is an important complication of PSS because of increased urinary excretion of ammonia and uric acid. Renal, cystic, and urethral calculi usually are green and contain an ammonia or uric acid component.

- If urolithiasis is a complicating feature, pollakiuria, dysuria, and hematuria may occur.
- Psychogenic polydipsia and subsequent polyuria are frequent findings in dogs.

Diagnosis

Suspect congenital PSS in the following patients:

- Young dogs and cats with intermittent CNS, GI, or urinary tract signs
- Young animals with unexplained weight loss, failure to grow, unthriftiness, or hypoglycemia
- Dogs (except dalmatians and bulldogs) or cats with urate urolithiasis
- Dogs and cats of any age with clinical and biochemical evidence of hepatic insufficiency (especially HE) and absence of histologic evidence of severe intrahepatic disease

▼ ***Key Point*** In young animals with clinical features of a congenital PSS but without a demonstrable shunt on portography or portal scintigraphy, consider hepatic microvascular dysplasia (see later in this chapter).

Although congenital PSS may be suspected because of historical, physical, laboratory, and radiographic findings, a definitive diagnosis requires identification of a shunt by ultrasonography, contrast radiography, transcolonic or transplenic portal scintigraphy, or exploratory laparotomy.

Signalment

- Congenital PSS is more common in purebred than in mixed-breed dogs. The genetic basis is unknown, although an increased incidence has been recognized in Yorkshire terriers, miniature schnauzers, Irish wolfhounds, Cairn terriers, Maltese dogs, Australian cattle dogs, Old English sheepdogs, Labrador retrievers, and golden retrievers.
- Domestic shorthaired cats are affected more commonly than are purebred cats. Of affected purebreds, Persian and Himalayan cats are at increased risk.
- No sex predilection has been noted. Affected male dogs and cats are often cryptorchid.
- Age is an important diagnostic clue, because most animals develop signs by 6 months of age. A congen-

ital PSS is also a diagnostic consideration in middle-aged and older dogs, because signs may be subtle and occasionally animals go undiagnosed until as old as 10 or 12 years of age.

History

- Many affected animals have a history of stunted growth or failure to gain weight compared with unaffected littermates.
- Prolonged recovery after general anesthesia or excessive sedation after treatment with tranquilizers, anticonvulsants, or organophosphates can be attributed to impaired hepatic metabolism of these substances.
- Signs of encephalopathy may be exacerbated by a protein-rich meal; GI bleeding associated with parasite infection, ulcers, or drug therapy; and administration of methionine-containing urinary acidifiers or lipotrophic agents.
- Clinical improvement after fluid therapy is common and most likely attributed to correction of dehydration and promotion of urinary excretion of ammonia and other toxins. Improvement with broad-spectrum antibiotic therapy reflects the effect of antibiotics on the toxin-producing intestinal flora.

Physical Examination

- Findings may be unremarkable except for small body stature or weight loss.
- The neurologic examination is normal or, if overt signs of HE are present, neurologic findings are consistent with diffuse cerebral disease.
- Ascites and edema are rare unless the shunt is complicated by marked hypoalbuminemia (less than 1 g/dl).
- Many affected cats have copper-colored irises.

Laboratory Evaluation

Routine hematologic and biochemical findings often are unremarkable. Although individual parameters might be only mildly abnormal, test results often reflect a pattern suggesting hepatocellular dysfunction in the absence of significant cholestasis or hepatocellular necrosis.

- Hematologic findings include microcytosis, target cells, poikilocytosis (especially in cats), and mild nonregenerative anemia. Microcytosis is associated with abnormal iron metabolism (impaired iron transport or iron sequestration) rather than absolute iron deficiency. These RBC changes can be subtle but important diagnostic clues in an otherwise normal CBC.
- Urinalysis findings include dilute urine, ammonium biurate crystalluria, and mild bilirubinuria.
- Coagulation tests are normal.
- Hepatocellular dysfunction is suggested by hypoproteinemia, hypoalbuminemia, hypoglobulinemia, hypoglycemia, decreased BUN, and mild hypocholesterolemia. Hypoalbuminemia is a consistent finding in dogs but not in cats. Total serum bilirubin concentration is normal.
- Serum liver enzyme (ALP and ALT) levels are normal to mildly (2–4 times) increased, consistent with a lesion of hepatic atrophy and minimal hepatocellular injury or intrahepatic cholestasis. Increases in ALP activity in these young animals may actually be due to the bone isoenzyme.
- Measure SBA concentrations to document hepatic dysfunction in dogs and cats suspected of having congenital PSS. Fasting SBA concentrations may be normal or increased, but PPSBA concentrations are consistently abnormal and usually exceed 10 µmol/L.

▼ ***Key Point*** The pattern of a normal FSBA concentration with a markedly increased PPSBA level is characteristic of PSS. A consistently normal PPSBA concentration makes a diagnosis of congenital PSS highly unlikely.

- In preliminary studies in dogs with congenital PSS, the sensitivity of urinary bile acids (UBA) (urine sample taken 4 to 8 hours after eating) was 100%, compared with 84% for FSBA and 98% for PPSBA.
- Hyperammonemia is a common finding in animals with PSS, but fasting blood ammonia concentration may be normal. The ATT is consistently abnormal and is equal in sensitivity to PPSBA concentrations for detecting hepatic dysfunction associated with PSS (see "Diagnostic Strategy for Liver Disease").

Radiography and Ultrasonography

Stabilize the patient by instituting therapy for HE prior to giving anesthesia for portography or for surgical correction (see under "Medical Therapy" in this section).

- ***Abdominal radiography*** commonly reveals microhepatica in dogs but not in cats. Mild renomegaly of unknown clinical significance also is common. Intra-abdominal detail may be poor because of lack of abdominal fat. Ammonium urate urinary calculi may be visible on survey radiographs if they contain substantial amounts of magnesium and phosphate.
- ***Routine abdominal ultrasonography*** may demonstrate intrahepatic and extrahepatic shunts. Intrahepatic shunts are more reliably detected with this procedure than are extrahepatic PSS. Urinary calculi also can be identified.
- ***Transcolonic portal scintigraphy*** using technetium 99m pertechnetate is a non-invasive and highly sensitive test (available at some referral institutions) for detecting whether a shunt is present; however, it does not provide reliable anatomic information such as the type and location of the shunt.
- ***Ultrasound-guided transplenic portal scintigraphy*** has recently been described. This procedure provides

more anatomic detail with less radiation exposure than transcolonic portal scintigraphy.

- ***Positive-contrast portography*** is the procedure of choice to accurately characterize the type and location of a PSS. Techniques include splenoportography, mesenteric (or jejunal) portography, and cranial mesenteric or celiac arterial portography. An operative mesenteric portogram is preferred because it allows evaluation of the entire portal vein, does not require special equipment, and results in few complications.

Technique for Mesenteric Portography

1. Place the animal under general anesthesia (see Chapter 2 for anesthesia of the patient with liver disease).
2. Isolate a loop of jejunum through a ventral midline incision.
3. Place two ligatures around a jejunal vein, and place an over-the-needle catheter (Abbocath, Abbott) within the vessel. Tie the ligatures and secure the catheter to the vessel.
4. Temporarily close the abdominal incision.
5. Inject a water-soluble contrast agent (Conray, Mallinckrodt, or Iohexol, Winthrop) as a bolus (2 ml/kg) into the catheter.
6. If a rapid film changer is not available, take a lateral and ventrodorsal radiograph as the final milliliter is injected.

Interpretation

- If a single PSS is identified, it should be further characterized as intrahepatic or extrahepatic, because this has important surgical ramifications (see Chapter 72).
- If multiple extrahepatic PSSs are identified, portal pressure determination and gross and microscopic findings of the liver are used to distinguish between congenital and acquired causes (see the next section).
- Failure to visualize the intrahepatic portal system is not a reliable indicator of vascular atresia but may correlate with a greater occurrence of postoperative complications after complete or partial shunt ligation.

Liver Biopsy

- The liver is grossly small but otherwise fairly normal in appearance.
- In some animals, biopsy findings are unremarkable.
- Liver biopsy lesions can be subtle but most consistently reveal hepatocyte atrophy with small or absent portal veins. Varying degrees of arteriolar hyperplasia, lipogranulomas, and biliary hyperplasia may be seen. Hepatocellular vacuolization is sometimes noted and may be severe. These biopsy findings reflect decreased portal blood flow and are indistinguishable from those seen in animals with hepatic microvascular dysplasia, primary hypoplasia of the portal veins, or portal vein obstruction or after experimental surgical creation of a PSS.
- Microscopic CNS abnormalities include polymicrocavitation of the brain stem and cerebellum and an increased number of astrocytes in the cerebral cortex.

Treatment

Surgery

- The treatment of choice for dogs and cats with a single PSS is surgical attenuation or complete ligation of the shunt (see Chapter 72). Although complete shunt ligation is preferred for improved long-term outcome, concurrent hypoplasia of the portal system (whether as a primary vascular disorder or secondary to prolonged portosystemic shunting), may increase intrahepatic vascular resistance and predispose the patient to portal hypertension. Consequently, attenuate the shunt to the maximum degree that can be tolerated without causing portal hypertension.
- Highly successful alternative approaches for gradual progressive closure of the shunt use surgically placed ameroid constrictors or cellophane bands around the shunt or intravascular thrombogenic coils within the lumen of the shunt (see Chapter 72). Theoretical advantages of slow attenuation of the shunt (over days to weeks) include reduced risk of postoperative portal hypertension and neurologic dysfunction and decreased surgical and anesthetic time.

▼ ***Key Point*** Gradual occlusion of the shunt should allow time for hepatic regeneration, expansion of the portal vascular system, and accommodation of portal blood flow without portal hypertension.

Medical Therapy

Medical management of dogs and cats with PSS is palliative and is directed primarily at control of HE with a moderately protein-restricted diet supplemented with soluble fiber, lactulose, and neomycin (see Table 71-1).

- The short-term response to therapy for HE is often dramatic, and the animal usually is clinically normal even prior to surgical shunt ligation.
- If surgical shunt correction is not feasible or is declined by the owner, long-term medical management may control clinical signs for as long as 2 to 3 years. However, medical management of PSS does not reverse the progressive hepatic atrophy and alterations in carbohydrate, lipid, and protein metabolism.
- Acute decompensation of encephalopathy requires fluid therapy for correction of dehydration, correction of electrolyte and acid-base imbalances, and maintenance of blood glucose levels (see Table 71-1).

- When severe CNS depression or coma prevents the oral administration of lactulose and neomycin, administer these drugs via an enema (see Table 71-1).
- Identify and correct precipitating causes of encephalopathy whenever possible, such as hypoglycemia, GI bleeding from hookworm infection, and hypokalemia (see Table 71-1).
- Management of urate urolithiasis is discussed in Chapter 79.

Perioperative Complications

Other perioperative complications of shunt ligation include seizures, portal hypertension, intra-operative hypothermia and hypoglycemia, anesthetic complications, fever and positive blood cultures, portal vein thrombosis, coagulopathy, acute pancreatitis, and cardiac arrhythmias.

Postoperative Seizures

Occasionally, seizures or status epilepticus are a complication of surgical shunt ligation. Dogs older than 18 months of age may be at increased risk. The pathogenesis is obscure, but seizures do not appear to be caused by simple hypoglycemia or HE. It is possible that the brain may have adapted to an altered metabolism. The prognosis for recovery from this complication is poor. Long-term anticonvulsant therapy is often required if the patient survives the acute postoperative period.

▼ ***Key Point*** Evaluate for identifiable metabolic causes of postoperative seizures, such as hyperammonemia, hypoglycemia, hypoxia, electrolyte imbalances, acid-base imbalances, and systemic hypertension.

- In addition to routine management of HE and correction of underlying metabolic imbalances (including thiamine administration in cats), manage seizures with IV phenobarbital (at reduced doses) or loading doses of potassium bromide (see Table 71-1 and Chapter 127).
- If seizures cannot be controlled, administer IV propofol to induce general anesthesia for 12 to 24 hours. Place an endotracheal tube and use a respirator to maintain pO_2 and pCO_2. Maintain anesthesia by propofol drip or isoflurane gas anesthesia. Consider mannitol (0.5–1 g/kg IV) for control of cerebral edema (see Table 71-1).
- Consider preoperative anticonvulsant therapy to help control or prevent postoperative seizures in PSS patients (see Table 71-1). Felbamate, levetiracetam, or topiramate are possible choices in dogs. Because of the short half-life of these drugs, therapeutic blood levels can be reached within a week. Topiramate can be used in cats. If postoperative seizures do not occur, anticonvulsant therapy can be tapered over a 4-week period after surgery and then discontinued.

Prognosis

Dogs

The prognosis for resolution of signs after total surgical ligation of the shunt in dogs is excellent if the dog survives the immediate postoperative period.

- In dogs with partial shunt ligation, the prognosis is not as good. Although clinical signs may resolve after surgery, and response appears favorable in the first few years, long-term follow-up (>3 years) suggests recurrence of signs will occur in 40% to 50% of dogs with partial shunt ligations.
- If clinical signs recur in dogs that have had partial ligation, reevaluate by transcolonic portal scintigraphy. If shunting persists, perform surgical exploration for complete shunt closure by suture ligation or ameroid constrictor.

Cats

The response to surgical correction of a congenital PSS in cats appears to be less encouraging than in dogs. With partial shunt ligation, clinical improvement is usually noted after surgery, but relapse of neurologic abnormalities is common. Persistent seizures and blindness are also more likely to occur when partial rather than total ligation is performed.

HEPATIC MICROVASCULAR DYSPLASIA

Hepatic microvascular dysplasia (HMD) refers to congenital histologic vascular abnormalities of the liver in dogs (and rarely in cats) that result in abnormally increased SBA concentrations and may be associated with clinical signs of portosystemic shunting of blood. It has been hypothesized (but not proven) that HMD results in intrahepatic microscopic portosystemic shunting of blood. Because the shunt fraction is small compared with shunting that occurs with a single macroscopic congenital PSS, the clinical signs are less severe (or absent) and SBA concentrations are only mildly increased. Portal hypertension is not a clinical feature of HMD for most affected dogs.

- The relationship among HMD, congenital PSS and primary hypoplasia of the portal veins is unclear. These disorders have similar hepatic histologic features (hepatic arteriolar hyperplasia, small or absent portal veins, and hepatic lipogranulomas), which are a stereotypical histologic response of the liver to inadequate portal vein flow. These same histologic findings also develop after experimental surgical creation of a PSS. These disorders may represent varying expressions of a more general developmental vascular disorder.
- It is likely that most animals with PSS have some degree of HMD, which may explain the persistence

of increased SBAs and histologic vascular lesions following complete surgical ligation of a PSS in some cases. If vascular dysplasia accompanying PSS is severe enough (e.g., primary hypoplasia of the portal veins), complete PSS ligation cannot be performed without the development of portal hypertension.

Etiology

HMD has been studied extensively in Cairn terriers, where it is believed to be an inherited disorder. A polygenic mechanism of inheritance is suspected.

Clinical Signs

Affected dogs and cats may be asymptomatic (especially true for Cairn terriers) or show signs similar to those seen with congenital PSS.

- Drug intolerance for products dependent on hepatic metabolism may be the only manifestation in otherwise asymptomatic patients.
- In symptomatic animals, signs are variable and include anorexia, lethargy, vomiting, diarrhea, PU/PD, dysuria and hematuria (due to urate urolithiasis), and HE and seizures.

Diagnosis

Consider HMD in dogs and cats with clinical features of congenital PSS, increased SBA concentrations, and typical liver biopsy findings and in those that do not have a demonstrable shunt.

- In symptomatic animals, it is essential to rigorously pursue the diagnosis of congenital PSS (as described in the previous section), because the clinical and histologic features of HMD alone are similar to those of congenital PSS. Specific surgical correction is the optimal treatment if a shunt is identified.
- Also consider the possibility that a dog or cat with increased SBA concentrations may have HMD and be asymptomatic for the disorder (especially Cairn terriers). An animal with HMD may have clinical signs due to an unrelated non-hepatic disease. Detection of increased SBA concentrations may focus diagnostic efforts on the liver, causing the clinician to overlook the true cause of the clinical signs.

Signalment

- Yorkshire terriers and Cairn terriers are most commonly affected. However, HMD has been diagnosed in many other small breeds of dogs, such as Maltese, dachshund, poodle, Shih Tzu, Lhasa apso, cocker spaniel, and WHWTs.
- Domestic shorthair cats are at increased risk for HMD.
- Dogs with HMD tend to be older at presentation than dogs with congenital PSS.

Physical Examination

Physical examination is often within normal limits unless signs of HE are present.

Laboratory Evaluation

- Dogs with HMD consistently have increased SBA concentrations, but not as increased as in dogs with PSS. A shunting pattern is typically seen: normal or low FSBA concentrations with moderately increased PPSBA concentrations. Indocyanine green clearance values are also consistently abnormal.
- Biochemical findings in dogs with HMD are usually unremarkable except for mild to moderate increases in ALT activity.

▼ ***Key Point*** As opposed to dogs with congenital PSS, dogs with HMD do not usually have microcytosis, hypoalbuminemia, decreased BUN, hypocholesterolemia, hypoglycemia, hyperammonemia, or ammonium biurate crystalluria.

- Preliminary results show that decreased protein C concentrations occur in 98% of dogs with congenital PSS but only 30% of dogs with HMD. Whether this test will be useful for differentiation of PSS versus HMD awaits further clinical studies.

Radiography and Ultrasonography

- Radiographically, the liver is usually normal in size but may be equivocally small in some cases.
- On ultrasonography the liver may be subjectively decreased in size and the portal vasculature may be decreased. Bladder or kidney stones are uncommon.
- Transcolonic portal scintigraphy is usually normal or only mildly abnormal in HMD, as opposed to the increased shunt fractions seen with congenital PSS. Since this is a relatively sensitive method for detecting congenital PSS, a normal exam would make PSS unlikely and support a diagnosis of HMD.
- Portography will fail to identify a large shunting vessel. Cairn terriers with HMD have abnormal truncation of the terminal branches of the portal veins and delayed clearing of contrast, which gives the parenchyma a “blush” appearance.

Liver Biopsy

A wedge biopsy of the liver is preferred over a needle biopsy because the vascular lesions are subtle and a wedge biopsy provides more hepatic lobules for evaluation.

- Grossly, the liver is normal in size and color compared with the small liver seen with congenital PSS.
- The histologic features of HMD are typical for inadequate portal vein flow and include small or absent portal veins, hepatic arteriolar hyperplasia, and

hepatic lipogranulomas. These findings are similar to those seen in dogs with congenital PSS, primary hypoplasia of the portal vein, portal vein obstruction, or after experimental surgical creation of a PSS.

▼ ***Key Point*** Biopsy more than one lobe in HMD because the histologic lesions can vary among liver lobes, with some lobes appearing very abnormal and others appearing normal.

Treatment and Prognosis

- No treatment is indicated for animals whose symptoms are subclinical.
- If clinical signs of HE are present, they can often be successfully managed with a moderately protein-restricted diet. Additional therapy with lactulose and antibiotics is sometimes warranted (see Table 71-1).
- Follow-up in 11 dogs for a mean period of 15 months (range of 1 week to 4.5 years) indicated a good clinical response to dietary therapy alone. Repeated SBA concentrations remained unchanged. How often dogs that are asymptomatic for HMD progress and develop clinical signs is unknown.
- Anecdotal reports suggest some severely affected dogs may develop a progressive hepatopathy with portal hypertension and multiple extrahepatic PSSs, similar to primary hypoplasia of the portal veins (see below).

PRIMARY PORTAL VEIN HYPOPLASIA

Primary portal vein hypoplasia (PPVH) is a congenital abnormality of portal vascular development seen in young medium- to large-breed dogs. Small intrahepatic portal venules are predominantly affected, although hypoplasia of the extrahepatic portal vein may occur in 30% of dogs. Underdevelopment of the portal system leads to obstruction to portal blood flow resulting in portal hypertension and development of multiple extrahepatic PSSs.

- Dogs described in the literature with *idiopathic noncirrhotic portal hypertension* have clinical and pathologic findings that resemble portal vein hypoplasia, and these are now considered the same disorder.
- In addition to the vascular changes, variable amounts of fibrosis may be present in portal areas, leading to the suggestion that *hepatoportal fibrosis* of young dogs is a variant of portal vein hypoplasia.
- It has also been proposed that HMD (discussed in the previous section) is a milder variant of PPVH and that the term HMD should be abandoned. Although histologic features are similar, the clinical presentations of HMD and PPVH are distinctly different. HMD is not typically associated with portal hypertension (or even clinical signs in many cases), whereas the clinical features of PPVH are primarily related to marked portal hypertension and subsequent portosystemic shunting. Thus, we advocate retaining the clinical distinction between HMD and PPVH until definitive clarification is available.

Signalment and Clinical Signs

The mean age is about 2 years. Medium- or large-breed dogs appear to be at increased risk. In one study, one unrelated and three related Doberman pinschers were reported. Related cocker spaniels have also been described.

- Common clinical signs include lethargy, weight loss or stunted growth, intermittent vomiting and diarrhea, ascites, and polydipsia. Neurologic signs of hepatoencephalopathy may occur but are inconsistent.
- The duration of clinical signs may range from a few weeks to a year. Most dogs have persistent signs for 2 to 3 months.

▼ ***Key Point*** Clinical signs of PPVH are similar to those seen in dogs with single congenital PSSs, except that ascites is common in PPVH and rare in dogs with congenital PSS.

Diagnosis

Laboratory Evaluation

- Laboratory findings are consistent with hepatic dysfunction and portosystemic shunting and include microcytosis, hypoalbuminemia, decreased BUN, and mild increases in ALP and ALT (2–4 times normal).
- A pattern of normal to mildly increased FSBA concentrations accompanied by markedly increased PPSBA values is consistent with portosystemic shunting.
- Hyperammonemia and an abnormal ATT are also consistent features.
- Ascitic fluid is typically a transudate.

Radiography and Ultrasonography

- Survey abdominal radiographs reveal microhepatica and poor intra-abdominal contrast.
- Microhepatica and abdominal effusion are common findings on ultrasonography. Liver echotexture is variable. Multiple extrahepatic PSSs appear as enlarged tortuous vessels caudal to the liver. Splenomegaly may also be detected.
- Ultrasonography can also provide important information regarding other disorders associated with portal hypertension, multiple PSSs, and ascites. With chronic end-stage liver disease, the liver may be small and hyperechoic with multiple regenerative nodules. Congenital hepatic arteriovenous fistulas appear as tortuous, anechoic tubular structures in the liver.

Laparotomy and Contrast Portography

Multiple PSSs can be confirmed by contrast portography or at exploratory laparotomy (or necropsy). Multiple PSSs usually appear as multiple tortuous vessels that communicate with the caudal vena cava in the area of the left kidney.

- The portal pressure can be measured to document portal hypertension (normal portal pressure is 6 to 13 cm of water).
- Patency of the portal vein should be verified (by mesenteric portography or at surgery) since portal vein obstruction could cause similar clinical and radiographic features. With PPVH, the extrahepatic portion of the portal vein is patent but may be underdeveloped.
- Congenital hepatic arteriovenous fistulas can be diagnosed by celiac arteriography or exploratory laparotomy.

Liver Biopsy

Liver biopsy is essential to confirm the diagnosis and rule out primary intrahepatic disorders such as chronic hepatitis and cirrhosis that can cause secondary portal hypertension and multiple acquired PSSs and that would have a different treatment and long-term prognosis.

- Grossly, the liver in PPVH is small and smooth or slightly irregular.
- Microscopically, the portal veins in the portal triads are small or absent. Other features include arteriolar hyperplasia, hepatocyte atrophy, and absence of inflammation with variable bile duct proliferation, lymphatic distention, and portal fibrosis (which is sometimes severe).
- Progressive fibrosis has been documented in some dogs with PPVH undergoing serial liver biopsies.

Treatment and Prognosis

Specific treatment for PPVH is not available. Initiate symptomatic therapy to control the consequences of portal hypertension and portosystemic shunting, such as ascites and HE (see Table 71-1 and "Principles of Treatment for Liver Disease"). The long-term prognosis is variable, but some dogs can live for years on medical management. Owners should be discouraged from electing euthanasia for affected dogs until medical management has been tried.

- Avoid indiscriminate dietary protein restriction since it can worsen hypoalbuminemia and promote ascites formation. Although ascites is a common presenting sign, it may resolve over time and diuretics can be discontinued.
- Use H_2 receptor blockers indefinitely because perforated duodenal ulcer is a potential cause of death in PPVH (see Table 71-1).
- Consider colchicine (0.025 mg/kg PO q24h) and ursodiol (15 mg/kg PO q24h) to prevent progressive hepatic fibrosis.

▼ ***Key Point*** Surgical ligation of multiple acquired PSSs is contraindicated. Ligation may result in fatal portal hypertension because shunts form as a protective compensatory response to portal hypertension. Also, do not perform caudal vena caval banding.

HEPATIC ARTERIOVENOUS FISTULA

Intrahepatic arteriovenous (AV) fistulas are vascular communications between the hepatic artery and the portal vein that result in portal hypertension, ascites, and secondary PSSs. They occur rarely in dogs and cats.

Etiology

Intrahepatic AV fistulas may be congenital, which is most common, or acquired as a result of abdominal trauma, hepatic surgery, hepatic neoplasia, cirrhosis, or rupture of a hepatic artery aneurysm.

Clinical Signs

Signs are similar to those of congenital PSS and PPVH and include anorexia, lethargy, vomiting, diarrhea, PU/PD, and encephalopathy in a young animal (usually less than 1.5 years).

Diagnosis

Historical and physical findings are similar to those in congenital PSS, with the notable exception that marked ascites is a consistent finding with hepatic AV fistulas but is uncommon with congenital PSS.

- Other causes of ascites to be differentiated include hypoproteinemia and right-sided congestive heart failure and other causes of portal hypertension and multiple PSSs, such as PPVH (see the preceding section and Table 71-10).
- Auscultate the abdominal wall over the area of the liver for a continuous murmur (bruit) caused by runoff of arterial blood into the portal system.

Laboratory Evaluation

- Laboratory abnormalities are similar to those seen in congenital PSS and PPVH and include hypoproteinemia, normal or mildly increased serum liver enzyme activity, and abnormal liver function tests including FSBA, PPSBA, blood ammonia, and ATT.
- Ascitic fluid typically is a transudate.

Radiography and Ultrasonography

- Survey radiographs show marked ascites.
- On abdominal ultrasonography, hepatic AV fistulas appear as tortuous, anechoic tubular structures in the liver. Multiple extrahepatic PSSs may also be identified.

Laparotomy

- Confirm the diagnosis by celiac arteriography or exploratory laparotomy. Grossly, AV fistulas appear as thin-walled, tortuous, pulsating vascular channels that distort the hepatic parenchyma and elevate the overlying hepatic capsule.

Treatment

Partial hepatectomy is indicated for treatment of hepatic AV fistulas involving one liver lobe (see Chapter 72). Dearterialization is required if multiple lobes are involved.

- Despite resection of involved liver lobes, hepatic function may not return to normal because of persistent shunting of portal blood through acquired PSS or concurrent PPVH.
- Medical management of HE with a moderately protein-restricted diet, lactulose, and antibiotics is indicated (see Table 71-1).

HEPATOBILIARY NEOPLASIA

Neoplasms involving the liver can be categorized as primary hepatic tumors (of either epithelial or mesodermal origin), hemolymphatic tumors, or metastatic tumors (Table 71-11). Hemolymphatic tumors (especially lymphoma) are the most common type of neoplasia involving the liver of cats. Metastatic tumors to the liver are most common in dogs, especially hemangiosarcoma, islet cell carcinoma, pancreatic carcinoma, and fibrosarcoma. Hepatic lymphoma also occurs frequently in dogs.

Primary hepatic tumors occur infrequently in dogs and cats. They are usually of epithelial origin and are derived from either hepatocytes or biliary epithelium. They can be either benign or malignant.

- A benign tumor of the hepatocytes is called a *hepatocellular adenoma* (or hepatoma), and its malignant counterpart is called a *hepatocellular carcinoma.*

▼ ***Key Point*** A hepatocellular carcinoma is the most common primary hepatic tumor in dogs.

- A benign tumor arising from the biliary epithelium is called a *biliary adenoma.* The malignant form is called a *biliary carcinoma.* Biliary carcinomas may be intrahepatic, extrahepatic, or within the gallbladder. The intrahepatic form is most common in dogs and cats. Cystic forms of these tumors (cystadenocarcinoma, cystadenoma) have also been described.

▼ ***Key Point*** Biliary carcinomas and adenomas are the most common primary hepatic tumors in cats.

- Hepatocellular carcinoma and bile duct carcinoma occur in three pathologic forms: (1) solitary, a single large mass in one liver lobe with or without smaller masses in other lobes; (2) multifocal nodular, discrete nodules of varying sizes in several liver lobes; and (3) diffuse, infiltration of large portions of the liver with non-encapsulated, highly invasive neoplastic tissue. Solitary masses are most likely to be successfully resected surgically. In dogs with hepatocellular carcinoma, approximately half of the tumors are solitary and half are multifocal or diffuse. Biliary carcinomas are more likely to be the multifocal or diffuse form.

Table 71-11. HEPATIC NEOPLASIA IN DOGS AND CATS

Primary Hepatic Neoplasia
Epithelial Origin
Hepatocellular carcinoma
Hepatocellular adenoma
Biliary carcinoma (cholangiocarcinoma, biliary cystadenocarcinoma)
Biliary adenoma (including biliary cystadenoma)
Hepatic carcinoid
Mesodermal Origin
Hemangiosarcoma
Hemangioma
Leiomyosarcoma
Fibrosarcoma
Liposarcoma
Myxosarcoma
Osteosarcoma
Myelolipoma
Fibroma
Hemolymphatic Tumors
Lymphoma
Mast cell tumor
Myeloproliferative disorders
Plasma cell tumor
Metastatic Hepatic Neoplasia
Hemangiosarcoma
Islet cell carcinoma
Pancreatic carcinoma
Fibrosarcoma
Osteosarcoma
Transitional cell carcinoma
Intestinal carcinoma
Renal cell carcinoma
Pheochromocytoma
Thyroid carcinoma
Mammary carcinoma

Etiology

The cause of spontaneous primary hepatic neoplasms in dogs and cats is not usually determined. Some potential causes based on reports of experimental and spontaneous hepatic tumors include aflatoxins, nitrosamines, aramite, liver flukes *(Clonorchis* spp. *Platynosomum concinnum),* and radioactive compounds such as strontium-90 and cesium-144. In contrast to humans, no association with viral infections has been identified in spontaneous tumors of dogs and cats.

Clinical Signs

Dogs and cats with hepatic neoplasia usually show vague signs of hepatic dysfunction that often do not appear until the more advanced stages of hepatic disease.

- The most consistent signs in dogs are anorexia, lethargy, weight loss, PU/PD, vomiting, and abdominal distention. Other signs include jaundice, diarrhea, and excessive bleeding.
- Signs of CNS dysfunction such as depression, dementia, or seizures can be attributed to HE, hypoglycemia, or CNS metastases.
- Anorexia and lethargy are the most common presenting signs in cats; ascites and vomiting are uncommon in cats as compared with dogs.
- When the liver is secondarily involved with metastases, the clinical signs may reflect the primary tumor location or other metastatic sites rather than the hepatic involvement.

Diagnosis

Suspect hepatobiliary neoplasia in any older animal with clinical and biochemical evidence of hepatic disease accompanied by hepatomegaly.

Signalment

- Primary hepatic neoplasms are most common in dogs and cats that are older than 10 years of age.
- Labrador retrievers were found to be disproportionately represented in one study of dogs with biliary carcinoma.
- Male dogs and cats may be at increased risk for hepatocellular carcinoma.
- Male cats and female dogs have an increased risk for biliary carcinoma.

Physical Examination

- Findings often include a cranial abdominal mass or marked hepatomegaly. Hepatomegaly is less likely with metastatic tumors.
- Ascites or hemoperitoneum may contribute to abdominal distention. Tumor rupture and hemorrhage is most likely with hepatocellular adenoma, hepatocellular carcinoma, and hepatic hemangiosarcoma.
- Anemia and pale mucous membranes may be attributed to excessive hemorrhage from a ruptured neoplasm or anemia of chronic disease.
- Jaundice is a less frequent finding with hepatic tumors unless the tumor mass causes obstruction of the common bile duct.
- Severe weight loss and cachexia are common but nonspecific findings.
- Myasthenia gravis causing weakness was suspected to be a paraneoplastic syndrome in a dog with biliary carcinoma.

Laboratory Evaluation

Hematologic and biochemical findings in animals with hepatic neoplasia are not specific and are indicative of hepatic disease and its complications.

- Potential hematologic findings include anemia and leukocytosis. Anemia is usually nonregenerative but may be regenerative if associated with excess bleeding or tumor rupture. When hematopoietic or lymphoid malignancies secondarily involve the liver, abnormal cells or pancytopenia may be detected on peripheral blood smears because of concurrent bone marrow involvement.
- Mild to marked increases in serum liver enzyme (ALT and ALP) activity are common in dogs with primary hepatic tumors (60–100% of cases) but less so with metastatic neoplasia. In contrast, most cats with nonhematopoietic hepatic neoplasms have increased serum ALT or AST activity, but serum ALP activity is usually normal. Increased serum AST activity may be the most sensitive indicator of metastatic hepatic disease in dogs (80% of cases) but lacks specificity.
- Hyperbilirubinemia appears to be a more frequent finding in dogs with metastatic neoplasia than in those with primary hepatic tumors (59% versus 25%).
- Hypoglycemia, sometimes severe, occasionally is noted in dogs with hepatocellular carcinoma and less frequently with hepatocellular adenoma, leiomyosarcoma, and hemangiosarcoma. Serum insulin concentrations are normal to decreased. Potential mechanisms of hypoglycemia include excess utilization of glucose by the tumor, release of insulin-like factors from the tumor, release of other substances from the tumor such as somatostatin, and secondary hepatic parenchymal destruction with impaired glycogenolysis or gluconeogenesis.
- Other biochemical findings are quite variable and include hypoalbuminemia, hyperglobulinemia, and increased SBA concentrations. The magnitude of increase in SBA concentrations in dogs with hepatic neoplasia can be quite small; SBA concentrations may be within normal limits.
- Although clinical evidence of impaired hemostasis is infrequent, prolongation of the PT and APTT may be identified in dogs with hepatic neoplasia.

- Analysis of abdominal fluid usually indicates a transudate or modified transudate; however, neoplastic cells or a bloody effusion are occasionally noted.
- Increased serum alpha-fetoprotein concentration may be an indicator of hepatocellular carcinoma and biliary carcinoma in dogs. Increased alpha-fetoprotein secretion also occurs with marked hepatic regeneration and chronic hepatitis. Alpha-fetoprotein concentrations in cats with hepatic neoplasia have not been reported.

Radiography

- Abdominal radiographic findings in animals with hepatic neoplasia include symmetrical or asymmetrical hepatomegaly and ascites.
- Perform thoracic radiographs to detect pulmonary metastases.

Ultrasonography

The diagnosis of hepatic neoplasia cannot be made based on ultrasonographic findings alone; however, ultrasonography often reveals focal, multifocal, or diffuse changes in hepatic echotexture.

- Hepatocellular carcinoma usually appears as a focal hyperechoic mass.
- Primary or secondary neoplasia and nodular hyperplasia often appear as focal or multifocal hypoechoic or mixed echogenic lesions.
- *Target lesions,* consisting of an echogenic center surrounded by a more sonolucent rim, are often neoplastic.
- Hepatic lymphoma is quite variable and may appear as a mild diffuse hyperechogenicity or hypoechogenicity, multifocal hypoechoic lesions, or a mixed echogenic pattern; alternatively, the appearance may be normal.

Liver Biopsy

Definitive diagnosis of hepatic neoplasia requires liver biopsy and histopathologic evaluation.

- *Laparotomy* is the procedure of choice for a single, large hepatic mass because excision of the mass can also be performed concurrently.
- *Ultrasound-guided biopsy* is useful to diagnose focal or diffuse hepatic involvement, but the small size of the biopsy can make differentiation of nodular hyperplasia versus primary hepatic neoplasia difficult. A wedge biopsy obtained at surgery is often necessary.
- *Blind percutaneous needle biopsy* and *FNA* cytology are most useful for diagnosis of diffuse hepatic neoplasias such as lymphoma, myeloproliferative disorder, and mast cell tumor.

Treatment

Surgery

Surgical removal of the affected liver lobe is the treatment of choice for primary hepatic neoplasms such as hepatocellular adenoma or carcinoma that involve a single lobe (see Chapter 72). Early detection prior to metastasis to other liver lobes affords the best chance for surgical control.

- Surgical resection of a bleeding mass may provide palliative therapy despite the presence of metastatic disease.
- Perform a complete exploratory of the abdominal cavity for evidence of metastases, and biopsy hepatic lymph nodes.
- When all lobes are affected, the prognosis is poor.

Chemotherapy

▼ ***Key Point*** Chemotherapy is not an effective means of control for primary liver tumors in dogs and cats.

Secondary hepatic neoplasms such as lymphoma, mast cell tumor, or myeloproliferative disease might temporarily respond to chemotherapeutic intervention (see Chapters 26 through 28).

HEPATIC NODULAR HYPERPLASIA

Nodular hyperplasia of the liver is a common benign postmortem finding in dogs more than 8 years of age. In one study, hepatic nodular hyperplasia was present in all dogs older than 14 years of age. It appears to be an age-related change, but the cause is unknown. It is not a preneoplastic disorder. The number of nodules ranges from just a few to multiple nodules in a random distribution throughout all liver lobes. They may be microscopic or macroscopic with distortion of the hepatic surface. With extensive involvement, nodular hyperplasia can grossly mimic macronodular cirrhosis or neoplasia. Occasionally, single hyperplastic nodules can become quite large and mimic a hepatocellular adenoma both clinically and microscopically.

Clinical Signs

- Nodular hyperplasia is not usually associated with clinical signs.

Diagnosis and Treatment

- Hepatic nodular hyperplasia can cause mild to moderate increases in serum liver enzymes, especially ALP activity. Other tests of liver function are typically normal.

- These benign lesions should be considered in the differential diagnosis when hepatic nodules are identified during ultrasonography, laparoscopy, or surgery. Ultrasonographically, many hyperplastic nodules are not detected because they are isoechoic to adjacent liver tissue. However, they may have a variety of echotextures and appear similar to primary or secondary hepatic neoplasia, requiring histopathology to distinguish these disorders. Preliminary studies suggest magnetic resonance imaging may be useful in differentiating benign from neoplastic focal hepatic lesions in dogs.
- FNA cytology commonly reveals vacuolated hepatocytes suggestive of fat or glycogen accumulation. Extramedullary hematopoiesis composed of predominantly segmented and band neutrophils may also be identified.

▼ ***Key Point*** Needle biopsies often do not provide adequate tissue for pathologists to diagnose nodular hyperplasia.

- If needle biopsy only describes vacuolated hepatocytes, the clinician may be misled to search for causes of metabolic disease, such as hyperadrenocorticism.
- A wedge biopsy may be necessary to differentiate nodular hyperplasia from hepatocellular carcinoma and hepatoma.
- No treatment is required.

HEPATIC CYSTS

Single or multiple diffuse hepatic cysts occasionally are identified in the liver of dogs and cats, usually as incidental findings at necropsy but occasionally in the live animal.

Etiology

Hepatic cysts can be congenital or acquired, although the distinction is often difficult to make. In general, acquired cysts are usually solitary and congenital cysts are often multiple.

- Congenital polycystic disease of the liver and kidneys has been reported in Cairn terriers and WHWTs.
- Polycystic renal disease in cats has been associated with cystic dilation of the intrahepatic bile ducts (see Chapter 77).
- Acquired cysts may represent benign bile duct adenomas or biliary cystadenomas or may occur secondary to trauma.
- Peliosis hepatis, a vasculoproliferative disorder characterized by cystic, blood-filled spaces in the liver, is a rare disease in dogs and cats. Infection with *Bartonella henselae* was confirmed by polymerase chain reaction of liver tissue in a dog with peliosis hepatis.

Clinical Signs

- Most solitary hepatic cysts do not cause any clinical signs unless they compress or displace adjacent structures. Signs are more likely to occur when congenital polycystic disease is accompanied by dilation of the extrahepatic biliary tract.
- Abdominal enlargement secondary to an enlarged cyst or abdominal fluid accumulation can be a presenting sign. Peliosis hepatis may be associated with intra-abdominal hemorrhage.

Diagnosis and Treatment

- Hepatic cysts should be considered in the differential diagnosis of any cavitated hepatic mass lesion detected on palpation, radiography, or ultrasonography.
- Surgery can confirm the diagnosis and allow excision of large solitary cysts (see Chapter 72).

FELINE INFLAMMATORY LIVER DISEASE

Inflammatory diseases of the liver are the second most common type of feline liver disease, after hepatic lipidosis. The cause, pathogenesis, natural history, and optimal treatment of inflammatory liver disease in cats are largely unknown. Various terms have been used to describe these disorders, such as cholangitis or cholangiohepatitis complex, suppurative cholangiohepatitis, non-suppurative cholangiohepatitis, lymphoplasmacytic cholangiohepatitis, lymphocytic cholangitis, progressive lymphocytic cholangitis, lymphocytic portal hepatitis, sclerosing cholangitis, and biliary cirrhosis.

- Recently, the World Small Animal Veterinary Association (WSAVA) Liver Diseases and Pathology Standardization Research Group developed a classification system with the goal of worldwide standardization of terminology for histologic evaluation of liver diseases in dogs and cats.
- The term *cholangitis* is preferred over *cholangiohepatitis* because the inflammation primarily originates in the bile ducts, and extension beyond the limiting plate into the hepatic parenchyma (cholangiohepatitis) is not always a feature. Cholangitis is further divided into neutrophilic (acute or chronic) or lymphocytic cholangitis. This classification scheme will be used for the purposes of the following discussion.

Neutrophilic Cholangitis

Neutrophilic cholangitis (also called *suppurative cholangitis*) is the most common form of cholangitis in cats.

- Histologically, the lesion is characterized by neutrophilic inflammation within the walls or lumen of bile ducts. The neutrophilic inflammation may disrupt the limiting plate and extend into the

hepatic parenchyma, causing necrosis of periportal hepatocytes.

- Chronic neutrophilic cholangitis (previously referred to as lymphoplasmacytic or non-suppurative cholangitis or cholangiohepatitis) is characterized by a mixed inflammatory response (neutrophils plus lymphocytes and plasma cells). Other features of chronicity include marked biliary hyperplasia, concentric periductal fibrosis, and bridging portal fibrosis.

▼ ***Key Point*** Chronic neutrophilic cholangitis may progress to biliary cirrhosis. As opposed to the small liver in dogs with end-stage cirrhosis, cats with biliary cirrhosis typically have hepatomegaly because of profound biliary hyperplasia.

Etiology

▼ ***Key Point*** Acute neutrophilic cholangitis is most likely caused by ascending bacterial infection from the intestine into the biliary tract.

- Bacterial organisms isolated from bile or liver tissue are primarily gram-negative and anaerobic enteric bacteria such as *E. coli* (most common), *Staphylococcus,* alpha-hemolytic *Streptococcus, Bacillus, Actinomyces, Bacteroides,* and *Clostridia.*
- Chronic bacterial infections elsewhere in the body (sinusitis, splenic abscess, pyelonephritis) and septicemia may also be associated with neutrophilic cholangitis.
- Chronic neutrophilic cholangitis may represent a persistent bacterial infection, or the lesion may have been initiated by bacteria but an immune-mediated response may result in a chronic self-perpetuating disorder. Other possible causes of neutrophilic cholangitis may include viral, toxin-induced, or drug-induced disease.
- Infectious agents infrequently associated with lesions of cholangitis in cats include liver flukes (see previous discussion in this chapter), *Toxoplasma*-like organisms, and *Hepatozoon canis.*

Clinical Associations and Predispositions

▼ ***Key Point*** Neutrophilic cholangitis in cats is commonly associated with IBD and chronic subclinical pancreatitis ("triaditis").

- In cats, the pancreatic and bile ducts join into a common channel prior to opening into the duodenum at the sphincter of Oddi. Underlying IBD may be the key feature that predisposes to both cholangitis and pancreatitis. Inflammation of the duodenal mucosa could alter the normal function of the sphincter of Oddi. IBD commonly causes vomiting in cats, and vomiting could raise the intraduodenal pressure and predispose the patient to reflux of duodenal juice into the pancreatic and biliary systems. Since the normal bacterial count in the proximal small intestine is higher in cats than in dogs, it may be more likely to induce pathology in cats.
- Congenital biliary tract malformations or biliary reconstructive surgery may also predispose the patient to ascending bacterial infection.
- Concurrent extrahepatic biliary tract abnormalities include cholecystitis and sludged bile or choleliths, which may cause bile duct obstruction.
- Cats with cholangitis may develop secondary hepatic lipidosis, possibly related to anorexia and weight loss.

Clinical Signs

- *Acute neutrophilic cholangitis* causes acute onset of vomiting, anorexia, lethargy, and weight loss.
- *Chronic neutrophilic cholangitis* causes intermittent or persistent vomiting, anorexia, lethargy, and weight loss lasting weeks to years. Signs of HE, ascites, and excessive bleeding are uncommon unless chronic neutrophilic cholangitis has progressed to biliary cirrhosis.

Diagnosis

Suspect neutrophilic cholangitis in any cat with non-hemolytic jaundice, especially if accompanied by fever (although not all cases are febrile). Definitive diagnosis requires liver biopsy to distinguish this disease from other hepatic disorders, such as hepatic lipidosis, hepatic FIP, and neoplasia.

History and Physical Examination

- Cats with acute neutrophilic cholangitis typically have an acute clinical presentation of short duration (<5 days). Young cats appear to be at increased risk. A history of antibiotic-responsive illness is common.
- In contrast, cats with chronic neutrophilic cholangitis are usually middle age or older.
- Physical examination findings include fever, jaundice, abdominal pain, hepatomegaly, and dehydration. Fever and abdominal pain are more likely with acute cholangitis.

▼ ***Key Point*** Ascites may be present if chronic neutrophilic cholangitis has progressed to cirrhosis.

Laboratory Evaluation

- For both acute and chronic disease, liver enzyme elevations are variable. Although cholangitis is typically considered a cholestatic disorder, the ALP may be normal, especially in the acute form. This may occur because ALP is an induced enzyme with a lag period before it increases in the serum.
- Increased ALT is a more consistent finding and probably indicates inflammation is extending beyond the

portal area and limiting plate, resulting in hepatocellular necrosis (cholangiohepatitis).
- Hyperbilirubinemia and bilirubinuria are common in both the acute and the chronic forms of cholangitis. FSBAs and PPSBAs are consistently increased.

▼ ***Key Point*** Neutrophilia with a left shift is most frequent in cats with the acute form of neutrophilic cholangitis, whereas hyperglobulinemia is a frequent finding in cats with the chronic form.

- Cats with chronic neutrophilic cholangitis frequently have a mild nonregenerative anemia. A coagulopathy may occur secondary to vitamin K malabsorption, hepatocyte failure, or DIC. Hypoalbuminemia, decreased BUN, and hyperammonemia suggest advanced disease.
- Consider evaluating serum cobalamin level (B_{12}) and feline pancreatic lipase immunoreactivity because of the association of neutrophilic cholangitis with IBD and pancreatitis (see Chapters 69 and 73).
- In endemic tropical locations, rule out liver flukes by fecal exams or a therapeutic trial of praziquantel.

Radiography and Ultrasonography

- Abdominal radiographs may reveal a liver that is normal or increased in size. Radiopaque choleliths may also be detected.
- Ultrasonographically, cats with neutrophilic cholangitis have no detectable parenchymal abnormalities, a diffuse hepatic hypoechogenicity, or a coarse or nodular liver texture. This helps differentiate cholangitis from lipidosis, which causes hyperechogenicity of the liver.
- Ultrasonography is also useful to evaluate for concurrent abnormalities of the biliary tract and pancreas, such as common bile duct obstruction, cholelithiasis, sludging of bile, cholecystitis, and pancreatitis.

Liver Biopsy

Definitive diagnosis requires liver biopsy to distinguish neutrophilic cholangitis from other hepatic disorders, such as hepatic lipidosis, hepatic FIP, and neoplasia.

- If concurrent biliary obstruction occurs, obtain a liver biopsy specimen and aerobic and anaerobic bile cultures at laparotomy during surgical relief of the obstruction (see Chapter 72). Duodenal and pancreatic biopsies are also indicated. At laparotomy, the gallbladder and common bile duct frequently are thickened, firm, and distended. Inspissated bile and choleliths may be present.
- In the absence of obstruction, ultrasound-guided liver biopsy is adequate for diagnosis in most cats. Laparoscopic liver biopsy provides larger tissue samples than those obtained with ultrasound guidance. Perform an aerobic and anaerobic bacterial culture of liver tissue (or bile obtained by cholecystocentesis).
- Cytologic evaluation of impression smears of bile or liver tissue has been recommended since bacteria are more easily detected cytologically than histopathologically.

Treatment

General Supportive Care

- Treat neutrophilic cholangitis with fluid therapy, nutritional support, and supplementation of potassium and B vitamins (see Table 71-1).
- Give vitamin K_1 (0.5–1.5 mg/kg SC or IM q12h for three doses) if hemostasis evaluation suggests vitamin K deficiency.
- Avoid dietary protein restriction unless overt signs of HE are present. If concurrent IBD is suspected, dietary modifications may include commercial GI or novel protein diets (see Chapter 69).

Antibiotics

▼ ***Key Point*** Antibiotics are the primary therapy for acute neutrophilic cholangitis. They are also used in the initial therapy of chronic neutrophilic cholangitis prior to initiating glucocorticoid therapy, in order to eliminate any bacterial component.

If possible, base the choice of antibiotic on culture and sensitivity testing results; otherwise, consider the following recommendations: Continue antibiotics for a minimum of 6 to 8 weeks. In some cats with persistent elevation of serum bilirubin and liver enzymes, continue antibiotic therapy for 3 to 6 months.

- For initial treatment, consider ampicillin (20–40 mg/kg PO, IV, IM or SC q8h), amoxicillin (10–20 mg/kg PO, IV, or SC q8–12h), amoxicillin-clavulanate (62.5 mg/cat PO q12h), or a cephalosporin. Combine one of these with metronidazole (7–10 mg/kg PO q12h) for broader spectrum against anaerobes, as well as modulation of cell-mediated immunity and treatment of concurrent IBD.
- For refractory cases, use enrofloxacin (2.5 mg/kg PO, IM, or IV q12h) or a 1-week course of an aminoglycoside.

Prednisolone

- Prednisolone is recommended for treatment of cats with chronic neutrophilic cholangitis because of its anti-inflammatory and immunosuppressive properties. However, efficacy of corticosteroids for treatment of chronic neutrophilic cholangitis has never been proven.
- Give prednisolone, 2 to 4 mg/kg q24h (once daily or divided), until clinical remission, then taper over 6 to 8 weeks to 1 to 2 mg/kg once every other day.

Hepatoprotective Therapy

- Give ursodiol (Actigall, Ciba Geneva) to all cats with neutrophilic cholangitis once extrahepatic biliary obstruction is eliminated because of its hepatoprotective (anti-inflammatory, immunomodulatory, and antifibrotic effects) properties (see Table 71-2). It appears to be well tolerated and safe in cats.
- Consider other hepatoprotectants, such SAMe or vitamin E (see Table 71-2).

Surgery

Surgical intervention is indicated if biliary obstruction (from sludged bile or choleliths) is detected on ultrasound examination. Surgical procedures for the biliary tract are described in Chapter 72. Use supportive care (including treatment of coagulopathy) for stabilization prior to the procedure. Indications for surgical intervention in the treatment of neutrophilic cholangitis include the following:

- Biliary decompression for extrahepatic biliary obstruction
- Sludge removal and bile duct and gallbladder irrigation
- Cholelith removal
- Cholecystectomy for necrotizing cholecystitis

Biliary diversion techniques such as cholecystoduodenostomy and cholecystojejunostomy are most commonly performed when biliary obstruction is present; however, the mortality rate ranges from 23% to 32% within 6 months of surgery. Cats with biliary surgery that did survive had repeated intermittent bouts of fever, vomiting, and anorexia, which responded to antibiotics. Consequently, if biliary obstruction is present, procedures to establish patency of the biliary system without performing a biliary diversion surgery appear preferable.

Prognosis

Cats with acute neurophilic cholangitis may have a complete recovery after treatment with antibiotics. However, some of these cats progress to the chronic form.

▼ ***Key Point*** Many cats with chronic neutrophilic cholangitis continue to have smoldering disease requiring continued treatment for months or years.

Cats with neutrophilic cholangitis that survive less than 1 year commonly have concurrent diseases that probably contribute to their death.

Lymphocytic Cholangitis

Lymphocytic cholangitis (also called *progressive lymphocytic cholangitis or cholangiohepatitis*) is believed to be a distinct form of cholangitis in the cat. It appears to be rare in the United States but has been well described in Europe. An immune-mediated pathogenesis has been suggested. The histologic lesion is characterized by moderate to marked infiltration of small lymphocytes in portal areas, with variable portal fibrosis and bile duct proliferation. As the lesion progresses, the number of lymphocytes decreases but marked fibrosis disrupts the hepatic architecture.

- Persian cats may have a genetic predisposition.
- The most common clinical features are ascites, icterus, generalized lymphadenopathy, and hyperglobulinemia in young cats.
- Concurrent abnormalities of the extrahepatic biliary system, intestine, or pancreas are not seen.
- Treatment options for lymphocytic cholangitis are similar to those described previously for chronic neutrophilic cholangitis.

Lymphocytic Portal Hepatitis

Lymphocytic infiltration of portal areas without bile duct involvement or periportal necrosis is termed *lymphocytic portal hepatitis*. It is believed to be a nonspecific reaction and not a primary disease process.

- Lymphocytic portal hepatitis is a common finding in liver biopsies of cats older than 10 years of age (up to 82% of cats). In contrast, only 10% of cats younger than 10 years had this finding. It is not associated with IBD or pancreatitis. Liver enzyme elevations may or may not be present.
- Whether or not treatment with corticosteroids is indicated is unclear. The mean survival time in 23 cats with lymphocytic portal hepatitis was 29 months; 72% of these cats were not treated with corticosteroids.
- In cats with marked lymphocytic infiltration in the portal areas, it can be difficult to distinguish lymphocytic portal hepatitis or lymphocytic cholangitis from well-differentiated hepatic lymphoma.

CHOLECYSTITIS

Cholecystitis, or inflammation of the gallbladder, is a clinical problem that occurs uncommonly in both dogs and cats. Cholecystitis may be associated with cholangitis, cholangiohepatitis, gallbladder mucocele, cholelithiasis, and choledocholithiasis. Acute necrotic cholecystitis in dogs frequently is complicated by rupture of the gallbladder and septic bile peritonitis.

Etiology

- Bacteria appear to play an important role in cholecystitis. An enteric origin of bacteria seems most likely, because isolates are usually aerobic gram-negative bacteria (especially *E. coli,* but also *Klebsiella, Pseudomonas,* and *Salmonella* spp.) or anaerobes (*Clostridium* spp.). Intestinal bacteria may be refluxed

into the gallbladder, or they may be blood-borne from the hepatic circulation.
- *Campylobacter jejuni* bacteremia and acute cholecystitis have been documented in dogs. Although the GI tract was suspected to be the source of the bacteria, diarrhea was not a presenting clinical sign.
- Gas-producing organisms, such as *E. coli* and *Clostridium,* can cause emphysema of the gallbladder wall. Emphysematous cholecystitis is recognized most frequently in diabetic dogs.
- Cholelithiasis can predispose the patient to cholecystitis by obstructing the cystic duct, causing gallbladder overdistension and stasis, which enables proliferation of anaerobic organisms.
- Anatomic malformations of the gallbladder, biliary obstruction from any cause, and biliary surgery also predispose the patient to biliary infections.

Clinical Signs

- Signs include anorexia, lethargy, fever, abdominal pain, hepatomegaly, vomiting, diarrhea, and jaundice.
- Acute rupture of the gallbladder with septic bile peritonitis causes abdominal distension, collapse, and septic shock (see also Chapter 76).
- Signs may be acute or chronic and persistent or episodic.

Diagnosis

Differentiate cholecystitis from other cholestatic hepatobiliary disorders that have fever, inflammation, and similar clinical findings, such as acute pancreatitis or pancreatic abscess, cholangiohepatitis, cholelithiasis, hepatic abscess, and septicemia or endotoxemia.

Physical Examination

Physical examination findings include fever, cranial abdominal pain, jaundice, and shock (bile or septic peritonitis).

Laboratory Evaluation

- Laboratory findings are characteristic of severe cholestatic hepatobiliary disease, including hyperbilirubinemia, markedly increased ALP and GGT activity, increased ALT activity, increased SBA concentrations, and hypercholesterolemia.
- Other findings suggestive of inflammation or sepsis are neutrophilia with a left shift and hypoglycemia.
- Increased amylase and lipase levels have been reported in dogs with cholecystitis in the absence of clinical pancreatitis.
- Prolonged PT and APTT occur if chronic biliary obstruction causes vitamin K malabsorption.
- Other laboratory findings reflect dehydration and electrolyte and acid-base imbalances secondary to vomiting, dehydration, and sepsis.
- If cholecystitis is complicated by rupture of the gallbladder or biliary tract, abdominal fluid analysis is consistent with septic bile peritonitis. For a general discussion of peritonitis, see Chapter 76.

Radiography and Ultrasonography

- Potential radiographic findings include cholecystolithiasis, emphysema of the gallbladder wall, and, if perforation occurs, abdominal effusion.
- Ultrasonographic findings include distension of the gallbladder and cystic duct, increased echogenicity or hypoechoic thickening of the gallbladder wall, cholecystoliths, and increased echogenicity of gallbladder bile with or without bile sludge. Small amounts of abdominal effusion not evident on survey radiographs may also be identified.
- Ultrasonographic-guided percutaneous cholecystocentesis has been recommended to obtain bile for cytology and culture (aerobic and anaerobic). Perform blood cultures to isolate bacteria associated with bacteremia and acute cholecystitis. Culture for *C. jejuni* requires selective culture techniques.

Surgery

- Findings at exploratory surgery include thickening, necrosis, and rupture of the gallbladder, localized or generalized peritonitis, and calculi or inspissated bile in the gallbladder, cystic duct, or bile duct. Previous gallbladder rupture may be associated with omental or hepatic adhesions.
- Obtain aerobic and anaerobic cultures of the gallbladder mucosa and bile.
- Histologic examination of the gallbladder reveals varying degrees of necrosis, inflammation, and fibrosis.

Treatment

- Give parenteral vitamin K_1 prior to surgery to correct coagulopathy (see Table 71-1).
- Administer antibiotic therapy effective against aerobic gram-negative and anaerobic bacteria, as described previously for bacterial cholangitis (see under "Feline Inflammatory Liver Disease"). For initial treatment of acute cholecystitis with bacteremia or necrotic cholecystitis with septic peritonitis, combine amoxicillin or cephalosporin with an injectable aminoglycoside or enrofloxacin. Long-term treatment (6–8 weeks) with an oral antibiotic is indicated.
- Cholecystectomy is required in most cases (see Chapter 72). Surgically manage complications such as biliary obstruction, cholelithiasis, inspissated bile, and abdominal drainage for septic bile peritonitis (see Chapter 76).

Postoperative Care and Complications

- Correct all fluid, electrolyte, and acid-base imbalances.

- Common postoperative complications include vomiting, diarrhea, anorexia, hypoproteinemia, and hypokalemia.

Prognosis

- Death usually is attributed to sepsis and peritonitis.
- If the animal survives the immediate postoperative period, the long-term prognosis is good and the recurrence of biliary or hepatic disease is unlikely.

GALLBLADDER MUCOCELE

Gallbladder mucocele is an abnormal accumulation of mucus in the gallbladder lumen accompanied by cystic mucosal hyperplasia of the gallbladder mucosa.

- Dogs with gallbladder mucoceles can be asymptomatic early in the course of disease. Clinical and biochemical abnormalities occur when mucoceles are complicated by secondary bacterial infection, extrahepatic biliary obstruction, or marked distention of the gallbladder leading to ischemic necrosis, gallbladder rupture, and bile peritonitis.

▼ ***Key Point*** Gallbladder rupture is a common life-threatening complication of mucocele.

- The incidence of gallbladder mucocele appears to be increasing, and it is one of the most common causes of extrahepatic biliary tract disease in dogs.

Etiology

The cause of gallbladder mucocele formation in dogs is unknown.

- In humans, gallbladder mucoceles form secondary to functional or mechanical biliary obstruction associated with cholecystitis, cholangitis, or cholelithiasis.
- In dogs, it is not clear whether gallbladder mucoceles are a primary gallbladder disorder or whether biliary obstruction leads to increased mucus secretion. However, predisposing disorders causing mechanical biliary obstruction (infiltrative disease of cystic duct, cholelithiasis) are not typically identified. A primary motility disorder of the gallbladder with delayed gallbladder emptying could potentially predispose the patient to functional gallbladder obstruction.
- A primary bacterial or inflammatory disorder of the gallbladder and biliary tract appear unlikely, since aerobic and anaerobic cultures are frequently negative and gallbladder inflammation is inconsistent and, if present, occurs in association with gallbladder wall necrosis.
- Dogs with hyperadrenocorticism (or receiving corticosteroids) appear to be at increased risk for mucocele formation. Experimentally, progestational compounds can induce lesions of gallbladder cystic mucosal hyperplasia in dogs.
- Acute pancreatitis may be a concurrent finding or a postoperative complication of gallbladder mucocele surgery.
- Increased recognition of gallbladder mucoceles in dogs may suggest a role for nutritional or environmental factors, or it may be the result of increased use of abdominal ultrasonography.

Clinical Signs

- Common clinical signs include anorexia, lethargy, vomiting, icterus, diarrhea, weight loss, PU/PD, abdominal discomfort, and abdominal distention.
- Some dogs with gallbladder mucocele are clinically (and biochemically) normal.

Diagnosis

History and Physical Exam

- Gallbladder mucocele appears to be more likely in older (>10 years) small to medium-sized dogs. No sex predilection is apparent. Cocker spaniels and Shetland sheepdogs appear to be at increased risk.
- Signs are usually acute to subacute and less than 3 weeks in duration.
- Physical examination findings include depression, weakness, lethargy, abdominal pain, icterus, fever, hepatomegaly, tachypnea, and tachycardia. Most dogs with gallbladder rupture have abdominal pain.
- Physical examination may be unremarkable.

Laboratory Evaluation

- Hematologic findings often include leukocytosis (mature neutrophilia or neutrophilic with left shift) and monocytosis.
- Increased liver enzyme activity (ALP, ALT, AST, and GGT) and hyperbilirubinemia are common biochemical features. Other less consistent findings include hypercholesterolemia, hyperglobulinemia, hypoalbuminemia, and azotemia.
- Values for serum ALP and ALT, total bilirubin, and WBC count are higher in dogs with gallbladder mucocele and secondary rupture than in dogs without rupture. In one study, all dogs with high venous lactate concentrations had a ruptured gallbladder.

▼ ***Key Point*** Biochemical findings may be normal in some dogs with early gallbladder mucocele formation detected ultrasonographically.

Ultrasonography

▼ ***Key Point*** The ultrasonographic appearance of a gallbladder mucocele is characteristic. The gallbladder bile is echogenic and organized in a stellate or finely striated, "kiwi fruit" pattern.

- As opposed to biliary sludge, a gallbladder mucocele is not gravity dependent.
- Ultrasonographic findings suggestive of secondary gallbladder rupture include loss of gallbladder wall continuity, hyperechoic fat or fluid around the gallbladder, free abdominal fluid, and striated or stellate echogenic material outside the gallbladder.
- Additional findings may include extrahepatic biliary obstruction and pancreatitis.

Laparotomy

- At surgery, the gallbladder is often markedly distended and firm, with dark serosal discoloration.
- The gallbladder contents appear as a shiny, greenish-black to brown gelatinous material that often has a striated pattern.
- If gallbladder rupture has occurred, abdominal contamination with mucocele contents is present.
- Perform a liver biopsy and aerobic and anaerobic bacterial cultures of bile. Perform cholecystectomy, and flush the bile ducts to remove any residual gelatinous material (see Chapter 72). Submit the excised gallbladder for histopathologic examination.

Histopathology

- Histopathology of the gallbladder reveals cystic mucosal hyperplasia. Cholecystitis is an inconsistent finding and is most likely associated with areas of ischemic necrosis and rupture.
- Liver biopsy findings are nonspecific and include mild to moderate portal hepatitis and fibrosis with bile duct proliferation and vacuolar hepatopathy.

Treatment

▼ ***Key Point*** Cholecystectomy is the treatment of choice of gall bladder mucocele.

- Perform cholecystectomy when a gallbladder mucocele is diagnosed ultrasonographically in a dog with clinical and biochemical evidence of hepatobiliary disease. If gallbladder rupture is suspected, emergency surgery is warranted (see "Biliary Rupture").
- Also perform cholecystectomy for treatment of gallbladder mucoceles in dogs without clinical and biochemical abnormalities, since gallbladder rupture is a life-threatening and unpredictable complication.
- Preoperatively stabilize the patient with fluid therapy and antibiotics. Give broad-spectrum antibiotic therapy (amoxicillin combined with enrofloxacin) to treat secondary bacterial infections of the biliary tract or if gallbladder rupture is suspected. Base antibiotic therapy on results of culture and sensitivity testing of bile or peritoneal fluid (rupture) when possible.
- If a coagulopathy is detected, give vitamin K_1 for 24 to 48 hours prior to surgery (see Table 71-1).
- When gallbladder mucocele is diagnosed in an asymptomatic dog and concurrent systemic disorders or risk of anesthesia precludes surgery, consider antibiotic therapy to control secondary bacterial infections and monitor biochemically and ultrasonographically.
- The role of choleretics such as ursodiol to prevent progression of mucocele formation is unclear. Although ursodiol can increase the watery component of bile, it is contraindicated if biliary obstruction is present.

Prognosis

The long-term prognosis after cholecystectomy appears to be excellent if the dog survives the postoperative period.

- Postoperative complications include sepsis and biliary infection, leakage at the surgery site with bile peritonitis, obstruction of the common bile duct by residual mucus, and acute pancreatitis.
- Mortality rates are similar in dogs with gallbladder rupture and prompt surgical intervention compared with dogs without gallbladder rupture.
- Although a dramatic decrease in liver enzymes and bilirubin occurs after surgery, some dogs have mild, persistent liver enzyme elevations that may be due to a concurrent chronic inflammatory hepatopathy.

CHOLELITHIASIS

Cholelithiasis occurs infrequently in dogs and cats. Choleliths may be present in the gallbladder (cholecystolithiasis), common bile duct (choledocholithiasis), or rarely, hepatic and lobar ducts. Most choleliths in dogs and cats consist of insoluble bile pigments. Minor components such as calcium, bile salts, protein, magnesium, phosphorus, iron, carbonate, and cholesterol also have been identified. Cholesterol choleliths, the most common type of stone in humans, are less likely to form in dogs because the cholesterol content of dog bile is lower than that in humans, and dogs have a better capacity for maintaining biliary cholesterol in solution. Little is known about the cholesterol content of cat bile, but cholesterol choleliths have been reported.

Etiology

The cause of spontaneous cholelithiasis in dogs and cats often cannot be determined. It is generally believed that gallstone formation requires initial nidus formation, retention of particles in the gallbladder, and then sustained growth of the cholelith. The following factors may be important in the development of pigment stones:

- Bile stasis and sludged bile are primarily composed of mucin, which may act as a nidus for cholelith for-

mation by subsequently binding calcium bilirubin pigments and cholesterol crystals.
- Cholecystitis and cholangitis can be associated with cholelithiasis, especially in cats (see "Feline Inflammatory Liver Disease"). It is difficult to determine whether choleliths were formed as a consequence of bile stasis, inflammation, and bacterial infection or whether cholelithiasis initiated the inflammation, which led to secondary biliary stasis and infection.
- Bacteria such as *E. coli* contain beta-glucuronidase, which can deconjugate bilirubin to a less soluble form that precipitates with calcium.
- Dietary factors are unlikely with balanced diets; however, dogs fed an experimental diet that is low in protein and fat, high in carbohydrates, and supplemented with cholesterol will form pigment stones. This diet is deficient in taurine, which may contribute to cholelithiasis by precipitating bile acids.

Clinical Signs

Dogs and cats with cholelithiasis often are asymptomatic. Clinical signs are most likely when cholelithiasis is complicated by bacterial infection, extrahepatic bile duct obstruction, perforation of the gallbladder or bile ducts, or secondary hepatic involvement (cholangiohepatitis or biliary cirrhosis).

- Common signs include vomiting, anorexia, weakness, PU/PD, jaundice, weight loss, and dehydration.
- Signs may be acute or chronic and intermittent or persistent. An acute onset is most likely with sudden obstruction of the cystic or common bile duct by the cholelith or rupture of the gallbladder.

Diagnosis

Although it is uncommon, consider cholelithiasis in the differential diagnosis of any dog or cat with cholestatic hepatobiliary disease.

History and Physical Examination

- Aged, small-breed female dogs appear to be at increased risk.
- A long-standing history (months to years) of intermittent jaundice and vomiting is present in some affected animals.
- Physical examination may be unremarkable, or findings may include jaundice, abdominal discomfort, hepatomegaly, fever, and abdominal distention. Fever is usually indicative of concurrent biliary bacterial infection or septic or bile peritonitis. Abdominal distension due to fluid accumulation is seen with secondary rupture of the biliary tract.
- Excessive bleeding may be noted with chronic common bile duct obstruction.
- Acholic feces are indicative of complete bile duct obstruction.

Laboratory Evaluation

Laboratory findings may be unremarkable. Biochemical evaluation of symptomatic patients is not specific for cholelithiasis but is indicative of cholestatic hepatobiliary disease.

- Findings include moderate to marked increases in serum ALP and GGT activity and in cholesterol, SBA, and total serum bilirubin concentrations. Serum ALT activity usually is increased, indicating secondary hepatocyte damage associated with severe cholestasis or cholangiohepatitis.
- Potential hematologic findings include neutrophilia with a left shift, usually indicating bacterial cholangiohepatitis or cholecystitis or complications such as a ruptured gallbladder. A mild, nonregenerative anemia is common.
- With chronic extrahepatic bile duct obstruction, coagulation tests may be affected by vitamin K malabsorption.
- With biliary rupture, abdominocentesis reveals bile peritonitis.

Radiography

- On routine abdominal radiographs, choleliths may appear as radiopaque densities in the area of the gallbladder or bile ducts. However, pigment stones are usually radiolucent unless they contain calcium. Hepatomegaly is common.
- Other findings are determined by the presence of complications such as obstruction (a distended gallbladder), emphysematous cholecystitis (gas density in the area of the gallbladder), and peritonitis (loss of abdominal detail).

Ultrasonography

- Ultrasonography detects both radiolucent and radiopaque choleliths as hyperechoic densities in the gallbladder and bile ducts. Choleliths are differentiated from mural masses by the presence of acoustic shadowing and movement of the density with changes in position of the animal.
- Inspissated or sludged bile also appears in the gallbladder as an echogenic substance, but sludge does not cause acoustic shadowing. Sludged bile may indicate biliary stasis but can also be seen in sick, anorexic animals without clinical biliary tract disease.
- Complications of cholelithiasis can be identified ultrasonographically, such as distention of the gallbladder and bile ducts with cystic or common bile duct obstruction, thickening of the biliary tract associated with inflammation, abdominal fluid accumulation with rupture of the gallbladder, and absence of the gallbladder.

▼ ***Key Point*** Because the majority of choleliths do not cause clinical signs, surgical removal may not always be warranted.

Laparotomy

Perform exploratory laparotomy for definitive diagnosis and treatment of cholelithiasis (see Chapter 72). Pigment choleliths usually are greenish-brown to black and may be single or multiple. Perform the following diagnostic and therapeutic procedures during exploratory laparotomy:

- Evaluate the patency of the gallbladder and bile ducts.
- Remove choleliths for chemical analysis and bacterial culture.
- Identify and repair secondary biliary rupture.
- Collect samples of affected tissue (liver, gallbladder) and bile for aerobic and anaerobic bacterial culture and biopsy.

Histopathologic Evaluation

Histopathologic changes in the gallbladder, bile ducts, and liver may be absent with uncomplicated cholelithiasis. However, mild cholangitis (cholangiohepatitis) and cholecystitis are common.

Treatment and Prognosis

- Institute supportive therapy to correct fluid, electrolyte, and acid-base imbalances prior to surgery. Feed a well-balanced diet.
- If a coagulopathy is detected, give vitamin K_1 for 24 to 48 hours prior to surgery (see Table 71-1).
- Administer systemic antibiotics in animals with inflammatory biliary tract disease and cholelithiasis. Ideally, base the choice of antibiotic on culture and sensitivity testing of bile and hepatic tissue obtained at surgery. See the discussion of antibiotic therapy of biliary infections under "Neutrophilic Cholangitis."
- Management of complications of cholelithiasis, such as biliary obstruction or rupture, is discussed in the next sections. Surgery of the biliary tract is discussed in Chapter 72.
- Little is known about the likelihood of recurrence of cholelithiasis in dogs and cats, but if the underlying mechanism of cholelith formation is not reversed, recurrence is possible.

EXTRAHEPATIC BILIARY OBSTRUCTION

Extrahepatic biliary obstruction of the common bile duct or large hepatic ducts interrupts bile flow into the intestine.

Table 71-12. CAUSES OF EXTRAHEPATIC BILIARY OBSTRUCTION

Cholelithiasis
Inspissated (sludged) bile
Gallbladder mucocele
Cholangitis and cholecystitis
Acute pancreatitis, pancreatic abscess, pancreatic fibrosis
Biliary, hepatic, pancreatic or duodenal neoplasia
Biliary stricture
Biliary hematoma
Liver flukes
Diaphragmatic hernia with entrapment of the gallbladder

Etiology

Biliary obstruction can be a complication of primary biliary tract disorders such as gallbladder mucocele, cholelithiasis, or biliary tumors or can be caused by extrahepatic disorders such as pancreatic fibrosis and pancreatic or duodenal masses (Table 71-12).

Clinical Signs

- Signs of biliary obstruction include anorexia, vomiting, jaundice, weight loss, abdominal pain, diarrhea, acholic feces, and excessive bleeding.
- Diarrhea and steatorrhea are characterized by tan-colored feces and are attributed to failure to secrete bile acids, which results in malabsorption of fat and fat-soluble vitamins such as vitamin K.
- With prolonged extrahepatic biliary obstruction, vitamin K malabsorption and the subsequent decreased synthesis of vitamin K–dependent factors results in a coagulopathy.
- With complete biliary obstruction, the feces may become clay colored (acholic) because of a lack of bile pigments.

Diagnosis

The diagnostic strategy is to identify that biliary obstruction is present and then to identify the underlying cause of obstruction.

Physical Examination

- Findings include jaundice and hepatomegaly due to bile engorgement of the liver.
- A firm, distended gallbladder occasionally is palpated.
- Other findings are dependent on the underlying cause of obstruction, such as palpation of an abdominal mass (pancreatic or biliary neoplasia) and abdominal pain (acute pancreatitis, peritonitis).
- Fever may suggest bacterial cholecystitis or cholangiohepatitis, biliary rupture with peritonitis, pancreatitis, or pancreatic abscess.

Laboratory Evaluation

- Biochemical findings reflect marked cholestasis, including increased serum concentrations of ALP, GGT, cholesterol, bile acids, and bilirubin. Unfortunately, biochemical findings cannot distinguish whether cholestasis is caused by intrahepatic or extrahepatic mechanisms. In general, values for total bilirubin and ALP activity tend to be higher with extrahepatic biliary obstruction. Serum ALT and AST activity are concurrently increased due to secondary hepatic damage.
- On the CBC, a mild neutrophilia and mild, nonregenerative anemia are common. Neutrophilia with a left shift suggests the possibility of acute pancreatitis or abscess, bacterial cholangitis or cholecystitis, or biliary rupture.
- Findings on urinalysis include bilirubinuria and absence of urobilinogen.
- With vitamin K malabsorption, findings include prolonged PT, APTT, and activated clotting time. Platelet function defects have also been documented in dogs with biliary obstruction.

Radiography

Abdominal radiography is frequently non-diagnostic.

- Occasionally, a large, fluid-filled gallbladder can be seen superimposed over the liver. The liver may be normal to increased in size. Chronic biliary obstruction in dogs may lead to biliary cirrhosis and microhepatica.
- Other radiographic findings depend on the underlying cause of obstruction and may include cholelithiasis, emphysematous cholecystitis, pancreatitis, and mass lesions.

Ultrasonography

Ultrasonography is helpful to confirm extrahepatic biliary obstruction and to evaluate the underlying cause.

- In normal dogs, the cystic duct, common bile duct, and intrahepatic ducts are not visible. The common bile duct may be visible in some normal cats but is usually ≤ 4 mm. A common bile duct > 5 mm is suggestive of extrahepatic biliary obstruction.
- With biliary obstruction, the biliary system, including the gallbladder, cystic duct, common bile duct, and intrahepatic ducts, becomes progressively dilated. The earliest detectable change is distension of the gallbladder and cystic duct, which occurs within 24 hours. By 48 hours, the common bile duct also is distended. Distention of intrahepatic ducts is not detected until 4 to 7 days after obstruction. Dilated hepatic biliary ducts are differentiated from hepatic and portal veins by their tortuosity and irregular branching patterns.
- Ultrasonography may identify underlying causes of biliary obstruction such as gallbladder mucocele, cholelithiasis, pancreatitis, or mass lesions.

Hepatobiliary Scintigraphy

Hepatobiliary scintigraphy may be used to confirm biliary obstruction but is available only at tertiary referral centers.

Laparotomy

Exploratory laparotomy usually is required to confirm extrahepatic biliary obstruction and to identify the underlying cause. Perform the following diagnostic procedures:

- Evaluate bile duct and gallbladder patency.
- Identify location and cause of obstruction.
- Evaluate for evidence of secondary rupture of the biliary tract.
- Collect a sample of bile for aerobic and anaerobic bacterial cultures.
- Perform a liver biopsy.

Treatment

Surgery

Specific therapy requires surgery to correct the underlying cause of obstruction (see Chapter 72).

- Prior to surgery, stabilize the patient with fluid therapy. Give vitamin K_1 parenterally for 24 to 48 hours prior to surgery to correct a coagulopathy.
- With complete biliary obstruction, antibiotics do not enter the bile.

Medical Therapy

If biliary obstruction occurs secondary to acute pancreatitis, manage the pancreatitis medically (see Chapter 73) and reserve surgery for those patients in which biliary obstruction does not resolve with resolution of pancreatic inflammation.

BILIARY RUPTURE

Leakage of bile into the abdominal cavity results in chemical peritonitis that can be complicated by sepsis.

Etiology

- Biliary tract rupture is commonly caused by blunt or sharp abdominal trauma from automobile-induced injuries, gunshot injuries, and bite wounds. Rupture of the common bile duct is most likely with blunt abdominal trauma.
- Gallbladder mucocele and necrotizing cholecystitis can be associated with gallbladder rupture.

- Other causes of gallbladder rupture include cholelithiasis, biliary neoplasms, gallbladder infarction, and iatrogenic puncture during percutaneous liver biopsy.

Clinical Signs

- When gallbladder rupture occurs secondary to gallbladder mucocele, cholecystitis or cholelithiasis, acute onset of anorexia, vomiting, diarrhea, jaundice, abdominal pain, fever, and shock may occur.
- Signs of biliary duct rupture secondary to trauma tend to be chronic and develop more slowly than with rupture of the gallbladder. With traumatic biliary rupture, early signs such as abdominal pain and vomiting are frequently overshadowed by more immediate signs of shock, fractures, and other injuries.
- Other signs, such as anorexia, listlessness, weight loss, jaundice, ascites, and acholic feces, do not occur until days or weeks following the traumatic event.

Diagnosis

History and Physical Examination

- A history of recent abdominal trauma and progressive jaundice and abdominal distention suggests the possibility of biliary rupture.
- Physical examination findings consistent with biliary rupture include jaundice, abdominal distension, and acholic feces.
- Abdominal pain is most likely with acute rupture or septic peritonitis.
- Fever may occur with septic peritonitis or cholecystitis.

Laboratory Evaluation

- Laboratory findings include hyperbilirubinemia and increased ALP, ALT, and SBA concentrations.
- Abdominal fluid appears yellow or green. Chemical tests for bilirubin are positive and concentrations of bilirubin are at least 2 times higher in the abdominal fluid than in the serum.
- Cytologic examination reveals mixed inflammatory infiltrate and bile-laden macrophages or free green or yellow-brown material consistent with bile. In some dogs with biliary rupture, bile pigment is not visible but an acellular amorphous blue mucinous extracellular material ("white bile") may be observed. These dogs still have fluid bilirubin concentrations greater than twice the serum value.
- Bacteria may be seen if bile peritonitis is complicated by sepsis.

Radiography and Ultrasonography

- Abdominal radiographs reveal poor abdominal contrast due to fluid accumulation.
- On ultrasonography, the gallbladder may not be visible, and even a small amount of abdominal fluid may be detected.
- Other radiographic and ultrasonographic findings depend on the underlying cause of rupture, such as gallbladder mucocele, cholecystitis, cholelithiasis, and biliary neoplasia.
- When trauma is suspected as the cause of biliary rupture, take thoracic films to detect other complications such as pneumothorax, diaphragmatic hernia, and bile pleuritis.

Laparotomy

Confirm rupture of the biliary tract by laparotomy.

- Rupture of the gallbladder secondary to cholecystitis may be acute or chronic. With chronic gallbladder rupture, omental and hepatic adhesions are common. Biliary fistulas may develop from the gallbladder to other abdominal structures such as the diaphragm. Fistulas between the gall bladder and the diaphragm may result in bile pleuritis and biliary effusion.
- Submit abdominal fluid and affected biliary tissue for aerobic and anaerobic bacterial culture.

Treatment

Surgery is required to repair the biliary rupture and is discussed in Chapter 72. The prognosis is guarded.

▼ ***Key Point*** Dogs with septic peritonitis (positive bacterial cultures of the biliary effusion) are less likely to survive than are dogs with negative culture results.

- Prior to surgery, stabilize the patient with fluid therapy, give vitamin K_1 parenterally for 24 to 48 hours, and give antibiotics.
- Open abdominal drainage is not necessary for dogs with sterile biliary effusions but may be helpful in managing dogs with septic peritonitis (see Chapter 76).

SUPPLEMENTAL READING

Ettinger SJ, Feldman EC (eds): Textbook of Veterinary Internal Medicine, vol. 2, 6th ed. Philadelphia: WB Saunders, 2005.

Chapter

72 Surgery of the Liver and Biliary Tract

Stephen J. Birchard

Surgery of the liver and biliary tract is commonly performed in small animals and can be very challenging. Animals frequently are presented with surgical diseases of these organs, such as liver tumors and obstruction or infection of the biliary system. Some of the procedures described in this chapter require specialized training and facilities. Others, such as liver biopsy, partial hepatectomy, and simple exploration of the biliary tract, can be performed in a standard veterinary practice. Regardless of the procedure, preparation for the surgery by reviewing anatomy, pathophysiology, and specific techniques is very important for a successful outcome. Preparation of the patient prior to surgery also is extremely important because most of these diseases have serious metabolic effects.

SURGERY OF THE LIVER

Anatomy

Liver Lobes

- The liver is divided into six lobes: the right lateral, right medial, caudate, quadrate, left medial, and left lateral.
- The caudate lobe is divided into the caudate process and the papillary process.

Liver Attachments

- The major liver attachments to other organs and the body wall are the triangular, hepatogastric, and hepatoduodenal ligaments.
- The falciform ligament extends from the liver to the diaphragm and ventral abdominal wall. This mesenteric remnant can be quite large and fat-filled in obese animals. Consider removing this structure during liver surgery to gain better exposure of the cranial abdominal structures.
- The hepatorenal ligament is a thin fold of peritoneum that extends from the renal fossa of the caudate lobe to the ventral surface of the right kidney.

Blood Supply

Portal Vein

- The portal vein receives blood from the spleen, pancreas, and intestines.
- The major hepatic branches of the portal vein are the right lateral trunk, right medial branch, and left lateral trunk.
- The portal vein is the confluence of the cranial and caudal mesenteric veins and the splenic vein.
- The portal vein can be seen at the base of the mesoduodenum. It forms the ventral boundary of the epiploic foramen.
- The portal vein eventually empties into the liver and supplies approximately 80% of the blood flow of the liver. The remaining 20% comes from the hepatic arteries.
- In the fetus, the ductus venosus connects the portal vein to the caudal vena cava, allowing blood to bypass the liver. This vessel closes soon after birth in normal dogs. If it remains patent, it is called a *patent ductus venosus* and is one of the several types of portosystemic shunts.

Hepatic Arteries and Veins

- The hepatic artery is a branch of the celiac artery. Variable numbers of hepatic artery branches supply the liver lobes. The hepatic arteries are located in the vicinity of the hepatoduodenal ligament and are adjacent to the common bile duct. The cystic artery, which supplies the gallbladder, is a branch of the left branch of the hepatic artery.
- Six to eight large hepatic veins drain the liver lobes to the caudal vena cava.
- The hepatic veins enter the vena cava at the hilus of the liver and are obscured by the liver parenchyma.

Preoperative Considerations

Liver diseases cause a variety of significant hematologic and metabolic disorders in animals. Prior to surgery, perform appropriate diagnostics to confirm the disease and check for involvement of other organs. (See Chapter 71 for diagnosis of liver problems.)

Of particular concern to the surgeon are the following potential problems:

- *Hypoproteinemia*—Evaluate serum proteins and consider administration of plasma, colloids, or hyperalimentation if significantly low.
- *Anemia*—Evaluate the animal's hemogram and establish a baseline packed cell volume so that changes can be kept in perspective. Blood loss before, during, and after liver surgery is common and should be monitored closely.
- *Coagulopathy*—Analyze the animal's coagulation profile and correct abnormalities if possible (see Chapter 23). Fresh whole blood transfusion before or during surgery may be necessary.
- *Diffuse disease*—Hepatic neoplasia may result in metastatic lesions. Thoracic and abdominal radiography and abdominal ultrasonography are helpful in determining the extent of disease.
- *Impaired liver function*—Manage hepatic encephalopathy, if present, medically (see Chapter 71) to stabilize the animal prior to surgery.
- *Hypoglycemia*—Consider giving the animal intravenous (IV) fluids supplemented with glucose before and during surgery (e.g., 5% dextrose in lactated Ringer's solution).

▼ ***Key Point*** Diffuse hepatic disease may cause serious metabolic problems that can be compounded by anesthesia and surgery. Analyze liver function tests, such as serum bile acid and blood ammonia concentrations (see Chapter 71), to determine the animal's ability to undergo anesthesia and surgery.

- *Liver trauma*
  - Thoroughly evaluate all animals with a history of trauma to rule out thoracic trauma such as pneumothorax, pulmonary contusions, and other cardiopulmonary problems (see Chapter 166). Evaluate for damage to other organs such as the urinary tract, gastrointestinal tract, and neurologic and skeletal systems.
  - Animals with liver trauma usually have hemoperitoneum. Severe blood loss will cause clinical signs of shock and should be treated (see Chapter 156 for treatment of hypovolemic shock).

▼ ***Key Point*** Most animals with liver trauma can be treated conservatively (e.g., IV fluids, whole blood transfusion, or autotransfusion of abdominal blood if not contaminated with bacteria or neoplastic cells).

Liver Biopsy and Partial Hepatectomy—Surgical Procedure

Objectives

- Examine the entire liver and biliary system for grossly evident abnormalities.
- Obtain tissues for biopsy or completely remove the lesion by partial hepatectomy.
- Minimize intraoperative blood loss.

Equipment

- Standard general surgery pack and suture
- Balfour and malleable retractors
- Tru-Cut biopsy needle, Anchor Soft Tissue Biopsy Device (Anchor Products Co., Addison, IL), or skin punch biopsy instrument
- Tissue stapling device (e.g., Autosuture TA, U.S. Surgical, Norwalk, CT) (optional)
- Gelfoam

Technique

1. Place the animal in dorsal recumbency and prepare the entire ventral abdomen and caudal one-third of the sternum for aseptic surgery.
2. Perform a standard ventral midline abdominal approach. If additional exposure is necessary, also perform a left or right paracostal abdominal incision or a caudal median sternotomy.
3. Use laparotomy sponges to protect the abdominal wall and place Balfour retractors to expose the liver and associated viscera.
4. Identify areas of liver to be removed or biopsied. If necessary, mobilize involved liver lobes by incising the triangular ligaments. Greater exposure of the liver can be achieved by placing a laparotomy sponge between it and the diaphragm.
5. Liver biopsy can be achieved by a variety of techniques:
   a. Obtain tissue samples from the periphery of the lobe, using the "guillotine" technique.
   b. Use absorbable suture to surround a small segment of liver and tie the suture tight to cut through the parenchyma and strangulate the blood vessels and bile ducts (Fig. 72-1). Alternatively, place the suture in a horizontal mattress pattern.
   c. Excise the tissue distal to the ligature, using a scalpel or Metzenbaum scissors. Check for bleeding and, if necessary, place a small piece of Gelfoam over the cut surface for hemostasis.
   d. Alternatively, use a Tru-Cut needle or skin biopsy punch to obtain small pieces of liver tissue. These are especially helpful if the lesion is centrally located in the liver lobe rather than peripherally. Be sure to include some normal tissue in the biopsy specimen.
6. Remove large lesions by partial hepatectomy (Fig. 72-2):
   a. Divide the liver parenchyma proximal to the lesion, using large crushing clamps or finger fractionation (gently squeezing the liver parenchyma between fingers to isolate vessels). Ligate the

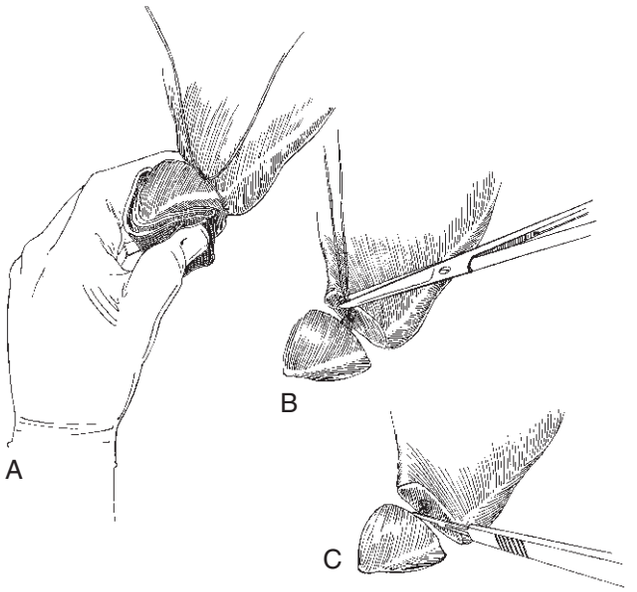

Figure 72-1. Guillotine method for intraoperative liver biopsy. Place a loop of absorbable suture around the tip of a liver lobe and tie tightly to cut through the liver parenchyma, ligating the vessels. Cut the suture ends and then cut the vessels to allow removal of the biopsy specimen.

ducts and vessels with absorbable sutures (e.g., 3-0 or 4-0 chromic catgut).

b. Alternatively, use surgical staples (e.g., U.S. Surgical Autosuture TA) to crush the tissue and ligate the vessels in one step.

c. Complete removal of an entire liver lobe requires carefully placed ligatures to attenuate the large arteries and veins at the liver hilus. Oversew or transfix the vessels to prevent ligature slippage. Place large clamps on the vessels prior to resection of the lobe to prevent cranial retraction of the vessel (Fig. 72-3).

Postoperative Care and Complications

- Monitor for postoperative hemorrhage (oozing of blood from the incision, distention of the peritoneal cavity, pale mucous membranes). Administer blood transfusion if the hematocrit drops below 20%.
- Give supportive therapy with IV fluids and glucose until oral intake of food and water resumes.
- Monitor for evidence of pancreatitis (vomiting, abdominal pain, increased serum amylase and lipase). Delay resuming oral intake and keep on IV fluid therapy until this resolves.
- After massive liver resection, monitor liver function by evaluating bilirubin and serum bile acid concentrations. Liver function reportedly becomes abnormal after resection of 60% or more of the liver.

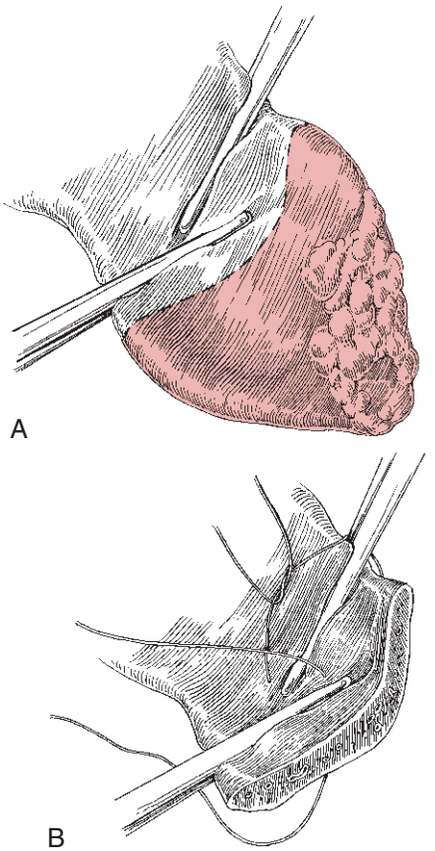

Figure 72-2. Partial hepatectomy. Lesions at the periphery of the liver lobe can be removed by placing crushing clamps across the lobe, proximal to the lesion, and then cutting distal to the clamps. Use absorbable sutures to ligate vessels proximal to the clamps. Tie these ligatures tightly as in the guillotine method for liver biopsy (see Fig. 72-1).

SURGERY FOR PORTOSYSTEMIC SHUNTS

Portosystemic shunts are abnormal vascular communications between the portal vein and a systemic vein. Diagnosis and medical treatment of this condition are discussed in Chapter 71. Animals with portosystemic shunts can initially improve with medical management. However, the definitive and most effective therapy for long-term resolution of clinical signs is surgical attenuation of the shunt vessel. With recent advances in the intraoperative and postoperative management of these animals, morbidity and mortality rates associated with surgery have decreased to very acceptable levels.

Anatomy

Portosystemic shunts are divided anatomically into *extrahepatic* and *intrahepatic* (Fig. 72-4). Definition of shunt anatomy preoperatively is important because

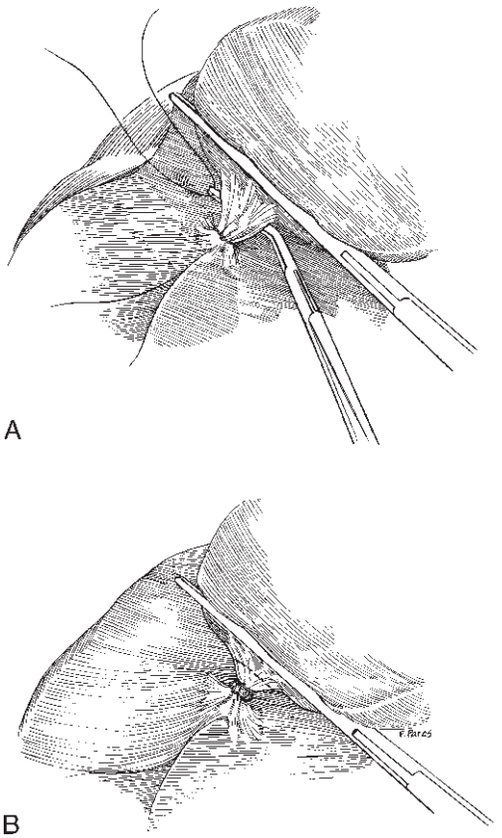

Figure 72-3. Double ligation *(A)* and transection *(B)* in total liver lobectomy.

intrahepatic shunts are much more difficult to correct surgically than are extrahepatic shunts. Also, familiarity with the anatomy helps decrease surgical time and patient morbidity.

Extrahepatic Shunts

Extrahepatic shunts are caudal to the liver. These are vascular communications that usually occur between the portal vein and the caudal vena cava (portacaval shunt) or the azygos vein (portoazygos shunt). Extrahepatic portacaval shunts frequently empty into the left side of the caudal vena cava just adjacent to the epiploic foramen. Shunts involving the left gastric vein can be found near or on the lesser curvature of the stomach.

Intrahepatic Shunts

Intrahepatic shunts communicate with the caudal vena cava within or cranial to the liver parenchyma and can involve either the right or left branches of the hepatic portal vein.

Preoperative positive contrast portography helps differentiate between intrahepatic and extrahepatic shunts. Using these studies, the portal vein can be correlated to the thoracolumbar spine. The first branch of the hepatic portal vein (the right lateral trunk) is located at the 12th thoracic vertebra. If any part of the shunt is caudal to the 13th thoracic vertebra (T13), it is probably extrahepatic. If the entire shunt is cranial to T13, it is probably intrahepatic.

Preoperative Considerations

- Stabilize the animal by medically treating the hepatic encephalopathy for 1 to 2 weeks (see Chapter 71).
- Treat hypoglycemia, if present, with 5% dextrose in a balanced electrolyte solution administered IV.
- If the animal is anorexic, consider giving nutritional support via nasogastric tube or some other feeding device and use a low-protein diet.
- Avoid lactated Ringer's solution for maintenance fluid administration. Lactated Ringer's can make the animal alkalotic and worsen the hepatic encephalopathy.

Anesthesia

▼ ***Key Point*** Animals with portosystemic shunts have markedly reduced capacity to metabolize anesthetic drugs in the liver.

- Avoid using drugs such as the barbiturates and phenothiazine derivatives.

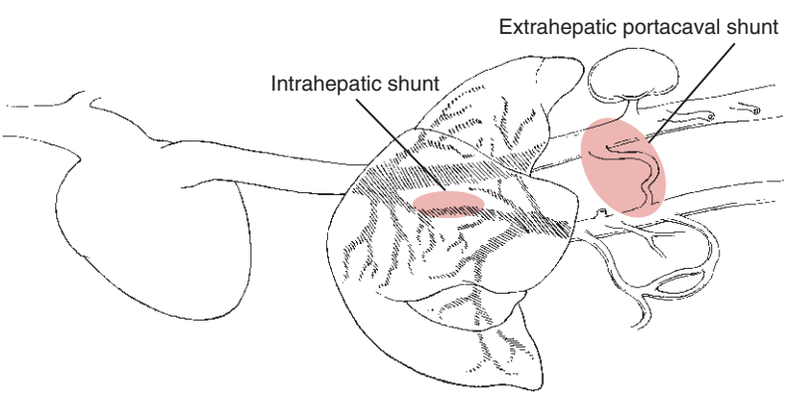

Figure 72-4. Schematic representation of an extrahepatic portacaval shunt and an intrahepatic portacaval shunt.

- Use diazepam (at a reduced dosage; see Chapter 2) as a premedicant, if needed.
- Induce anesthesia via mask induction with isoflurane and oxygen or ketamine/diazepam combination (see Chapter 2).
- Maintain anesthesia with isoflurane and oxygen via endotracheal tube.
- In addition to routine monitoring, monitor blood pressure because changes may occur during manipulation of the shunt.
- Administer 5% dextrose in a balanced electrolyte solution IV during anesthesia and surgery to prevent severe hypoglycemia.

Surgical Procedure

Objectives

- Place a jejunal vein catheter to monitor portal pressures.
- Identify and attenuate the portosystemic shunt to redirect portal blood flow to the liver.
- Avoid causing portal hypertension.

Equipment*

- Standard general surgery pack and retractors (Balfour, malleable)
- Over-the-needle IV catheter (e.g., Sureflo, Terumo Medical, Elkton, MD), water manometer, IV extension set, three-way stopcock, heparinized saline
- Small and large right-angled forceps
- DeBakey tissue-holding forceps
- Ameroid constrictors of various sizes (Research Instruments NW Inc., Sweethome, OR)

Technique

1. Place the animal in dorsal recumbency and prepare the entire ventral abdomen and caudal one-third of the sternum for aseptic surgery.
2. Perform a routine ventral midline abdominal approach. If the shunt is intrahepatic, it also may be necessary to perform a caudal sternotomy.
3. Explore the abdomen and identify the shunt.
   a. *Extrahepatic shunts* usually are found by retracting the duodenum ventrally and to the left, and then following the mesoduodenum cranially and dorsally to the level of the epiploic foramen. Ventral retraction of the lesser omentum usually exposes the shunt entering the left side of the caudal vena cava. Be careful not to injure the hepatic arteries, which lie adjacent to the shunts located in this position. Some shunts can be found by creating a small window in the greater omentum and looking in the vicinity of the splenic vein, or by making a window in the lesser omentum and looking craniodorsal to the lesser curvature of the stomach. Portoazygos shunts are identified by following the abnormal vessel as it courses dorsally through the diaphragm. Shunts in other locations require careful exploration of the cranial abdomen for location. It may be necessary to locate other branches of the portal vein, such as the splenic vein or the left gastric vein, in order to find the shunt.
   b. The location of *intrahepatic shunts* varies. Exposure may be facilitated by median sternotomy and ventral-to-dorsal division of the diaphragm. The intrahepatic shunt may be seen entering the caudal vena cava cranial to the liver. These shunts are usually closely adherent to the peritoneal surface of the diaphragm. Alternatively, the shunt or the branch of the portal vein entering the shunt may be seen and dissected caudal to the liver. Dissection and attenuation of intrahepatic shunts can be very difficult, even for experienced surgeons.
4. Carefully skeletonize a small portion of the shunt vessel and pass an ameroid constrictor around it. The constrictor is composed of a hydroscopic material (casein) encased in a metallic ring. It gradually occludes the shunt over a period of weeks, reducing the incidence of portal hypertension. Choose a constrictor size (range from 3.5–9 mm internal diameter) that allows placement on the shunt with no immediate occlusion of the vessel lumen.
5. If the shunt is too large for an amerioid constrictor, or it is impossible to pass the constrictor around the shunt (common in intrahepatic shunts), perform suture ligation of the shunt using silk suture. Slowly ligate the shunt while monitoring portal pressure via a jejunal vein catheter (over-the-needle IV catheter placed in a jejunal vein and connected to a water monometer).

▼ ***Key Point*** During shunt ligation, do not allow portal pressure to rise >10 cm above the preligation value or to reach an absolute value >20 cm H_2O.

6. Carefully observe the abdominal viscera, especially the pancreas and intestine, for evidence of portal hypertension (e.g., bluish color and congestion of venous vessels). Use both the portal pressure values and tissue appearance to be sure that portal hypertension is not developing during ligation.
   a. Reduce the degree of attenuation if there is any evidence of portal hypertension.
   b. Complete ligation is possible in rare cases; however, many animals respond well to only partial ligation of the shunt.
7. Remove the jejunal catheter and ligate the jejunal vein if necessary.
8. Close the abdominal incision in a routine fashion.

*Also see equipment listed under Median Sternotomy, which may be needed if the shunt is intrahepatic (Chapter 167).

Postoperative Care and Complications

- Monitor for portal hypertension. *Acute* portal hypertension is a life-threatening complication that may develop any time from immediately to several hours postoperatively. Watch for the following clinical signs of postoperative portal hypertension: acute collapse, severe abdominal pain, abdominal distention (ileus), pale mucous membranes, slow capillary refill, and diarrhea with frank blood and mucosal shreds.

▼ ***Key Point*** If acute portal hypertension is suspected, reoperate immediately to remove the shunt ligature.

- *Chronic* portal hypertension usually is manifested by ascites. Treatment generally is not necessary, and the ascites usually resolves in 1 to 3 weeks.
- Prevent hypoglycemia by giving 5% dextrose in saline until the animal resumes oral feeding.
- Add potassium to the fluid to prevent hypokalemia (see Chapter 5 on fluid therapy).
- Continue medical management of hepatic encephalopathy (see Chapter 71).
- If the animal is doing well clinically, discontinue the lactulose and neomycin after 2 to 4 weeks.
- Continue feeding a low-protein diet (e.g., Prescription Diet k/d [Hill's]) until liver function improves significantly. Measure pre- and post-prandial serum bile acid concentrations 3 and 6 months postoperatively to evaluate improvement in liver function. If no clinical improvement is seen, consider follow-up portography and religation of the shunt vessel if continued shunting of blood is seen.

SURGERY OF THE BILIARY TRACT

Anatomy

Gallbladder

- The gallbladder is a pear-shaped sac located between the quadrate and right medial lobes of the liver.
- In a medium-sized dog, it has a capacity of 15 ml.
- Bile drains from the gallbladder to the cystic duct, and then to the common bile duct.
- The gallbladder is divided anatomically into three parts: the fundus (blind end), body (middle portion), and neck.
- Histologically, the gallbladder wall consists of a mucosal lining, layer of smooth muscle fibers, submucosal layer, and serosal covering.
- Blood supply is via the cystic artery, a branch of the hepatic artery.

Bile Ducts

- Hepatic cells discharge bile into minute canaliculi, which coalesce to form interlobar ducts and then hepatic ducts.
- Hepatic ducts and the cystic duct drain into the bile duct (or common bile duct).
- The common bile duct is present in the lesser omentum, and the free portion is about 5 cm in length. It travels through the duodenal wall as an intramural portion that is 1.5 to 2.0 cm in length, and empties into the major duodenal papilla. The minor pancreatic duct in dogs empties immediately adjacent to the opening of the bile duct at the major duodenal papilla. In cats, the common bile duct and major pancreatic duct join and subsequently enter the duodenum at the major papilla as a common duct.

Preoperative Considerations

- Correct dehydration and serum electrolyte imbalances before surgery.
- If the animal is not already being treated for infection, administer prophylactic antibiotics (directed toward gram-negative and anaerobic bacteria).

▼ ***Key Point*** If the bile duct is totally obstructed, coagulopathy may be present because of decreased absorption of vitamin K, with decreased activity of vitamin K–dependent clotting factors.

- Give vitamin K_1 (AquaMEPHYTON) at 1 to 3 mg/kg divided q12h subcutaneously (SC), 36 hours before surgery if necessary. If immediate surgery is required, give a fresh whole blood transfusion.

Cholecystectomy—Surgical Procedure

Cholecystectomy is indicated for severe diseases of the gallbladder, such as damage to the gallbladder or cystic duct secondary to trauma, severe cholecystitis, gallbladder mucocele, neoplasia, and biliary calculi.

Objectives

- Remove the gallbladder while minimizing trauma to surrounding tissues.
- Prevent leakage of bile to the peritoneal cavity.
- Avoid damage to the remainder of the biliary duct system.

Equipment

- Standard general surgery pack and suture
- Small and large gallbladder forceps and other right-angled forceps
- Hemostatic stainless steel clips
- Sterile cotton-tipped applicators

Technique

1. Prepare the animal as previously described for liver biopsy and hepatic surgery.
2. Isolate the gallbladder from the remainder of the peritoneal cavity with moistened laparotomy sponges.

3. Dissect the gallbladder from the liver by blunt dissection. Sterile cotton-tipped applicators are helpful to separate the gallbladder from the surrounding hepatic tissue. Babcock forceps or stay sutures can be used to manipulate the gallbladder during this dissection.
4. Isolate and double-ligate the cystic duct and cystic artery with absorbable sutures or hemostatic clips.
5. Place gallbladder forceps and incise the cystic duct and artery just distal to the forceps. Remove forceps and gallbladder.
6. Submit the gallbladder for aerobic and anaerobic bacterial culture and histopathology.
7. Close the abdominal incision in a routine fashion.

Cholecystotomy—Surgical Procedure

Cholecystotomy is indicated to remove biliary calculi, to flush the gallbladder of inspissated or infected bile, or to facilitate passing a catheter into the common bile duct to relieve obstruction. The gallbladder should be healthy and have a good blood supply to ensure satisfactory healing. If the gallbladder is infected, inflamed, or necrotic, perform cholecystectomy.

Objectives

- Open and inspect the gallbladder and its contents.
- Avoid spillage of bile into the peritoneal cavity.
- Provide a watertight seal of the cholecystotomy incision using absorbable suture material.
- Submit samples of tissue, calculi, and/or bile for analysis and culture.
- Thoroughly flush the gallbladder and biliary ducts to remove stones and infected material.

Equipment

Equipment is the same as for cholecystectomy plus the following:

- Fine absorbable suture with taper or taper-cut needle (4-0, 5-0 polydioxanone or polyglactin 910).
- Infant feeding tube or small (5-French) Brunswick rubber catheter.

Technique

1. Prepare and position the animal as previously described for liver biopsy and hepatic surgery. The surgical approach is the same as for a cholecystectomy.
2. Isolate the gallbladder from the remainder of the peritoneal cavity with laparotomy sponges.
3. Use stay sutures (5-0 silk) on the gallbladder on each side of the proposed incision.
4. Incise the gallbladder fundus, using a #11 scalpel blade and Metzenbaum or tenotomy scissors. Evacuate the contents and save samples of bile or calculi for analysis and culture.

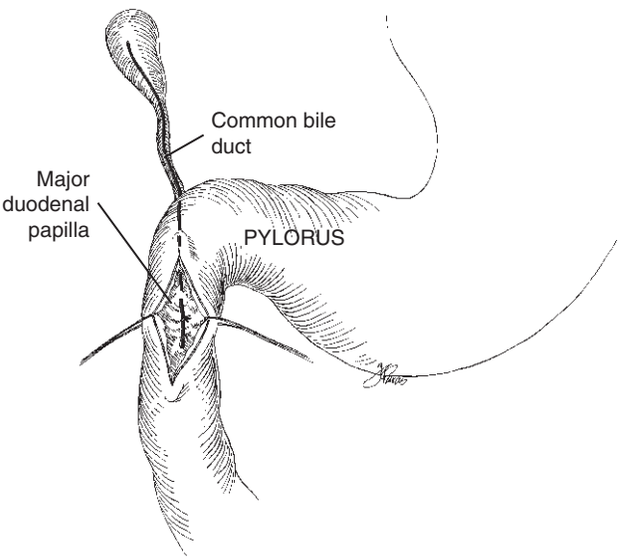

Figure 72-5. Placement of an indwelling stent catheter in the common bile duct. The catheter is placed via a duodenotomy. Insert the catheter retrograde through the major duodenal papilla and into the gallbladder. Leave the end of the catheter in the duodenal lumen and ligate in place with 4-0 or 5-0 catgut; close the duodenotomy incision.

5. Flush the gallbladder with warm, sterile saline.
6. To ensure patency, cannulate and flush the cystic and common bile ducts with an infant feeding tube or 5-French Brunswick catheter.
7. If necessary, perform a duodenotomy approximately 2 to 4 cm distal to the pylorus to pass a catheter retrograde into the common bile duct through the major duodenal papilla. Place a stent catheter if recurrent bile duct obstruction is expected or to stent a ruptured biliary duct (Fig. 72-5) (see more detailed description of stent catheter placement under "Surgical Repair of Traumatic Biliary Rupture").
8. Close the gallbladder incision in a one- or two-layer inverting pattern (e.g., Cushing and/or Lembert), using 4-0 or 5-0 absorbable suture and a taper needle.
9. Close the abdominal incision in a routine manner.

Cholecystoenterostomy—Surgical Procedure

Cholecystoenterostomy is surgical anastomosis of the gallbladder to the intestinal tract. The major objective is to bypass the cystic and common bile ducts when these ducts are irreversibly obstructed. Examples of indications are severe scar tissue in the bile ducts (sequela of cholangitis), non-resectable neoplasia, severe cholangiohepatitis with sludged bile (in cats), and large bile duct calculi that cannot be removed. The gallbladder can be anastomosed to the duodenum (cholecystoduodenostomy) or to the jejunum (cholecystojejunostomy).

Objectives

- Establish flow of bile from the gallbladder directly to the duodenum or jejunum to bypass the cystic and common bile duct.
- Maintain sufficient lumen size to allow free flow of bile from the gallbladder to the intestine.
- Prevent bile or intestinal leakage.
- Provide a tension-free anastomosis.

Equipment

- Equipment is the same as for cholecystotomy.

Technique

1. Prepare and position the animal as previously described for liver biopsy and hepatic surgery. The surgical approach is identical to that for cholecystectomy.
2. Using blunt dissection, gently free the gallbladder from the surrounding liver tissue.
3. Bring a loop of duodenum or jejunum close to the gallbladder and place stay sutures in both structures.
4. Incise the gallbladder along the fundus and the intestine on its antimesenteric surface.
5. Perform a two-layered anastomosis, using absorbable suture (e.g., 4-0 PDS). The inner layer is a simple continuous, full-thickness closure; the outer layer is a Cushing pattern. Make sure the anastomosis is at least 2.5 cm in diameter. This large opening helps prevent sequestration of intestinal contents in the gallbladder that could result in severe cholecystitis and cholangitis.
6. Close the abdominal incision in a routine manner.

Surgical Repair of Traumatic Biliary Rupture

Rupture of the biliary tract causes severe chemical and possibly septic peritonitis. Diagnosis and initial management of animals with bile peritonitis is discussed in Chapter 76. Perform surgical correction of bile leakage promptly because metabolic consequences are serious and life-threatening.

Objectives

- Evaluate the entire liver and biliary tract for evidence of damage.
- Identify the source of bile leakage and control it.
- Treat the peritonitis with copious lavage and abdominal drainage.
- Maintain patency of major biliary pathways.
- Provide nutritional access for hyperalimentation in patients in critical condition.

Equipment

Equipment is the same as for cholecystotomy plus the following:

- Stent tubing (e.g., 5-French Brunswick catheter, infant feeding tube, or Silastic tubing)

Technique

1. The preparation of the animal and surgical approach are the same as for cholecystectomy.
2. Evacuate fluid from the peritoneal cavity.
3. Examine the entire liver and biliary system for evidence of trauma and injury. Examine the remainder of the abdominal organs for abnormalities.
4. Find the source of bile leakage:
   a. If the gallbladder is intact, express it and look for leakage.
   b. If the above is unsuccessful, perform a duodenotomy over the major duodenal papilla and catheterize the common bile duct, using a 5-French Brunswick catheter or infant feeding tube. Flush the bile duct with sterile saline and look for leakage.
5. Correct the leakage.
   a. If the rent is in the gallbladder, perform cholecystectomy. Suture the rent if in a large bile duct. Use fine absorbable suture material (4-0 or 5-0 polydioxanone).
   b. If primary closure is not possible, stent the torn duct by passing a soft catheter up the common bile duct via the major duodenal papilla. Make sure that the end of the catheter is at least 2 to 3 cm proximal to the rent. Secure the catheter to the duodenal mucosa by placing one or two ligatures of 5-0 catgut. Cut the catheter, leaving 2 to 3 cm in the lumen of the duodenum, and close the duodenal incision in a routine manner. In 1 to 2 weeks, the catheter will dislodge and be passed through the intestinal tract. If the catheter has not passed in 3 weeks, remove via endoscopy.
   c. Rupture of small hepatic ducts can be treated by simple ligation of the duct. Collateral biliary ducts should allow for continued flow of bile from that liver lobe.
6. Lavage the abdomen with copious amounts of warm, sterile saline.
7. Close the abdomen routinely.

Postoperative Care and Complications

- Maintain IV fluid therapy until oral intake resumes.
- Monitor for evidence of bile peritonitis: painful abdomen, fever, leukocytosis, icterus, and bile-stained fluid on abdominal tap.
- If cultures from the biliary tract are positive, administer long-term (6 weeks) antibiotic therapy.

▼ ***Key Point*** Mortality associated with bile peritonitis is significantly higher if bacterial contamination is also present.

- Monitor for evidence of pancreatitis; withhold food and water if it occurs (maintain the animal on IV fluids).
- Reevaluate every 3 to 6 months for recurrence of biliary obstruction or ascending infection of the biliary tract after cholecystoenterostomy.

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Chapter

73 Diseases and Surgery of the Exocrine Pancreas

Robert G. Sherding / Stephen J. Birchard / Susan E. Johnson

The pancreas is a V-shaped gland in the cranial abdomen composed of an exocrine portion (the acinar cells) and an endocrine portion (the islets of Langerhans). The normal functions of the exocrine pancreas are summarized in Table 73-1. The clinically important disorders of the exocrine pancreas include pancreatitis, exocrine pancreatic insufficiency, and neoplasia. Diseases of the endocrine pancreas are discussed in Chapters 34 and 35.

PANCREATITIS

Pancreatitis is an acute or chronic inflammatory condition of the pancreas that develops when premature intrapancreatic activation of digestive enzymes results in progressive autodigestion of the pancreas. Clinically, pancreatitis can be acute or chronic and mild or severe. The clinical forms of pancreatitis are categorized in Table 73-2.

▼ ***Key Point*** Dogs most frequently develop acute pancreatitis. Cats are more likely to develop chronic pancreatitis.

Etiology and Risk Factors

In most animals with spontaneous pancreatitis, an etiology is not identified and the pathogenesis is poorly defined. Based on clinical associations found in naturally occurring cases and on various experimental models for producing pancreatitis, the following have been implicated as etiologic or predisposing factors:

- ***Nutrition***—Obesity (dogs), long-term intake of high-fat low-protein diet
- ***Hyperlipidemia***—As a result of recent ingestion of a fatty meal, miniature schnauzer hyperlipidemia, lipodystrophy, or endocrinopathy (e.g., hyperadrenocorticism, diabetes mellitus, or hypothyroidism)
- ***Reflux of duodenal contents***—Into the pancreatic duct as bile, fatty acids, activated enzymes, or bacteria
- ***Obstruction of the pancreatic duct or papilla***—As a result of duodenitis, edema, spasm, calculi, neoplasia, metaplasia, or aberrant intestinal parasite migration
- ***Biliary tract disease***—Especially cholangitis in cats
- ***Gastrointestinal disease***—Especially inflammatory bowel disease in cats
- ***Infection***—For example, ascending enteric bacteria, parvovirus, feline infectious peritonitis, *Toxoplasma gondii, Babesia canis,* pancreatic flukes *(Eurytrema procyonis),* or liver flukes *(Amphimerus pseudofelineus)*
- ***Hypercalcemia***—When total serum calcium exceeds 15 mg/dl, as can occur in hypercalcemia of malignancy, hyperparathyroidism, and vitamin D intoxication
- ***Hyperstimulation***—By organophosphate toxicity, cholinergic agonists, scorpion venom, and caerulein (an analogue of cholecystokinin)
- ***Idiosyncratic drug reactions***—Corticosteroids, potassium bromide, L-asparaginase, azathioprine, sulfonamides, etc.
- ***Zinc toxicosis***
- ***Pancreatic trauma***—Abdominal injury, surgery, or lithotripsy
- ***Pancreatic ischemia***—For example, hypovolemia, thrombosis, and gastric dilatation-volvulus
- ***Genetic predisposition***—Miniature schnauzers, etc.

Pathogenesis

Pancreatitis results from the premature intrapancreatic activation of trypsin and other digestive enzymes, resulting in acinar cell necrosis and pancreatic autodigestion.

- Once initiated, amplification and progression of pancreatitis involves factors such as nitric oxide, oxygen-derived free radicals, and various inflammatory mediators, cytokines, and interleukins.
- Severity is enhanced by pancreatic microvascular injury, pancreatic ischemia, systemic inflammatory response, disseminated intravascular coagulation (DIC), and intestinal bacterial translocation (Table 73-3).

▼ ***Key Point*** Intrapancreatic activation of trypsin and other digestive enzymes leads to autodigestion of the pancreas. Impaired pancreatic microcirculation is a key factor in the progression from mild self-limiting pancreatitis to severe necrotizing pancreatitis.

Table 73-1. FUNCTIONS OF THE EXOCRINE PANCREAS

Secretory Products	Functions
Digestive enzymes*	
Trypsins	Protein digestion
Chymotrypsins	Protein digestion
Elastases	Protein digestion
Carboxypeptidases	Protein digestion
Amylase	Polysaccharide digestion
Phospholipase	Lipid digestion
Lipase	Lipid digestion
Colipase	Coenzyme facilitator of lipase
Bicarbonate and water†	Neutralization of gastric acid entering duodenum
Pancreatic trypsin inhibitor	Protection against autodigestion
Pancreatic intrinsic factor	Facilitation of cobalamin (vitamin B_{12}) absorption
Antibacterial proteins	Antibacterial (regulation of small intestinal microflora)
Miscellaneous	Facilitation of zinc absorption
	Trophic effect on intestinal mucosa

*Acinar cells secrete enzymes in response to cholecystokinin, which is released into the blood from the proximal intestine when partially digested food enters the duodenum from the stomach. Proteolytic enzymes are secreted as inactive precursors (zymogens) that are not activated until they enter the intestinal tract. Enteropeptidase from the duodenal mucosa activates trypsinogen to active trypsin; trypsin then activates the other proteases and phospholipase.

†Centroacinar and duct cells produce bicarbonate-rich secretion in response to secretin released into the blood from the proximal intestine when acid enters the duodenum from the stomach.

Table 73-2. CATEGORIES OF PANCREATITIS

Acute Pancreatitis
(abrupt onset, acute episodes may recur)

Mild (Edematous)
Self-limiting
Minimal necrosis and vascular compromise
No multisystemic effects or complications
Uncomplicated recovery

Severe (Hemorrhagic)
Self-perpetuating (progressive)
Extensive necrosis and vascular compromise
Severe complications
Multisystem failure
Guarded prognosis

Chronic Pancreatitis
(may be continuous and "smoldering" or recurrent and episodic)

Mild
Minimal morphologic damage
Absence of complications

Severe
Progressive irreversible destruction of acinar and islet cells
Severe pancreatic fibrosis and atrophy
Complications:
- Exocrine pancreatic insufficiency
- Diabetes mellitus
- Extrahepatic bile duct obstruction

- Natural protective mechanisms against autodigestion involve pancreatic secretory trypsin inhibitor, $alpha_1$-proteinase inhibitor, and alpha-macroglobulins. These become overwhelmed as pancreatitis develops.
- Pathologically, pancreatitis can be categorized as acute edematous, acute necrotizing, acute suppurative, or chronic nonsuppurative. Sequelae include pseudocyst, abscess, fibrosis, and atrophy.

Clinical Signs and Manifestations

Clinical signs of acute pancreatitis are extremely variable, ranging from inapparent to mild to fulminant "acute abdomen" crisis. Signs may be vague, especially in cats. In chronic pancreatitis, episodic signs may correspond to periodic flare-ups of inflammation. In some cases, clinical signs are dominated by secondary complications (e.g., DIC) or sequelae (e.g., diabetes mellitus).

▼ ***Key Point*** The "classic" signs of vomiting and abdominal pain are frequent in dogs with acute pancreatitis but are relatively uncommon in affected cats.

Canine Pancreatitis

Pancreatitis most frequently occurs in middle-aged and older dogs that are overweight. A recent history of dietary indiscretion or a high-fat meal is common.

- Vomiting (90% of severe cases), anorexia (91%), and depression are the most consistent signs.
- Cranial abdominal pain is found in 58% of dogs, varying from mild to intense (manifested as restlessness, panting, trembling, hunched-up abdomen, praying position of relief, seeking of cool surfaces, and pain on palpation).
- Cranial abdominal mass may be palpable in some dogs.
- Dehydration is detected in 50% of dogs.
- Diarrhea (sometimes hemorrhagic) is reported in 33% of dogs.
- Fever is seen in 32% of dogs, usually attributable to the inflammatory response. It does not necessarily imply infection.
- Weakness or, in severe cases, acute collapse from shock may be observed.

Feline Pancreatitis

Cats are more likely to have chronic "smoldering" pancreatitis, manifested by nonspecific signs of lethargy, anorexia, and weight loss, with or without vomiting. Cats with severe acute pancreatitis can have any of the clinical sign seen in dogs, but less consistently.

The reported frequency of clinical signs and physical findings in cats with severe pancreatitis is as follows:

- Lethargy (100% of cases)
- Inappetence (97%)

Table 73-3. FACTORS IN THE PATHOGENESIS OF PANCREATITIS

Factor	Proposed Role in Pathogenesis
Pancreatic Enzymes	
Trypsin	Perpetuation of proteolytic damage of pancreatic tissue (autodigestion)
	Perpetuation of activation of more trypsin and other proteases
	Consumption of plasma protease inhibitors
	Coagulation/fibrinolysis (DIC)
	Activation of kinin system and release of histamine from mast cells, contributing to edema and hemorrhage
Phospholipase A	Cell membrane damage (necrosis, non-cardiogenic pulmonary edema)
	Liberation of toxins (e.g., myocardial effects)
Elastase	Vascular damage (progression of edematous to hemorrhagic pancreatitis)
Chymotrypsin	Activation of xanthine oxidase (generation of oxygen-derived free radicals; see below)
Lipase	Local fat necrosis (peritonitis, "calcium soaps," hypocalcemia)
Inflammatory Mediators	Systemic inflammatory response syndrome
	Vasodilation, hypotension, shock
	Local inflammation and aggregation of leukocytes; peritonitis
Oxygen-Derived Free Radicals	Damage of tissues by disrupting cell membranes through peroxidation of lipids in the membrane
	Endothelial cell injury (pancreatic edema and hemorrhage, DIC)
Coagulation/Fibrinolysis	Disseminated intravascular coagulopathy
	Thrombosis of pancreatic blood vessels
	Ischemic pancreatic necrosis

DIC, disseminated intravascular coagulation.

- Dehydration (92%)
- Hypothermia (68%)
- Icterus (64%)
- Vomiting (35%)
- Abdominal pain (25%)
- Palpable abdominal mass (23%)
- Dyspnea (20%)
- Diarrhea (15%)
- Ataxia (15%)
- Fever (7%)

▼ ***Key Point*** Concurrent inflammatory bowel disease and cholangitis are frequent in cats with pancreatitis. This may be related to the anatomic arrangement of the bile and pancreatic ducts that join and have a common opening into the duodenum in cats.

Acute Complications

Most of the following complications seriously worsen the prognosis in pancreatitis:

- Shock, collapse, and hypothermia (due to hypovolemia and endotoxemia)
- Peritonitis (sterile exudate) and intra-abdominal fat necrosis
- Jaundice (intrahepatic cholestasis, hepatocellular necrosis, biliary obstruction, lipidosis in cats)
- Hepatic lipidosis (in cats)
- Sepsis
- DIC (bleeding, thrombosis, infarction)
- Acute oliguric renal failure
- Intestinal hypomotility (ileus)
- Hypocalcemia (rarely, overt tetany)
- Hyperglycemia (due to hyperglucagonemia and hypoinsulinemia)
- Cardiac arrhythmias (myocardial depressant factors, myocardial ischemia or necrosis)
- Respiratory distress (rarely, non-cardiogenic pulmonary edema or pleural effusion)

Chronic Complications and Sequelae

- ***Pancreatic pseudocysts and abscesses***—Characterized by persistence or recurrence of signs associated with a cavitated pancreatic mass that contains liquefied necrotic debris, which can be sterile (pseudocyst) or infected (abscess)
- ***Chronic relapsing pancreatitis***—Characterized by chronic smoldering disease with periodic flare-ups
- ***End-stage pancreatic fibrosis and atrophy***—Manifested as diabetes mellitus, exocrine pancreatic insufficiency, or both
- ***Liver disease***—Resulting from common bile duct obstruction or concurrent cholangiohepatitis

Diagnosis

The diagnosis of pancreatitis is based on the combination of clinical signs, physical examination, routine laboratory findings, assays for circulating pancreatic enzymes, radiography, ultrasonography, and in some cases, pancreatic biopsy.

Clinical Signs and Physical Findings

- Suspect pancreatitis in animals presented for vomiting, depression, anorexia, and abdominal pain. Most dogs have vomiting, abdominal pain, or both; how-

ever, only 33% of cats have vomiting as a sign and only 25% are painful.
- Nearly 33% of dogs are febrile, compared with only 7% of cats. More than 66% of cats with severe acute pancreatitis are hypothermic.
- Identifiable risk factors increase the index of suspicion (e.g., obesity, recent fatty meal, miniature schnauzer breed, and endocrinopathy).
- A palpable right cranial abdominal mass or fluid suggests a pancreatic lesion.

Hematologic Findings

Dogs

- In dogs with severe pancreatitis, the most frequent findings are neutrophilic leukocytosis (55% of cases), with or without a left shift; thrombocytopenia (59%); and hemoconcentration (dehydration) or anemia (29%).
- Neutropenia with a degenerative left shift occurs occasionally with severe necrosis, peritonitis, sepsis, or endotoxemia.
- Red blood cell (RBC) fragments and macroplatelets are consistent with subclinical DIC.

▼ ***Key Point*** Evaluate hemostasis in pancreatitis dogs with thrombocytopenia that may be developing DIC.

Cats

- In cats with severe pancreatitis, the most frequent findings are anemia (55% of cases) or hemoconcentration (30%) and leukocytosis (30%) or leukopenia (15%).

Routine Serum Chemistries and Urinalysis

Several nonspecific abnormalities may be found on routine serum chemistries:

- Azotemia (increased blood urea nitrogen and creatinine), resulting frequently from dehydration and hypovolemia (prerenal) or occasionally from renal damage and acute oliguric renal failure
- Metabolic acidosis and hypokalemia
- Hypocalcemia (usually subclinical; tetany is rare)

▼ ***Key Point*** Hypokalemia is more common in cats with pancreatitis (50% of cases) than in dogs (5%) and is a negative prognostic indicator.

- Elevated serum liver enzymes (ALT, AST, ALP, GGT) and hyperbilirubinemia, can result from hepatocellular injury (due to ischemia, sepsis, or toxins from the pancreas), biliary obstruction, or concurrent cholangitis (cats).
- Hyperglycemia (usually transient, but some animals are diabetic after recovery)
- Fasting hyperlipemia (hypertriglyceridemia and hypercholesterolemia)
- Urinalysis is usually normal with concentrated specific gravity except in cases complicated by diabetes mellitus (glucosuria) or renal failure (isosthenuria).

▼ ***Key Point*** Because elevated levels of amylase, lipase, blood urea nitrogen, and creatinine are common in both renal failure and pancreatitis, assess urine specific gravity (USG) as a reflection of renal concentrating ability; USG > 1.025 indicates adequate renal function.

Serum Amylase and Lipase

Dogs

Serum amylase and lipase concentrations have traditionally been used as indicators of pancreatic inflammation, but these enzymes lack sensitivity and specificity and thus are only appropriate as aids for the diagnosis of canine pancreatitis. Amylase and lipase are normal in one-third to one-half of dogs with histologically confirmed pancreatitis, and up to one-half of dogs with elevation of one or both enzymes do not actually have pancreatitis. Serum amylase and lipase are frequently increased in non-pancreatic diseases.

- Serum amylase and lipase also originate from non-pancreatic sources and may be increased in many renal, gastrointestinal, liver, and neoplastic diseases.
- Delayed renal clearance of enzymes combined with increased secretion due to hypergastrinemia can cause elevations in azotemic patients.
- Corticosteroids in high doses can cause a significant increase (up to fivefold) in serum lipase in the absence of pancreatitis.
- The magnitude of amylase or lipase elevation does not correlate with the severity of the pancreatitis or the prognosis.

Cats

Serum amylase and lipase do not appear to be diagnostically useful in the cat. Most cats with pancreatitis often have minimal or no increase in amylase or lipase.

Serum Trypsin-Like Immunoreactivity Assay

The serum trypsin-like immunoreactivity (TLI) assay is an exocrine pancreatic function test that detects circulating trypsinogen and trypsin. For normal reference ranges see under "Exocrine Pancreatic Insufficiency."

- Serum TLI may be increased in pancreatitis (>50 µg/L in dogs; >100 µg/L in cats) associated with enzyme leakage from the inflamed pancreas.
- Increased serum TLI has good specificity, but its diagnostic usefulness is limited by its low sensitivity (30–60%). TLI has some value as a diagnostic aid in cats. For the diagnosis of canine pancreatitis, TLI

offers minimal advantage over conventional serum lipase and amylase.

Serum Pancreatic Lipase Immunoreactivity Assay

The serum pancreatic lipase immunoreactivity (PLI) assay is an exocrine pancreatic function test that detects circulating pancreas-specific lipase. For normal reference ranges, see under "Exocrine Pancreatic Insufficiency."

- Increased serum PLI (>200 µg/L in dogs; >12 µg/L in cats) appears to be a sensitive indicator of pancreatitis (82% in dogs; nearly 100% in cats) with specificity of approximately 90%.
- Studies suggest that PLI is not increased by gastritis, chronic renal failure, or corticosteroid therapy.
- PLI requires a 0.5-ml fasting serum sample and is commercially available at the Gastrointestinal Laboratory, Department of Small Animal Medicine and Surgery, College of Veterinary Medicine, Texas A&M University, College Station, TX 77843-4474 (website: www.cvm.tamu.edu/gilab).

▼ ***Key Point*** Preliminary studies suggest that the serum pancreatic lipase immunoassay may be the most accurate and reliable diagnostic test available for pancreatitis in dogs and cats.

C-Reactive Protein Assay

C-reactive protein (CRP) concentration is an acute phase reactant produced by the liver in response to inflammation, necrosis, and infection, and is a useful serum marker of systemic inflammation associated with pancreatitis. Canine CRP assays are commercially available (e.g., the gastrointestinal laboratory at Texas A&M; see preceeding section).

- CRP serum level may be an indicator of the severity of pancreatitis.
- CRP may be useful for monitoring response to therapy in dogs with pancreatitis.

Other Pancreatic Function Tests

The following tests have been evaluated as potential indicators of pancreatic inflammation; however, they do not appear to be clinically useful for the diagnosis of pancreatitis in dogs and cats:

- Assay for urine or plasma trypsin activation peptide (TAP)
- Assay for trypsin-alpha$_1$-proteinase inhibitor complexes in plasma
- Plasma protease inhibitor consumption (alpha$_1$-proteinase inhibitor, alpha$_2$-macroglobulin)
- Amylase isoenzyme analysis (for pancreas-specific isoenzyme)
- Assay for serum phospholipase A$_2$

Radiography

Radiography is a useful diagnostic aid for canine pancreatitis and for ruling out other conditions with similar presenting signs.

Dogs

The following radiographic findings are subjective indicators of pancreatitis in dogs but are not present in all cases:

- Increased density and loss of abdominal contrast and detail in the right cranial abdomen (localized peritonitis, ground-glass appearance)
- Displacement of the descending duodenum ventrally and to the right and the pyloric antrum to the left, producing a widened angle or mass effect between the antrum and the duodenum on ventrodorsal radiographs
- Gastric distention and static gas pattern (ileus) in the duodenum and transverse colon
- Delayed passage of barium from the stomach and through the duodenum; also, thickening, corrugation, or spasticity of the duodenum

Thoracic radiography may identify complicating pulmonary edema, pleural effusion, or aspiration pneumonia.

Cats

The abdominal radiographic abnormalities described for dogs are rarely seen in cats with acute pancreatitis. Hepatomegaly and abdominal effusion may be identified in some cats. Thoracic radiography is the same as for dogs.

Ultrasonography

Ultrasonography has high specificity (>85%) but moderate sensitivity (<70%). Detection rates are highest for moderate to severe pancreatitis. The sonographic findings in dogs and cats are similar.

- Pancreatitis is suggested by irregular pancreatic enlargement, decreased or mottled echogenicity of the pancreas, hyperechoic peripancreatic mesentery, and peripancreatic effusion.
- Dilatation of the pancreatic duct, bile ducts, or gallbladder are seen occasionally.

▼ ***Key Point*** Normal radiographic and ultrasonographic evaluations do not rule out pancreatitis, especially in cats.

- Pancreatic pseudocysts and abscesses appear as poorly defined, cavitated pancreatic masses. Consider ultrasound-guided needle aspiration of pseudocysts for diagnosis and therapeutic drainage. Pseudocysts

are more common than abscesses, and serial ultrasound examinations have shown that many pseudocysts resolve spontaneously without complications.

Computed Tomography

Abdominal computed tomography (CT) scanning is not a reliable diagnostic test for pancreatitis in dogs and cats.

Pancreatic Biopsy

Biopsy of the pancreas by laparoscopy or laparotomy can be used for confirming pancreatitis when less invasive diagnostics are equivocal and for staging the histopathologic category (i.e., necrotizing, suppurative, chronic mononuclear with fibrosis, or neoplastic). The pancreas may grossly appear normal in some cases. Take multiple biopsies as the lesions can be patchy in distribution, especially in mild or chronic cases.

Medical Treatment

Mild acute pancreatitis often is self-limiting and may resolve spontaneously in a few days. Severe acute pancreatitis is a life-threatening multisystemic crisis that requires intensive therapy. The goal of treatment is to rest the pancreas, provide supportive care, and control complications as they arise to allow time for the pancreatic inflammation to subside. In addition, identify and correct potential causative factors (see under "Etiology and Risk Factors"). Surgical intervention may be required for pancreatic abscessation or biliary obstruction.

Fluid and Electrolyte Therapy

Use IV fluid therapy to correct dehydration, control hypovolemia, maintain electrolyte balance, and support perfusion of the pancreatic microcirculation.

- For fluid volume replacement and maintenance, administer an IV, balanced crystalloid solution (e.g., lactated Ringer's) in sufficient volume to replace deficits, replace ongoing losses, and meet maintenance requirements (see Chapter 5). To treat shock, give up to 60 to 90 ml/kg IV in the first hour and consider other therapy described in Chapter 156.
- Supplement potassium with 20 to 30 mEq of KCl per liter of maintenance fluids, and adjust according to monitoring of serum potassium.
- Treat hypocalcemia as needed with calcium gluconate IV.
- Acid-base status is unpredictable in pancreatitis. Avoid unnecessary bicarbonate administration that can worsen hypocalcemia.
- Monitor urine output (for oliguria) and respiratory function (for pulmonary edema).
- In hypoproteinemic patients (serum albumin is <2.0 g/dl), consider infusion of colloid solution (hetastarch at a dosage of 10–20 ml/kg q24h IV), plasma, or whole blood (10–20 ml/kg) for maintenance of plasma oncotic pressure (see Chapter 5). Colloid may also enhance pancreatic microcirculation, reduce pancreatic edema, and help prevent secondary renal failure, pulmonary edema, and pleural effusion. Fresh plasma or whole blood also can replace circulating proteinase inhibitors (alpha-macroglobulins) that are consumed in pancreatitis.
- Use glucocorticoids only in patients presented in shock and only short term (one or two doses, as described for treatment of shock in Chapter 156). Glucocorticoids may impair clearance of circulating proteinase-macroglobulin complexes.

Control of Vomiting

For vomiting animals, restrict oral intake until vomiting is controlled.

- Use metoclopramide, chlorpromazine, or ondansetron to control vomiting (see Chapter 67, Table 67-3)
- Control gastric acid secretion with a drug such as famotidine (see Chapter 67, Table 67-3).
- Avoid anticholinergics because they potentiate ileus of the gastrointestinal tract.

Control of Abdominal Pain

- Use rest and confinement to help minimize pain.
- For initial pain relief, use buprenorphine (Buprenex at a dosage of 0.005–0.010 mg/kg SC, IM, or IV q6–12h) or oxymorphone (0.05–0.20 mg/kg SC, IM, or IV q2–6h), beginning at the lower dosage range in cats or with IV use and titrating higher as needed. Transdermal fentanyl patches and other analgesic options can also be used (see Chapter 6 for additional options for pain control).
- Avoid nonsteroidal anti-inflammatory drugs in pancreatitis because of risks of gastrointestinal ulceration and the potential for adverse renal and hepatic effects.
- Oral pancreatic enzyme supplements and insulin have been beneficial for pain relief in humans with chronic pancreatitis, but this effect has not been evaluated in animal patients.

Control of Bacterial Complications

Most animals with pancreatitis do not have bacterial infection, but translocation of enteric bacteria is possible. Potential indications for antibiotics include persistent fever, leukocytosis with left shift, systemic sepsis, aspiration pneumonia, septic peritonitis, pancreatic abscess, or failure to improve with therapy.

- The use of prophylactic antibiotics in pancreatitis is controversial and requires good clinical judgement. For initial routine prevention, administer ampicil-

lin (20 mg/kg q8h IV) or a cephalosporin (e.g., cephalothin or cephazolin) (20 mg/kg q6–8h IV).
- For treatment of suspected or confirmed infections, use ampicillin combined with enrofloxacin (Baytril at 5 mg/kg SC, IM, or PO q12h) or amikacin (Amikin at 5 mg/kg q8h IM or IV). If renal failure is present, adjust the aminoglycoside dosage or choose an alternative antibiotic.

Nutritional Support

- For dogs with pancreatitis, only restrict food intake for as brief a period as possible while vomiting is brought under control (i.e., 48 hours or less). As soon as food is tolerated orally, resume feeding. Use a diet that is moderately restricted in fat and protein.
- Feed cats with pancreatitis whenever possible to prevent hepatic lipidosis.
- Alternatively, use an endoscopically placed jejunostomy tube or other tube feeding strategy (see Chapter 3). Constant-rate infusion of a tube-fed diet may be tolerated even in vomiting animals.
- Use partial parenteral nutrition or total parenteral nutrition only when enteral nutrition fails or when necessary for animals with persistent vomiting.

Inhibition of Pancreatic Secretion

- Pancreatic enzyme secretion is normally stimulated by ingestion of food, particularly fats and proteins. The traditional approach to treating pancreatitis has been to restrict oral intake (nothing per os) to place the pancreas at "physiologic rest." However, this has not been proven to be effective, and evidence suggests that enteral nutrition enhances the speed and rate of recovery from pancreatitis (see under "Nutritional Support").
- The benefits are doubtful for experimental treatments such as glucagon, somatostatin, cholecystokinin inhibitors, and enzyme inhibitors that are intended to suppress pancreatic secretion.

Removal of Activated Enzymes

These measures promote natural plasma antiprotease activity or removal of activated proteases.

- Alpha$_2$-macroglobulin binds circulating activated enzymes for removal by the mononuclear phagocyte system. Fresh frozen plasma (10–20 ml/kg) or whole blood transfusion may benefit patients with fulminant pancreatitis by supplying macroglobulin. It also benefits hypoalbuminemia.
- Avoid glucocorticoids because they may have a detrimental effect on removal of macroglobulin-enzyme complexes.
- Peritoneal lavage using a dialysis catheter can help remove intraperitoneal enzymes, inflammatory mediators, and toxins. Although it is not practical to recommend as a routine method of treatment, it can be beneficial in cases of pancreatitis with abdominal effusion.

Treatment of Acute Complications

Disseminated Intravascular Coagulation

- Prevent by IV fluid therapy to promote perfusion of the microcirculation.
- Treat DIC with heparin (75–150 IU/kg q8h SC) (see Chapter 23).
- Give fresh frozen plasma or whole blood.

Oliguric Renal Failure

- Prevent by vigorous IV fluid therapy to control hypovolemia.
- If oliguria occurs (<1 ml of urine per kilogram per hour), ensure adequate circulatory volume expansion with IV fluids and give furosemide (Lasix at 2 mg/kg IV; repeat once or twice up to 4–6 mg/kg, if necessary). For refractory oliguria, give a constant-rate infusion of dopamine and other measures as described in Chapter 77.

Other Acute Complications

- Control hyperglycemia (if glucose exceeds 300 mg/dl) with short-acting regular crystalline zinc insulin (see Chapter 34).
- Control cardiac arrhythmias if they occur (see Chapters 145 and 146).
- Control non-cardiogenic pulmonary edema if it occurs (see Chapter 162).

Treatment of Chronic Complications and Sequelae

- Surgical intervention is indicated for management of septic peritonitis (see Chapter 76), for drainage or excision of pancreatic abscesses, and for cholecystoduodenostomy (after active pancreatitis is resolved) to relieve persistent biliary obstruction (see Chapter 72).
- Insulin is indicated if persistent hyperglycemia consistent with diabetes mellitus occurs (see Chapter 34).
- Pancreatic enzyme supplementation is indicated for exocrine pancreatic insufficiency (see discussion later in this chapter).
- In cats in endemic areas, diagnose infections caused by pancreatic flukes *(Eurytrema procyonis)* or liver flukes *(Amphimerus pseudofelineus)* by identifying the characteristic single-operculated fluke ova in the feces. Treat with praziquantel (Droncit at 40 mg/kg PO q24h for 3 days), or fenbendazole (Panacur at 50 mg/kg PO q24h for 10–14 days).

Prevention of Recurrences

- Identify and control underlying risk factors (see previous discussion under "Etiology and Risk Factors").
- Feed a fat-restricted diet and avoid fatty "treats."

Surgical Treatment of Pancreatitis

Medical treatment, as outlined in this chapter, is preferred for most animals with pancreatitis. However, surgery may be appropriate in certain patients. The decision to operate on an animal with pancreatitis is very difficult because such patients frequently are poor anesthetic and surgical risks. The surgical procedure may cause the animal's overall condition to worsen. Consider all options and thoroughly discuss the prognosis and potential complications with the owner prior to surgery.

Indications for Surgery

- *Failure to respond to appropriate medical therapy:* Assuming an accurate diagnosis, consider an exploratory laparotomy if the patient's condition deteriorates or does not improve with medical treatment.
- *Presence of a pancreatic abscess or other mass:* Consider surgery if repeated ultrasonographic examinations reveal persistence or enlargement of a pancreatic abscess, pseudocyst, or other mass and if the patient's condition dictates aggressive action.
- *Severe icterus due to extrahepatic biliary obstruction:* As previously discussed, inflammation and tissue swelling associated with pancreatitis can cause biliary obstruction (see Chapter 71). Serial serum chemistries and repeated ultrasonographic examinations are helpful in making this diagnosis and determining trends. If the obstruction and associated icterus do not improve with medical therapy, consider surgical exploration and biliary decompression.
- *Severe pancreatitis and septic peritonitis:* Severe peritonitis may occur with pancreatitis (see Chapter 76). Surgical lavage and drainage may be necessary.

Preoperative Considerations

- Thoroughly assess the animal and review the history and clinical course of events.
- Consider patient factors that may increase the complication rate, such as age, debilitation, sepsis, hypoproteinemia, DIC, diabetes mellitus, and disorders of other organ systems.
- Determine the coagulation status in animals with severe pancreatitis, biliary obstruction, or possible DIC.
- If the animal is not already receiving antibiotics, administer IV antibiotics at or before induction of anesthesia and continue postoperatively if necessary.

Surgical Procedure

Objectives

- Surgically expose the pancreas and determine the type and extent of the disease; remove devitalized tissue.
- Obtain fluid and tissue samples for culture, sensitivity, and histopathology.
- Open, drain, and omentalize pancreatic abscesses or pseudocysts.
- Thoroughly explore the abdominal cavity for evidence of associated lesions or other problems, such as obstruction of the common bile duct.
- Lavage the peritoneal cavity to remove necrotic tissue debris, toxins, enzymes, and exudate.
- Provide abdominal drainage in cases of severe peritonitis.

Equipment

- Standard general surgery pack and suture
- 5 Fr. infant feeding tube or red rubber catheter

Technique

1. Aseptically prepare the ventral abdomen.
2. Perform a standard ventral midline abdominal approach from the xiphoid to the pubis.
3. Expose the right limb of the pancreas by exteriorizing the small intestine and retracting the duodenum ventrally. Expose the left limb of the pancreas by retracting the transverse colon caudally.
4. Carefully and gently examine the pancreas for masses, abscesses, inflammation, and necrosis.
5. Gently break down adhesions and open areas of abscessation digitally to establish ventral drainage. Obtain samples of fluid or tissue for bacterial culture and histopathology. Carefully and judiciously debride necrotic pancreatic tissue and fat. Do not disrupt the pancreatic blood supply during dissection (see Chapter 35 under description of partial pancreatectomy). Minimize trauma to normal or non-necrotic pancreatic tissues. Submit all tissues for histopathology.
6. After draining, flushing, and debriding necrotic tissue, consider omentalization of large pancreatic abscesses or pseudocysts. Grasp the caudal edge of the greater omentum and place it into the abscess cavity. Place several tacking sutures (synthetic absorbable) from the omentum to the edges of the abscess cavity. As in omentalization of prostatic abscesses (see Chapter 85), the omentum will provide increased blood flow and lymphatic drainage and will fill dead space.
7. Carefully examine the gallbladder and biliary ducts for evidence of obstruction.
   a. Gently squeeze the gallbladder to determine if bile is expressible through the common bile duct.
   b. Consider retrograde catheterization of the common bile duct, using an infant feeding tube or red rubber catheter, if complete obstruction is suspected. A stent catheter can be left in the common bile duct if necessary (see Chapter 72). This procedure is somewhat risky because a duodenotomy is necessary and duodenal healing may be impaired by the severe local inflammation created by the pancreatitis. Close the duodenal

incision routinely, and place an omental patch over the incision.
8. Thoroughly lavage the peritoneal cavity with warm sterile saline.
9. Establish abdominal drainage by placing closed suction drains (e.g., Jackson-Pratt) or, in animals with severe peritonitis, by leaving the abdomen open (see Chapter 76). Otherwise, close the abdomen routinely.

Postoperative Care and Complications

- Maintain all aspects of medical therapy for pancreatitis (see previous discussion in this chapter). Consider plasma transfusions or IV colloids for hypoproteinemia (see Chapter 5) and whole blood transfusions for postoperative anemia (packed cell volume < 20%).
- See Chapter 35 for postoperative care of the partial pancreatectomy patient.
- See Chapter 76 for postoperative care of peritonitis.
- Consider total parenteral nutrition for animals with severe pancreatitis and open abdominal drainage (see Chapter 3).
- See under "Medical Treatment" in this chapter for dietary recommendations.
- Complications include septic shock, hypoproteinemia, worsening of pancreatitis and peritonitis, abdominal pain, and dehiscence of intestinal incisions.

Prognosis

Although most patients recover, pancreatitis is a life-threatening disease that frequently has a prolonged and unpredictable clinical course; thus, a guarded prognosis is warranted. The prognosis is poor when pancreatitis is complicated by septic shock, DIC, acute renal failure, or bowel infarction.

EXOCRINE PANCREATIC INSUFFICIENCY

Exocrine pancreatic insufficiency (EPI) occurs when 90% or more of pancreatic secretory capacity is lost. The key functions of the exocrine pancreas (see Table 73-1) that fail in EPI include the following:

- Secretion of enzymes for digestion of carbohydrate, protein, and fat
- Secretion of bicarbonate for neutralization of gastric acid entering the duodenum
- Secretion of pancreatic intrinsic factor for facilitating the intestinal absorption of cobalamin in the ileum
- Secretion of antibacterial proteins for regulation of the intestinal microflora

The results are maldigestion of nutrients, acid injury to the duodenal mucosa, deficiency of cobalamin and fat-soluble vitamins, and overgrowth of small intestinal bacterial flora. Clinically, these are manifested as chronic diarrhea, weight loss, and malnutrition.

Etiology

EPI results from severe irreversible loss of pancreatic acinar cells caused by atrophy, inflammation, hypoplasia, or neoplasia. Canine pancreatic acinar cell atrophy is by far most common. Chronic pancreatitis occasionally causes EPI in both dogs and cats. Rarely, EPI is associated with pancreatic hypoplasia in puppies or pancreatic adenocarcinoma in older dogs and cats (see the next section).

Pancreatic Acinar Atrophy

The most common cause of EPI is degenerative pancreatic acinar atrophy (PAA) of young dogs. The progressive loss of acinar tissue results in nearly total absence of digestive enzyme secretion. The endocrine part of the pancreas is spared.

- Many breeds can be affected, especially large breeds. The highest prevalence is in the German shepherd and rough-coated collie, breeds in which the predisposition to PAA appears to be inherited as an autosomal recessive trait.
- Studies in German shepherds suggest that PAA may be the end stage of autoimmune-mediated atrophic lymphocytic pancreatitis. Infiltration of cytotoxic T lymphocytes in the early preclinical stages has been demonstrated.

Chronic Pancreatitis

The end stage of progressive inflammatory destruction of the pancreas is fibrosis and atrophy, which can result in EPI. In addition to exocrine failure, substantial islet destruction can affect endocrine function, resulting in concurrent diabetes mellitus.

- Any breed of dog can be affected, but most are smaller breeds and are middle age or older.
- Chronic pancreatitis is the most common cause of EPI in cats.

Clinical Signs

Chronic small bowel diarrhea and weight loss are the most consistent clinical signs.

- PAA can occur at any age, but typically the onset of signs is prior to 4 years of age. Pancreatitis-associated EPI can occur at any age but most often is recognized in middle-aged and older dogs.
- Diarrhea in EPI is related to nutrient maldigestion and malabsorption and is characterized by large volumes of soft, semiformed, or unformed feces. The soft voluminous feces are also pale, fatty, and rancid-smelling. The owner may describe improvement with fasting or feeding of a highly digestible or fat-restricted diet, suggesting a malabsorptive process.

Table 73-4. NORMAL VALUES FOR PANCREATIC FUNCTION TESTS

Function Test	Canine	Feline
Serum TLI assay*	5–35 µg/L	12–82 µg/L
Serum PLI assay*	2.2–102 µg/L	2.0–6.8 µg/L
Fecal proteolytic activity (radial enzyme diffusion)* (3-day mean)	6–24 mm	6–17 mm
Fecal proteolytic activity (azocasein hydrolysis) (3-day mean)	19–200 ACU/g	29–207 ACU/g
Fecal elastase activity (ELISA)	>20 µg/g	
Serum cobalamin*	249–733 ng/L	290–1500 ng/L

*Available as mail-in test through Gastrointestinal Laboratory, Department of Small Animal Medicine and Surgery, College of Veterinary Medicine, Texas A&M University, College Station, TX, www.cvm.tamu.edu/gilab.
ACU, azocasein unit; ELISA, enzyme-linked immunosorbent assay; PABA, para-aminobenzoic acid; PLI, pancreatic lipase immunoreactivity; TLI, trypsin-like immunoreactivity.

- Weight loss or failure to gain weight occur despite a ravenous appetite and increased food intake. Intense hunger may cause pica and coprophagia in some dogs.
- Borborygmus and severe flatulence are common.
- The haircoat is often dull and poor in quality, with excessive shedding. Greasy soiling of hair around the perineum is often noted.
- There may be a history of recurring signs of pancreatitis when this is the underlying cause of EPI (see the prior section).

Diagnosis

The presenting signs of diarrhea and weight loss are nonspecific; thus, EPI must be differentiated from other causes of intestinal malabsorption and chronic small bowel diarrhea (see Chapter 69).

In EPI, routine hematology, serum chemistries, urinalysis, and radiographs are generally unremarkable. Serum amylase and lipase remain in the normal range because of non-pancreatic sources of these enzymes. The diagnosis of EPI is based on pancreatic function tests.

Serum Trypsin-Like Immunoreactivity Assay

The species-specific serum TLI assays are highly sensitive and specific pancreatic function tests for the diagnosis of EPI in both dogs and cats. The TLI measures total circulating trypsinogen and trypsin in a single fasted (8–12 hours) serum sample. TLI is readily available on a mail-out basis at reference veterinary laboratories (see Table 73-4).

▼ ***Key Point*** The serum TLI assay is the diagnostic test of choice for confirmation of EPI.

- In dogs with EPI, serum canine TLI is <2.5 µg/L (normal, 5–35 µg/L).
- In dogs with partial or early EPI, canine TLI is 2.5 to 5 µg/L.
- In cats with EPI, serum feline TLI is <8 µg/L (normal, 12–49 µg/L).
- The TLI assay is not affected by intestinal disease.
- Impaired renal elimination of trypsinogen may elevate TLI in renal failure patients.

Serum Pancreatic Lipase Immunoreactivity

The serum PLI assay is an exocrine pancreatic function test that detects circulating pancreas-specific lipase (see Table 73-4). The PLI test is more sensitive and specific than the TLI assay for diagnosing acute pancreatitis (see under "Pancreatitis"); however, the TLI test is more accurate and is preferred over PLI for the diagnosis of EPI.

Fecal Proteolytic Activity

Semiquantitative assays of fecal proteolytic activity by azocasein hydrolysis or radial enzyme diffusion are indirect methods of evaluating pancreatic function.

- Because the serum TLI assay is more accurate, reliable, and practical, TLI has replaced fecal proteolytic assays for diagnosis of EPI in both dogs and cats.
- Collect fecal specimens on each of 3 consecutive days because of daily variation. Freeze samples immediately for shipment to the laboratory. Fecal proteolytic activity is abnormally low in EPI (see Table 73-4).

Fecal Elastase Activity

Pancreas-specific elastase has been measured by fecal enzyme-linked immunosorbent assay as an indicator of exocrine pancreatic function in dogs.

- A single fecal sample is usually adequate, although low activity is occasionally found in normal dogs, as well as EPI dogs (see Table 73-4).
- Fecal elastase <10 µg/g is consistent with EPI and >20 µg/g has good predictive value for ruling out EPI. This test is not widely available.

Serum Cobalamin

Serum cobalamin (vitamin B_{12}) reflects pancreatic secretion of intrinsic factor, intestinal absorptive function, and status of the intestinal microflora.

- Serum cobalamin is frequently decreased in both dogs and cats with EPI, presumably due to the lack of pancreatic intrinsic factor combined with increased uptake by the overabundant intestinal bacterial flora. For normal values, see Table 73-4.
- Cobalamin deficiency is a nonspecific finding that also is common in chronic intestinal disease.

Treatment

Successful treatment of EPI requires lifelong pancreatic enzyme replacement. Dietary modification and adjunctive treatment with cobalamin, fat-soluble vitamins, antibiotics, and antacids are beneficial in some cases.

Immunosuppressive therapy directed toward the autoimmune pathogenesis of PAA in German shepherds has shown questionable benefit and is not recommended.

Pancreatic Enzyme Replacement

For best results, use dried, powdered porcine pancreatic extracts (e.g., Viokase-V [Fort Dodge], Pancrezyme [Virbac], or PancreVed [Vedco]). Bioavailability of other commercially available forms varies widely. Tablets, capsules, and enteric-coated formulations are less effective.

- For dogs, add 1 to 2 tsp of powdered pancreatic extract per meal to the food just prior to feeding and divide the daily food intake into two to three meals per day. For cats, give 0.5 tsp per meal. Moisten dry food with water.
- When the diarrhea is in remission and the animal is gaining weight, titrate to the minimum effective maintenance dose (1 tsp added to each of two meals daily is adequate for most dogs).
- Rarely, oral bleeding and irritation results from powdered enzyme supplementation. This adverse effect is dose dependent and resolves with a decrease in dosage.
- Chopped raw beef or pork pancreas (50–100 g per meal) has been used successfully to treat dogs with EPI, as an alternative to pharmaceutical extracts; however, this should be a last resort because of the risks of transmitting food-borne and zoonotic diseases (campylobacteriosis, salmonellosis, etc.).
- In cats that refuse food with commercial pancreatic extracts, chopped raw bovine pancreas (1–2 oz with each meal) has been used. A supply of raw pancreas can be stored frozen and can retain enzyme activity for several months.

▼ ***Key Point*** The effectiveness of enzyme supplementation is not increased by concurrent use of sodium bicarbonate, bile acids, or preincubation of enzymes with the food prior to feeding. Enteric-coated enzymes, capsules, and uncrushed tablets are less effective than powdered pancreatic extracts.

Diet Modification and Vitamins

- Most dogs with EPI can be fed an ordinary maintenance diet; however, if the response to enzyme supplementation is incomplete, consider substituting a diet that is highly digestible, low in fiber, and mildly restricted in fat.
- Consider daily use of a multivitamin supplement that contains the fat-soluble vitamins (A, D, E, and K). In dogs, vitamin E (tocopherol) may be severely depleted; thus, give vitamin E at 400 units PO daily for the first month.
- Cobalamin (vitamin B_{12}) deficiency is common in dogs and cats with EPI; thus, determine serum cobalamin levels at the start of treatment (see Table 73-4). Give deficient dogs cobalamin at a dosage of 250 to 500 µg SC weekly for 6 to 8 weeks, and give cats cobalamin at a dosage of 100 to 250 µg SC weekly for 6 to 8 weeks.
- Folate deficiency and vitamin K–responsive coagulopathies have been reported in cats with EPI.

What to Do if There Is Failure to Respond

1. Evaluate serum cobalamin and treat if too low. Severe cobalamin deficiency can cause intestinal malabsorption and may explain persistent diarrhea. Also evaluate serum folate.
2. Modify the diet and the enzyme brand, form, and dosage according to the above recommendations; if there is no response, go to step 3.
3. Administer antibiotics (e.g., doxycycline, metronidazole, or tylosin) for small intestinal bacterial overgrowth (see Chapter 69). If there is no response, go to step 4.
4. Administer an oral H_2 receptor blocker with meals, such as famotidine (Pepcid) (0.5–1 mg/kg PO q12h), to reduce acidic inactivation of enzymes. These reduce activity of gastric lipase and may not be effective for improving overall digestion. If there is no response, go to step 5.
5. Reassess the diagnosis and evaluate for intestinal mucosal disease via endoscopic biopsy.

PANCREATIC NEOPLASIA

Pancreatic neoplasms can be hormone-secreting tumors that arise from islet cells (insulinoma and gastrinoma are discussed in Chapter 35), or they can arise from the exocrine pancreas as adenomas or adenocarcinomas of acinar or duct cell origin. Pancreatic tumors occur most frequently in older dogs and cats (>9 years of age).

- Benign exocrine pancreatic adenomas are rare, well-encapsulated tumors that are usually incidental findings and are not associated with clinical signs.
- Exocrine pancreatic adenocarcinomas are more common and are discussed here. These are highly aggressive malignancies that metastasize early to the liver, regional lymph nodes, mesentery, duodenum, stomach, and occasionally lungs, often prior to the onset of clinical signs.

▼ ***Key Point*** Multifocal nodular hyperplasia of the pancreas is a common incidental finding in older dogs and cats. It does not affect pancreatic function or cause clinical signs. No treatment is necessary.

Clinical Signs

Pancreatic adenocarcinoma is usually in the advanced stages by the time presenting clinical signs develop.

- Clinical signs are usually insidious and nonspecific, often resembling chronic pancreatitis. Vomiting, anorexia, weight loss, depression, and abdominal pain are usually noted first.
- Bile duct obstruction or extensive liver metastases may lead to obstructive jaundice.
- Duodenal invasion and obstruction may lead to persistent intractable vomiting.
- Peritoneal carcinomatosis may lead to abdominal effusion.
- Pancreatic carcinoma in cats has been associated with paraneoplastic alopecia primarily involving the ventrum and legs, with hyperkeratosis, exfoliation, and painful footpad lesions.

Diagnosis

Suspect pancreatic adenocarcinoma in animals with progressive signs resembling chronic pancreatitis or obstructive jaundice, especially when a right cranial abdominal mass is identified by palpation or abdominal radiography or ultrasonography.

- Serum bilirubin and liver enzymes usually are elevated. Serum pancreatic enzymes may be increased. Tumor production of lipase and extreme hyperlipasemia have been associated with pancreatic and hepatic neoplasia in dogs.
- Cytology of abdominal effusion or fine-needle aspirates of the tumor mass are diagnostic in about 25% of cases but more often are inconclusive.
- In most cases, use exploratory laparotomy and surgical biopsy for definitive diagnosis and staging. Alternatively, use laparoscopic or ultrasound-guided needle biopsies. Because chronic pancreatitis and pancreatic adenocarcinoma can have a similar gross appearance, histopathologic evaluation is necessary.

Treatment and Prognosis

Attempted surgical resection (pancreatectomy) (see Chapter 35) is sometimes palliative (e.g., for relief of bile duct or duodenal obstruction); however, in most cases surgery is not beneficial and is virtually never curative. Adjunctive chemotherapy has little or no benefit. The prognosis is grave.

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Chapter

74 Constipation and Anorectal Diseases

Robert G. Sherding

The presenting signs of anorectal disease can include any of the following: dyschezia, hematochezia, constipation, anal discomfort (licking, scooting), ribbon-like feces, fecal incontinence, anal discharge, malodorous perineum, matting of perianal hair, and perianal dermatitis. Physical examination establishes the diagnosis of anorectal disease in most cases. In many anorectal diseases, surgery is required for effective treatment (see Chapter 75).

CONSTIPATION

Constipation is a clinical sign characterized by absent, infrequent, or difficult defecation associated with retention of feces within the colon and rectum. When feces are retained for a prolonged period of time, they become progressively harder and drier and, eventually, become impacted as the mucosa continues to absorb water from the fecal mass. Terms associated with constipation are defined below:

- ***Obstipation***—A condition of intractable constipation in which the colon and rectum become so impacted with excessively hard feces that defecation cannot occur.
- ***Megacolon***—A condition in which the colon becomes extremely and irreversibly dilated and hypomotile. Megacolon occurs most frequently in cats with idiopathic smooth muscle dysfunction that leads to severe colonic dilation, recurrent constipation, and obstipation. Megacolon also can occur in both dogs and cats secondary to chronic colorectal obstruction.
- ***Dyschezia***—A clinical sign often associated with constipation, characterized by difficult or painful evacuation of feces from the rectum and usually associated with lesions in or near the anal region.
- ***Tenesmus***—A clinical sign characterized by straining to defecate, usually ineffectively or painfully; thus, it often accompanies dyschezia.

Etiology

Underlying causes and predisposing factors for constipation are listed in Table 74-1 and include dietary factors, environmental factors, painful defecation, anorectal or colonic obstruction, neuromuscular diseases, fluid and electrolyte disturbances, and drug-related effects.

Ingestion of Foreign Material

Ingested foreign material, such as indigestible fibrous material (especially hair in cats from their grooming behavior) and abrasives (especially bones in dogs), may become incorporated in the fecal mass and result in the formation of hard fecal impactions that are difficult and painful to evacuate from the colon.

Environmental Conditions

Environmental conditions that are not conducive to defecation or that vary from the daily routine to which a pet is accustomed may cause the pet to inhibit the urge to defecate, leading to constipation. This occurs, for example, when the pet is kept in strange surroundings, such as in a kennel or veterinary hospital, or when its daily outdoor exercise routine is changed. Indoor cats may suppress the urge to defecate when their litter box is too dirty or there is territorial competition with other cats in the household.

Painful Defecation

Painful anorectal diseases (anal sacculitis, perianal fistulas) and painful orthopedic disorders that limit positioning for defecation (diseases of the pelvis, spine, or hips) may result in voluntary inhibition of defecation and lead to constipation.

Rectocolonic Obstruction

Anorectal or colonic obstruction that mechanically impedes the passage of feces may result from intraluminal causes, such as foreign bodies, perineal hernia, and stenosing neoplastic or inflammatory lesions, or from extraluminal causes, such as prostatic enlargement, paraprostatic cysts, compressive pelvic fractures, perianal tumors, and pseudocoprostasis (feces matted in perianal hair).

Neuromuscular Disease

Neuromuscular disorders may lead to constipation by interfering with colonic innervation or smooth muscle

Table 74-1. CLASSIFICATION AND CAUSES OF CONSTIPATION

Category	Cause
Dietary factors	Ingested foreign material mixed with feces (hair, bones, cloth, garbage, cat litter, stones, wood, plant material) Inadequate water intake
Environmental/psychological factors	Dirty litter box Prolonged inactivity Confinement (hospitalization, boarding) Change in habitat or daily routine
Painful defecation	Anorectal disorders Anal sac impaction, infection, or abscess Anorectal stricture, tumor, or foreign body Myiasis Perianal fistulae Perianal bite wound cellulitis or abscess Pseudocoprostasis Orthopedic disorders Spinal disease or injury Injuries of the pelvis, hip joints, or pelvic limbs
Rectocolonic obstruction	Extramural Prostatic hypertrophy, tumor, abscess, or prostatitis Paraprostatic cyst Pelvic fracture (malunion) Pelvic collapse due to nutritional bone disease Perianal tumor Pseudocoprostasis Intramural or intraluminal Rectocolonic stricture, tumor, or foreign body Perineal hernia or rectal diverticulum Rectal prolapse Fecalith
Neuromuscular dysfunction	Lumbosacral spinal cord disease (injury, deformity, degeneration, neoplasia) Bilateral pelvic nerve injury Dysautonomia (Key-Gaskell syndrome) Hypothyroidism Idiopathic megacolon
Fluid and electrolyte abnormalities	Dehydration (e.g., chronic renal disease) Hypokalemia Hypercalcemia (hyperparathyroidism, etc.)
Drug-induced effects	Anticholinergics Adrenergic antagonists Calcium channel blockers Phenothiazines and benzodiazepines Opiates and opioids Diuretics Antihistamines Aluminum hydroxide antacids Sucralfate Kaolin-pectin Barium sulfate Iron Laxatives (abuse or chronic overuse)

function or with the ability of the animal to assume the normal defecation stance. For example, this may occur in association with disease or injury of the lumbosacral spinal cord (canine intervertebral disc disease), spinal deformity (e.g., Manx cats), endocrine disease (hypothyroidism), and dysautonomia, a progressive fatal autonomic polyneuropathy. When innervation of the anus is also impaired, fecal incontinence may be an associated clinical sign.

The pathogenesis of idiopathic megacolon involves a primary or secondary dysfunction of colonic smooth muscle (see later under "Megacolon").

Fluid and Electrolyte Disorders

Dehydration can cause the feces to become excessively dry and hard, predisposing the animal to constipation. Hypokalemia and hypercalcemia can impair colonic

smooth muscle function. A combination of these may explain the frequent constipation seen in chronic renal failure, especially in cats.

Drug-Related Constipation

Drug-induced constipation may be a side effect of motility-modifying drugs (anticholinergics, opiates, loperamide), antihistamines, barium sulfate, aluminum hydroxide, and diuretics.

Clinical Signs

- ***Reduced or absent defecation:*** Constipated animals are usually presented because of failure to defecate over a period of days. The owner may notice tenesmus or frequent attempts to defecate with little or no passage of feces. Constipation tends to be a recurrent problem in some patients, especially in cats.
- ***Dyschezia:*** Difficult or painful defecation usually indicates anorectal disease. The animal first may cry out as it attempts to defecate, usually with straining (tenesmus) during the attempt; then it may cease the effort, walk around anxiously, and repeatedly try again.
- ***Abdominal discomfort:*** Constipated animals may develop a hunched-up appearance.
- ***Paradoxical diarrhea:*** Mucosal irritation caused by impacted feces may provoke a secretion of fluid and mucus, which passes around the retained fecal mass and is expelled paradoxically as diarrhea during attempts to defecate.
- ***Other signs:*** Prolonged constipation may lead to anorexia, weight loss, lethargy, vomiting, and dehydration.

Diagnosis

▼ ***Key Point*** The presence of constipation usually is determined from the history and confirmed by rectal and abdominal palpation of colonic distention with hard, impacted feces. The goal of diagnosis is to identify predisposing factors (see Table 74-1).

- Use abdominal radiography to confirm constipation, assess the degree of colonic impaction with feces, and identify megacolon.
- Depending on severity and clinical signs, consider serum chemistries, neurologic examination, neurodiagnostics, abdominal ultrasonography, contrast barium enema radiography, and colonoscopy to identify underlying causes of constipation or predisposing factors. Diagnostics are indicated when constipation is recurrent.

History

Question the owner to identify the potential dietary, environmental, behavioral, psychological, and medication-related factors or predispositions listed in Table 74-1.

Physical Examination

- Perform a digital anorectal examination to detect painful or obstructive lesions of the anorectal area and pelvic canal. Sedation may be required.
- Evaluate the pelvic limbs, coxofemoral joints, pelvis, and lumbosacral spine for orthopedic problems that could cause painful defecation or difficulty maneuvering into position for defecation.
- Perform a neurologic examination (see Chapter 125) to identify underlying neurologic deficits that may be involved in causing constipation.
- In cats with constipation caused by dysautonomia (Key-Gaskell syndrome), additional manifestations of progressive autonomic failure that may be seen include urinary and fecal incontinence, megaesophagus, bradycardia, mydriasis, decreased lacrimation, and prolapse of the nictitating membranes.

Routine Laboratory Evaluations

Perform a serum biochemical profile, urinalysis, and complete blood count (CBC) in animals with recurrent constipation or during an episode of severe obstipation.

- This may identify underlying systemic disease that could cause constipation related to dehydration or electrolyte disturbances (e.g., chronic renal failure).
- In severely obstipated animals, especially those that are vomiting and depressed, this detects the metabolic consequences of prolonged fecal retention (e.g., fluid and electrolyte imbalances, endotoxemia, and azotemia) and guides supportive treatment.

Abdominal Radiography

Perform abdominal radiography to determine the following:

- Confirm the extent of colonic impaction with densely packed feces
- Identify the extreme dilation of the colon that indicates megacolon
- Identify radiopaque foreign material (e.g., bone chips) in the retained feces that indicates a dietary cause of constipation
- Identify pelvic, coxofemoral, or spinal lesions that can cause constipation
- Identify underlying prostatic enlargement that might cause constipation

Other Diagnostic Evaluations

These diagnostics may be warranted in selected patients with recurrent constipation:

- ***Thyroid function testing***—Evaluate thyroid function in dogs with recurrent constipation and other signs compatible with hypothyroidism (see Chapter 31).

- ***Abdominal ultrasonography***—Use this to evaluate the urogenital tract when prostatic disease, paraprostatic cyst, or pelvic canal neoplasia is suspected.
- ***Barium enema contrast radiography***—Use this to evaluate the lumen of the colon when an intraluminal obstructive lesion is suspected (e.g., rectal stricture or neoplasia).
- ***Colonoscopy***—Use this to evaluate the lumen of the colon after all retained feces have been removed.
- ***Neurodiagnostic evaluations***—Use myelography, magnetic resonance imaging (MRI), electromyography, and nerve conduction studies to evaluate the lumbosacral spinal cord and spinal nerves in selected patients in which impaired anorectal innervation is suspected (see Chapter 125).

Treatment Overview

Simple constipation with mild to moderate impaction of feces and without systemic signs (depression, vomiting, dehydration) can be managed on an outpatient basis using rectal suppositories or oral laxatives combined with dietary modification and measures to enhance water intake. Oral laxatives can be prescribed (see a later section) and the patient can be reevaluated after 48 hours.

Severe constipation and obstipation may initially require evacuation of impacted feces from the colon (using enemas, manual extraction, or both) with correction of complicating dehydration and electrolyte imbalances.

- The subsequent goals of therapy are to eliminate or control any of the underlying causes of constipation (see Table 74-1) that are identified and to prevent recurrences using dietary modification, laxatives, and promotility agents as needed.
- Surgical correction is required for obstructing neoplasms, strictures, pelvic malunions, and anorectal diseases.
- Subtotal colectomy is often the most effective way to manage cats with advanced megacolon and recurrent obstipation that are unresponsive to medical therapy (see Chapter 70).

Initial Relief of Constipation

Use rectal suppositories, enemas, or manual extraction under anesthesia to initially relieve constipation.

Rectal Suppositories

To promote defecation in patients with mild constipation, give one to three pediatric rectal suppositories of docusate, glycerin, or bisacodyl. Rectal suppositories can be used alone or in combination with an oral laxative (Table 74-2). Pet and owner compliance are often limiting factors with suppositories.

- Docusate rectal suppository: An emollient (stool softener) laxative
- Glycerin: A lubricant laxative
- Bisacodyl: A stimulant laxative

Enema Therapy

Enema solutions are used to soften hard, impacted feces and promote evacuation. Warm the enema solution prior to instillation and use a lubricated rubber catheter or feeding tube to administer the calculated dose slowly so as not to induce vomiting. Commonly used enema solutions (see Table 74-2) include the following:

- Warm isotonic saline or tap water (5–10 ml/kg of body weight)
- Lactulose as an osmotic stool softener
- Docusate as an emollient (stool softener)
- Mineral oil as a lubricant

▼ ***Key Point*** Do not mix mineral oil and docusate. Docusate promotes mucosal absorption of mineral oil, and mineral oil coats the feces, preventing the emollient effect of docusate.

- Sodium phosphate solution, which has softening, bulk-producing, and irritant effects, can only be used in medium-sized and large dogs with normal hydration and renal function

▼ ***Key Point*** Caution! Never use phosphate enemas in cats or small dogs because of life-threatening hypernatremia, hyperosmolality, hyperphosphatemia, and hypocalcemia.

Manual Extraction of Impacted Feces

In severe constipation or obstipation, restore fluid and electrolyte balance parenterally and evacuate the colon manually under general anesthesia with endotracheal tube in place.

- Use colonic irrigation with warm isotonic saline as an enema solution to soften the impacted feces.
- Extract retained fecal masses by gentle transabdominal manipulation to milk the feces into the distal rectum for digital or forceps removal (using a sponge or whelping forceps).
- To avoid excessive bowel trauma in animals with extensive fecal impaction, it may be advisable to evacuate the colon manually in stages over 2 to 3 days.

Oral Laxative Therapy

Oral laxative medications and dietary supplements can be prescribed as needed for control of constipation and to prevent recurrences (Table 74-2). Laxatives lubricate feces, promote water penetration to soften feces, enhance intestinal mucosal fluid and electrolyte transport, or stimulate colonic propulsive motility. They are classified by their properties and mechanisms of action as bulk forming, lubricant, emollient, osmotic, stimulant, or promotility.

Table 74-2. LAXATIVE THERAPY FOR CONSTIPATION

Treatment	Product (Manufacturer)	Dosage Regimen
Oral Laxatives		
Bulk-Forming Laxatives		
Psyllium	Metamucil (Searle)	1–5 tsp daily with food
Unprocessed whole grain and bran cereal	Fiber One (General Mills) and others	1–5 tbsp daily with food
Canned pumpkin	Pie filling (Libby)	1–5 tbsp daily with food
Commercial high-fiber diet	Many	Use as daily food source
Lubricant Laxatives		
White petrolatum	Laxatone (Evsco)	1–5 ml daily PO
Mineral oil*	Many	Not recommended
Emollient Laxatives		
Docusate sodium	Colace (Shire)	Cat: 50 mg daily PO Dog: 50–200 mg daily PO
Docusate calcium	Surfak (Geneva)	Cat: 50–100 mg daily PO Dog: 100–240 mg daily PO
Osmotic Laxatives		
Lactulose	Duphalac Syrup (Reid-Powell), Cephulac (Marion Merrell Dow)	0.5–1.0 ml/kg q8–12h PO
Magnesium hydroxide	Phillips Milk of Magnesia (Glenbrook)	2–8 tablets daily PO
Polyethylene glycol and electrolytes†	Colyte (Schwarz), GoLytely (Braintree)	25–40 ml/kg PO, repeat in 2–4 hours (for bowel prep)
Stimulant Laxatives		
Bisacodyl	Dulcolax (Boehringer Ingelheim)	Cat: 5 mg daily PO Dog: 5–20 mg daily PO
Senna	Senokot (Purdue Frederick)	1–4 tablets q12–24h PO
Castor oil†	Many	5–30 ml PO (bowel prep)
Promotility Drugs		
Cisapride	Compounded pharmaceutical	Cat: 1.0 mg/kg q8h or 1.5 mg/kg q12h PO Dog: 0.25–0.5 mg/kg q8–12h PO
Tegaserod	Zelnorm (Novartis)	0.05–0.1 mg/kg q12h PO
Ranitidine	Zantac (Glaxo)	Cat: 3.5 mg/kg q12h PO Dog: 2.0 mg/kg q12h PO
Nizatidine	Axid (Eli Lilly)	2.5 mg/kg q24h PO
Rectal Suppositories		
Glycerin	Many	1–3 pediatric
Docusate sodium	Colace (Shire)	1–3 pediatric
Bisacodyl	Dulcolax (Boehringer Ingelheim)	1–3 pediatric
Enemas		
Isotonic saline solution (or tap water)		5–10 ml/kg
Lactulose	Duphaloc, Cephulac (see above)	5–30 ml
Docusate sodium	Colace (Shire)	5–30 ml
Mineral oil	Many	5–30 ml or 1–2 ml/kg
Sodium phosphate‡	Fleet Children's Enema (Fleet)	1–2 ml/kg or 1 enema unit
Bisacodyl	Fleet Bisacodyl Enema (Fleet)	1–2 ml/kg or 1 enema unit

**Caution:* May cause lipid aspiration pneumonia and may interfere with absorption of fat-soluble vitamins; combination with docusate may cause undesirable absorption of mineral oil.
†Used mainly to prepare the colon for radiography or endoscopy.
‡Do *not* use in cats or small dogs.

▼ ***Key Point*** Many oral laxatives require normal water intake and patient hydration for optimal activity.

The use of an oral laxative often must be individualized by adjusting the dose until the desired frequency of defecation and fecal consistency is obtained.

▼ ***Key Point*** The most clinically effective and useful laxatives are dietary fiber, lactulose, and promotility drugs such as cisapride.

High-Fiber Bulk-Forming Laxatives

Fiber-based laxatives are added to food to promote soft feces and normal colonic motility as an initial approach for long-term control of mild constipation, especially in dogs. These bulk-forming agents are non-absorbable polysaccharide and cellulose derivatives that exhibit hydrophilic properties within the bowel. This method of treatment is available as commercial high-fiber diets or as fiber additives for the regular diet, such as unprocessed cereal grains, wheat bran, or psyllium (see

Table 74-2). Efficacy depends on normal hydration and vigorous water intake.

▼ ***Key Point*** High-fiber diets may worsen obstipation in cats with megacolon or dehydration. Highly digestible low-residue diets may be preferable.

Lubricant Laxatives

Laxatives such as mineral oil and white petrolatum are used to soften and lubricate the feces to facilitate evacuation (see Table 74-2).

- *Flavored petrolatum* is the preferred oral lubricant laxative; however, it is only effective for treatment or prevention of mild constipation. Administer it between meals so that it does not interfere with the absorption of fat-soluble vitamins.
- *Mineral oil enemas* are sometimes useful for assisting manual extraction of feces, but do not give mineral oil orally because it can lead to inhalation lipid pneumonia.

Emollient Laxatives

Docusate sodium, docusate calcium, and *docusate potassium* are mild laxatives available in enema and oral forms that promote water penetration into the feces, thereby softening the feces (see Table 74-2).

- Do not mix docusate and mineral oil.
- Efficacy requires normal patient hydration.

Osmotic Laxatives

These laxatives consist of poorly absorbed disaccharides (e.g., lactose or lactulose), ions (e.g., magnesium hydroxide or magnesium citrate), or inert osmotic agents (e.g., polyethylene glycol) that osmotically retain water in the bowel lumen to produce soft or fluid feces.

- A mild osmotic laxative effect can be produced in some animals by the addition of milk (lactose) to the diet in a quantity that exceeds the digestive capacity of small intestinal lactase.
- *Lactulose* is a non-absorbable disaccharide (see Table 74-2) that is fermented by colonic bacteria to lactic acid and other organic acids that exert an osmotic effect and stimulate colonic fluid secretion and propulsive motility. Lactulose is a very safe laxative for long-term use. An excessive dosage can cause abdominal discomfort, diarrhea, and flatulence.

▼ ***Key Point*** Lactulose is the most clinically useful and effective osmotic laxative. It is an excellent all-purpose laxative for both dogs and cats.

- *Magnesium hydroxide* (Milk of Magnesia) is an over-the-counter product for people; it is generally not recommended for dogs and cats (see Table 74-2). Magnesium is contraindicated in patients with renal failure.
- *Magnesium citrate* and *polyethylene glycol-electrolyte* solutions (see Table 74-2) are used primarily for bowel preparation for colonoscopy. The large doses required are given by orogastric intubation, which limits their usefulness for routine treatment of constipation.

Stimulant Laxatives

Stimulant laxatives are over-the-counter agents that increase propulsive motility of the bowel. Bisacodyl is the most effective drug in the group; others are senna, castor oil, and cascara (see Table 74-2). They are contraindicated in the presence of an obstructive lesion.

- *Bisacodyl* is available for oral, rectal suppository, and enema administration. It works by stimulating colonic smooth muscle and the myenteric plexus. Although beneficial on a short-term basis in conjunction with measures to soften the feces, long-term use may damage the myenteric plexus.
- *Senna* (Senokot) is a natural vegetable-based laxative.
- *Castor oil* is hydrolyzed in the intestines to ricinoleic acid, which stimulates colonic motility and secretion. Castor oil is not useful for outpatient treatment because of poor patient acceptance. Some clinicians use a dose of castor oil to stimulate defecation in hospitalized patients prior to abdominal imaging and other procedures.

Promotility Drugs

Promotility drugs have a prokinetic effect on the gastrointestinal tract, including propulsive motility of the colon. They are contraindicated in the presence of an obstructive lesion.

- *Cisapride* is a 5-HT_4 serotonergic agonist that is highly effective for stimulating colonic propulsive motility (see Table 74-2). Anecdotal experience suggests it may be the most effective drug for medical therapy of megacolon in cats, although many cats become refractory after several months and require colectomy. The current availability of cisapride in the United States is limited to compounding pharmacies. Cisapride was taken off the market because of fatal ventricular arrhythmias that occurred in people, but these have not been documented in dogs and cats.
- *Tegaserod* and *prucalopride* are new serotonergic (5-HT_4) agonist promotility drugs that may have application in animal patients.
- *Ranitidine* and *nizatidine* are H_2 blockers that stimulate gastrointestinal and colonic motility through inhibition of synaptic acetylcholinesterase, which increases acetylcholine (see Table 74-2). These drugs have less potent prokinetic effects than cisapride.

Adjunctive Treatment and Preventive Measures

Following evacuation of retained feces from the colon, institute measures to prevent and control recurrences

of constipation. Identify and eliminate or correct underlying causes or predisposing factors (see Table 74-1).

- Prevent ingestion of constipating or abrasive materials such as bones.
- Prevent loose hair ingestion by adopting a routine of regular grooming, especially in cats.
- Provide dogs with a daily exercise routine and frequent opportunities to defecate.
- Provide cats with clean litter daily to encourage regular defecation.
- Provide access to fresh water at all times to encourage water intake.
- Adjust or discontinue the use of any medications that promote constipation.
- Treat predisposing prostatic, endocrine (hypothyroidism), spinal, and orthopedic disorders.
- Correct painful or obstructing anorectal lesions, by surgery if necessary (see Chapter 75).

MEGACOLON

Megacolon, which occurs most frequently in cats, is characterized by a colon that becomes severely and irreversibly dilated and hypomotile.

Etiology

- ***Idiopathic:*** In 70% of cases, feline megacolon is an idiopathic hypomotility disorder involving colonic smooth muscle. This *dilated megacolon* is usually irreversible. In vitro studies have demonstrated decreased active contraction of megacolonic smooth muscle in response to neurotransmitters (acetylcholine, substance P, cholecystokinin), membrane depolarization (potassium), and electrical stimulation. Innervation of the colon is intact, and histopathology of the muscle and nerves is unremarkable.
- ***Obstructive:*** In up to 25% of cases, megacolon is secondary to an underlying cause of persistent rectocolonic obstruction, such as perineal hernia, anorectal stricture, anorectal neoplasia, or pelvic canal stenosis caused by fracture malunion. This *hypertrophic megacolon* is potentially reversible with early removal of the obstruction.
- ***Neurologic:*** Neurologic dysfunction may account for 5% of megacolon cases, for example, lumbosacral spinal cord disease, Manx cat deformity, or dysautonomia.

Clinical Signs

- Megacolon occurs mostly in middle-aged and older cats with a 2:1 predilection for male cats. It is most prevalent in domestic shorthair (46%), domestic longhair (15%), and Siamese (12%) cats.
- Recurrent constipation and obstipation are the primary signs (see under "Constipation"). Episodes of constipation usually become more frequent and severe with progressive decline in motor function of the colon.

Diagnosis

Severe irreversible dilation of the colon is the hallmark of megacolon.

- Severe colonic impaction with feces is evident by abdominal palpation and abdominal radiography.
- Perform rectal palpation to rule out anorectal obstructive disease.
- Evaluate for evidence of neurologic disease that could result in secondary megacolon.

Treatment

Treatment is based on evacuation of impacted feces, correction of predisposing causes, and prevention of constipation episodes by the use of laxatives such as lactulose (osmotic) and cisapride (prokinetic) as described previously under "Constipation" (see Table 74-2 for dosages). Dietary adjustments alone are not usually sufficient to control constipation in cats with megacolon.

▼ ***Key Point*** In cats, use subtotal colectomy for severe recurrent constipation, obstipation, or megacolon that is unresponsive to medical management (see Chapter 70).

- Eventually most cats with idiopathic megacolon become refractory to medical management and require subtotal colectomy that removes 95% of the colon (see Chapter 70). Results are satisfactory to excellent with this palliative procedure in most cats. Diarrhea and increased frequency of defecation are common postoperatively but resolve after 2 to 4 weeks.
- In cats with obstipation from pelvic fracture malunion, pelvic osteotomy and reconstructive surgery can allow return of normal colonic function if obstipation has been present for less than 6 months; otherwise, perform subtotal colectomy.

PROCTITIS

Proctitis, or inflammation of the rectum, can cause tenesmus, diarrhea, and hematochezia. Therefore, it must be differentiated from other anorectal diseases. Proctitis usually is a manifestation of colitis or inflammatory bowel disease, which are discussed in Chapter 69.

ANORECTAL PROLAPSE

Etiology

Anorectal prolapse is seen most frequently in puppies and kittens as a consequence of an underlying disorder

that produces persistent straining to defecate, especially endoparasitism. It also can be associated with straining caused by urogenital conditions. Predisposing causes include the following:

- Intestinal diseases that cause diarrhea and tenesmus (e.g., proctitis, colitis, and parasites)
- Anorectal diseases that cause dyschezia
- Anal sphincter incompetence in Manx cats
- Dystocia
- Lower urinary tract diseases (e.g., cystitis, urethral obstruction, and calculi) and prostatic diseases that cause stranguria

Clinical Signs

- *Partial prolapse* involves only the rectal mucosa and appears as a red, swollen, doughnut-shaped ring of prolapsed mucosa.
- *Complete prolapse* involves all layers of the rectal wall and appears as an edematous, cylindrical-shaped mass. The prolapsed tissue may be viable (pink or red and moist) or necrotic (blackened and dry).

Diagnosis

Insert a thermometer, blunt instrument, or finger in the space between the prolapsed tissue and the anal sphincter to probe for a cul-de-sac. If there is none and resistance is not met, the prolapsed tissue is an intussusception of ileum or colon (see Chapter 69) rather than an anorectal prolapse.

Conservative Treatment

Successful management of anorectal prolapse includes repair of the prolapse and identification and treatment of the underlying cause. Evaluate the anus, rectum, intestines, and urogenital tract by palpation, urinalysis, fecal examinations, proctoscopy, and diagnostic imaging studies, as appropriate.

▼ ***Key Point*** Effective treatment of anorectal prolapse requires reduction of the prolapse and medical therapy to reduce tenesmus and prevent recurrence.

- To treat minor prolapse in which the tissue is viable, lubricate and manually reduce the prolapse.
- Place a temporary (2–3 days) anal purse-string suture to prevent recurrence, especially in animals with persistent straining. Leave the purse-string suture loose enough to allow passage of feces. Feed a digestible low-fiber diet while the purse-string suture is in place.
- To enhance anal tone in animals with diarrhea, give loperamide (Imodium AD) (0.1–0.2 mg/kg PO q6–8h).
- To relieve persistent straining and spasm refractory to loperamide, use anticholinergic-antispasmodic drugs such as dicyclomine (Bentyl, Marion Merrell Dow), 0.15 to 0.20 mg/kg q8–12h PO or SC.
- For proctitis, consider an anti-inflammatory retention enema:
  - Hydrocortisone retention enema (Cortenema, Reid-Rowell), 10 to 60 ml q12–24h
  - Mesalamine retention enema (Rowasa, Reid-Rowell) for dogs only, 10 to 60 ml q12–24h

Surgery

- Perform colopexy if conservative management fails and to prevent recurrent prolapse (see Chapter 70).
- Perform resection and anastomosis (i.e., "prolapse amputation") if the prolapsed tissue is necrotic and non-viable (see Chapter 75).

PERINEAL HERNIA

Etiology

Perineal hernia occurs when weakened perineal musculature (levator ani and lateral coccygeus), also called the pelvic diaphragm, fails to support the rectal wall, resulting in persistent rectal distention and impaired defecation. Aged, intact male dogs are most frequently affected, but perineal hernia also occurs in female dogs and in cats. The pathogenesis of the muscle weakening is poorly understood. Persistent straining related to constipation or prostatic disease may play a role in some animals. Neurogenic atrophy of the perineal musculature may play a role in dogs. Male hormones have been implicated because the disease is extremely rare in neutered and female dogs. Chronic constipation and megacolon are predispositions in cats.

The hernia usually contains an outpouched rectum and can be unilateral or bilateral; unilateral hernias are predominantly right-sided. The hernia sac may also contain retroperitoneal fat, the prostate gland, and rarely abdominal organs such as the urinary bladder or intestines. The rectal defects associated with perineal hernia have been classified as follows:

- ***Sacculation***—Unilateral loss of support that allows expansion of the rectal wall to one side.
- ***Dilation***—Bilateral loss of support that allows generalized distention of the rectum.
- ***Deviation or flexure***—The rectum curves or bends to one side within the hernia sac.
- ***Diverticulum***—An outpouching of mucosa that occurs through a defect in the rectal wall.

Clinical Signs

Perineal hernia causes a perineal swelling or bulge in association with signs of constipation, obstipation, dyschezia, and tenesmus.

- Dysuria may occur when the urinary bladder is retroflexed into the hernia, causing urethral obstruction.

- Perineal hernia in cats may be a complication of megacolon.

Diagnosis

Diagnosis is based on palpation of a reducible perineal bulge ventrolateral to the anus and rectal palpation of the weakened pelvic diaphragm with dilatation or deviation of the rectum.

Treatment

The goal of initial treatment is evacuation of retained feces from the rectum (see under "Constipation"). Urethral catheterization or cystocentesis also may be necessary initially to relieve urinary obstruction.

- In a mild perineal hernia, normal defecations can be maintained by laxative therapy and stool-softening diets (see under "Constipation").
- Castration of male dogs with a mild perineal hernia may prevent progression of the disorder.
- Corrective perineal herniorrhaphy surgery combined with castration provides the best long-lasting results in most cases (see Chapter 75).

▼ ***Key Point*** Perform castration as an adjunct to perineal hernia repair in male dogs.

- Surgery may not resolve clinical signs in cats with perineal hernia secondary to megacolon.

ANORECTAL FOREIGN BODIES AND FECALITHS

Etiology

- Ingested foreign bodies such as bones, toys, sticks, and sewing needles can sometimes pass unobtrusively through the gastrointestinal tract and become lodged transversely within the rectum or at the anal sphincter.
- Foreign objects occasionally are inserted into the anus of an animal by malicious or abusive people.
- Aged cats sometimes present because of inability to pass a firm lump of feces (fecalith) that is lodged in the anal canal between the internal and the external sphincters.

Clinical Signs and Diagnosis

When a foreign body or fecalith is lodged in the anal canal or rectum, defecation becomes painful or impossible and dyschezia, tenesmus, and secondary fecal impaction occur. Diagnosis is usually confirmed by rectal examination. Radiography is occasionally required.

Treatment

Most anorectal foreign bodies and fecaliths can be detected and removed by rectal palpation; sedation or anesthesia is often necessary. In some cases a proctoscope may facilitate foreign body extraction. There are two potentially serious complications of anorectal foreign bodies:

- Rectal laceration resulting in retroperitoneal cellulitis
- Anorectal stricture (see the next section)

ANORECTAL STRICTURE (STENOSIS)

Etiology

Strictures of the anus or rectum can result from the following causes:

- Trauma caused by passage of sharp foreign bodies (especially bones)
- Postsurgical scarring after anorectal surgery
- Iatrogenic instrument trauma during treatment of obstipation
- Chronic inflammation associated with anal sac disease, perianal fistulae, or proctitis
- Annular stenosing anorectal adenocarcinoma

Clinical Signs and Diagnosis

Anorectal strictures cause dyschezia, tenesmus, hematochezia, and secondary constipation. The onset of signs is usually 2 to 3 weeks following rectal injury. The stricture can usually be identified by digital rectal palpation, proctoscopy, or barium enema contrast radiography.

Treatment

- Most anorectal strictures are successfully managed by a series of bougienage or balloon dilations under anesthesia. The balloon diameter is 10 to 20 mm in cats and small dogs, 20 to 30 mm in medium dogs, and 30 to 40 mm in large dogs. Dilate to 40 to 60 psi for 1 minute, 3 times in succession, and repeat the dilation procedure every 7 to 10 days for three treatments or until defecation is normal.
- Concurrently, give triamcinolone (5–10 mg by intralesional injection just prior to dilation), or prednisolone (1 mg/kg PO q12h) for 2 weeks and taper.
- If conservative dilation therapy fails, perform surgical correction (see Chapter 75).
- Severe and neoplastic strictures require resection and anastomosis by rectal pull-through (see Chapter 75).

ANAL SPASM

Etiology

This rare idiopathic form of severe dyschezia occurs when the anal sphincter contracts in spasm when the animal attempts to defecate.

Clinical Signs

When attempting to defecate, the animal may cry out in pain, move about frantically before stopping to make another attempt to defecate, turn and stare at its hindquarters, and appear extremely anxious. There appears to be a cycle of painful defecation, leading to defensive contraction of the anal sphincter, leading to more pain.

Diagnosis

- Most affected dogs are German shepherds of temperamental disposition.
- Digital palpation of the rectum is vigorously resented, and the anal sphincter muscle feels hypertrophied and tightly contracted in spasm. Visually, the external sphincter muscle appears hypertrophied.
- To attribute dyschezia to anal spasm, it is important to rule out other identifiable causes of dyschezia (e.g., anal sac disease, perianal fistulae, and anal stricture) by thorough anorectal examination under anesthesia, including proctoscopy.

Treatment

- Conservative treatment using anal sac evacuation, topical analgesics, antispasmodics, sedatives, or stool softeners is usually unsuccessful.
- Pin hole–sized perianal fistulae can be easily overlooked and cause identical clinical signs; thus, consider trial medical therapy for perianal fistula (see a later section) to see if the dyschezia subsides, especially in high-risk breeds such as German shepherds.
- Diffuse fibrosis of the anal ring can be less apparent than well-developed strictures and can cause dyschezia that resembles anal spasm; thus, consider empirical bougienage or balloon dilation of the anal ring under anesthesia followed by prednisolone (see under "Anorectal Stricture").
- As a last resort for palliation of anal pain and spasm, resection of one or both anal branches of the pudendal nerve may be required. Fecal incontinence is a frequent postoperative complication of this procedure.

ANAL AND RECTAL ATRESIA

Etiology

Imperforate anus (atresia ani) and rectal agenesis (rectal atresia) are rare congenital malformations of cloacal development that result in an absence of a patent anal opening for defecation.

Clinical Signs

Complete obstruction of feces produces clinical signs within the first several days of birth. The affected neonatal puppy or kitten develops abdominal distention and discomfort, bulging of the perineum, tenesmus, restlessness, vomiting, and loss of appetite. Without treatment the neonate becomes obtunded and dies.

Diagnosis

- The diagnosis is established by failure to defecate and absence of an anal opening. Variations in the malformation range from an imperforate anal membrane covering the anal opening (atresia ani) to varying degrees of rectal agenesis (rectal atresia) in which the rectum ends in a blind pouch at some distance cranial to the anus.
- The terminal end of the rectum can be delineated radiographically by the intraluminal air when a lateral radiograph is exposed with the animal's hind end slightly elevated.
- In some animals, imperforate anus is associated with genitourinary defects such as rectovaginal fistula.

Treatment

The treatment for atresia ani is surgical opening and removal of the retained anal membrane, usually producing favorable results (see Chapter 75). For rectal atresia, surgical correction is more difficult and may require combined abdominal surgery and rectal pull-through. The prognosis is guarded because of postoperative complications of fecal incontinence, anal stricture, or megacolon.

RECTOVAGINAL FISTULA

Rectovaginal fistula is a rare congenital malformation of females characterized by passage of fecal material through the vaginal opening. In many cases there also is an imperforate anus.

- Persistent fecal incontinence through the vagina leads to perivulvar dermatitis.
- Colonic distension usually occurs when the puppy or kitten begins eating solid food.
- The defect can be surgically corrected, but the prognosis is guarded (see Chapter 93).
- Other related, rare anorectal anomalies include rectovestibular fistula, anovaginal cleft, and rectourethral fistula.

ANAL SAC DISEASE

Anal sac disorders are the most common problem of the anal area in small animals, especially dogs. Anal sac

disease has been classified as impaction, inflammation (sacculitis), infection, abscess, and rupture:

- ***Impaction***—This is usually bilateral and indicated by a sac that is distended, mildly painful on palpation, and not readily expressed. The impacted contents are thick, pasty, and dark brown or grayish brown.
- ***Anal sacculitis***—This may be unilateral or bilateral and is associated with moderate to severe pain on palpation; the sacs contain a thinner-than-normal, yellowish or blood-tinged purulent fluid.
- ***Anal sac abscess***—This is usually unilateral and characterized by marked distention of the sac with pus, cellulitis of surrounding tissues, erythema of the overlying skin, and fever.
- ***Rupture***—Abscessed anal sacs may rupture through the adjacent skin, producing a draining fistulous tract.

These probably represent a continuum in that impacted anal sacs tend to become inflamed and secondarily infected, and the infection may lead to abscessation and, finally, to rupture or fistulation.

All breeds of dogs can be affected. Anal sac disease is uncommon in cats and usually involves only impaction.

Etiology

The specific cause of anal sac disease is poorly understood. It is believed to be associated with conditions that promote inadequate emptying of the sacs, which should normally occur during defecation when feces of normal consistency are forced through a normally functioning anal sphincter. Abnormal retention of anal sac secretions initiates the impaction–inflammation–infection cycle.

▼ ***Key Point*** Always consider the possibility that anal sac disease might be secondary to a generalized dermatologic disease or endocrinopathy (e.g., hypothyroidism).

Clinical Signs

- The most frequent clinical signs of anal sac disease are related to anal discomfort and include scooting the hind end on the floor, tenesmus, and licking and biting the anal area, perineum, or base of the tail.
- Chewing and licking may result in areas of self-inflicted (pyotraumatic) dermatitis.
- Tail chasing, malodorous perianal drainage, and change in temperament may be noted.

Diagnosis

The diagnosis of anal sac disease is based on the clinical signs and examination of the anal sacs. Examine and evacuate the anal sacs by palpation with a gloved index finger inserted in the rectum and a thumb compressed against the skin ventrolateral to the anus.

Treatment

▼ ***Key Point*** Anal sacculectomy as described in Chapter 75 is the treatment of choice for animals with recurrent anal sac disease.

Anal Sac Impaction and Sacculitis

- Manual evacuation of the sac contents to reestablish drainage is all that is required in many animals.
- Follow-up examination and expression of the anal sacs again in 1 to 2 weeks is advisable.
- A high-fiber diet (see Table 74-2) may help prevent recurrence.

Recurrence of Impaction or Sacculitis

- Irrigation with povidone-iodine solution using a tomcat urinary catheter or lacrimal needle and instillation of an antibiotic (e.g., otic or ophthalmic antibiotic ointment) into the sac may be helpful, along with expression of the sacs every 3 to 4 days.
- Consider systemic antibiotics based on culture and sensitivity testing of the sac contents for animals with troublesome recurrences.

Anal Sac Abscesses

- Drain, irrigate with povidone-iodine solution, and treat with systemic antibiotics.
- Treat recurrent anal sacculitis or abscess by surgical excision of the sacs (see under "Anal Sacculectomy" in Chapter 75). Delay anal sacculectomy until the severe inflammation associated with abscessation has resolved.

PERIANAL FISTULA

Perianal fistula (anal furunculosis) is a chronic progressive disease characterized by deep ulcerating sinuses and fistulous tracts in the perianal tissues. The disease occurs most frequently in German shepherds and Irish setters more than 5 years of age, but it occurs sporadically in Labrador retrievers and various other large-breed dogs.

Etiology

The pathogenesis is not well understood. It may involve infection and abscessation of the apocrine glands and other glandular elements in and around the anus, promoted by the moist, contaminated environment of the area and the broad-based tail with low tail carriage typical for many German shepherds. The pathogenesis appears to involve cell-mediated immune mechanisms, supported by the effectiveness of immunosuppressive therapy in many cases.

Clinical Signs

- Dogs with perianal fistulas usually present with signs of dyschezia, tenesmus, and severe anal discomfort (constant licking of the anal area and scooting).
- Hematochezia, constipation, fecal incontinence, and foul-smelling purulent perianal discharge may be present.

Diagnosis

Visual examination of the perianal area establishes the diagnosis. Because of severe pain, sedation or anesthesia is required for thorough examination of the area.

- The sinus tracts and fistulae first appear as small, draining puncture holes in the perianal skin; there is inflammation and hyperpigmentation of the surrounding skin.
- These small tracts enlarge and coalesce to form large, interconnecting sinuses and areas of ulceration and granulation tissue. The fistulous tracts may extend deep into the perirectal tissues, and the anal sacs may be infected or ruptured.
- Fibrosis may lead to anorectal stricture in chronic cases.
- Histopathologic findings include hidradenitis, chronic necrotizing pyogranulomatous inflammation of skin and hair follicles, cellulitis, necrosis, and fibrosis.

Treatment

Medical therapy can be used alone or can be combined with surgical therapy. Medical approaches include hair removal and cleansing of the perianal area, systemic antibacterial therapy, dietary therapy using novel protein diets, and immunosuppressive therapy using cyclosporine, tacrolimus, or azathioprine.

Medical Therapy

Clip hair from around the anal region and base of the tail and cleanse the area with chlorhexidine scrub. Use one of the following treatment approaches:

- *Cyclosporine* (Atopica, Novartis) (5 mg/kg PO q24h) produces improvement in nearly all dogs within 2 to 4 weeks and a full remission and healing in 85% of dogs within 16 weeks. The recurrence rate is 40%, necessitating additional medical treatment or surgery.
- *Tacrolimus* (0.1% topical ointment) is applied once daily to the perianal area after cleansing as a cost-effective alternative to systemic cyclosporine with similar actions, fewer side effects, and a 50% remission rate.
- *Azathioprine combined with metronidazole* is an alternate, less expensive form of immunotherapy that usually produces improvement, but the rate of complete healing may not be as high as with cyclosporine or tacrolimus. Azathioprine (Imuran) is dosed at 2 mg/kg PO q24h.
- *Novel protein diets combined with immunotherapy* is an alternative approach that has benefited some dogs.
- *Broad-spectrum antibiotics* (a cephalosporin or fluoroquinolone such as enrofloxacin, combined with amoxicillin-clavulanate or metronidazole) may be palliative and can be used in conjunction with other medical treatments.

Surgery

Numerous surgical techniques have been advocated (see Chapter 75), including varying degrees of excision and debridement of diseased tissue, chemical ablation, laser excision, electrocautery, cryosurgery, and tail amputation. It is advisable to tailor the aggressiveness of the technique to the extensiveness of the lesions and to preserve as much normal tissue and anal function as possible.

Prognosis

- Early diagnosis and medical or surgical intervention avoids radical surgical excision, which in turn means less risk of postoperative complications and a better prognosis.
- Complications such as fecal incontinence, anal stenosis, and recurrence of the lesions can lead to an unacceptable outcome.

PSEUDOCOPROSTASIS

Etiology

Pseudocoprostasis is a condition of obstruction of the anal opening in which the surrounding hair becomes densely matted with feces. It occurs most often in long-haired breeds of dogs and cats, especially during bouts of diarrhea. Obesity is a contributing factor in some animals.

Clinical Signs

The anal obstruction leads to anal irritation, inability to pass feces, and constipation.

- The animal usually is restless and attempts to bite or lick the anal region.
- The owner may complain of an unexplained foul odor from the animal.
- The matted hair often results in an underlying dermatitis that may attract flies and lead to a maggot infestation (myiasis) of the perianal area.

Diagnosis

Visual examination of the anal region is sufficient for diagnosis.

Treatment

- Clip hair mats, cleanse the underlying irritated skin, and apply a topical antibacterial ointment. When the obstructing hair mats are removed, defecation should occur normally.
- If the animal has secondary colonic impaction of feces, measures to evacuate the colon may also be required (see under "Constipation").
- Diagnose and treat underlying diarrheal disease that may have predisposed the animal to matting of perianal hair with feces.
- Correct obesity that may be a contributing factor.

MUCOCUTANEOUS AND PERIANAL DERMATITIS

- Anal irritation often causes licking, biting, and rubbing at the anal area that leads to perianal dermatitis.
- Generalized pruritic skin conditions may cause perianal dermatitis (e.g., allergic dermatitis), fleas, etc.
- Eosinophilic granuloma complex of cats may involve the perianal region (see Chapter 53).
- The mucocutaneous junction where the perianal skin meets the anal mucosa may be severely inflamed and ulcerated in conjunction with other mucocutaneous areas in animals with immune-mediated skin disease (e.g., pemphigus complex, pemphigoid diseases, or lupus erythematosus complex; see Chapter 48), cutaneous drug eruption, cutaneous vasculitis, or various necrotizing dermatoses (see Chapter 49).

Perianal dermatitis often can be treated topically; however, the key is to recognize that it is usually secondary to an underlying anorectal or dermatologic disorder that must be identified and treated. For information regarding specific dermatologic disorders, see the respective chapters.

RECTAL, ANAL, AND PERIANAL TUMORS

The most common rectal tumor in the dog is the benign adenomatous polyp. Malignant tumors of the rectum (adenocarcinoma, lymphoma) can occur anywhere in the colon and rectum of dogs and cats. These are discussed with intestinal neoplasia in Chapter 69.

The most common tumor of the anal region is benign perianal (circumanal) gland adenoma of dogs. Other benign tumors of the anal area are rare and include lipoma and leiomyoma. The two most common anal malignancies are perianal (circumanal) gland adenocarcinoma and apocrine gland (anal sac, anal gland) adenocarcinoma. Perianal tumors are also discussed in Chapter 30.

Other malignant tumors of the anal region include squamous cell carcinoma, melanoma, lymphoma, and mast cell neoplasia.

Benign Rectal Polyps

Benign adenomatous polyps of the rectum are common in middle-aged and older dogs. They are usually solitary, focal, pedunculated or sessile masses in the rectal mucosa. Rectal polyps may cause clinical signs of rectal bleeding, hematochezia, dyschezia, tenesmus, or excessive licking of the anal region. The clinical signs are often mistaken for chronic colitis. Polyps also may be inapparent or incidental findings.

Diagnosis

Polypoid rectal masses can usually be detected by rectal palpation. Many rectal polyps can be exteriorized through the anus by everting the rectal mucosa with gentle traction to allow visual inspection.

- Rectal polyps appear dark red and lobulated (raspberry-like appearance). They are friable and bleed easily.
- Proctoscopy is beneficial for identifying more proximal lesions.
- Biopsy is required for definitive diagnosis.

Treatment

Complete surgical excision is the treatment of choice for rectal polyps. Techniques include endoscopic polypectomy, surgical resection by rectal pull-through, or cryosurgery.

- Always submit excised tissue for histopathologic evaluation, because the visual appearance of polyps and adenocarcinomas can be identical.
- The prognosis is excellent. Recurrence is uncommon, and malignant transformation is very rare in animals.

Perianal (Circumanal) Gland Adenoma

These androgen-dependent tumors occur most often in older, intact male dogs and they usually appear as small, firm, well-circumscribed nodules in the skin surrounding the anus.

Clinical Signs

Perianal gland adenomas may be incidental findings unassociated with clinical signs or they may cause anal irritation with scooting and licking at the anal area. In addition, they sometimes ulcerate and periodically bleed.

Treatment

The treatment of choice is excision (see Chapter 75) and adjunctive castration because of their hormone dependency.

- Castration alone can produce regression of these tumors; however, excisional biopsy at the time of castration is necessary to rule out malignancy.

- Estrogens are inhibitory for perianal gland adenomas; however, they cannot be recommended for prolonged use because of their myelotoxic effects.

Perianal Gland Adenocarcinoma

These tumors occur most often in aged female dogs and may resemble an ulcerated perianal gland adenoma, except that they are locally invasive and may cause diffuse infiltration and thickening of surrounding tissues.

Clinical Signs

- Their appearance can be confused with a perianal fistula lesion or a ruptured anal sac.
- These tumors eventually metastasize to regional lymph nodes (sublumbar) and beyond.

Diagnosis and Treatment

For potentially malignant lesions of the perianal area, excisional biopsy is the diagnostic procedure of choice (see Chapter 75).

- First perform thoracic and abdominal radiography and abdominal ultrasonography to evaluate for lung or lymph node metastasis.
- Early excision of malignant tumors of the anal region can be effective; however, when extensive local invasion or regional lymph node metastasis has occurred, the prognosis for a cure is poor.
- Repeated partial excisions, radiation therapy, cryosurgery, and chemotherapy have been used for palliative therapy in patients with inoperative malignancies of the anal region.

Apocrine Gland Adenocarcinoma

Apocrine gland adenocarcinoma arises in the anal sac and affects middle-aged and older dogs (median age, 10 years). A recent large case series found equal gender distribution, although other studies have found higher prevalence in spayed females.

Clinical Signs

These small perianal tumors are often incidental findings on palpation of the anal sacs, or they cause signs referable to perianal irritation or obstructive constipation. However, 25% to 50% of affected dogs present with paraneoplastic hypercalcemia, with or without polyuria-polydipsia and anorexia.

- More than 50% of these tumors can produce parathyroid hormone-related protein (PTHrP) that causes a paraneoplastic humoral hypercalcemia of malignancy (see Chapter 32). Even very small tumor nodules can produce this syndrome.
- These tumors are malignant and metastasize to sublumbar lymph nodes and distant sites, such as the lungs.

Treatment

Surgical excision is the treatment of choice. The reported median survival has varied from 6 months to 1.5 years. Hypercalcemic cases and animals with evidence of metastasis at the time of diagnosis have a shorter survival.

- For medical treatment of associated hypercalcemia, see Chapter 32.
- Adjunctive radiotherapy and/or chemotherapy may be appropriate, especially for incompletely excised or metastatic tumors (see Chapters 26 and 30).

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Chapter

75 Anorectal Surgery

Ronald M. Bright

Surgery of the rectum and anus is associated with a high rate of complications. The high bacterial population of the rectum increases the risk of wound infection and dehiscence. Bowel preparation with multiple enemas can mechanically remove large numbers of bacteria; however, enemas should not be done within 8 hours of anorectal surgery to avoid leakage of rectal contents during surgery. Prophylactic antibiotics are indicated with surgery of this area due to high numbers of bacteria. Synthetic absorbable sutures or monofilament nonabsorbable sutures are recommended for surgery of the rectum and anus.

ANATOMY

The rectum begins at the brim of the pelvis and joins the anal canal just inside the anal opening. The anal canal is approximately 1 to 2 cm in length. The circumanal glands, anal glands, and anal sacs are associated with the anus.

The rectum receives its blood supply from the caudal mesenteric artery and its branch coursing caudally, the cranial rectal artery. This artery forms anastomoses with the middle and caudal rectal arteries, which arise, in the male, from the prostatic artery, and in the female, from the internal pudendal arteries. At the caudal demarcation of the rectum are two anal sphincters (internal and external). Fecal continence is maintained by these sphincters, and surgery in this area always threatens their integrity.

RECTAL PROLAPSE

Rectal prolapse is almost exclusively limited to young dogs and cats. The most common cause is straining to defecate, associated with severe colitis or proctitis due to endoparasites. Other causes include foreign bodies, rectal neoplasia, dystocia, and, in the cat, persistent straining related to urethral obstruction or cystic calculi.

Differentiate this condition from prolapsed intussusception. In the latter condition, a probe can be inserted and advanced cranially into a space between the cylindrical mass and the edge of the anus. This cannot be done with rectal prolapse.

Preoperative Considerations

- Treat underlying diseases (e.g., parasitism) while attempting conservative management of rectal prolapse.
- Initial management consists of cleaning and lubricating the prolapse, determining viability of the tissue, and then manually reducing the prolapsed tissue followed by a loose pursestring suture. The pursestring suture should be loose enough to allow passage of loose feces, but tight enough to keep the prolapsed tissue reduced.
- Feed a digestible low-fiber diet for 7 to 8 days while the pursestring suture is in place.
- Failure of conservative management may necessitate a surgical procedure.
- The preferred surgical procedure is colopexy (see Chapter 70), unless there is non-viable tissue within the prolapsed segment of rectum that requires resection and anastomosis.

Surgical Procedure: Resection and Anastomosis

Objectives

- Remove devitalized tissue involved in the rectal prolapse.
- Remove excessive rectal tissue that continues to prolapse in spite of manual reduction or use of the pursestring suture technique alone or in conjunction with a colopexy.

Equipment

- General surgery pack
- A 3-cc syringe case

Technique

1. Place the animal in sternal recumbency in a perineal stand.
2. Insert a well-lubricated 3-cc syringe case into the rectum.
3. Place three or four stay sutures around the circumference of the prolapsed tissue through all the layers

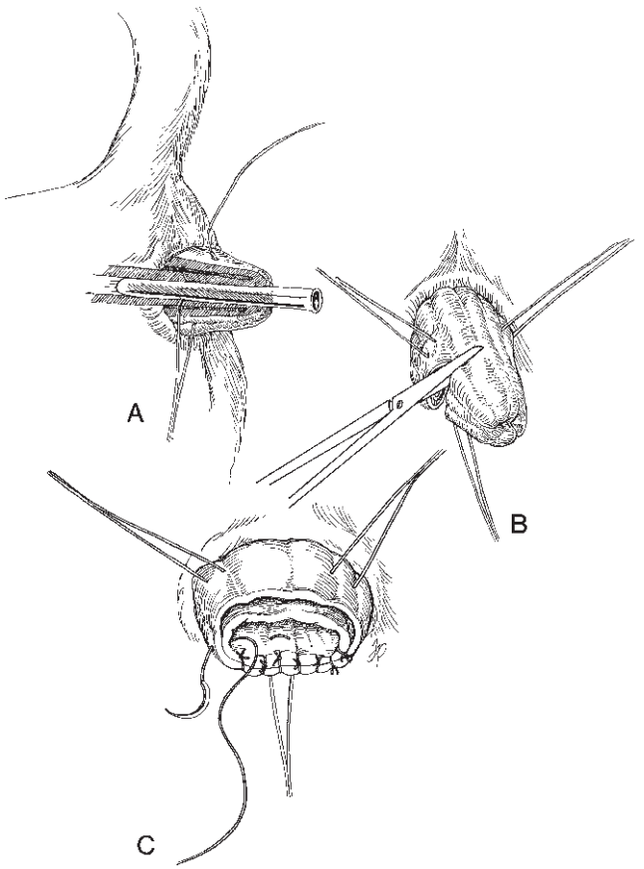

Figure 75-1. Resection and anastomosis of rectal prolapse.

of tissue. The needle should be against the syringe case at its deepest penetration (Fig. 75-1*A*).

4. Resect the prolapse around 180 degrees of the circumference, caudal to the stay sutures (Fig. 75-1*B*).
5. Place synthetic absorbable sutures (3-0 or 4-0) through the full thickness of the incised bowel, being sure to incorporate the serosal layers. A simple interrupted appositional pattern is preferred (Fig. 75-1*C*).
6. Incise the remaining 180 degrees and suture as described in Step 5. Push the rectum cranially into the pelvic canal.

Postoperative Care and Complications

Short T erm

- Give a stool softener (see Chapter 74) with food, which is offered the day after surgery. Continue giving the stool softener for 2 weeks.
- Closely monitor for leakage from the anastomotic site for at least 48 hours by observing the animal's temperature, level of activity, eating habits, and signs of excessive pain around the anorectal region. Be careful when placing a rectal thermometer.
- Recurrence of rectal prolapse may occur. A pursestring suture may have to be used again or a colopexy performed if it has not been done previously.

Long T erm

Long-term complications can include the following:

- Recurrence of rectal prolapse
- Fecal incontinence
- Anorectal stricture

ANORECTAL STRICTURE

Causes of anorectal stricture can be benign (e.g., inflammation) or malignant (e.g., adenocarcinoma):

- Inflammatory causes include perianal fistulas, prior anorectal surgery (including cryosurgery), and accidental trauma.
- Adenocarcinoma of the rectum and anus is the most common cause of stricture, resulting in a scirrhous, annular ring-type lesion.

Preoperative Considerations

Simple, annular non-neoplastic lesions that are not too cranial in location may respond to a series of bougienage or balloon dilations. During this therapy, give prednisolone for 10 to 14 days (1 mg/kg q12h).

- For other lesions (e.g., adenocarcinoma), resection/anastomosis (described below) is the treatment of choice.

Surgical Procedure: Resection/Anastomosis with Rectal Pull-Through

Objective

- Restore bowel lumen size that will accommodate the passage of feces with minimal resistance while preserving competence of the anorectal sphincter.

Equipment

- General surgery pack
- Senn retractors

Technique

1. Clip and aseptically prepare the perineal region.
2. Place a pursestring suture in the anus.
3. When the lesion is cranial to the anorectal junction, make an incision circumferentially around the anal ring.
4. Continue the perirectal dissection to normal tissue just cranial to the stricture ring. Avoid trauma to the sphincter muscles.
5. Place four stay sutures circumferentially through the normal rectal wall just ahead of the stricture.
6. Resect the diseased rectal tissue.

7. Pull the healthy tissue being held by the stay sutures caudally and appose to the anus. Avoid suturing under tension; mobilize more rectal tissue if necessary.
8. Close the tissues in two layers: subcutaneous tissue apposed to seromuscular layer of rectum (monofilament absorbable suture), and skin to rectal mucosa (monofilament non-absorbable suture).

Postoperative Care and Complications

Short Term

- Feed the animal the following day.
- Give stool softeners (see Chapter 74) for 2 weeks following surgery.
- Monitor for leakage from the anastomotic site, especially during the first 48 hours.
- Fecal incontinence may occur.

Long Term

- A pelvic abscess due to earlier leakage from the anastomosis can occur.
- Postoperative stricture can occur, especially if tension was present at the suture line.

Prognosis

The prognosis is poor if the stricture is due to an adenocarcinoma. It is poor to guarded if the stricture is related to an inflammatory process.

ANAL STRICTURE LIMITED TO THE ANAL RING

Causes, preoperative considerations, and objectives are similar to those for anorectal strictures, as described in the previous section.

Surgical Procedure

Technique

1. Cut the stricture in four places around the anal ring at 3, 6, 9, and 12 o'clock.
2. Make the incisions perpendicular to the ring. Extend one-half of each incision outward into the skin and the other half inward through the fibrotic mucosa.
3. Suture the incisions in the opposite direction to the edge of the anal ring with monofilament non-absorbable sutures.
4. Alternatively, excise the stricture and suture rectal mucosa to skin with monofilament non-absorbable sutures.

ATRESIA ANI

This condition exists in several forms, the most common being type I (imperforate anus) and type II, in which the rectal pouch is located cranial to the membrane overlying the anus. Regardless of the type, the main problem is loss of continuity between the rectum and anus during embryonal development of the cloacal membrane.

Preoperative Considerations

- Plain film radiography of the abdomen and pelvis with the animal standing helps to differentiate between type I and type II.
- Because the patient usually is only days or weeks old, there is a relatively high anesthetic risk.

Surgical Procedure

Objective

- Relieve the obstruction of feces in the rectum by opening the anus and reconstructing the anorectal junction.

Equipment

- General surgery pack
- Iris scissors
- Fine mouse-tooth thumb forceps or Simkin thumb forceps

Technique

Type I

1. Incise the skin overlying the anus in a cruciate pattern.
2. Protect the anal sphincter.
3. Incise the rectal pouch just under the incision in a cruciate pattern.
4. Suture the rectal circumference to the subcutaneous tissues and skin with 4-0 or 5-0 monofilament non-absorbable suture in a one-layer simple interrupted appositional pattern.

Type II

1. Incise the membrane overlying the anus in a cruciate pattern.
2. Continue the perirectal dissection cranially until the rectal pouch is identified.
3. Incise the blind pouch as described in Step 3 for type I.
4. Appose the rectocutaneous tissues as described in Step 4 for type I.

Postoperative Care and Complications

Short Term

- Monitor closely for suture line breakdown and infection of the surgical site.
- Because of the young age of these patients, give aggressive fluid therapy (including dextrose to prevent hypoglycemia) during surgery and well into the postoperative period.

- Initially, fecal incontinence often is a problem but resolves spontaneously in some animals.

Long Term

- Fecal incontinence may continue indefinitely.
- Stricture is a possible sequela to anorectal surgery.
- Megacolon that sometimes accompanies atresia ani may be permanent and constipation may be an ongoing problem.

PERIANAL FISTULAE

Perianal fistulae are multiple draining tracts that surround the anus and are chronic in nature. German shepherds and Irish setters are affected most commonly (see Chapter 74 for a complete description of this disease).

Preoperative Considerations

- Consider conservative therapy, consisting of perianal cleansing with an antiseptic solution and application of hot packs.
  - Antibiotic therapy for 2 to 3 weeks may ameliorate the pain associated with this condition. Medical therapy using cyclosporine or topical tacrolimus has reportedly been successful for many dogs with perianal fistulas (see Chapter 74)
- In some cases, surgical intervention will be necessary. Regardless of the procedure, surgical excision of diseased tissue is a compromise between complete excision and minimization of trauma to spare the external anal sphincter.
- An anal sacculectomy should accompany any excisional procedure.

Surgical Procedure

Objective

- Remove diseased tissue around a portion of the anus and, if necessary, around its entire circumference.

Equipment

- General surgery pack

Technique

1. Make a skin incision to incorporate all the diseased tissue surrounding the anus.
2. Dissect and continue into the deeper tissues until the cranial extent of the fistulous tracts is determined.
3. Take care to prevent damage to the external anal sphincter muscle or its innervation.
4. In some instances, a portion of the sphincter muscle may be removed coincidentally when attempting to excise the diseased tissue.
5. In severe cases, remove a doughnut-shaped piece of tissue, leaving healthy rectal tissue underneath.
6. Transversely incise the rectum to allow removal of the anus and diseased tissue.
7. Suture the subcutaneous tissue layer to the seromuscular layer of the rectum with 3-0 monofilament absorbable suture. Suture the rim of rectal mucosa directly to the skin, using 3-0 monofilament nonabsorbable suture.

Postoperative Care and Complications

- Keep the incision and underside of the tail clean, using hydrotherapy twice a day. A thin layer of petroleum jelly placed around, but not in, the incision is helpful for preventing fecal soiling and irritation.
- Give stool softeners for 1 to 2 weeks.
- Incisional dehiscence may occur but is usually treated conservatively (let heal by second intention).
- Fecal incontinence may occur after extensive resections.
- Recurrence of fistulas can occur. Treat by excision of affected tissues.

PERINEAL HERNIA

Perineal hernia results from weakening of the perineal muscles (i.e., the levator ani and lateral coccygeus) and external anal sphincter. Hernias may result in rectal sacculation and herniation of prostate, fat, urinary bladder, or bowel (see Chapter 74). The exact cause is uncertain but is thought to be related to any condition that causes chronic tenesmus (constipation, prostatomegaly). Other possible causes include hormonal imbalance and degenerative changes to the levator ani musculature.

Preoperative Considerations

- Castration usually accompanies a herniorrhaphy. It is thought to help prevent recurrence by decreasing tenesmus related to prostatomegaly.
- Urethral obstruction secondary to bladder entrapment requires emergency treatment (cystocentesis and placement of a urethral catheter).
- Administer an intravenous prophylactic broad-spectrum antibiotic immediately preoperatively.

Surgical Procedure: Herniorraphy

Objectives

- Replace contents of hernial sac into the peritoneal cavity.
- Reconstruct the pelvic diaphragm.
- Prevent deviation of the rectum and retroflexion of the bladder and prostate gland.

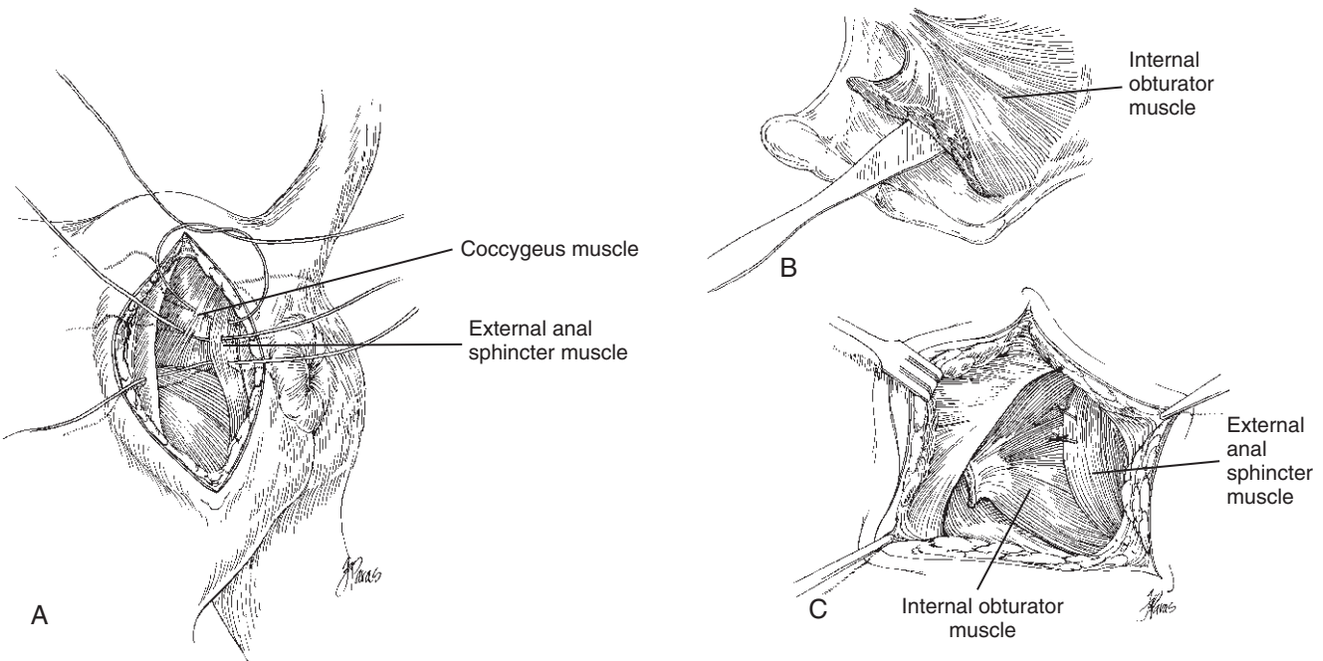

Figure 75-2. Repair of perineal hernia. Close the dorsal portion using the coccygeus and external anal sphincter muscles *(A)*. Close the remainder of the defect by elevating the internal obturator muscle *(B)* and suturing it to the external anal sphincter muscle *(C)*.

Equipment

- General surgery pack
- Self-retaining retractors
- $^1/_4$-inch Penrose drain

Technique

1. Place the animal in sternal recumbency and secure the tail forward over the back.
2. Place a pursestring suture around the anus.
3. Make a half-curved or a curvilinear incision, beginning just lateral to the base of the tail and extending ventrally below the perineal bulge.
4. Using blunt dissection, remove the tissue overlying the hernia sac; open the sac with scissors.
5. Gently replace the herniated viscera into the abdominal cavity.
6. Dissect the tissue overlying the external anal sphincter, exposing the muscle striations.
7. Identify dorsolaterally the levator ani and lateral coccygeal muscles.
8. Palpate the sacrotuberous ligament and use it as the lateral landmark.
9. Carefully isolate the neurovascular bundle containing the pudendal nerve and the internal pudendal vessels and place a $^1/_4$-inch Penrose drain around it to identify its presence as sutures are placed.
10. Repair the dorsal aspect of the hernia first by preplacing three or four sutures between the coccygeal musculature and the external anal sphincter. Monofilament non-absorbable sutures or synthetic absorbable sutures such as PDS or Maxon are preferred (Fig. 75-2*A*).
11. The sacrotuberous ligament may be incorporated with the coccygeal muscle when insufficient musculature is present. Tie the sutures.
12. Identify the obturator muscle and isolate by bluntly dissecting the overlying tissue.
13. Incise the caudal border of the internal obturator muscle and elevate the muscle with a periosteal elevator until the caudal border of the obturator foramen can be seen (Fig. 75-2*B*).
14. Partially or completely incise the tendon of the obturator muscle to allow the muscle to be drawn dorsomedially (Fig. 75-2*C*).
15. Preplace similar sutures between the obturator muscle and the external anal sphincter. Avoid penetrating the rectum. Tie the sutures after gently apposing the tissues.
16. Close the subcutaneous tissues (monofilament absorbable sutures) and skin (monofilament nonabsorbable sutures) routinely.

Alternative Techniques

- Porcine small intestinal submucosa has been used successfully as a primary means of repair in dogs or to augment the internal obturator muscle when it is too weak or thin to hold sutures securely. It can also be used as a last resort in those cases of failed herniorraphy.
- A staged approach has also been described in bilateral or complicated perineal hernias. This approach

uses a laparotomy as the initial step in the surgical treatment of bilateral or complicated perineal hernias in dogs.

1. Perform a ventral midline abdominal approach
2. Perform a colopexy (see Chapter 70) to reduce rectal sacculation or deviation of the rectum.
3. Perform either a vas deferens pexy, or cystopexy to prevent herniation of the urinary bladder. Vas deferens pexy involves fixing the vas deferens, after castration, to the interior abdominal musculature. Cystopexy involves creating a permanent adhesion between the apex of the urinary bladder and the peritoneum. Scarify the serosa of the urinary bladder with a scalpel, and then make an incision in the peritoneum and abdominal muscle adjacent to the bladder apex (similar to technique for colopexy). Suture the scarified bladder to the abdominal wall incision with 3 or 4 interrupted sutures (polydioxanone or monofilament non-absorbable)

- In those instances where there is a midline ventral component to the herniation, a semitendinosus muscle flap has been used as a salvage technique.

Postoperative Care and Complications

Short Term

- Administer postoperative analgesics (see Chapter 6).
- Straining to urinate or hematuria suggests iatrogenic trauma to the urethra by a misplaced suture.
- Rectal prolapse may occur, especially if a bilateral repair was done. Staging the repair of right and left sides several weeks apart usually eliminates this complication.
- Fecal incontinence may result from damage to the pudendal or caudal rectal nerves or to the sphincter muscle itself. If damage to innervation is bilateral, the animal usually will not regain continence.
- Urinary incontinence sometimes occurs postoperatively but is infrequent. It appears to be associated with bladder retroflexion before surgery.
- Wound infection may result because of improper suture placement through the rectal wall, penetration of the anal sac, or contamination. This usually is seen in the first 48 to 72 hours postoperatively.

Long Term

- Fecal or urinary incontinence may persist for weeks or months and sometimes indefinitely.
- Recurrence is directly correlated with the skill of the surgeon and the severity of the hernia. Castration may help to decrease recurrence regardless of the skill level of the surgeon.
- Colopexy and vas deferens pexy can be performed on recurrent hernias or if the initial hernia is severe. The colopexy procedure is described in Chapter 70. See "Supplemental Reading" for more information on the vas deferens pexy.

Prognosis

- If the surgery is performed by an experienced surgeon, the prognosis is good.
- Use of the obturator flap technique is believed to be associated with fewer problems postoperatively and with a lower recurrence rate.

ANAL SACCULECTOMY

The primary goal of anal sac surgery is correction of long-standing anal sac infection (see Chapter 74) that is refractory to conservative therapy.

Preoperative Considerations

- Do not perform anal sacculectomy during the acute inflammatory stage of infection.
- Administer antibacterial therapy, flush the anal sacs with antiseptic solutions, and use hot packs to control the sacculitis. (See Chapter 74 for a complete discussion of anal sac diseases.)
- Tumors of the apocrine glands of the anal sac are an indication for surgery (see Chapter 74). If neoplasia is suspected, obtain thoracic and abdominal radiographs (or abdominal ultrasound) to check for evidence of metastasis.
- A recent study suggests that complications associated with the standard open technique were greater than when using a closed technique.

Surgical Procedure

Objectives

- Remove the entire anal sac.
- Preserve anorectal function by carefully avoiding excessive trauma to the external anal sphincter muscle and its corresponding innervation.

Equipment

- General surgery pack
- Electrocautery
- Iris scissors (optional)

Technique

1. Place a scissors blade into the duct of each anal sac (Fig. 75-3*A*).
2. Use thumb forceps to place countertraction on the duct before cutting so that all structures can be exposed.
3. After incising the sac, identify the lining by its gray color.
4. Place mosquito forceps at opposite ends of the anal sac lining.

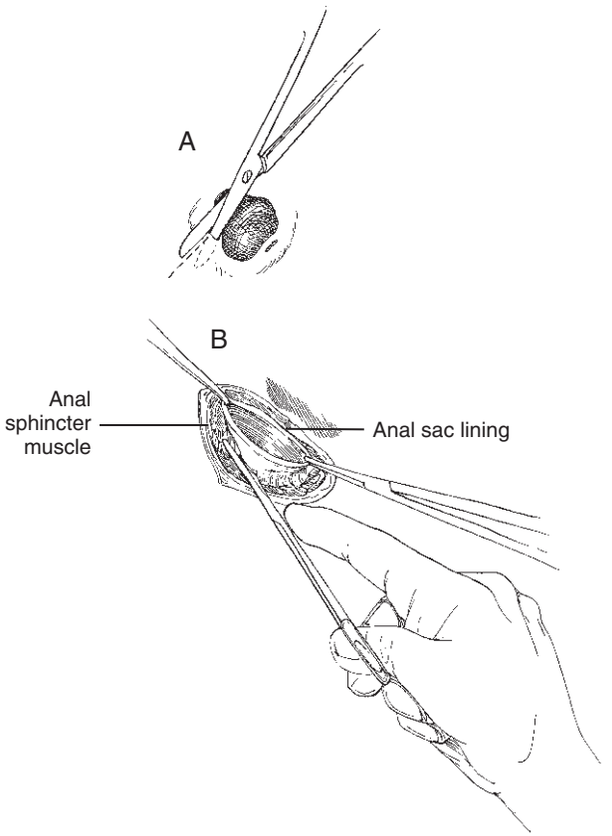

Figure 75-3. Surgical technique for resection of the anal sac.

5. Use small Metzenbaum or iris scissors to bluntly dissect the sac free of its attachments, including the fibers of the external anal sphincter (Fig. 75-3*B*).
6. When dissecting medial to the anal sac duct, preserve the caudal rectal artery.
7. Use fine, monofilament absorbable sutures to close defects in the anal sphincter and subcutaneous tissues after flushing thoroughly with saline. Close the skin with monofilament non-absorbable suture.

Alternative Technique

1. I now prefer a "closed" technique using a 6-French Foley catheter. Gently flush each anal sac to be removed with saline or a dilute antiseptic solution.
2. Place a 6-French silicone or latex catheter into the anal sac and fill the catheter bulb gently with saline until the anal sac can be easily palpated below the skin.
3. Occasionally, the inflated bulb will tend to migrate out of the anal sac as it is distended. Place a suture across the anal duct opening to prevent this.
4. The distended bulb makes identification and palpation of the gland simple. Gentle traction on the catheter by an assistant enhances the dissection of the sac from its surrounding attachments including the fibers of the external anal sphincter muscle. The wall of the sac is off-white or gray in appearance compared to the reddish color of the external anal sphincter.
5. Dissection with the inflated Foley catheter bulb allows the surgeon to stay close to the sac and minimize injury to the sphincter muscle fibers.
6. Once the sac is dissected free, excise the duct along its length toward the duct opening.
7. Flush the pocket that remains vigorously with saline. Repeat the flush three to four times as the subcutaneous tissues and skin are closed.
8. Close the deep tissues (including external anal sphincter muscle) and subcutaneous tissues with monofilament absorbable sutures.
9. Use 3-0 or 4-0 absorbable multifilament synthetic suture to appose the skin as it is softer and is less irritating to the tender perianal tissues. Remove sutures in approximately 10 to 14 days.

Postoperative Care and Complications

Short Term

- Hemorrhage due to inadequate hemostasis may continue after closure of the skin.
- Rarely, temporary or permanent fecal incontinence may result.
- Wound infection is more likely because of the location of the surgical site.
- Tenesmus or dyschezia may occur for a few days but usually resolves spontaneously.

Long Term

- Fistulous tracts may form after sacculectomy and are the result of incomplete excision of the anal sac lining.
- Wounds that do not heal after surgery may indicate a concurrent anal sac tumor.

Prognosis

- The prognosis is good with complete excision of the sac lining and preservation of the external anal sphincter.

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Chapter

76 Peritonitis

Stephen J. Birchard

Peritonitis is a common problem in small animals. Primary peritonitis can occur in cats (feline infectious peritonitis; see Chapter 10), but other forms of peritonitis in dogs and cats are usually secondary to other diseases or injuries. Advances in the diagnosis and treatment of peritonitis have lowered mortality rates. However, peritonitis continues to be a serious and life-threatening condition that requires aggressive management.

In this chapter, the general topic of peritonitis is discussed. For more detailed information on the treatment of the specific causes of peritonitis, refer to appropriate chapters.

ANATOMY

The peritoneum is a serous membrane composed of mesothelial cells. It consists of the parietal peritoneum that lines the abdominal cavity and the visceral peritoneum that covers the abdominal viscera. The peritoneum has tremendous surface area (i.e., 50–100% of body surface area). The peritoneal cavity is closed in the male but open in the female through the reproductive tract. A small amount of fluid that lubricates the abdominal viscera is produced by the peritoneum.

ETIOLOGY

Viral

Feline infectious peritonitis is an example of primary peritonitis (see Chapter 10).

Bacterial

Gastrointestinal Perforation or Leakage

▼ ***Key Point*** Loss of bowel wall integrity accounts for the majority of cases of bacterial peritonitis in dogs and cats.

Leakage of bowel contents allows release of bacteria, predominantly anaerobes and gram-negative aerobes. Fluid and ingesta may also leak if gross bowel wall disruption occurs, resulting in a complex interaction of bacterial, chemical, and foreign body factors in the pathogenesis of peritonitis.

Bowel leakage can occur by a variety of mechanisms:

- *Perforation*—The bowel can be penetrated by external objects such as gunshot or a sharp object.
- *Neoplasia or granuloma*—Leakage from a necrotizing gastrointestinal (GI) neoplasm (carcinoma, lymphoma) or granuloma can occur.
- *Corticosteroids*—Colonic perforation can occur secondary to the administration of high doses of corticosteroids in animals with spinal compression.
- *Foreign bodies*—Sharp intestinal or linear foreign bodies frequently cause perforation (see Chapter 69). Also, intraluminal pressure on the intestinal wall by a foreign body can eventually lead to ischemic necrosis and leakage.
- *Blunt trauma*—Devitalization of the bowel can occur secondary to tearing of the mesenteric blood supply.
- *Strangulation*—Any process causing obstruction of the intestinal blood supply causes loss of mucosal integrity and eventually full-thickness necrosis (see Chapter 69). Loss of the so-called mucosal barrier can result in translocation of bacteria and/or endotoxins into the peritoneal cavity.
- *Dehiscence*—Unsatisfactory healing of a GI incision may result in leakage through the wound and subsequent peritonitis.

Pyometra

Bacterial infection of the uterus can lead to peritonitis by leakage through the fallopian tubes or overt rupture of a pus-filled uterus (see Chapter 90).

Prostatic or Liver Abscess

Abscesses of the prostate gland (see Chapter 84) or liver (see Chapter 71) may leak bacteria to the peritoneal cavity spontaneously or iatrogenically during surgical exploration.

Surgical Contamination

A breakdown in aseptic technique can result in contamination of the peritoneal cavity and peritonitis.

Chemical

Urinary Tract

Leakage of urine from any part of the urinary tract can cause chemical peritonitis.

- Causes of urinary tract disruption include trauma (blunt or penetrating), bladder or urethral rupture due to obstruction, and traumatic catheterization (see Chapters 77, 79, and 81). Urinary tract disruption due to blunt trauma frequently is associated with pelvic and sacral fractures or luxations.
- Bacterial peritonitis can complicate the chemical peritonitis from urine leakage if urinary tract infection was present before the leakage occurred.

Biliary Tract

- Trauma to the biliary tract can cause leakage of bile due to rupture of the gallbladder or one of the bile ducts.
- Spontaneous leakage of bile can occur with rupture of the gallbladder due to diseases like necrotizing cholecystitis and mucocele. Bacterial peritonitis may also complicate this situation.
- Bile is irritating to the peritoneum. However, several days may elapse before an affected animal is presented for clinical signs of peritonitis and biliary disease.

▼ ***Key Point*** A clinical study in dogs and cats found a grave prognosis for animals with combined bacterial and bile peritonitis.

Gastrointestinal Tract

- Gastric fluid contains hydrochloric acid and therefore is very irritating to the peritoneum. Proximal intestinal fluid contains bile and pancreatic enzymes that may cause a combination of chemical and bacterial peritonitis.
- Leakage of gastric fluid may occur due to trauma or any of the other causes of tissue breakdown listed under "Gastrointestinal Perforation or Leakage."
- Gastric fluid may leak secondary to perforating ulcers or necrotizing gastric neoplasms (see Chapter 67).
- Tissue necrosis secondary to gastric dilatation-volvulus can cause leakage of gastric contents.
- Gastric contents are not always sterile. Bacterial contamination associated with leakage of ingesta can complicate the peritonitis and result in a combination of chemical and septic peritonitis.

Chyle

- Disruption of the mesenteric lymphatics, lymph nodes, or cisterna chyli can cause leakage of chyle into the peritoneal cavity.
- Neoplasia or other diseases causing erosion or obstruction of the lymphatics are more likely causes than disruption due to trauma.
- Chyle is irritating to the peritoneum, although in some animals it is reabsorbed by the abdominal lymphatics.

Pancreatitis

- Leakage of pancreatic enzymes and various chemical mediators of inflammation from the inflamed pancreas causes peritonitis (see Chapter 73).
- Local peritonitis is very common with pancreatitis. Severe, necrotizing pancreatitis or pancreatic abscess may cause generalized peritonitis.

Traumatic

Penetrating trauma that involves the peritoneal cavity, such as a gunshot or knife wound, will cause peritonitis even if the viscera are not injured.

Iatrogenic (Surgical)

- Varying degrees of peritonitis result from surgical manipulation of the peritoneum or abdominal structures.
- Analysis of peritoneal fluid after routine abdominal surgery shows increased neutrophils and increased serum lipase concentrations, suggesting pancreatic inflammation.
- Typically, peritonitis from routine visceral manipulation is clinically insignificant. Poor surgical technique, such as rough handling of tissues, allowing tissues to become desiccated, and lack of aseptic technique, can result in more serious peritonitis.

Foreign Body

Sutures

- Implantation of excessive, large, or contaminated sutures can result in focal peritonitis.
- Non-absorbable braided sutures (e.g., Braunamid, B. Braun Melsungen) that are contaminated can cause chronic focal peritonitis and resultant sinus tracts and abscesses.

▼ ***Key Point*** Avoid placing non-absorbable, multifilament sutures in the peritoneal cavity or viscera.

Surgical Sponges

- Failure to remove surgical sponges can result in focal or diffuse peritonitis. Even sponges considered sterile can cause a significant foreign body reaction. Contaminated sponges cause abscesses and possibly severe, septic peritonitis.
- Prevention of this complication is essential.
- Count surgical sponges before and after surgery to be sure that none have been left in the abdomen.
- Use sponges that contain a radiopaque marker to allow diagnosis of a sponge foreign body with abdominal radiography.

Other Foreign Bodies

- Failure to remove surgical instruments can cause a foreign body reaction, irritation of viscera, and strangulation of blood supply to structures.
- Talc used on surgical gloves can cause a foreign body, granulomatous peritoneal reaction. After donning surgical gloves, rinse with sterile saline before opening the peritoneal cavity.
- Bacterial peritonitis is a potential complication of peritoneal dialysis caused by contamination during the procedure or ascending infection via the indwelling dialysis catheter.

DISTRIBUTION AND LETHAL FACTORS

Local Peritonitis

- Local peritonitis is common and usually does not require aggressive surgical management.
- The abdominal structures, such as the omentum and mesentery, are able to "wall off" inflammatory processes and prevent spread to the entire cavity.
- The production of fibrin by the peritoneum is also an important process in confining bacteria and debris to an isolated area of the peritoneal cavity.
- Permanent adhesions can be a sequela of local peritonitis, but they rarely cause a significant clinical problem in dogs and cats.

Diffuse Peritonitis

- Diffuse or generalized peritonitis occurs when the processes of confinement are overwhelmed and the entire cavity is affected.
- Diffuse peritonitis is a serious condition that requires aggressive medical and usually surgical therapy.
- Movement of the diaphragm, intestinal peristalsis, and gravity encourage dissemination of bacteria throughout the peritoneal cavity.
- Surgical manipulation of contaminated tissues can convert local to diffuse peritonitis.

Lethal Factors

Certain substances or combinations of substances have been shown to be especially devastating to the animal with peritonitis.

▼ ***Key Point*** The addition of blood, fluid, or barium (or other foreign material) to bacterial contamination of the peritoneum can cause severe, frequently fatal peritonitis.

- Hemoglobin and bacteria are a lethal combination in peritonitis. Hemoglobin tends to reduce the ability of the neutrophils to phagocytize bacteria.
- Barium sulfate, in addition to bacteria, has the same effect as hemoglobin.
- Excessive peritoneal fluid acts as an adjuvant in peritonitis. Fluid causes dissemination of bacteria and interferes with neutrophil migration along visceral and peritoneal surfaces.
- Contamination of the peritoneal cavity with multiple species of bacteria, such as occurs with bowel leakage, causes a more severe peritonitis than that due to one species.
- The combination of chemical and bacterial peritonitis is especially devastating. Proteolytic and lipolytic enzymes cause tissue necrosis, an ideal medium for bacterial growth.

CLINICAL SIGNS

Pain

The peritoneum is a very sensitive membrane. Irritation of the peritoneum can cause abdominal discomfort.

- The mildly affected animal is resistant to abdominal palpation.
- Signs of severe pain include reluctance to move and tachycardia and tachypnea.
- The animal may assume the "praying mantis" posture in an attempt to alleviate peritoneal pain.
- Peritoneal pain may cause the animal to contract the abdominal muscles, giving the abdomen a "tucked up" appearance.

Fever

- Pyrexia may or may not be present.
- Fever does not always imply sepsis but is more likely when bacterial contamination complicates peritoneal inflammation.
- An animal with overwhelming peritonitis, dehydration, and shock may have a subnormal temperature.

Vomiting

Vomiting may result from irritation of serosal surfaces, ileus, or the primary disease causing peritonitis.

Dehydration

- The peritoneum responds to inflammation by producing large amounts of protein-rich fluid.
- Loss of fluid from the peritoneum, inadequate intake of water and food, vomiting, and fever rapidly cause significant dehydration and hypovolemia.

Shock

- Hypovolemic shock can develop rapidly with peritonitis as a result of the processes described under "Dehydration," as well as the sequence of events described in Chapter 156 on shock.
- Septic shock also is possible with diffuse peritonitis owing to release of bacteria to the peritoneal cavity,

followed by absorption to the systemic circulation. Lysis of gram-negative bacteria that have leaked from the bowel causes endotoxemia. These endotoxins have a direct cytotoxic effect, as well as causing many systemic changes such as vasodilation and blood pooling, hypoglycemia, and acidosis.

DIAGNOSIS

History

- Thoroughly review the animal's history to gain clues to the presence of peritonitis and possible etiologies.
- Give special attention to any history of trauma or prior abdominal surgery.
- Determine if the animal recently ate any foreign bodies that could have caused bowel perforation.
- Determine if the animal has had any signs of gastric or colonic ulceration. A history of hematemesis, melena, or hematochezia is indicative of a more serious lesion of the GI tract and increases the suspicion of perforation.
- Determine if the signalment and history are typical of pancreatitis.

Physical Examination

- Look for the clinical signs listed previously.
- Carefully palpate the abdomen for evidence of pain, fluid, ileus, or masses. Perform a rectal examination to evaluate for evidence of pelvic trauma, prostate or urethral problems, or hematochezia.
- Evaluate for fever.

Diagnostic Tests

Fluid Analysis

Abdominocentesis

See Chapter 3 for a description of the technique for abdominocentesis.

- Animals with peritonitis will have many neutrophils (>500/μl) and may have bacteria on cytologic examination. Absence of bacteria suggests a sterile peritonitis, such as can occur with chemical peritonitis.
- The presence of bacteria within phagocytes confirms septic peritonitis. Bacteria within and outside phagocytes suggest that the infection is overwhelming the defense mechanisms. The presence of cocci and rods indicates mixed infection, such as can occur with GI perforation. Gram stain of the fluid can differentiate gram-negative rods (usually aerobes such as *Escherichia coli*) from gram-positive rods (usually anaerobes such as *Clostridium* spp.).
- Large numbers of red blood cells (RBCs) indicate hemorrhage associated with the peritonitis. This can occur with trauma, bleeding tumors, or disseminated intravascular coagulation.
- Recent studies indicate that animals with septic peritonitis have decreased abdominal fluid glucose compared with their serum.

Diagnostic Peritoneal Lavage

See Chapter 3 for a description of the technique for diagnostic peritoneal lavage (DPL).

- Observe the gross appearance of the fluid. Opaque fluid is likely from animals with peritonitis.
- Analyze the fluid for neutrophils (>500/μl is considered a positive finding), toxic neutrophils, bacteria, bilirubin, creatinine higher than serum concentration, amylase > 200 IU, and vegetable fibers.
- Animals that have had recent surgery normally have a high number of nucleated cells in the peritoneal cavity (>6000/μl).

Hematology

- Neutrophilia may be present with or without toxic neutrophils. A left shift (an increase in the number of band neutrophils) indicates more significant inflammation. A degenerative left shift (more bands than segmented neutrophils) indicates an overwhelming, life-threatening inflammatory process.
- Chronic blood loss or chronic infection may result in anemia.
- Hypoproteinemia due to loss or sequestration of albumin is very common in peritonitis.

Serum Chemistry Profile

- Many parameters may be altered, depending on the type of peritonitis and the associated clinical signs.
- Electrolytes (sodium, potassium, and chloride) may be depleted in animals that are vomiting. Acidotic animals may be hyperkalemic. Dehydration can artificially elevate electrolyte concentrations.
- Hypoglycemia may be present in animals with septic peritonitis.
- Serum urea nitrogen is elevated in animals with uroperitoneum and in animals suffering from prerenal azotemia due to dehydration or shock. Hyperkalemia may also be seen in animals with uroperitoneum.
- Serum pancreatic enzymes (amylase, lipase, trypsin) frequently are mildly elevated in all types of peritonitis, and they are moderately to markedly elevated when underlying pancreatitis is the cause of peritonitis.
- Serum liver enzymes and bilirubin are variably increased in all types of peritonitis and may be markedly increased in sepsis, biliary tract rupture, liver abscess, and pancreatitis.

Radiography

Plain Radiography

- Plain abdominal radiography usually reveals a loss of contrast and lack of soft tissue detail either focally or throughout the abdomen. Fluid may be present in the peritoneal cavity.
- Pneumoperitoneum may be seen if any portion of the GI tract has perforated or there has been penetrating abdominal trauma. Radiographs obtained using horizontal projection can confirm air in the peritoneal space, because it rises to the dorsum of the cavity (see Chapter 4).

Contrast Studies

- Perform positive-contrast urethrography, cystography, and/or intravenous (IV) pyelography if uroperitoneum is suspected (see Chapter 4).
- Perform positive-contrast GI studies to diagnose perforation (see Chapter 4). Avoid using barium as the contrast agent when perforation is suspected, because barium leakage into the peritoneal cavity can be devastating (treat with immediate laparotomy, peritoneal lavage, and drainage). Instead, use a water-soluble, non-ionic, iodinated contrast agent, such as iohexol (Omnipaque).

Ultrasonography

- Ultrasonography can confirm the presence of peritoneal fluid and can be used to assist in sampling the fluid for analysis. It is especially valuable for evaluating the pancreas as a potential cause of peritonitis.
- Soft tissue masses or abscesses may be detected (see Chapter 4).

TREATMENT

Management of peritonitis consists of supportive care and definitive measures to eliminate or correct the cause. The decision to treat the animal medically or surgically depends on the cause and the animal's response to treatment. If a surgical disease is not suspected and the peritonitis is mild, medical treatment alone may suffice. However, promptly initiate surgical treatment if the peritonitis is moderate or severe, is not improving with medical treatment, or is due to a surgical lesion such as a perforated intestine or biliary or urinary rupture.

Medical Management

Fluids

IV fluids are probably the most important supportive treatment. The type of fluids used depends on the type of peritonitis and the metabolic alterations present in the patient.

- In most cases, use lactated Ringer's solution supplemented with potassium to prevent or correct hypokalemia.
- After correcting the dehydration, give fluids at a maintenance rate, plus continuing losses, until the animal is able to maintain hydration with oral intake. (See Chapter 5 for fluid therapy details.)

Antibiotics

Systemic antibiotics are indicated in bacterial peritonitis. Choose antibiotics based on culture and sensitivity testing of peritoneal fluid.

- In the absence of culture results, use broad-spectrum bactericidal drugs. Results of Gram stain of abdominal fluid (see under "Diagnosis") can be used to guide antibiotic choice.
- Combinations of antibiotics may be necessary if a mixed population of bacteria is present. For example, combine ampicillin or one of the cephalosporins (e.g., cefazolin) with enrofloxacin for peritonitis due to a mixed bacterial population. Alternatively, if the animal has normal renal function, combine ampicillin with an aminoglycoside (e.g., amikacin or gentamicin). Other options include penicillins, clindamycin, or metronidazole for anaerobes and other fluoroquinolones for gram-negative rods.

Lavage and Drainage

▼ ***Key Point*** One of the most important treatments for peritonitis is drainage of fluid and debris from the peritoneal cavity.

Abdominal drains such as Penrose drains or sump drains (e.g., a fenestrated Brunswick catheter inside a fenestrated Penrose drain) are ineffective for draining the entire peritoneal cavity for any longer than a few hours. However, these types of drains can be effective for the initial drainage of the abdomen or for animals that are producing large amounts of abdominal fluid.

- Open abdominal drainage has been used successfully in experimental and clinical peritonitis and is described under "Surgical Management."

▼ ***Key Point*** Recent studies have found closed suction drains (e.g., Jackson Pratt drains) to be effective in the treatment of generalized peritonitis (see description under "Surgical Management").

- Lavage of the peritoneal cavity has been recommended but is controversial. Addition of fluid to the peritoneal cavity may potentiate generalized peritonitis and should only be used when all of the lavage fluid can be drained. Therefore, lavage should be reserved for those patients that undergo surgical treatment of the problem. Lavage consists of copious

amounts of warm, sterile saline. Continue lavage until the fluid removed from the peritoneal cavity appears clear.
- Addition of antibiotics or antiseptics to the lavage fluid has *not* been shown to have any benefit over the use of saline alone in conjunction with systemic antibiotics.
- Do not use aminoglycosides in peritoneal lavage during anesthesia, especially if systemic neuromuscular blocking agents are being used. Aminoglycosides can potentiate the effect of these agents. Also, aminoglycosides will be absorbed and can reach toxic blood levels if they also are being given parenterally.
- Avoid using povidone-iodine (Betadine) in lavage fluid in animals with peritonitis, because it can also be absorbed and cause severe toxicity, possibly due to absorption of large amounts of iodine.

Surgical Management

Correction of lesions resulting in peritonitis is covered in the appropriate chapters.

Preoperative Considerations

- As discussed under "Medical Management," correct fluid and electrolyte disorders, when possible, before surgery.
- Begin antibiotic treatment before surgery if contamination is present or is likely to occur during the surgery.

Closed versus Open Peritoneal Drainage

A key decision for the surgeon is whether to use closed or open drainage methods for peritonitis. Closed suction drains are reasonably effective for septic peritonitis. Complications with the use of these drains are less than with open drainage. Consider the following factors when deciding which type of peritoneal drainage to use:

- Type and severity of the peritonitis
  - If the source of the peritonitis can be definitively corrected at surgery, consider choosing closed peritoneal drainage.
- Ability of the patient to withstand the complications of open drainage
- Financial considerations (closed drainage patients tend to require less intensive therapy)
- Hospital facilities and personnel
- Personality of the patient
  - Open peritoneal drainage would be very difficult in a fractious animal.

Technique for Closed Peritoneal Drainage

1. After the laparotomy has been performed and the cause of the peritonitis has been corrected, lavage the abdominal cavity with warm, sterile saline. Use copious amounts of saline to flush bacteria and debris from the cavity. Discontinue flushing when the lavage solution appears clear on removal from the abdomen.
2. Place the drain(s) (e.g., Jackson Pratt drain) either directly adjacent to the source of the peritonitis or along the ventral midline to facilitate drainage of fluid from the entire abdomen.
3. If necessary, use absorbable sutures to tack the omentum to the peritoneum away from the drain to prevent occlusion.
4. Exit the drain from the abdominal cavity through separate stab incisions lateral to the ventral midline abdominal incision.
5. Close the abdominal incision routinely.
6. Frequently empty the drain reservoir, and characterize the type and amount of fluid.
7. Remove the drain when little or no fluid is being recovered and the patient's other clinical parameters are significantly improved (usually 3–5 days postoperatively).

Technique for Open Peritoneal Drainage

1. After the laparotomy has been performed and the cause of the peritonitis has been corrected, lavage the abdominal cavity with warm, sterile saline. Use copious amounts of saline to flush bacteria and debris from the cavity. Discontinue flushing when the lavage solution appears clear on removal from the abdomen.
2. Partially close the abdominal incision. Place large horizontal mattress or simple continuous sutures of monofilament polypropylene or nylon (1-0 or 2-0) in the linea alba to reduce the incisional gap to approximately 3 to 4 cm in width. Leave the remaining tissue layers open (Fig. 76-1*A*).
3. Cover the incision with a sterile dressing consisting of (from inside out) sterile petrolatum-impregnated gauze, sterile laparotomy sponges or towels, cotton, conforming gauze, and tape. Make the bandage large enough to extend several centimeters beyond the cranial and caudal aspect of the incision, and construct it so that slippage will not occur.
   a. Large monofilament polypropylene eyelet sutures can be placed, and umbilical tape "laces" used to hold the laparotomy pads or towels in place (Fig. 76-1*B*).
4. Change the bandage aseptically two or more times daily, depending on the quantity of fluid drainage. Sedate the patient if necessary for bandage changes. Gently break down omental or falciform ligament adhesions to the sutures with a sterile-gloved hand between bandage changes. If necessary, obtain samples of peritoneal fluid periodically for cytology and culture.
   a. Weigh the bandage before and after placement on the animal to estimate fluid loss (500 ml = 1 lb). Use this information to help

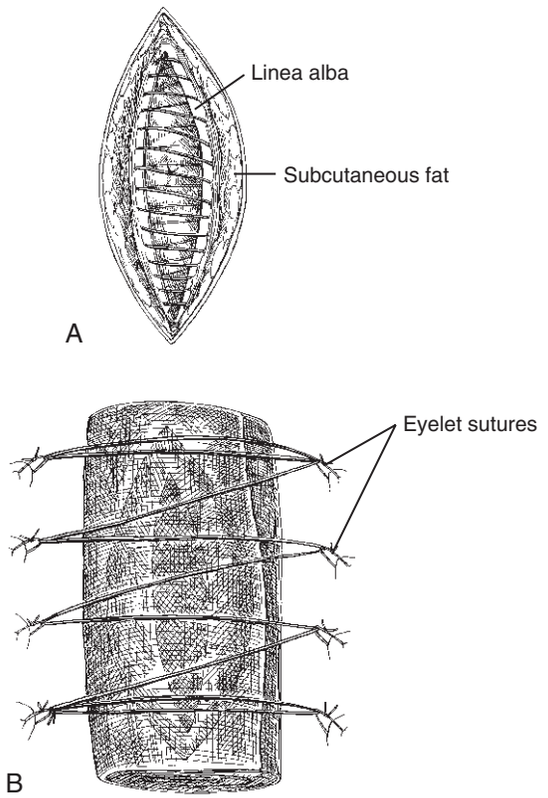

Figure 76-1. Partial closure technique for open abdominal drainage. *A,* Partially close the linea alba with a loosely placed, simple continuous suture using a monofilament non-absorbable material. *B,* To hold the primary layer of the abdominal bandage in place, put several eyelet sutures in the skin, then use umbilical tape to "lace" through the eyelets over the abdominal sponge.

calculate fluid requirements and to monitor the trend of abdominal fluid production.

5. In most patients, the abdomen can be closed within 5 to 7 days of the original surgery (see below). Perform abdominal closure by removing the original sutures in the fascia and proceeding with routine closure. Additional culture samples from the peritoneum may be obtained just before closure.

The decision on when to close the abdominal incision is subjective. Base this decision on several factors:

- Overall progress of the patient
- Quantity, character, and cytology of fluid drainage from the abdomen
- Resolution of fever and neutrophilia with a left shift

Postoperative Care and Complications

- Keep the bandage as clean as possible. Indwelling urinary catheterization may be necessary in a male dog, or the animal can be kept on an elevated grate to prevent urine soaking of the bandage.
- Open drainage of the abdomen can cause several complications:
  - *Loss of fluid and protein from the peritoneal cavity*—Supportive care with IV fluids and colloids is very important. Hyperalimentation (or total parenteral nutrition) also is necessary if the animal is not eating adequately (see Chapter 3 for nutritional management of the critical care patient).
  - *Electrolyte depletion, especially potassium*—Supplement IV fluids with potassium if necessary (see Chapter 5).
  - *Discomfort from the peritonitis and from the open abdomen*—Administer analgesics as necessary (e.g., morphine, butorphanol, buprenorphine, or oxymorphone) (see Chapter 6).
  - *Herniation of abdominal viscera or omentum*—This may occur if the bandage slips or is damaged by the animal. Gently lavage any tissue that becomes contaminated with sterile saline or remove surgically. Restrict exercise.

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Section 7

Disorders of the Urogenital System

Mary A. McLoughlin

Chapter 77

Diseases of the Kidney and Ureter

David Grant / S. Dru Forrester

ACUTE RENAL FAILURE

Acute renal failure (ARF) is a syndrome caused by an abrupt decline in renal function that occurs over a period of hours to days. Clinical signs result from inability of the kidneys to excrete metabolic wastes and adequately regulate fluid, acid, base, and electrolyte balance. Consistent laboratory findings include azotemia with decreased urine concentrating ability (urine specific gravity usually <1.025).

▼ ***Key Point*** When azotemia is identified, it is important to distinguish among prerenal, renal, and postrenal causes.

- ***Prerenal azotemia*** can result from any disorder that decreases renal perfusion (e.g., dehydration, heart failure, or hypovolemia) or that results in increased production of urea (e.g., gastrointestinal hemorrhage). With few exceptions (Table 77-1), dogs and cats with purely prerenal causes of azotemia produce concentrated urine (i.e., specific gravity >1.035 in dogs and >1.040 in cats). In addition, prerenal azotemia quickly resolves when the cause of decreased renal perfusion is corrected (e.g., fluid therapy).
- ***Renal azotemia*** is caused by renal failure and occurs when 75% of nephrons are nonfunctional. Dogs and cats with renal failure have concomitant azotemia and inability to adequately concentrate urine. Isosthenuria (specific gravity of 1.008–1.012) often exists, and urine specific gravity (USG) is almost always <1.025, although some cats with renal failure maintain ability to concentrate urine up to 1.035. In contrast with prerenal causes, renal azotemia usually does not resolve quickly with treatment.
- ***Postrenal azotemia*** results from decreased elimination of urine from the body, most often due to urethral obstruction or a rupture in the urinary system. There usually is something in the history (e.g., trauma or stranguria) or physical examination (e.g., abdominal fluid, swelling or discoloration of the perineal area, or masses within the prostate, urethra, or urinary bladder) that suggests a postrenal cause of azotemia. Additional tests such as radiography (plain and contrast), ultrasonography, and abdominal fluid analysis are helpful in confirming postrenal azotemia. Postrenal azotemia also rapidly resolves after correction of the underlying cause.

Etiology

ARF in dogs or cats results from acute tubular necrosis (i.e., nephrosis) and less frequently from renal inflam-

Table 77-1. DISORDERS ASSOCIATED WITH AZOTEMIA AND INADEQUATE URINE CONCENTRATION DESPITE NORMAL RENAL FUNCTION IN DOGS AND CATS

Drugs
Corticosteroids
Diuretics
Fluid therapy
Endocrine Diseases
Diabetes mellitus (ketoacidosis)
Hyperadrenocorticism
Hyperthyroidism
Hypoadrenocorticism
Other Disorders
Hepatic disease
Hypercalcemia
Pyometra
Urinary obstruction (postrenal azotemia)

Table 77-2. CAUSES OF ACUTE TUBULAR NECROSIS IN DOGS AND CATS

Nephrotoxicosis	Renal Ischemia
Therapeutic Agents	***Hypovolemia***
Aminoglycosides	Dehydration
Amphotericin B	Hemorrhage
Tetracycline (IV)	Hypoadrenocorticism
Cisplatin	***Decreased Cardiac Output***
Thiacetarsamide	Congestive heart failure
Paromomycin	Arrhythmias
Calcitriol analogues	Anesthesia
Streptozotocin	***Renal Vasoconstriction***
Endogenous Substances	ACE inhibitors
Hypercalcemia	NSAIDs
Hemoglobinuria	***Renal Thrombosis***
Other Substances	Bacterial endocarditis
Ethylene glycol	Disseminated intravascular coagulation
Iodinated contrast agents (IV)	
New methylene blue (IV)	
Lily plants	
Cholecalciferol rodenticide	

NSAIDs, nonsteroidal anti-inflammatory drugs.

mation (i.e., nephritis). Acute tubular necrosis is caused by nephrotoxins or renal ischemia (Table 77-2). Nephritis usually is due to infectious diseases in small animals.

- *Toxins:* Renal tubular toxins are responsible for about 20% to 25% of cases of ARF. Ethylene glycol is responsible for the overwhelming majority of ARF cases due to toxins. Less commonly, drugs (e.g., aminoglycosides) are a cause of ARF.
- *Ischemia:* Renal ischemia probably causes ARF more often than was once considered. Approximately one-third of dogs with ARF have a condition that predisposes to renal ischemia. In general, renal ischemia is most likely to cause ARF in patients that have preexisting renal disease or that have multiple, concomitant disorders that cause renal injury.
- *Nephritis:* Nephritis causes ARF in a small number of cases, probably less than 10%. Leptospirosis is the most common infectious cause of ARF (see Chapter 19), but pyelonephritis also may cause ARF, especially if concomitant urinary obstruction exists. Rarely, ARF occurs in dogs with rickettsial infections such as Rocky Mountain spotted fever (see Chapter 17). Recently, Lyme disease has been associated with ARF in dogs (i.e., Lyme nephritis) (see Chapter 18).
- *Idiopathic:* Even after thorough evaluation, a cause for ARF cannot be identified in approximately 20% to 25% of patients.

Clinical Signs

Clinical findings in patients with ARF are nonspecific and include lethargy, depression, inappetence, vomiting, and diarrhea. Urine volume varies, and in most cases the patient is presented for other signs before the owner has a chance to observe a change in urinary habits. Most patients with ARF have normal to decreased urine output, although some have polyuria (e.g., aminoglycoside toxicosis).

Diagnosis

▼ ***Key Point*** Make sure to distinguish between ARF and chronic renal failure (CRF) because ARF is a potentially reversible condition that requires aggressive treatment initially.

Distinguish between ARF and CRF on the basis of findings from history, physical examination, and routine laboratory evaluation (Table 77-3). Evaluation of renal size by abdominal radiography or ultrasonography also is helpful. In some cases, a renal biopsy is necessary to make a definitive diagnosis of ARF or CRF.

History

- Carefully question owners about potential for exposure to nephrotoxins. Ethylene glycol toxicosis cannot be excluded in any patient that is allowed outdoors, especially in free-roaming pets. Ask the owner if the animal has been given any over-the-counter medications such as nonsteroidal anti-inflammatory drugs (NSAIDs) (ibuprofen, aspirin).
- Ask about the patient's urine volume. Many dogs and cats with CRF have a history of polyuria/polydipsia (PU/PD), whereas oliguria or anuria usually indicates ARF.

Physical Examination

- Nonspecific findings on physical examination of patients with ARF include depression, dehydration, hypothermia, and oral ulcerations.

Table 77-3. DIFFERENTIATION BETWEEN ACUTE AND CHRONIC RENAL FAILURE

	Acute Renal Failure	Chronic Renal Failure
Clinical Findings	Acute onset of inappetence, depression, and vomiting (less than 1 week)	Chronic inappetence, vomiting, depression, weight loss (usually weeks to months)
	Usually moderate to severe depression	Often alert, responsive, and only slight depression
	Urine volume often decreased	Polyuria/polydipsia common
	Good body condition	May be thin
	Kidneys enlarged, painful but possibly normal	Kidneys small, irregular but possibly normal
	Bone density always normal	Bone density may be decreased
Lab Findings	Normal or increased hematocrit, but anemia may be present	Nonregenerative anemia, but hematocrit may be normal
	BUN and SCr previously normal but increasing progressively	BUN and SCr previously increased and typically stable
	Normal to increased serum potassium	Normal to decreased serum potassium
	Moderate to severe metabolic acidosis	Mild to moderate metabolic acidosis
	Urinary casts in some patients	Urinary casts usually absent
	Proteinuria or glucosuria may result from acute tubular necrosis	Proteinuria often present but usually due to glomerular disease

BUN, blood urea nitrogen; SCr, serum creatinine.

- Abdominal palpation may reveal enlarged, painful kidneys in patients with ARF, whereas finding small, irregularly shaped kidneys suggests CRF.
- Fever may be present in patients with ARF due to infectious diseases such as leptospirosis or pyelonephritis.
- Icterus in a patient with ARF suggests multisystemic disease such as leptospirosis, Rocky Mountain spotted fever, or disseminated intravascular coagulation.

Laboratory Evaluation

Hemogram

- Hemogram changes in patients with ARF usually are nonspecific and may include leukocytosis, with or without a left shift, and monocytosis. Increased hematocrit and plasma protein are consistent with dehydration. Mild anemia may occur secondary to gastrointestinal hemorrhage or hemodilution after fluid therapy. Finding a normocytic, normochromic, nonregenerative anemia (packed cell volume [PCV] <30%) is common in patients with CRF.

Biochemistries

- Serum chemistry abnormalities include azotemia and hyperphosphatemia. Hyperkalemia is very suggestive of ARF because patients with CRF usually have normal or low serum potassium. Some patients with ARF, especially due to ethylene glycol intoxication, may have hypocalcemia.
- Blood gas evaluation most often shows metabolic acidosis. Calculate the anion gap ([Na + K] − [Cl + HCO_3]) to help characterize metabolic acidosis; normal values for the anion gap are 12 to 18 mEq/L. An increased anion gap may occur with CRF, ARF, diabetic ketoacidosis, or lactic acidosis, but values >40 are almost always due to ethylene glycol intoxication or salicylate poisoning, which can be investigated by questioning the owner and performing an ethylene glycol test (measures blood levels of ethylene glycol).

Urinalysis

Analysis of urine, collected by cystocentesis where possible, should include evaluation of urine specific gravity, routine dipstick tests, and sediment examination.

- USG in patients with ARF is either isosthenuric (1.007–1.012) or minimally concentrated (usually <1.025).
- Dipstick analysis may reveal proteinuria or glucosuria, without concomitant hyperglycemia, due to renal tubular damage.
- Examine urine sediment for pyuria, bacteriuria, crystalluria, or cylindruria (renal casts).
  - Pyuria or bacteriuria suggests urinary tract inflammation or infection, respectively, and indicates the need for bacterial urine culture.
  - Hippurate or calcium oxalate crystals in patients with ARF suggest ethylene glycol intoxication.
  - White or red blood cell casts indicate renal inflammation or hemorrhage, respectively. However, most patients with pyelonephritis do not have white blood cell casts.
  - Renal epithelial cellular casts occur in patients with ARF due to acute tubular necrosis (i.e., nephrotoxicosis or ischemia).

Urine Culture

- Culture of urine collected by cystocentesis is indicated in patients with ARF to rule out urinary tract infection (UTI), a potentially reversible cause of renal injury.

Abdominal Radiography

- Plain radiographs of the abdomen help to objectively evaluate renal size and identify radiopaque uroliths that may be associated with urinary obstruction or infection.

Contrast Radiography

- Contrast radiography may be indicated to help identify urinary tract rupture or obstruction as a cause of postrenal azotemia (see Chapter 4).
- Excretory urography is indicated for evaluation of the kidneys and ureters. To avoid additional renal injury, establish adequate hydration prior to administration of IV contrast agents. Except for identifying rupture or obstruction of the upper urinary tract, excretory urography is of limited value in patients with renal failure because the kidneys cannot excrete contrast material well enough to produce useful images.
- Perform contrast urethrocystography when obstruction or rupture of the urinary bladder or urethra is suspected.

Ultrasonography

- Abdominal ultrasonography is helpful for evaluating renal size, changes in echogenicity, pyelectasia, perinephric effusions, and architecture and for identifying uroliths and signs of urinary tract obstruction (hydroureter, hydronephrosis). Ultrasonography is preferred over excretory urography for evaluation of the kidneys in patients with ARF (see Chapter 4).

Renal Biopsy

- Collection of renal tissue for histologic evaluation is unnecessary in most cases of well-defined ARF.
- Renal biopsy, however, may be helpful in the following situations:
  - When it is not possible to distinguish between ARF and CRF on the basis of clinical and laboratory findings
  - When the cause of ARF is not apparent and the mechanism of renal injury seems to be ongoing
  - When response to treatment is inadequate and expensive forms of treatment such as dialysis are being considered
- Renal biopsy is contraindicated in patients with coagulopathies (thrombocytopenia), renal cysts or abscesses, or hydronephrosis. Use caution in patients that have only one kidney.

Testing for Leptospirosis

- If leptospirosis is even a remote possibility, submit serum samples for determination of *Leptospira* titers (see Chapter 19 for guidelines on interpreting results of titers) as this is a potentially reversible cause of ARF.
- At minimum, evaluate *Leptospira* titers for serovars *L. pomona, L. grippotyphosa, L. bratislava, L. canicola,* and *L. icterohaemorrhagiae.*

Treatment

▼ ***Key Point*** Objectives of treating ARF are to minimize additional renal injury, promote diuresis if oliguria exists, and combat metabolic consequences of uremia.

- With time, renal injury in patients with ARF may be repaired so that there is adequate renal function to maintain homeostasis. This requires 2 to 4 weeks of aggressive medical treatment in many patients.
- Discontinue all potentially nephrotoxic drugs to avoid additional renal injury; if a potentially nephrotoxic drug must be administered, adjust the dosage appropriately. For drugs that undergo renal excretion, dividing the dose by the creatinine concentration or multiplying the dosing frequency (in hours) by the creatinine concentration provides a rough adjustment for the increased exposure to drugs in patients with renal failure.
- Rapidly correct all prerenal factors (dehydration, decreased cardiac output) so that renal perfusion is maintained.
- Administer treatment as necessary to control consequences of uremia such as vomiting, metabolic acidosis, hyperkalemia, and hyperphosphatemia.
- If an underlying cause of ARF or renal injury can be identified (pyelonephritis, leptospirosis), administer specific treatment to eliminate the disorder.

Initial Patient Management

- Determine baseline values for PCV, plasma or total protein, blood urea nitrogen (BUN), serum creatinine, phosphorus, potassium, calcium, sodium, and total carbon dioxide (CO_2).
- Record values for body weight and hydration status. Use body weight after rehydration as a reference for future comparisons.
- Aseptically place an indwelling IV catheter, preferably in a jugular vein. In addition to convenience for the patient, jugular catheters allow collection of blood, measurement of central venous pressure, and IV administration of hypertonic solutions (see Chapter 5).
- If oliguria (i.e., urine volume <1 ml/kg/hr) persists after apparent rehydration, place an indwelling urinary catheter so that urine volume can be objectively measured. Connect the urinary catheter to a closed collecting system. Unless absolutely necessary, avoid administering antimicrobials to patients with indwelling urinary catheters because it may predispose to development of resistant UTI.

Fluid Therapy

A comprehensive discussion of fluid therapy is provided in Chapter 5.

Initial Treatment

- Calculate the dehydration deficit using the following formula to determine volume of fluids (milliliters) to correct dehydration initially:

$$\% \text{ Dehydration} \times \text{Body Weight (kg)} \times 1000$$

- If cardiac function is normal, correct dehydration within 6 hours by administering fluids IV.
- Ideally, select the type of fluid on the basis of serum electrolyte concentrations and acid-base status. It usually is safe to use lactated Ringer's solution in most patients unless hyperkalemia exists. If serum potassium concentration is unknown, initial administration of 0.9% sodium chloride is more appropriate.
- Clinical dehydration may not be apparent in all patients with ARF; however, most of these patients have a history of inappetence, vomiting, and/or diarrhea. Therefore, it generally is safe to assume subclinical dehydration (3–5% of body weight) and treat accordingly. In most cases, it is better to cause slight overhydration than to risk persistent mild dehydration, which may contribute to prerenal azotemia and potentiate ischemic renal injury.

Maintenance Treatment

- After rehydration, the volume of fluids to administer IV for maintenance needs equals the sum of ongoing losses (e.g., vomiting or diarrhea), insensible losses, and urine volume ("in and outs"; see Chapter 5). The fluid rate/volume should be recalculated every 4 to 6 hours to prevent dehydration or hypervolemia.

▼ ***Key Point*** Select a fluid such as Plasma-Lyte M or Normosol-M to facilitate maintenance of normal serum electrolytes. Avoid lactated Ringer's solution and 0.9% sodium chloride because they contain too much sodium and too little potassium to be maintenance solutions. If a maintenance fluid is not available, alternate lactated Ringer's solution with 5% dextrose to avoid hypernatremia; add potassium to fluids as needed to maintain serum potassium concentration, especially during the recovery phase of ARF.

- Depending on the severity of renal injury, IV fluid therapy may be necessary for 1 to 3 weeks.

Discontinuing Fluids

- Gradually taper the volume of fluids administered to patients with ARF, once BUN and serum creatinine return to normal or oral intake of fluid is tolerated without vomiting.
- Provide unlimited access to water and decrease the patient's daily fluid volume administered IV by one-half every 24 hours.
- Monitor hydration (body weight, skin turgor, moistness of mucous membranes) closely while IV fluids are gradually discontinued.
- Monitor BUN, serum creatinine, and electrolytes every 1 to 2 days to detect need for additional treatment.

Reversing Oliguria

▼ ***Key Point*** Do not attempt to stimulate diuresis (increased production of urine) with diuretics in patients that are dehydrated or that have non-oliguric renal failure. This will worsen or cause dehydration and electrolyte disturbances, which adversely affect renal function.

If oliguria (<1 ml of urine per kilogram per hour) persists after correction of dehydration, additional treatment is indicated to increase urine production. Urine formation does not necessarily indicate improved renal function; however, it generally is easier to maintain serum electrolytes and acid-base balance in patients that are not oliguric. If there is any doubt whether oliguria exists, place an indwelling urinary catheter so that urine output can be measured.

IV Fluid Therapy

- IV administration of balanced electrolyte solutions promotes diuresis in normal patients and those with non-oliguric renal failure but usually is not effective in patients with ARF.
- Administer fluids to correct dehydration or cause slight volume expansion (3% to 5% of body weight) only and not 1.5 to 3 times maintenance volumes. Patients with ARF cannot adequately handle excessive IV fluids because of acute renal tubular dysfunction and are predisposed to overhydration, which may cause peripheral and pulmonary edema.

Mannitol (20% or 25%)

- Osmotic diuretics such as mannitol are often used initially to stimulate urine production in patients that remain oliguric after rehydration. In addition, mannitol may have beneficial free radical–scavenging properties.
- To avoid thrombophlebitis in peripheral veins it is preferable to administer hypertonic solutions (>10%) through a jugular vein.
- Initially, administer 0.25 to 0.5 g/kg IV over 5 to 10 minutes. If treatment is effective, increased urine production begins within 15 minutes. The goal is to produce 1 to 2 ml of urine per kilogram per hour.

- Continue mannitol every 6 to 8 hours as needed.
- If urine flow does not increase after initial treatment, repeat the dose every 15 minutes up to a total dose of 1.5 g/kg. Do not administer additional mannitol because vascular overload may occur.

Furosemide

- Loop diuretics, such as furosemide, may be administered to promote diuresis when an osmotic diuretic has been unsuccessful. Do not use furosemide in patients with aminoglycoside-induced ARF, because it can worsen renal injury.
- Administer furosemide at a dose of 2.2 mg/kg IV initially. If urine production increases, continue every 8 hours.
- If urine production does not increase within 30 to 60 minutes, administer a dose of 4.4 mg/kg IV. If there still is no response, administer furosemide 6.6 mg/kg IV. If the third attempt is unsuccessful, additional furosemide treatment is unlikely to be effective.

Dopamine

- Dopamine often is used to stimulate urine production when patients do not respond to other treatment. Infusion of low doses of dopamine causes dilation of renal vasculature and increased urine production.
- Dilute dopamine in 0.9% saline or 5% dextrose and infuse at a rate of 1 to 3 µg/kg/min using an infusion pump or pediatric infusion set.
- Ideally, a separate IV line should be used so that changes in rate of dopamine infusion can be made without interfering with administration of other IV fluids. However, patients with severe oliguria may need to receive dopamine mixed in a small volume of fluids to avoid overhydration.
- Monitor patients during infusion of dopamine, preferably by continuous electrocardiography, to detect tachycardia or cardiac arrhythmias, which indicate the need to slow the rate of infusion.
- If urine production increases, continue dopamine for 12 to 24 hours or until urine flow can be maintained with IV fluids.
- Continued infusion of dopamine after 6 hours is likely to be ineffective if urine production does not increase.

Furosemide and Dopamine Combination

- There is some evidence to suggest that concomitant treatment with furosemide and dopamine may be more effective than either drug used alone.
- We prefer to use both drugs simultaneously by administering dopamine as directed in the previous section and also giving furosemide at a dose of 1 mg/kg IV every hour.
- Treatment beyond 6 hours is unlikely to be beneficial.

Dialysis

Hemodialysis is the treatment of choice for ethylene glycol and salicylate toxicosis, life-threatening electrolyte disturbances, severe fluid overload, and cases in which oliguria persists despite measures to stimulate urine production. This requires an intensive care facility equipped for this procedure. For financial reasons, limited availability of hemodialysis, intense labor and complications of peritoneal dialysis, and guarded to grave prognosis for recovery in many cases of ARF, most owners elect euthanasia when dialysis is the only treatment that can maintain their pet.

Managing Electrolyte Disturbances

Hyperkalemia

Hyperkalemia is a potentially life-threatening electrolyte abnormality that occurs in patients with oliguria.

- Serum potassium concentrations between 6 and 8 mEq/L usually do not cause clinically important problems and are best treated by IV administration of 0.9% sodium chloride.
- If serum potassium concentration exceeds 8 mEq/L or if signs of cardiotoxicosis occur (bradycardia, prolonged P-R intervals, absent P waves, tall and peaked T waves, widened QRS complexes, ventricular arrhythmias), other treatment is indicated in addition to IV fluids. Administer sodium bicarbonate (0.5–1.0 mEq/kg) IV over 15 to 20 minutes. Sodium bicarbonate may be preferred in patients with ARF because they often have concomitant acidemia. Sodium bicarbonate causes potassium to move into cells, which lowers serum potassium concentration for several hours.
- Alternatively, administer 0.5 U/kg of regular insulin IV with 1 to 1.5 grams of dextrose for every unit of insulin. This also causes potassium to shift inside cells.
- If life-threatening cardiac arrhythmias exist, administer 10% calcium gluconate (0.5–1.0 ml/kg IV over 10 to 15 minutes) to effect. During treatment, monitor the electrocardiogram (ECG) for shortening of the QT interval and progressive bradycardia, and slow or discontinue calcium infusion if these occur. Calcium gluconate directly antagonizes effects of hyperkalemia on the myocardium for 10 to 15 minutes. It does not affect serum potassium; therefore, concurrent treatment with either bicarbonate or dextrose and insulin is indicated to lower serum potassium.

Hypokalemia

- Hypokalemia may occur during the recovery phase of ARF due to excessive urinary losses and decreased oral intake. Therefore, monitor serum potassium every 1 to 2 days to detect hypokalemia.

- Add potassium chloride to IV fluids as needed to correct hypokalemia (see Chapter 5 for specific guidelines).

Hyperphosphatemia

Hyperphosphatemia occurs secondary to decreased renal elimination of phosphorus in patients with ARF.

- IV administration of fluids helps lower serum phosphorus.
- Additional treatment to control hyperphosphatemia (i.e., feeding a phosphate-restricted diet and administering phosphate binders) can be instituted when the patient tolerates oral feeding.

Correction of Acid-Base Abnormalities

- Metabolic acidosis is the most common and clinically important acid-base disturbance that occurs in patients with ARF. Acidosis occurs because of the kidneys' inability to reabsorb bicarbonate and excrete hydrogen ions.
- Acidosis predisposes to cardiac arrhythmias, decreased cardiac output, decreased renal perfusion, hyperkalemia, and obtundation.
- Patients with blood pH values above 7.2 or a total CO_2 >12 mEq/L usually respond to IV administration of fluids alone.
- If blood pH is less than 7.2 or the total CO_2 is <12 mEq/L, administer sodium bicarbonate to help normalize acid-base status.
  - Calculate the initial bicarbonate dose (mEq) using the following formula: (base deficit) × (body weight in kg) × 0.3. If base deficit is unknown, substitute the value for (20 – total CO_2).
  - Administer one-quarter to one-half of the deficit over the first 1 to 2 hours, then add the remaining volume of bicarbonate to calcium-free IV fluids and administer over the next 12 hours.
  - Reassess blood gas data or total CO_2 to determine the need for additional bicarbonate therapy. If these values are not available, add bicarbonate at a dosage of 1 to 5 mEq/kg, depending on severity of initial acidemia, to IV calcium-free fluids to be administered over the next 12 to 24 hours.
- Refer to Chapter 5 for a detailed discussion of managing acid-base abnormalities.

Control Vomiting

Vomiting is a common complication of ARF due to effects of uremic toxins on the chemoreceptor trigger zone and emetic center and due to gastrointestinal ulceration, which results from decreased renal elimination of gastrin and subsequent gastric hyperacidity.

- Administer an H_2-receptor antagonist to help control uremic gastritis.
  - Administer cimetidine (Tagamet, SmithKline Beecham) IV initially at a dose of 10 mg/kg q12h. As uremia resolves, decrease the dose to 5 mg/kg IV q12h.
  - Alternatively, administer ranitidine (Zantac, Roche) at a dose of 2 mg/kg IV q8h in dogs and 2.5 mg/kg IV q12h in cats.
  - If vomiting persists, administer a centrally acting antiemetic.
  - Metoclopramide (Reglan, Robins) may be administered at a dose of 0.2 to 0.4 mg/kg IV q6–8h. Because it is a dopamine antagonist, do not use it concomitantly with dopamine.
  - Alternatively, administer chlorpromazine (Thorazine) at a dose of 0.25 to 0.5 mg/kg IV or IM q6–8h. Because chlorpromazine may cause hypotension and decrease renal perfusion, avoid using it in patients that are dehydrated. Do not combine chlorpromazine and metoclopramide as this can potentiate neurologic side effects.
  - Refer to Chapter 67 for other recommendations for treating gastritis and the control of vomiting.

Monitoring Patients

The objectives of monitoring patients are to evaluate response to treatment, avoid potential complications, and help establish a prognosis. Patients generally are monitored more frequently during initial treatment or when life-threatening complications such as severe metabolic acidosis, oliguria, or hyperkalemia exist and less often when there is improvement or stabilization of the patient's condition. Parameters that are evaluated include hydration status, body weight, urine volume, and laboratory values.

- Record body weight and hydration status 2 to 4 times daily. Clinical estimation of hydration status and fluid losses can be inaccurate. Once a patient is rehydrated, rapid changes in body weight generally reflect net fluid losses or gains and signal the need for a change in the rate of fluid administration.
- Measure hematocrit and total protein values at the end of rehydration and then at minimum daily to help evaluate hydration status.
- Measure serum chemistries and electrolytes at the end of rehydration and then at minimum daily for the first 4 to 7 days.
- Monitor blood gas values or total CO_2 and serum potassium several times daily if severe metabolic acidosis or hyperkalemia exists.
- To prevent overhydration, monitor changes in central venous pressure in patients with cardiac disease or persistent oliguria. In addition, a system of measuring "ins" and "outs" helps guide fluid therapy in these patients (see Chapter 5).
- Place an indwelling urinary catheter in patients that appear to have anuria or oliguria after rehydration. This helps determine the need for measures to stimulate urine production and guides fluid therapy to prevent overhydration.

Treatment of Underlying Causes of ARF

Leptospirosis

- Administer penicillin (20,000–40,000 U/kg IV q12h) or ampicillin (22 mg/kg IV q8h) initially. When vomiting resolves, administer doxycycline (5 mg/kg PO q12h) for 2 weeks to eliminate the carrier state of leptospirosis.

Ethylene Glycol (Antifreeze) Toxicosis

If a patient is presented within 6 hours of ingesting ethylene glycol, induce vomiting, lavage the stomach, and administer activated charcoal. If it has been less than 24 hours since ingestion, administer agents to slow conversion of ethylene glycol to its toxic metabolites. Unfortunately, most patients with ethylene glycol intoxication are presented after ARF develops and the following treatments are not effective. Remember, not all antifreeze products are ethylene glycol. Products containing propylene glycol are available and are less toxic. If in doubt as to which was consumed, treat for ethylene glycol exposure.

Ethanol

- Ethanol (20%) acts as a substrate for alcohol dehydrogenase and decreases metabolism of ethylene glycol. It remains the preferred treatment for ethylene glycol intoxication in cats.
- In dogs, administer 5.5 ml/kg IV q4h for five treatments, then q6h for four additional treatments.
- In cats, administer 5 ml/kg IV q6h for five treatments, then q8h for four additional treatments.

4-Methylpyrazole

- 4-Methylpyrazole (5%) inhibits alcohol dehydrogenase and does not cause central nervous system depression like ethanol. It is the preferred treatment for ethylene glycol intoxication in dogs.
- Administer 0.4 ml/kg IV initially, then 0.3 ml/kg IV at 12 and 24 hours after ingestion, and then a final dose of 0.1 ml/kg IV at 36 hours after ingestion.
- 4-Methylpyrazole is not effective for treatment of ethylene glycol intoxication in cats at dosages administered to dogs and therefore is not generally recommended. There is some evidence to suggest that when 4-methylpyrazole is administered 3 hours after ingestion of ethylene glycol it is safe and effective at preventing renal failure in cats. The dosing schedule is 125 mg/kg IV initially followed by 31.25 mg/kg at 12, 24, and 36 hours after ingestion.

Prevention

Because of expensive treatment and a guarded prognosis, make every effort to prevent ARF whenever possible.

- Warn owners about the danger of ethylene glycol if their pet lives outdoors.
- Do not use nephrotoxic drugs unless absolutely necessary (use enrofloxacin instead of aminoglycosides for severe gram-negative infections). If a nephrotoxic drug must be used, make sure the patient is well hydrated prior to treatment. Monitor serum drug concentrations, biochemical parameters, and urinalyses.
- Older patients often have chronic renal disease and are very susceptible to acute renal injury associated with dehydration or hypotension. Avoid stress and make sure the pet has access to fresh water at all times. Tell owners to avoid administering over-the-counter pain medications such as aspirin or ibuprofen. If general anesthesia is planned, administer IV fluids before and during anesthesia to maintain renal perfusion.

CHRONIC RENAL FAILURE

CRF is a syndrome characterized by inability of the kidneys to perform excretory, regulatory, and synthetic functions due to a loss of nephrons over a period of months to years. Loss of excretory function causes retention of urea nitrogen, creatinine, phosphorus, and other substances that are eliminated by glomerular filtration. Decreased ability of the kidneys to regulate fluid, electrolyte, and acid-base balance causes polyuria and/or polydipsia, hypokalemia, and metabolic acidosis, as well as other abnormalities. Failure of the kidneys to synthesize erythropoietin and calcitriol causes nonregenerative anemia and renal secondary hyperparathyroidism, respectively.

Etiology

Some breeds are predisposed to development of CRF due to congenital or familial renal disease; however, most dogs and cats with CRF are older and have acquired disease. Although many disorders may predispose to development of CRF in middle-aged to older patients, an underlying cause often is not identified. Regardless of the inciting cause, CRF tends to be a progressive and irreversible disorder.

- *Congenital and familial diseases* that cause CRF in dogs and cats are listed in Table 77-4.
- *Infectious and inflammatory disorders* may cause glomerular or tubulointerstitial damage that progress to CRF. Immune-mediated glomerular injury (e.g., glomerulonephritis) secondary to infectious or inflammatory diseases often progresses to cause CRF, especially in dogs. Tubulointerstitial inflammation associated with pyelonephritis, leptospirosis, or feline infectious peritonitis may progress to cause CRF.
- *Amyloidosis* may cause CRF secondary to deposition of amyloid in glomeruli or in the renal medulla.

Table 77-4. BREEDS WITH CONGENITAL OR FAMILIAL RENAL DISEASE

Breed	Renal Disease
Abyssinian cat	Renal amyloidosis
Basenji	Renal tubular dysfunction
Beagle	Unilateral renal agenesis, renal amyloidosis
Bernese mountain dog	Glomerulonephritis
Cairn terrier	Polycystic renal disease
Cocker spaniel	Hereditary nephritis
Doberman pinscher	Glomerulonephritis
Domestic longhaired and Persian cats	Idiopathic polycystic kidney disease
English foxhound	Renal amyloidosis
Lhasa apso	Renal dysplasia
Norwegian elkhound	Tubulointerstitial fibrosis
Pembroke Welsh corgi	Telangiectasia (idiopathic renal hematuria)
Samoyed	X-linked nephritis
Shih Tzu	Renal dysplasia
Soft-coated wheaten terrier	Renal dysplasia, protein-losing glomerulopathy

- *Neoplasia* of the kidneys infrequently causes CRF. Renal lymphoma in cats is the most common neoplastic cause of CRF.
- *Nephrotoxic substances* (drugs, toxins, hypercalcemia) usually cause ARF; however, CRF may persist after recovery from the acute insult.
- *Hyperthyroidism* in cats is often associated with CRF. Although the relationship is not yet fully understood, renal arteriolar hypertension is thought to play a role (see Chapter 31).
- *Idiopathic* glomerular or tubulointerstitial disease is the most common cause of CRF in dogs and cats. Despite thorough diagnostic evaluation, most patients do not have evidence of an inciting cause of renal injury.

Clinical Signs

Clinical signs in patients with CRF depend on the degree of renal insufficiency and the underlying cause.

- Lethargy, depression, and weight loss are frequent nonspecific signs.
- Gastrointestinal signs such as inappetence, vomiting, and diarrhea often occur in uremic patients; oral ulcerations also may be observed. Constipation is common in cats with CRF.
- Weakness and exercise intolerance may result from anemia.
- Polyuria and polydipsia often are reported by owners and may be the first abnormality noted.

Diagnosis

▼ ***Key Point*** Try to identify any concomitant disorders that may contribute to progression of CRF; these include pyelonephritis, hypertension, hyperthyroidism, hypercalcemia, renal neoplasia, and urinary obstruction.

History

- Ask owners about potential for exposure to nephrotoxic substances, including any over-the-counter medications.
- To help distinguish between CRF and ARF, ask how long clinical signs have been present. Most patients with CRF have changes in appetite, body weight, urine volume, and/or water consumption that have been present for several weeks to months, whereas clinical signs in patients with ARF have been present for <1 week.

Physical Examination

- Assess hydration status by evaluating skin turgor and moistness of mucous membranes.
- Examine the oral cavity for ulcerations that occur with uremia and pale mucous membranes that may be associated with anemia.
- Perform ophthalmic evaluation to detect changes consistent with hypertension, including retinal hemorrhages or detachments, or tortuous vessels.
- During abdominal palpation, try to evaluate renal size and consistency. Both kidneys usually can be palpated in cats, whereas in dogs only the left kidney can reliably be identified on physical examination. Small, firm, and/or "lumpy-bumpy" kidneys are typical of CRF, although kidneys in patients with CRF may be of normal size and consistency. Enlarged kidneys most often occur with ARF, especially in dogs. In cats, however, renomegaly may result from disorders that cause CRF such as hydronephrosis, feline infectious peritonitis, renal lymphoma, and polycystic kidney disease.
- Ascites, and less frequently peripheral edema, may be observed in patients with hypoalbuminemia due to severe glomerular disease.
- In cats, palpate the neck region for thyroid nodules.
- In dogs, perform a rectal examination to identify any potential causes of postrenal azotemia such as urinary bladder, urethral, or prostatic masses.

Laboratory Evaluation

- Hemogram often reveals nonregenerative anemia in patients with CRF. Infectious, inflammatory, or neoplastic diseases may cause hyperproteinemia.
- Serum chemistry abnormalities include azotemia and hyperphosphatemia.

▼ ***Key Point*** Approximately 75% of nephrons must be nonfunctional before azotemia occurs. This means that BUN and serum creatinine are insensitive indicators of renal function, and patients may have severe renal disease in the absence of azotemia.

- Hypokalemia often occurs in cats with CRF.
- Urinalysis shows decreased renal concentrating ability and isosthenuria (urine specific gravity of 1.008–1.013) in most patients. Some cats with CRF retain concentrating ability with values for urine specific gravity up to 1.035.

Urine Culture

- Culture urine obtained by cystocentesis to rule out UTI in all patients with CRF.

Leptospira Titers

- In addition to being a cause of ARF, leptospirosis can cause clinical signs related to decreased renal function for several weeks. If exposure is possible, measure serum microscopic agglutination titers (see Chapter 19).

Radiography

- Survey abdominal radiographs are helpful for evaluating renal size and identifying other abnormalities of the urinary tract such as radiopaque uroliths.
- Excretory urography may be indicated for evaluation of suspected pyelonephritis, hydronephrosis, and obstructive uropathy; however, reduced renal excretory function often limits usefulness of this technique (see Chapter 4).

Ultrasonography

- Ultrasonography is the preferred technique for identifying abnormalities in renal size and architecture.
- This can also be useful for diagnosing obstructive nephropathies, nephrolithiasis, neoplasia, polycystic kidneys, and renal dysplasia (see Chapter 4).

Renal Biopsy

- Consider collection of renal tissue for histologic evaluation when results could alter treatment or help give the owner a more accurate prognosis (biopsy techniques are described in Chapter 78).
- Disorders in which a renal biopsy may provide useful information include glomerular diseases (glomerulonephritis, amyloidosis) and renal neoplasia.

Systemic Blood Pressure

- Measure systemic blood pressure because 50% to 90% of dogs and cats with CRF are hypertensive.
- Indirect measurement of blood pressure using Doppler ultrasonic or oscillometric (e.g., Dinamap) techniques is most practical and convenient in the clinical setting.
- Collect three consecutive measurements of systolic, mean, and diastolic pressures and use the mean of these values.
- Hypertension is defined as systolic pressure greater than 180 mm Hg, mean pressure >150 mm Hg, or diastolic pressure > 100 to 120 mm Hg. Hypertension is also discussed in Chapter 153.

Treatment

Renal Transplantation

- Renal transplantation has become a legitimate option for treatment of cats with CRF. Postoperative survival is between 70% and 85% with some cats living many years. Cats must be free of concurrent diseases prior to consideration. Consider transplantation when medical management is failing and clinical signs are becoming apparent but are not advanced. Transplantation requires lifelong care of the recipient and the donor, frequent administration of medications, lifelong immunosuppression for the recipient, and significant time and financial commitment by the owner. Cost typically exceeds $5000 for the initial hospitalization and surgery followed by lifelong drug and monitoring costs. Numerous private and university clinics offer this service.
- Canine renal transplantation is not widely offered due to its relatively poor success compared with feline transplantation. On average, dogs do not live longer than a year following transplantation. Costs far exceed those of cats due to the number of immunosuppressants dogs require and their larger size.
- Because CRF is an irreversible disorder that usually has no identifiable underlying cause, and transplantation is rarely chosen or appropriate, the goals of treatment are to make the patient more comfortable and slow the progression of disease, if possible. This is accomplished by the following measures:
  - Control the clinical signs of uremia.
  - Maintain fluid, electrolyte, and acid-base balance.
  - Provide adequate nutrition.
  - Minimize the progression of renal failure by treating concomitant disorders such as UTI and hypertension.

Dietary Management

Dietary management of patients with CRF consists of feeding a diet that is moderately restricted in the amount of protein, phosphorus, and sodium while providing adequate amounts of non-protein calories, vitamins, and minerals. This approach has been shown to prolong survival and the time before uremic crisis.

Protein Restriction

- The primary beneficial effect of feeding a restricted amount of high-quality protein (which contains only essential amino acids) is to control clinical signs of uremia by reducing the amount of nitrogenous wastes that result from protein catabolism.

- Currently recommended protein levels for dogs (2.0–2.2 g/kg/day) and cats (3.3–3.5 g/kg/day) may be achieved by feeding commercial or homemade diets.
- Adjust protein intake to prevent malnutrition as evidenced by hypoalbuminemia, worsening anemia, or weight loss.
- Severely restricted protein diets (1.25 g/kg/day) that are used to treat patients with urolithiasis should be reserved for patients that continue to have signs of uremia after moderate protein restriction and even then should be used carefully because of potential for protein malnutrition.

Phosphorus Restriction

- Feeding a phosphate-restricted diet also may lessen signs of uremia and could prevent progression of CRF by blunting renal secondary hyperparathyroidism and decreasing renal mineralization. Most protein-restricted diets are also phosphate restricted.

Sodium Restriction

- Restriction of dietary sodium may help control hypertension in patients with CRF.
- Gradually restrict sodium intake by changing to the new diet over a 2- to 4-week period to allow the kidneys time to adapt to changes in sodium intake. A sudden decrease in dietary sodium could precipitate hypovolemia, which could worsen renal function.
- Avoid severely restricted sodium diets such as those used to treat patients with congestive heart failure because they may cause volume depletion and renal hypoperfusion.

Calcitriol Supplementation

- Calcitriol concentrations can become deficient in patients with CRF due to failure of renal metabolism. Calcitriol supplementation has been suggested for CRF patients because of its purported suppressive effects on parathyroid hormone secretion. Parathyroid hormone is considered by some to be a uremic toxin, and renal secondary hyperparathyroidism can certainly cause loss of bone density. In uncontrolled studies of veterinary patients with CRF, calcitriol has been associated with decreased uremic signs. Currently, controlled studies are under way to evaluate the efficacy of calcitriol in CRF patients. Until these results are available, we do not recommend routine use of calcitriol in dogs and cats with CRF.

Managing Fluid/Electrolyte/Acid-Base Disorders

Fluid Balance

Because of tubular dysfunction, patients with CRF cannot adequately produce concentrated urine and have primary polyuria. Fluid balance is maintained by increased water consumption.

▼ ***Key Point*** Be sure that patients with CRF have unlimited access to fresh water at all times.

- If water intake is not adequate to maintain hydration, as is often the case in cats, owners can administer supplemental fluids subcutaneously or via a gastrostomy tube at home.

Potassium Balance

Hypokalemia is the most common abnormality of serum potassium in patients with CRF; it is more common in cats than in dogs. Hypokalemia most likely results from decreased oral intake, as well as excessive urinary loss of potassium.

- If the patient is not vomiting, oral administration of potassium is preferred.
- Administer potassium gluconate (Tumil-K) at a dose of 2 to 6 mEq/cat once or twice daily, depending on severity of hypokalemia and the cat's size.
- Initially, monitor serum potassium weekly to determine the appropriate maintenance dose; 2 to 4 mEq/cat once daily often is adequate.
- If parenteral potassium is necessary due to vomiting or severe hypokalemia, administer potassium chloride with IV fluids (see Chapter 5 for details).

Metabolic Acidosis

Metabolic acidosis is the most common acid-base abnormality in patients with CRF. Treatment generally is indicated if blood pH is <7.2 or total CO_2 is <12 mEq/L.

- Administer sodium bicarbonate at a dose of 8 to 12 mg/kg PO q8–12h (1 teaspoon of baking soda = 2000 mg sodium bicarbonate); start at the lower dose and give several times daily to avoid fluctuations in blood pH.
- Alternatively, administer potassium citrate at a dose of 0.3 to 0.5 mEq of potassium per kilogram PO q12h. One advantage of potassium citrate is that it can be used to treat both hypokalemia and metabolic acidosis, which may be present together.
- Monitor total CO_2 in 10 to 14 days and try to maintain values within the normal range (e.g., 18–24 mEq/L).
- Avoid administering urinary acidifiers or feeding diets that are intended to acidify urine because they may worsen metabolic acidosis.

Controlling Hyperphosphatemia

Dietary phosphate restriction usually is successful for controlling hyperphosphatemia initially; however, as renal failure progresses, additional measures are necessary. Administer phosphate binders with a phosphate-restricted diet to provide additional control.

- Aluminum hydroxide, calcium carbonate, and calcium acetate are effective phosphate binders.

- Administer aluminum hydroxide at an initial dose of 100 mg/kg/day.
- Alternatively, administer calcium carbonate (100 mg/kg/day) or calcium acetate (60 mg/kg/day) if hypercalcemia does not exist.
- Phosphate binders are most effective when the daily dose is divided and administered 3 to 4 times daily with meals.
- Monitor serum phosphorus and calcium concentrations every 2 to 4 weeks initially and adjust the dose of phosphate binder as needed to maintain normophosphatemia.
- Side effects of phosphate binders include constipation with aluminum hydroxide and diarrhea or hypercalcemia with calcium-containing products.

Treatment of Anemia

Treatment of anemia may be indicated when hematocrit is <25% in cats and <30% in dogs or when clinical signs such as fatigue, depression, weakness, or respiratory distress occur. It is likely that anemia is responsible for many of the signs of CRF that have been attributed to uremia. This is supported by the observation that correction of anemia is associated with substantial clinical improvement and quality of life despite continued or worsening azotemia.

Transfusion

- Administration of whole blood or packed red cells generally is reserved for patients with severe clinical signs (dyspnea, extreme lethargy) due to anemia. Because of cost, limited availability of blood products, and inconvenience of repeated transfusions, this is not an option for long-term maintenance of hematocrit in dogs and cats with CRF.

Erythropoietin

- At this time, administration of recombinant human erythropoietin (Epogen) is the most reliable method for correcting anemia due to CRF in dogs and cats. It may be cost prohibitive for some owners and has potentially significant side effects; however, its beneficial effects exceed its disadvantages for patients with severe anemia due to CRF. Because erythropoietin is a human drug and is not approved for use in veterinary patients, obtain informed consent from owners before treatment.

Treatment Protocol

- Prior to using erythropoietin, measure blood pressure and control hypertension.
- Evaluate iron status by measuring serum iron and total iron-binding capacity (TIBC) and calculating the percentage of saturation (serum iron divided by TIBC). If iron deficiency is detected (see Chapter 22), it should be corrected before administration of erythropoietin.
- Administer erythropoietin (75–100 U/kg SC 3 times weekly) until hematocrit reaches 37% to 45% in dogs and 30% to 40% in cats; this usually requires 8 to 12 weeks of treatment, depending on severity of anemia and individual patient response.
- Because of the time required to reach a normal hematocrit, it may be more cost effective to administer a transfusion, especially in larger patients, and then begin treatment with erythropoietin.
- Once hematocrit reaches the low normal range, decrease frequency of treatment with erythropoietin to twice weekly. If anemia recurs during twice weekly treatment, administer erythropoietin 3 times weekly again. Most patients can be maintained with a dose of 75 to 100 U/kg 2 or 3 times per week.
- Because of tremendous demand for iron during treatment with erythropoietin, there is great potential for developing iron deficiency. Therefore, it may be best to administer iron to all patients receiving erythropoietin. Oral ferrous sulfate has been recommended for cats (50–100 mg/cat/day) and dogs (100–300 mg/dog/day); however, iron products often are unpalatable and cause gastric irritation. One over-the-counter ferrous sulfate product (Slow Fe) appears to be less likely to cause gastric irritation and may be suitable for veterinary patients.

Monitoring

- Monitor patients carefully during treatment with erythropoietin to determine efficacy and detect side effects.
- Measure hematocrit weekly until it reaches the normal range and remains stable for 4 weeks on a maintenance dosage and then every 1 to 2 months.
- Determine iron status 1 month after beginning treatment and every 2 to 3 months thereafter. Increase iron supplementation if serum iron is <84 µl/dl or the percentage of saturation is <20%.
- Measure blood pressure once monthly during initial treatment then every 1 to 2 months thereafter. If hypertension exists, monitor blood pressure more frequently and begin treatment.

Side Effects

- In addition to seizures and exacerbation of hypertension, the most clinically important side effect of treatment is development of antibodies against erythropoietin. This is reported to occur in 25% to 30% of veterinary patients. Development of antibodies is characterized by a precipitous drop of hematocrit that is preceded by erythroid hypoplasia of bone marrow. If this occurs, discontinue erythropoietin. These patients become transfusion dependent because the antibodies also form against endogenous

erythropoietin, and hematocrit often is lower than before treatment with erythropoietin.

Controlling Hypertension

Because of the potential for serious consequences (blindness, worsening of renal failure), treat hypertension whenever it is identified in a CRF patient. The goal is to maintain normal systemic blood pressures (systolic <160 mm Hg, diastolic <90 mm Hg).

- Feed a diet that is moderately restricted in sodium; most diets formulated for patients with CRF fit this criterion.
- Hypertension in patients with CRF usually does not respond to dietary sodium restriction alone and also requires administration of antihypertensive drugs. Avoid administering drugs to control hypertension if blood pressure cannot be adequately monitored. It is best to start with a single drug at the lowest dose and gradually increase the dose; however, it is not uncommon for hypertensive dogs and cats to require multiple drugs administered simultaneously to control hypertension (see Chapter 153 for additional treatment recommendations).
- To determine efficacy of treatment, monitor blood pressure every 1 to 2 weeks until pressures stabilize within the normal range and then every 1 to 3 months indefinitely.
- *Calcium channel blockers* cause vasodilation and decreased blood pressure and are effective antihypertensive agents. Amlodipine (Norvasc) is a long-acting calcium channel blocker and seems to be the most effective antihypertensive drug in cats (0.625 mg/cat PO q24h).
- *Angiotensin-converting enzyme* (ACE) inhibitors such as enalapril or benazepril (0.25–0.5 mg/kg q12–24h) also may be used initially to control hypertension. ACE inhibitors are commonly chosen as a first line antihypertensive in dogs. They prevent formation of angiotensin II, resulting in arteriolar dilation, vasodilation, and decreased blood pressure. Because ACE inhibitors can worsen renal function, it is important to start with a low dose and gradually increase while monitoring renal function. If azotemia develops or worsens, discontinue ACE inhibitors.
- *Beta-blockers* appear to decrease blood pressure by decreasing cardiac output, inhibiting renin release, or decreasing sympathetic activity. Atenolol (0.25–1.0 mg/kg PO q8–12h) is preferred in patients with respiratory disease because it is a cardioselective beta-blocker and does not cause bronchoconstriction like propranolol (0.25–1.0 mg/kg PO q12–24h).

Monitoring Patients

Monitor patients with CRF to determine efficacy of treatment and need for adjustments in therapy. Frequency of evaluation depends on severity of metabolic complications and the patient's overall condition. Those with severe abnormalities obviously need more frequent monitoring than stable patients.

- Evaluate stable patients (those that are eating, drinking, and maintaining body weight) every 2 to 4 months.
- Perform physical examination to detect changes in body weight, hydration status, and general condition.
- Perform laboratory evaluation including CBC, serum chemistries, electrolytes, and urinalysis to determine need for adjusting treatment.

PYELONEPHRITIS

Pyelonephritis implies inflammation of the renal pelvis and kidney; however, it usually is used to describe bacterial infection of the kidneys. Altered host defense mechanisms (diabetes mellitus, hyperadrenocorticism, hydroureter, ectopic ureters, nephrolithiasis) predispose to development of pyelonephritis, although not all patients have an identifiable cause. In general, UTIs, including pyelonephritis, occur more often in dogs than cats. For additional information on UTIs, see Chapter 79.

Etiology

▼ ***Key Point*** Ascending infection from the urinary bladder is the most common route of renal infection.

Organisms that most often cause UTI in dogs and cats include *Escherichia coli, Staphylococcus, Streptococcus, Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus,* and *Enterobacter.*

Clinical Signs

- Acute pyelonephritis often is associated with lethargy, depression, dehydration, fever, and abdominal pain.
- Chronic pyelonephritis usually is subclinical or is characterized by vague signs such as weight loss, inappetence, and polyuria or polydipsia.
- Patients with pyelonephritis may have concomitant signs of lower UTI such as pollakiuria, stranguria, and dysuria.
- Discolored urine (hematuria) or malodorous urine also may be noted.

Diagnosis

Because there is no specific test that is diagnostic of pyelonephritis, a presumptive diagnosis usually is made on the basis of clinical findings and results of laboratory evaluation and diagnostic imaging.

History

- Clinical signs may be apparent from the history; however, many patients with pyelonephritis have no clinical signs.

Physical Examination

- Palpate the kidneys to detect enlargement or pain, which may occur with acute pyelonephritis.
- Physical examination usually is unremarkable in patients with chronic pyelonephritis.

Laboratory Evaluation

- *Serum chemistries* often are normal unless concomitant renal failure exists, causing azotemia and hyperphosphatemia.
- *Hemogram* changes may include leukocytosis characterized by mature neutrophilia with or without a left shift.
- *Urinalysis* may show decreased urine specific gravity, proteinuria, hematuria, pyuria, granular or smooth casts, and/or bacteriuria. Although white blood cell casts are diagnostic of renal inflammation, they often are not observed in patients with pyelonephritis.

Urine Culture

- Quantitative culture of urine collected by cystocentesis is indicated in patients with suspected pyelonephritis.
- A positive urine culture indicates UTI, but it must be interpreted with clinical findings and results of other diagnostic tests to make a presumptive diagnosis of pyelonephritis. For additional information on urine culture, see Chapter 79.
- Some patients with chronic pyelonephritis may have a negative urine culture because infection has been treated previously or resolved.

Radiography

- Results of excretory urography help support a diagnosis of pyelonephritis, but changes are neither sensitive nor specific (see Chapter 4).
- Dilation of ureters and renal pelves and blunted opacification of the collecting system may be observed in patients with pyelonephritis. Predisposing factors may also be identified (nephroliths, malformations).

Ultrasonography

- Ultrasonography is an excellent noninvasive method for evaluating patients with suspected pyelonephritis (see Chapter 4).
- Ultrasonographic findings of pyelonephritis include dilation of the renal pelvis and proximal ureter and generalized hyperechogenicity of renal cortices. Predisposing factors may also be identified (nephroliths, malformations).

Treatment

Treatment of patients with pyelonephritis includes correction of abnormal host defenses if possible and administration of appropriate antimicrobials.

- Ideally, select an antimicrobial based on results of urine culture and susceptibility.
  - Because treatment of patients with acute pyelonephritis must begin before culture results are available, select an antimicrobial such as ampicillin that is effective against many of the organisms that cause UTI and can be administered parenterally.
  - If life-threatening septicemia is suspected, administer a broad-spectrum combination such as ampicillin and enrofloxacin.
- Administer parenteral antimicrobials to patients with acute pyelonephritis until systemic signs such as fever, pain, and inappetence resolve (usually 2–3 days). Then administer oral antibiotics as for chronic pyelonephritis.
- Administer oral antimicrobials to patients with chronic pyelonephritis for a minimum of 6 to 8 weeks (Table 77-5).
- Monitor effectiveness of treatment by performing urine cultures 7 to 10 days after beginning treatment and 5 to 7 days after completing treatment.
- To detect relapsing or recurrent infections, repeat urine cultures every 4 to 8 weeks until negative findings are obtained from three consecutive cultures.

GLOMERULAR DISORDERS

Glomerular disorders are characterized by significant proteinuria that causes hypoalbuminemia. Glomerulonephritis and amyloidosis are the two most common disorders that cause glomerular disease in dogs and cats. In general, glomerular disorders are more commonly diagnosed in dogs than in cats.

Table 77-5. ANTIMICROBIAL DOSAGES FOR PYELONEPHRITIS

Drug	(mg/kg)	Frequency
Ampicillin/amoxicillin	25	q8h
Cephalexin	18	q8h
Tetracycline	18	q8h
Trimethoprim sulfa	15	q12h
Amoxicillin/clavulanic acid	16.5	q8h
Enrofloxacin	5 (dogs)	q12h
	2.5 (cats—maximum)	q12h

Etiology

- Many systemic infectious or inflammatory processes can cause production of immune complexes that adhere to glomeruli (i.e., glomerulonephritis) or that stimulate production of amyloid, which deposits in glomeruli (Table 77-6).
- Some breeds of dogs have a familial predisposition to development of glomerular disease (see Table 77-6).

Clinical Signs

- Signs that may result from hypoalbuminemia include weight loss, peripheral edema, and ascites. The combination of ascites or edema and hypoalbuminemia, proteinuria, and hypercholesterolemia is referred to as *nephrotic syndrome*. This syndrome is rare in dogs but relatively common in cats with glomerular disease.
- Inappetence, vomiting, and diarrhea may occur in patients that have developed CRF and azotemia secondary to glomerular disease.
- Some patients may have severe proteinuria and no clinical signs.

Table 77-6. CONDITIONS ASSOCIATED WITH GLOMERULONEPHRITIS IN DOGS AND CATS

	Cats	Dogs
Infectious	Feline infectious peritonitis	Heartworm disease
	Feline leukemia virus infection	Leishmaniasis
		Lyme disease
		Bacterial endocarditis
		Pyometra
		Ehrlichiosis
		Canine adenovirus-2 infection
Neoplastic	Lymphoma	Lymphocytic leukemia
	Myeloproliferative disorders	Transitional cell carcinoma
		Lymphoma
	Mast cell tumors	Bronchogenic adenocarcinoma
		Many others
Hereditary		Doberman pinscher
		Bernese mountain dog
		Beagle
		Soft-coated wheaten terrier
		Samoyed
		Bull terrier
		Standard poodle
		Golden retriever
		Cocker spaniel
Inflammatory	Systemic lupus erythematosus	Systemic lupus erythematosus
		Chronic dermatopathy
	Polyarthritis	Polyarthritis
		Immune-mediated hemolytic anemia
		Prostatitis
Endocrine		Hyperadrenocorticism
		Diabetes mellitus
Drugs		Corticosteroids
		Trimethoprim sulfadiazine

Diagnosis

▼ ***Key Point*** Look for historical, physical, and laboratory findings that might suggest the underlying cause of glomerular disease such as infectious, immune-mediated, parasitic, or neoplastic conditions.

History

- Try to determine potential for exposure to infectious diseases by asking owners about travel history, environment, and tick control. Certain infectious diseases are more common in some geographic areas and in pets that live outdoors or are housed in kennels or catteries.
- Ask owners about vaccination, heartworm preventive, and feline leukemia virus status.
- If the patient is an intact female, consider pyometra as a potential cause of glomerulonephritis and determine when the last heat cycle occurred.

Physical Examination

- Some patients with glomerular disease develop peripheral edema or ascites.
- Thin body condition, decreased muscle mass, and poor haircoat are common but nonspecific findings.
- Hypertension is common with glomerular disease. Perform a fundic examination to evaluate for tortuous vessels, hemorrhages, or detachments.
- Carefully examine patients for any signs of systemic infectious, inflammatory, or neoplastic disorders that may predispose to development of glomerular disease. These signs include the following:
  - Fever
  - Anterior uveitis or chorioretinitis
  - Dermatologic lesions such as chronic pyoderma or mucocutaneous ulcerations
  - Lymphadenopathy
  - Hepatomegaly or splenomegaly
  - Icterus
  - Abdominal pain
  - Enlarged uterus or other abdominal masses
  - Joint swelling, pain, or reluctance to walk
  - Signs consistent with hyperadrenocorticism such as thin skin, abdominal distention, and hyperpigmentation

Laboratory Evaluation

- *Hematologic abnormalities* are nonspecific and may include nonregenerative anemia, hypoproteinemia, and leukocytosis. Some infectious, inflammatory, or neoplastic disorders may be associated with thrombocytopenia. Occasionally, hyperproteinemia is observed because of increased globulins.
- *Serum chemistry abnormalities* may include hypoalbuminemia, hypercholesterolemia, and/or hyperglobu-

linemia. Azotemia and hyperphosphatemia are present in patients with CRF.

Urinalysis

▼ ***Key Point*** The hallmark of glomerular disease is the presence of significant proteinuria in the absence of hematuria, pyuria, and bacteriuria.

Urine specific gravity values are variable; most patients with glomerular disease retain the ability to concentrate urine unless CRF has developed.

Assessment of Proteinuria

- Dipstick analysis of urine protein is a semiquantitative test that is affected by urine concentration. Finding a 1+ protein in urine with a specific gravity >1.035 probably is not significant, but a 2 to 4+ proteinuria probably is significant at any urine specific gravity.
- Measurement of urine protein and creatinine for calculation of the protein-to-creatinine ratio is the most accepted test for confirming significance of proteinuria.
- In the absence of pyuria, hematuria, and bacteriuria, a urine protein-to-creatinine ratio of >1 indicates significant proteinuria.

Microalbuminuria

- Immunoassay kits are now available for determination of microalbuminuria (>1 mg/dl but <30 mg/dl) in dogs and cats. These tests detect concentrations of albumin smaller than would be considered abnormal by either the dipstick or the protein-to-creatinine ratio. Dipsticks designed to detect microalbuminuria in humans are unreliable in dogs.
- Microalbuminuria has been detected in numerous human diseases and is a predictor of sequelae and outcome for some of them. Positive tests have been found in dogs with such diseases as osteosarcoma, lymphoma, heartworm disease, hyperlipidemia, Samoyed nephropathy, and wheaten terrier nephropathy.
- The incidence of microalbuminuria increases with age in dogs. Administration of corticosteroids can induce microalbuminuria.
- Exercise and microscopic hematuria do not seem to cause microalbuminuria in dogs.
- Positive microalbuminuria has not been shown to resolve with treatment of underlying diseases. Correlation with development of progressive renal disease or with prognosis is uncertain at this time.
- At this point, microalbuminuria is probably best utilized as a monitoring and early detection tool in breeds with hereditary renal disease and in elderly patients. In these cases, microalbuminuria of increasing magnitude would seem to be an indication for evaluation of underlying causes of glomerular disease.

Ancillary Tests

▼ ***Key Point*** Because glomerular diseases may be associated with potentially treatable underlying disorders, perform diagnostic tests to help identify these conditions (Table 77-7).

- *Serologic tests* (as indicated by other clinical findings) to exclude occult heartworm disease, rickettsial diseases, feline leukemia and immunodeficiency virus infection, systemic mycotic infections, and systemic lupus erythematosus
- *Serum protein electrophoresis* to characterize hyperglobulinemia as polyclonal or monoclonal
- *Thoracic and abdominal radiographs* to detect signs of occult heartworm disease, systemic fungal infection, primary or metastatic neoplasia, and pancreatitis
- *Abdominal ultrasonography* to help identify pyometra and hepatic, splenic, or lymph node enlargement
- *Fine-needle aspiration cytology* to evaluate lymphadenopathy, splenomegaly, or hepatomegaly
- *Arthrocentesis* if there is lameness, joint swelling or pain, stiffness or reluctance to move, or no obvious cause for persistent fever

Renal Biopsy

- Perform renal biopsy if the results will influence treatment or provide additional prognostic information.

▼ ***Key Point*** The only method for distinguishing between glomerulonephritis and amyloidosis is microscopic examination of a renal biopsy.

Table 77-7. DIAGNOSTIC EVALUATIONS FOR GLOMERULONEPHRITIS

Cats	Dogs
Urine culture	Urine culture
CBC, chemistry panel	CBC, chemistry panel
FeLV/FIV ELISA	Heartworm antigen, ELISA
Thoracic/abdominal radiographs	Thoracic/abdominal radiographs
Abdominal ultrasound	Abdominal ultrasound
Heartworm Ag/Ab tests (in endemic areas)	Echocardiogram (if appropriate)
Blood pressure	Rickettsial and borrelia titers
Antinuclear antibody titer	ACTH stimulation test
	Blood pressure
	Antinuclear antibody titer
	Renal biopsy

ACTH, adrenocorticotropic hormone; Ag/Ab, antigen/antibody; CBC, complete blood count; ELISA, enzyme-linked immunosorbent assay; FeLV, feline leukemia virus; FIV, feline immunodeficiency virus.

- The distinction between amyloidosis and glomerulonephritis is important because amyloidosis has no reliable treatment and rapidly progresses to terminal renal failure. In contrast, glomerulonephritis tends to progress more slowly and may even resolve if the underlying infectious, inflammatory, or neoplastic disease can be eliminated.
- The most reliable methods for obtaining samples of renal tissue are percutaneously by ultrasound guidance or keyhole technique or at exploratory laparotomy (see Chapter 78 for discussion of renal biopsy techniques).
- Contact the laboratory to determine the appropriate medium in which to submit samples. In most cases, it is appropriate to place samples for routine histologic evaluation in formalin and samples for immunofluorescence in Michel's solution.
- Findings on routine histologic evaluation usually are sufficient to diagnose either glomerulonephritis or amyloidosis. Special stains such as Congo red may be used to help identify amyloid.
- Immunofluorescent studies are done to identify glomerular immune complexes; however, their presence is not specific for glomerulonephritis. Findings must be interpreted with results of clinical signs, laboratory tests, and routine histologic studies of the kidney.

Treatment

Management of Glomerulonephritis

Predisposing Causes

Eliminate any disorders that may predispose to additional glomerular injury.

- Treatment of some diseases (e.g., pyometra, heartworm disease, and hyperadrenocorticism) may be associated with resolution of proteinuria.
- In many cases, however, a cause for glomerular disease cannot be identified or is not amenable to treatment (e.g., feline leukemia virus infection, neoplasia, and feline infectious peritonitis).

Immunosuppressive Therapy

- In general, avoid immunosuppressive treatment (e.g., prednisone, azathioprine, and cyclophosphamide) of patients with glomerular diseases. At present, no studies have documented the efficacy of immunosuppressive agents for treatment of dogs or cats with glomerular disease, and these agents may actually worsen proteinuria and signs of renal failure.
- However, use immunosuppressive drugs if they are significantly indicated to treat an underlying disorder (e.g., systemic lupus erythematosus, leukemia, and lymphoma).

Antiplatelet Therapy

- Because of the role of platelet aggregation in the pathogenesis of glomerulonephritis, antiplatelet drugs may be helpful.
- Consider administering a low dose of aspirin (for dogs: 0.5–5 mg/kg PO q12–24h) to inhibit cyclooxygenase and impair platelet aggregation.
- Although studies to document beneficial effects of aspirin or any other antiplatelet drugs in dogs or cats with glomerulonephritis are lacking, a low dose of aspirin is unlikely to produce serious side effects. Limited evaluation of the human platelet inhibitor clopidogrel has shown some promise in inhibiting aggregation in cats.
- Use caution when administering any nonsteroidal anti-inflammatory drugs such as aspirin to patients with CRF because they can cause acute worsening of renal function.

Angiotensin-Converting Enzyme Inhibition

- Consider ACE inhibitors in dogs and cats with glomerular disease when an underlying cause cannot be found or when there is concurrent hypertension.
- Enalapril (0.5 mg/kg PO q12–24h) decreases proteinuria, slows progression of azotemia, and prolongs the life of dogs with idiopathic glomerulonephritis. Benazepril (0.5 mg/kg PO q12–24h) undergoes less renal excretion and has had beneficial effects in cats. It may be an appropriate alternative for dogs. Monitor blood pressure and serum biochemistry as ACE inhibitors can exacerbate renal failure.

Management of Amyloidosis

▼ ***Key Point*** No reliable treatment exists for patients with amyloidosis and most progress rapidly to develop terminal renal failure.

Dimethyl Sulfoxide

- Treatment with dimethyl sulfoxide (DMSO) has been associated with improvement in some dogs with amyloidosis.
- Because the drug has few serious side effects and for lack of any other effective treatment, a therapeutic trial with DMSO may be warranted.
- Dosage regimens have included 125 mg/kg twice daily and 80 mg/kg 3 times weekly; DMSO can be administered either orally or subcutaneously.

Colchicine

- The efficacy of colchicine in dogs or cats with amyloidosis is unknown. Colchicine impairs the secretion of serum amyloid A. This would suggest that if used

it is best started in cases that have not progressed to CRF.
- Consider colchicine (0.02–0.04 mg/kg PO q24h) in these cases. Side effects can include nausea, vomiting, and diarrhea.

Immunosuppressive Drugs

- Avoid administering immunosuppressive agents to patients with amyloidosis because they may potentiate renal amyloid deposition.

Dietary Management

- The ideal diet for dogs and cats with glomerular disease is unknown at this time.
- Evidence in humans with hypoalbuminemia secondary to glomerular disease suggests dietary protein restriction is associated with increases in serum albumin and may lessen proteinuria.
- Restriction of sodium intake probably is beneficial because most patients with glomerular disease are also hypertensive.
- Avoid dietary protein supplementation because this may actually increase glomerular injury and worsen proteinuria.
- Omega-3-fatty acid supplementation may be renoprotective for patients with glomerular disease and CRF.
- Currently, diets formulated for dogs or cats with CRF (such as Hill's K/D) address these points and are appropriate for patients with glomerular disease.
- Carefully monitor patients for signs of protein malnutrition (continued weight loss, worsening hypoalbuminemia and proteinuria, anemia), worsening renal function, and increased proteinuria.
- Measure BUN, serum creatinine, serum albumin, and the protein-to-creatinine ratio 2 weeks after changing diets.
- Continue dietary protein restriction if the renal function has not deteriorated, the magnitude of proteinuria is reduced or unchanged, and the serum albumin has remained stable or has increased.

Managing Complications

Renal Failure

- Renal failure is a common complication of glomerular disease (see the previous section in this chapter for recommendations on treatment of patients with CRF).

Ascites and Edema

- Ascites and peripheral edema may occur in patients with glomerular disease secondary to hypoalbuminemia and renal retention of excessive sodium and water.
- Avoid removing fluid from body cavities unless it significantly interferes with respiration. Removing fluid potentiates hypovolemia, protein loss, and formation of additional edema or ascites.
- Enforce cage rest for 2 to 3 days until ascites or edema decreases or resolves.
- Administer loop diuretics such as furosemide (2–4 mg/kg PO q8–12h for dogs; 1–2 mg/kg PO q12–24h for cats) cautiously and only if edema or ascites interferes with vital functions. Gradually taper the dose and discontinue when edema resolves.

Hypertension

- Measure blood pressure and treat patients with hypertension to avoid additional worsening of renal function (see "Controlling Hypertension" in this chapter and Chapter 153 for guidelines on treatment of hypertension).

Thromboembolism

- Thromboembolism, especially of pulmonary vessels, is a potential complication of glomerular disease. Factors that contribute to a hypercoagulable state in glomerular disease include platelet hyperaggregability and glomerular loss of antithrombin.
- Because of the guarded to grave prognosis associated with thromboembolism, consider preventive measures to minimize its occurrence.
  - Reduce magnitude of proteinuria.
  - Treat any underlying inflammatory condition.
  - Avoid indwelling IV catheters.
  - Maintain adequate hydration.
  - Avoid excessive use of diuretics.
  - Avoid treatment with corticosteroids.
- For additional information on management of patients with thromboembolic disease, see Chapter 153.

RENAL TUBULAR DISORDERS

Renal tubular disorders are caused by functional tubular defects that produce altered urine, and in some instances abnormal plasma concentrations, of some substances.

Etiology

Renal Tubular Acidosis

- Renal tubular acidosis (RTA) may be acquired or congenital and rarely is observed in small animals.
- Proximal RTA (type II) is characterized by wasting of bicarbonate. It occurs as part of the Fanconi-like syndrome in certain breeds of dogs (see the next section). Type II RTA has been associated with gentamicin-induced nephrotoxicosis in dogs.
- Distal RTA (type I) is characterized by inability of the distal tubule to secrete hydrogen ions and produce acidic urine. Type I RTA has been reported in a cat

with pyelonephritis and in another cat with hepatic lipidosis. Distal RTA can be a component of hypoadrenocorticism.

Fanconi-like Syndrome

- Fanconi-like syndrome is characterized by multiple proximal tubular dysfunctions, which cause glucosuria, proteinuria, and phosphaturia.
- It is suspected to be an inherited disorder and has been observed in basenjis, Norwegian elkhounds, Shetland sheepdogs, and schnauzers.
- Acquired Fanconi-like syndrome has been reported in dogs treated with aminoglycoside antibiotics.

Renal Glucosuria

- Primary renal glucosuria is characterized by defective proximal tubular transport of glucose. It is an inherited defect in Norwegian elkhounds but has been observed in other breeds.

Cystinuria

- Cystinuria is characterized by defective tubular transport of the amino acid cystine and other amino acids.
- Dogs with cystinuria can have carnitinuria and resultant carnitine and taurine deficiency. Consider measurement of plasma concentration of these amino acids.
- It occurs most often in dachshunds but has been observed in other breeds such as English bulldogs, Tibetan spaniels, and basset hounds.
- Cystine is sparingly soluble in urine, and animals with cystinuria are predisposed to development of cystine urolithiasis (see Chapter 79 for discussion of urolithiasis).

Nephrogenic Diabetes Insipidus

- Nephrogenic diabetes insipidus is characterized by failure of the kidneys to concentrate urine because of inability of the renal tubules to respond to normal amounts of antidiuretic hormone.
- It usually is an acquired disorder that occurs secondary to disorders (pyometra, hyperadrenocorticism, pyelonephritis, hypercalcemia) that interfere with renal tubular response to antidiuretic hormone; however, it also is a rare congenital defect in dogs.

Clinical Signs

Clinical findings vary depending on the renal tubular defect that exists.

- Signs of lower urinary tract disease such as stranguria, dysuria, and pollakiuria may occur with urolithiasis (e.g., cystinuria).
- Polyuria or polydipsia may occur with glucosuria, Fanconi-like syndrome, or nephrogenic diabetes insipidus.
- Stunted growth and weight loss may be observed in patients with glucosuria, congenital nephrogenic diabetes insipidus, and RTA.
- Vomiting often occurs due to gastric distention with water associated with extreme polydipsia in animals with congenital nephrogenic diabetes insipidus.
- Some metabolic disorders (glucosuria, cystinuria) may not be associated with clinical signs.

Diagnosis

History

- History identifies breeds at risk, as well as clinical findings that occur with metabolic disorders.

Physical Examination

- Physical examination findings often are nonspecific but may include decreased muscle mass, muscle weakness, distended urinary bladder, and palpable urocystoliths.

Laboratory Evaluation

- Hemogram results usually are normal.

Serum Chemistries

- Hypokalemia may occur in RTA and Fanconi-like syndrome.
- Hyperchloremia may be observed in RTA.
- Hypophosphatemia may develop in patients with Fanconi-like syndrome.

Urinalysis

- Normoglycemic glucosuria occurs in patients with renal glucosuria and Fanconi-like syndrome.
- Proteinuria occurs in Fanconi-like syndrome.
- Urine specific gravity shows hyposthenuria (<1.008) in patients with congenital nephrogenic diabetes insipidus and ranges from 1.001 to 1.018 in dogs with Fanconi-like syndrome.
- Cystine crystals may be observed in urine of dogs with cystinuria; these crystals are colorless and hexagonal and are most likely to form in concentrated, acidic urine.
- Urine pH values > 6 often occur in patients with RTA. In the presence of metabolic acidosis, patients with proximal RTA can produce acidic urine (pH <6), whereas patients with distal RTA cannot.

Blood Gas Evaluation

- Hyperchloremic metabolic acidosis with a normal anion gap is found in patients with RTA.

Ancillary Tests

- Infuse sodium bicarbonate to help distinguish between proximal and distal RTA. Animals with proxi-

mal RTA respond with increased urine pH and fractional excretion of bicarbonate, whereas those with distal RTA do not.
- Confirm Fanconi-like syndrome by performing renal clearance studies that show excessive urinary losses of protein, amino acids, glucose, bicarbonate, phosphate, and potassium.
- Perform a modified water deprivation test to confirm nephrogenic diabetes insipidus (see Chapter 36 for details on performing water deprivation tests).

Treatment

Renal Tubular Acidosis

- Identify and eliminate any underlying causes.
- Administer sodium bicarbonate (1–2 mEq/kg PO) to control acidemia; higher doses may be needed for patients with proximal RTA. Adjust dosage on the basis of response to treatment.
- Administer supplemental potassium if hypokalemia exists (see previous discussion in this chapter).

Fanconi-like Syndrome

- Discontinue drugs that might cause acquired disease.
- Try to maintain a plasma bicarbonate of 12 to 18 mEq/L by administering sodium bicarbonate as needed.
- Administer supplemental potassium as needed to correct hypokalemia.
- Monitor patients for development of severe acidosis, hypokalemia, or decreased renal function.
- Allow unlimited access to fresh water at all times.

Primary Renal Glucosuria

- This condition does not require any treatment.

Cystinuria

- Monitor patients for development of cystine uroliths and remove them surgically or employ medical treatment to promote dissolution (see Chapters 78 and 79). Consider supplementation with taurine and carnitine if plasma levels are low or clinical signs of deficiency are present.

Nephrogenic Diabetes Insipidus

- Treat the underlying cause if acquired diabetes insipidus exists.
- For congenital diabetes insipidus, feed a low-sodium diet and administer chlorothiazide (Diuril) at a dosage of 20 to 40 mg/kg PO q12h. This diuretic enhances proximal tubular reabsorption of sodium, chloride, and water, which decreases urine volume.

CYSTIC RENAL DISEASE

Cysts are epithelium-lined cavities that contain fluid. Renal cysts are dilated nephron segments that may be single or multiple (i.e., polycystic). Pseudocysts are accumulations of fluid that collect outside the renal parenchyma. They are not lined by epithelium and, therefore, are not true cysts.

Etiology

- *Familial* polycystic disease has been reported in Cairn terriers and longhaired cats. This disease is inherited as an autosomal dominant trait in Persian cats.
- *Acquired* cystic disease may develop in animals with any type of chronic renal disease.
- *Perinephric pseudocyst* is an uncommon condition reported mainly in cats. Pathogenesis is unknown.

Clinical Signs

- Progressive abdominal enlargement is the most common clinical sign. This generally is the only sign in cats with perinephric pseudocysts.
- Vomiting, anorexia, weight loss, and polyuria or polydipsia occur secondary to renal failure in animals with familial polycystic renal disease.
- Solitary or multiple cysts that do not enlarge are usually of little clinical significance.

Diagnosis

History

- History identifies the clinical signs of cystic renal disease, especially in breeds with familial predispositions. Question the owner about an affected dam, sire, or sibling.

Physical Examination

- Physical examination findings include abdominal enlargement and non-painful renomegaly.

Laboratory Evaluations

- *Hemogram* may show increased erythropoiesis in longhaired cats with idiopathic polycystic renal disease, possibly due to hypoxia-induced release of erythropoietin. Anemia may be present if CRF is present.
- *Serum chemistry profile* abnormalities include increased BUN and serum creatinine concentrations and hyperphosphatemia in renal failure.
- *Urinalysis*
  - Isosthenuria occurs in renal failure.
  - Bacteriuria and pyuria occur if secondary UTI is present.

Urine Culture

- Culture the urine if UTI is suspected or CRF is present.

Excretory Urography

- Excretory urography (see Chapter 4) confirms renomegaly in animals with polycystic renal disease and may show the cysts as multiple radiolucent areas in the renal parenchyma. In animals with perinephric pseudocyst, the kidney is demonstrated within the fluid-filled structure.

Ultrasonography

- Ultrasonography (see Chapter 4) is quite useful for detection and characterization of fluid-filled renal lesions. Their number, size, and anatomic relationships can be assessed.

▼ ***Key Point*** Ultrasonography is the procedure of choice for reliable diagnosis of polycystic kidneys and perinephric pseudocyst. Hepatic cysts may also be noted in cats with polycystic disease.

Aspiration

- Aspirate the cyst if necessary to confirm that it is a fluid-filled structure.

Treatment

- No specific treatment of cystic renal disease now exists. Bilateral polycystic kidneys result in CRF. A unilateral polycystic kidney can be treated by unilateral nephrectomy or partial nephrectomy (see Chapter 78) if necessary, provided that normal renal function is documented in the unaffected kidney.
- If renal failure exists, treat it medically (see CRF).
- Treatment for perinephric pseudocyst is surgical drainage and resection of the cyst wall (renal capsule). (See Chapter 78 for a general discussion of renal surgery.)

Prognosis

- The prognosis for animals with perinephric pseudocysts is good after surgical treatment.
- The prognosis for progressive bilateral polycystic kidney disease is poor. Advise the owner of the potential genetic aspects (autosomal dominant in Persian cats) of the disease.

NEPHROLITHIASIS AND URETEROLITHIASIS

Uroliths are polycrystalline concretions that are composed mainly of organic or inorganic crystalloids (90–95%) and a smaller but essential amount of organic matrix (5–10%). Uroliths form in the urinary space within the excretory pathway, and they usually are classified according to mineral composition.

▼ ***Key Point*** In dogs and cats, the majority of uroliths are found in the urinary bladder or urethra (see Chapters 79 and 81). Fewer than 10% are found in the renal pelvis.

Occasionally, nephroliths pass from the kidney and become ureteroliths.

Etiology

Urinary Tract Infection

- UTI by bacteria that hydrolyze urea (e.g., *Staphylococcus* or *Proteus*) is the most common cause of magnesium ammonium phosphate (struvite) urolithiasis in dogs. UTI also may occur secondary to urolithiasis that initially developed in the absence of infection.

Idiopathic

- Idiopathic conditions often cause urolithiasis. The pathogenic mechanisms of urolith formation in animals with calcium oxalate, sterile struvite, and silica urolithiasis are poorly understood.

Metabolic

- Metabolic disorders that cause excessive urinary excretion of sparingly soluble compounds may predispose an animal to urolithiasis.
- Inborn errors of metabolism predispose Dalmatians to urate urolithiasis, dogs with cystinuria to cystine urolithiasis, and animals with RTA to calcium phosphate urolithiasis.
- Portal vascular anomalies predispose affected dogs and cats to the development of urate urolithiasis because of hepatic dysfunction (see Chapter 71).
- Acquired metabolic disorders that predispose animals to urolithiasis include hyperparathyroidism (see Chapter 32), which may lead to the formation of calcium phosphate uroliths.

Dietary Factors

- High-magnesium alkalinizing diets promote struvite urolithiasis in cats.
- Diets containing large amounts of corn gluten or soybean hulls have been associated with formation of silica uroliths.
- Excessive dietary calcium or phosphorus intake may promote formation of calcium phosphate uroliths.

Clinical Signs

- Clinical signs associated with renal and ureteral uroliths are diverse and primarily depend upon the following:
  - Size, number, and location of the stones

  - Presence (degree and duration) or absence of obstruction to urine flow
  - Presence or absence of UTI
- Hematuria and signs of sublumbar or abdominal discomfort may be observed.
- Bilateral obstruction or unilateral obstruction with inadequate renal function in the contralateral kidney causes vomiting, anorexia, and depression, owing to postrenal azotemia/uremia.
- Urine may have a foul odor if UTI exists.
- An affected animal may have subclinical disease.

Diagnosis

History

- History identifies the breed predispositions (see Chapter 79) and clinical signs associated with nephrolithiasis and ureterolithiasis.

Physical Examination

- Physical examination abnormalities may include sublumbar or abdominal pain and/or renomegaly. Fever may be found in a patient with UTI-causing nephritis, especially with concurrent obstruction.

Laboratory Evaluations

Hemogram

- Hemogram usually is normal. Leukocytosis may be found when UTI causes pyelonephritis, especially with concurrent obstruction.

Serum Chemistries

- Increased BUN, serum creatinine, and serum phosphorus concentrations accompany renal failure, bilateral ureteral obstruction, or unilateral obstruction of a single functioning kidney.
- Hypokalemia, hyperchloremia, and metabolic acidosis may occur in cases of urolithiasis associated with RTA (see previous discussion).
- Hypercalcemia occasionally is found in animals with calcium-containing uroliths; however, most of these animals are normocalcemic.

Urinalysis

- Hematuria is a common finding.
- Suspect UTI when pyuria or bacteriuria is found.
- Urine pH tends to be alkaline with struvite uroliths and acidic with cystine uroliths. Urate and calcium oxalate uroliths may be associated with either alkaline or acidic urine.
- Examine sediment for struvite, ammonium urate, cystine, or calcium oxalate crystals. Crystalluria represents a risk factor for urolithiasis; however, do not presumptively identify the mineral content of uroliths solely on the type of crystalluria.

Urine Culture

- Urine culture is indicated in all patients with uroliths.

Radiography

- Confirm the presence, location, density, size, and number of uroliths with abdominal radiography.
- Urolith density is quite variable; however, oxalate, struvite, calcium phosphate, and silica uroliths usually are more radiodense than urate and cystine uroliths.
- Confirm the presence of nephrolithiasis and ureterolithiasis and the degree of urinary obstruction by excretory urography (see Chapter 4). Consider cystourethrography to identify concomitant lower urinary tract uroliths (see Chapter 79).

Ultrasonography

- Ultrasonography helps confirm the presence and location of uroliths, identify radiolucent uroliths, and assess the degree of obstruction.

Urolith Analysis

- *Quantitative (crystallographic) urolith analysis* is required to accurately determine mineral composition of uroliths.

▼ ***Key Point*** A tentative diagnosis of urolith composition often can be made using information from the clinical, laboratory, and radiographic findings.

- Perform *urolith culture* because in some cases bacteria can be cultured from calculi even when urine culture has failed to identify bacteria.

Treatment

The goals of treatment are to correct any predisposing factors if possible, eliminate existing calculi by surgical or medical treatment, and prevent recurrence. Refer to Chapter 4 for discussion of treatment for urolithiasis.

Non-obstructing, sterile nephroliths that do not increase in size, do not cause significant hematuria, and do not produce deterioration in renal function can be monitored without treatment. However, even for seemingly innocuous nephroliths, consider medical dissolution therapy if the mineral composition (struvite, urate, cystine) can be estimated with confidence.

Correct Underlying Causes

- When concomitant UTI exists, administer an appropriate antimicrobial drug and continue for 2 to 3 weeks after dissolution or removal of uroliths.
- Correct portosystemic shunts surgically, when possible (see Chapter 72).
- Remove parathyroid adenomas in patients with primary hyperparathyroidism (see Chapter 32).

Medical Treatment

- This is not effective for calcium oxalate, calcium phosphate, or silica uroliths. Struvite, urate, and cystine uroliths may respond partially or completely to medical calculolytic therapy (see Chapter 79 for a description of protocols).
- Monitor the patient to determine efficacy of medical dissolution therapy efforts.
- Reassess the size and location of uroliths using radiography and/or ultrasonography every 4 to 6 weeks.
- Perform urinalysis periodically (every 4–6 weeks).
- Crystalluria must be absent for medical dissolution therapy to be effective.
- Perform urine culture periodically (every 4 to 6 weeks) to verify continuing control of UTI.
- If uroliths enlarge or fail to steadily decrease in size, verify compliance with intended treatment instructions, and based on that consider other treatment options. The original assessment of urolith mineral type might be incorrect, or the urolith might be composed of more than one mineral.
- As nephroliths decrease in size, they may move into the ureter, causing partial or complete obstruction.

Surgical Treatment

- Surgical treatment is required in some situations (see Chapter 78).

▼ ***Key Point*** Promptly remove nephroliths or ureteroliths that obstruct urine flow to any substantial degree.

- If treatment of uroliths composed of calcium oxalate, calcium phosphate, or silica is required, surgical removal is indicated.
- Uroliths that fail to dissolve when treated with appropriate medical strategies may also require surgical removal.

Prevention

Prevention of recurrent urolithiasis depends upon the mineral type involved (see Chapter 79).

RENAL PARASITISM

Etiology

Dioctophyma renale is the canine kidney worm. *D. renale* infection is rare. Dogs become infected by ingesting the larvae or by ingesting a paratenic host, usually a fish, that contains encysted larvae.

Clinical Signs

- Dogs often are asymptomatic. Signs of renal failure do not occur with unilateral involvement.
- Abdominal enlargement may occur if the worm migrates into the peritoneal cavity and causes peritonitis.
- Hematuria may be observed.

Diagnosis

History

- History identifies clinical findings and potential for exposure to a paratenic host.

Physical Examination

- Physical examination findings may be normal, or abdominal enlargement may be found.

Laboratory Evaluations

- *Hemogram:* Eosinophilia, basophilia, and hyperproteinemia may be observed.
- *Serum chemistries:* Azotemia does not occur unless both kidneys are affected or unless one kidney is affected and the other kidney is impaired owing to some other cause.

Urinalysis

- The diagnosis is confirmed by observing characteristic double operculated ova in urine sediment. Renal infestation is required for a patent infection.
- Hematuria, pyuria, and proteinuria may occur secondary to urinary tract inflammation.

Abdominal Fluid Analysis

- With peritoneal involvement, findings are consistent with peritonitis (see Chapter 76).
- Look for parasitic ova in abdominal fluid.

Treatment

- No medical therapy is effective.

Surgical Treatment

- Perform a nephrectomy if severe unilateral renal infection exists and a nephrotomy if bilateral renal infection exists. (Surgical techniques for nephrectomy and nephrotomy are described in Chapter 78.)
- If peritonitis is present, perform an exploratory procedure to identify and remove all parasites.

Prevention

Do not allow dogs to ingest paratenic hosts or infected water.

RENAL NEOPLASIA

Etiology

Primary Tumors

- Renal cell carcinoma, transitional cell carcinoma, and embryonal nephroblastoma are the most common primary renal tumors in dogs. A syndrome of dermatofibrosis and renal cystadenocarcinoma occurs primarily in female German shepherds and may be a heritable trait.
- Renal cell carcinoma is the most common primary renal tumor in cats.
- Renal tumors in dogs and cats are usually malignant.

Metastatic Tumors

- Metastatic neoplasia is more common than primary renal neoplasia.
- The kidneys are often involved in patients with lymphoma, especially cats.
- Hemangiosarcomas, melanomas, mast cell tumors, and carcinomas also may metastasize to the kidneys.

Clinical Signs

- Clinical signs usually are vague and nonspecific. Lethargy, anorexia, and progressive weight loss may occur.
- Anorexia, vomiting, and polyuria or polydipsia may occur in patients that develop renal failure.
- Hematuria of renal origin may be observed.

Diagnosis

History

- History identifies the clinical signs of renal neoplasia.

Physical Examination

- Palpate the kidneys for renomegaly.
- Examine for tumors or masses in other organ locations.

Laboratory Evaluations

- *Hematology:* Polycythemia may occur with some renal tumors (e.g., carcinoma and fibrosarcoma) presumably owing to inappropriate production of erythropoietin.
- *Serum chemistries:* Azotemia and hyperphosphatemia due to renal failure may occur with bilateral renal neoplasia, especially in cats with lymphoma.
- Hematuria and proteinuria may be observed.

▼ ***Key Point*** About 50% of cats with renal lymphoma are positive for feline leukemia virus by enzyme-linked immunosorbent assay (ELISA) test.

Radiography

- Survey abdominal radiographs may reveal unilateral or bilateral renomegaly. An abdominal mass that cannot be identified as kidney sometimes is seen.
- When a renal mass is suspected, perform excretory urography to confirm renal involvement (see Chapter 4).
- Radiography of the thorax is needed to look for possible metastasis. This finding is most likely with renal cell carcinoma.

Ultrasonography

Ultrasonography of the abdomen helps confirm renal mass lesions.

Renal Biopsy

- In cats with bilateral renomegaly, cytologic examination of a fine-needle aspirate sample from a kidney often is diagnostic of lymphoma and eliminates the need for renal biopsy.
- For other neoplasms, perform a renal biopsy. Tissue for histologic evaluation is submitted to determine definitive diagnosis. Surgical biopsy may be necessary to allow direct exposure of the neoplasm.

Treatment

Chemotherapy

- Treat lymphoma with combination chemotherapy (see Chapter 27).

Surgery

- Evaluate the function of the contralateral kidney prior to nephrectomy.
- With the exception of lymphoma, surgical excision of the neoplastic kidney and its ureter is the treatment of choice (see Chapter 78). Consider adjunctive treatment (see Chapters 26 and 27).

Prognosis

The prognosis is guarded to poor for patients with malignant renal neoplasms.

RENAL AND URETERAL TRAUMA

Because of their location in the abdominal cavity, traumatic injury to the kidneys and ureters is uncommon in small animal patients. See Chapters 79 and 81 for discussion of bladder and urethral trauma.

Etiology

- *Blunt trauma* may be caused by vehicular injuries and falls from heights.
- *Penetrating trauma* may result from fight wounds, gunshot injuries, and other objects.

Clinical Signs

- In most cases, renal and ureteral trauma is mild and self-limiting.
- Rupture of the renal capsule, pelvis, or mid- to upper ureter causes extravasation of urine into the retroperitoneal space, which is associated with vague signs including abdominal pain and fever.
- Rupture of the distal ureter causes leakage of urine into the abdominal cavity. Clinical findings result from peritonitis and uremia and may include abdominal enlargement and pain.
- Macroscopic hematuria occurs frequently.
- Severe bruising to the ventral abdominal wall is often, but not always, seen with traumatically induced uroabdomen.
- Normal urination may be seen with unilateral ureteral rupture.

Diagnosis

▼ ***Key Point*** Suspect renal or ureteral trauma when there are vague signs of abdominal discomfort; macroscopic hematuria; or fractures of the caudal ribs, vertebrae, or pelvis, particularly.

History

- Question the owner about the possibility of trauma.

Physical Examination

- Observe for any external signs of trauma.
- Palpate the abdomen to detect evidence of pain and fluid accumulation.

Laboratory Evaluations

- *Hemogram* is usually normal.
- *Serum chemistry panel* may reveal azotemia if the injury is not acute and significant urine leakage has occurred.
- *Urinalysis* may show hematuria.

Abdominal Fluid Analysis

Note: Urine leakage may remain confined to the retroperitoneal space and not result in uroabdomen.

- Perform cytologic evaluation. Non-septic inflammation occurs most often with uroabdomen.
- Determine creatinine and potassium concentration in abdominal fluid for comparison with serum.
- When urine leaks into the abdominal cavity, the creatinine and potassium concentrations of the peritoneal fluid are greater than that of the serum initially.

▼ ***Key Point*** A fluid to serum ratio of >2:1 for either creatinine or potassium is highly sensitive and specific for uroabdomen.

- Urea is a small molecule; therefore, its concentration rapidly equilibrates with that of serum, making its measurement less useful for diagnosis of uroabdomen.

Radiography

Radiography provides the most useful information regarding the location of ureteral rupture.

Survey Abdominal Radiography

- Survey abdominal radiographic findings are rarely diagnostic of renal or ureteral trauma.
- Signs suggestive of trauma include displacement, asymmetry, and inability to visualize one or both kidneys.
- Urine leakage into the retroperitoneal space causes increased opacity and streaky, hazy areas in the retroperitoneum.
- Loss of abdominal contrast occurs when urine leaks into the peritoneal space.

Contrast Radiography

▼ ***Key Point*** Excretory urography is the diagnostic test of choice for patients with renal and ureteral trauma.

- Look for an accumulation of contrast material in the area of suspected leakage.
- If a kidney is not visualized, perform renal arteriography to evaluate the kidney's vascular supply.
- Perform thoracic radiography in all trauma patients to evaluate for consequences of thoracic trauma.
- Ultrasonography may be helpful to delineate the kidneys and retroperitoneal space.

Treatment

Supportive

- Stabilize the patient by administering fluids and other treatment for shock as needed (see Chapter 156).
- Observe the animal for evidence of a ruptured urinary tract. Other injuries may be self-limiting (e.g., renal contusions and hematoma).
- Provide abdominal drainage in animals with uroabdomen to stabilize them prior to surgery (see Chapter 76).

Surgery

- After stabilization and diagnostic evaluation, consider surgical treatment (see Chapter 78).
- Indications for surgery include leakage of urine into the abdomen or retroperitoneal space and crushing injury to the kidney or its vascular supply.

ECTOPIC URETER

Etiology

- Ureteral ectopia is a congenital abnormality whereby one or both ureters do not terminate in the correct location in the trigone of the urinary bladder.
- In females, ectopic ureters may terminate in the bladder neck, vagina, urethra, or uterus. In males, ectopic ureters end in the bladder neck and prostatic urethra.

Clinical Signs

- Urinary incontinence is usually observed by the owner around the time of weaning. Incontinence can be continual or intermittent.
- Animals with ureteral ectopia usually retain the ability to urinate normally. (See Chapter 83 for discussion of micturition disorders.)
- Urine may have a foul odor if a concurrent UTI exists.
- Soiling of the perineal hair and skin with urine may cause dermatitis.

Diagnosis

History

- Identify urinary incontinence in a young animal. (For a discussion of diagnostic approach and differential diagnosis for incontinence, see Chapter 83.)
- Female dogs are affected most frequently; however, male dogs and cats may also have ectopic ureters.

Physical Examination

- Verify urinary incontinence by observing a urine-soaked perineal area or after observation during hospitalization.
- Look for other congenital defects.

Laboratory Evaluations

- These are usually normal with the exception of urinalysis. Pyuria and bacteriuria often occur secondary to UTI.

Urine Culture

- Perform urine culture to rule out UTI.

Contrast Radiography

- *Excretory urography* (see Chapter 4) usually confirms the diagnosis of ureteral ectopia.
  - Dilated ureters and hydronephrosis may occur secondary to UTI.
  - Inflating the bladder with room air or CO_2 helps improve visualization of terminal ureters, and oblique films may be indicated to outline individual ureters.
- *Retrograde contrast urethrography* or *vaginourethrography* may help localize the site of ureteral termination.

Vaginoscopy and Cytoscopy

- Vaginoscopy or cytoscopy may be helpful to locate the terminal ureteral orifice and to evaluate for ureteral abnormalities.
- Surgical exploration occasionally is required to achieve a definitive diagnosis if cytoscopy is not available. Cytoscopy allows evaluation of ureteral orifice location. Intramural ectopic ureter may enter the bladder in a normal trigonal position.

Treatment

Surgical Treatment

- Surgical correction is the treatment of choice (see Chapter 78 for description of techniques).

▼ ***Key Point*** Surgical correction cures about 50% of patients with ectopic ureter; incontinence continues in approximately 50%. One-third of these animals respond to medical treatment.

Medical Treatment

- Treatment of UTI is indicated.
  - Culture urine to determine the species of infecting organism.
  - If pyelonephritis is suspected, administer an antimicrobial agent for 6 to 8 weeks.
  - Reculture urine 3 to 5 days after beginning treatment and again 5 to 7 days after discontinuing treatment.
- Adrenergic stimulants (agonistic) may reduce incontinence following surgery (see Chapter 83).

Prevention

- Counsel the owners regarding possible inheritance of ectopic ureter.
- Consider neutering the animal.

URETERAL OBSTRUCTION

Etiology

- *Neoplasia*
  - Primary ureteral tumors include leiomyosarcoma and leiomyoma.
  - Any abdominal tumor may compress a ureter, causing extramural obstruction.
  - Extension of tumors from the bladder (e.g., transitional cell carcinoma and rhabdomyosarcoma) and prostate (e.g., adenocarcinoma) may obstruct the ureters.

- *Uroliths* formed in the kidney may enter a ureter, causing obstruction (see discussion of calculi of kidney and ureter).
- *Blood clots* may lodge in the ureter secondary to renal hematuria.
- *Strictures* may be congenital or occur secondary to inflammation or surgery.

Clinical Signs

- Partial and unilateral obstruction may be subclinical. Bilateral obstruction causes signs of renal failure (see previous discussion).
- Signs may result from the underlying disease.
  - Hematuria and stranguria may occur with urinary bladder neoplasia and prostatic disease.
  - Straining to defecate may be observed with prostatic disease.
  - Ureterolithiasis may cause pain and abdominal discomfort.

Diagnosis

History

- Look for clinical signs of ureteral obstruction.
- Determine the possible history of abdominal surgery or trauma, urolithiasis, and neoplasia.

Physical Examination

- Palpate the abdomen for evidence of pain and abdominal masses.
- Perform a rectal examination to evaluate the prostate gland, pelvic urethra, and sublumbar lymph nodes.
- Palpate the urinary bladder to detect a mass.

Laboratory Evaluations

- *Hemogram* may be normal or show an inflammatory response (e.g., pyelonephritis).
- *Serum chemistry panel* is usually normal. Azotemia may occur if both kidneys are affected.
- *Urinalysis* may show hematuria or pyuria associated with inflammation, neoplasia, or urolithiasis.

Radiography

- *Survey abdominal radiographs* may demonstrate radiopaque ureteroliths or compressing masses.
- *Excretory urography* confirms the presence and location of ureteral obstruction. Dilation of the ureter proximal to the obstruction and hydronephrosis often occur.

Ultrasonography

- Noninvasively detects changes (e.g., hydronephrosis) consistent with ureteral obstruction.
- Preferred over excretory urography in patients with compromised renal function.
- Normal findings do not rule out a diagnosis of obstruction.

Treatment

The goals of treatment are to provide supportive care and to remove the underlying cause, if possible.

Medical Treatment

- If the obstruction is partial, urine is sterile, and the cause of obstruction may resolve spontaneously (e.g., blood clot), monitor the animal for a period of weeks to months.
- If partial obstruction occurs because of urolithiasis (e.g., struvite or urate), attempt dissolution of the urolith.

Surgical Treatment

- Surgery is indicated with evidence of progressive renal damage, persistent UTI, and no response to medical therapy.
- If ureteral neoplasia or stricture exists, surgical excision (nephrectomy/ureterectomy) is the treatment of choice.
- If possible, remove extramural masses that compress the ureter. Severe renal damage from chronic obstruction and/or pyelonephritis with concurrent ureteral obstruction is treated by nephrectomy/ureterectomy, provided that the contralateral kidney is functioning adequately.

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Chapter

78 Surgery of the Kidney and Ureter

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Biopsy of the kidney often gives the most reliable information regarding the presence of disease and the prognosis for improvement. When renal calculi are removed surgically, a nephrotomy is usually performed. When the renal pelvis and proximal ureter are dilated, a pyelolithotomy may be performed to remove calculi. Removal of the kidney (nephrectomy) is considered because of severe damage due to trauma, neoplasia, infection, or obstruction of the ureter. Reattachment of the ureter to the renal pelvis is extremely difficult without magnification and proper instrumentation and is infrequently attempted in veterinary practice. This disorder is more commonly treated by unilateral nephrectomy and ureterectomy. A ureterotomy may be performed to remove calculi from the lumen of the ureter. Ureteral anastomosis in small dogs and cats is a challenge for veterinarians. Magnification and microsurgical instrumentation are strongly encouraged during this procedure to improve outcome. Ureteroneocystostomy is a feasible treatment option for lesions of the middle and distal ureter and can also be used to treat some cases of ectopic ureter.

ANATOMY

Kidney

- The kidneys are normally found in the retroperitoneal space in a sublumbar location. The cranial pole of the right kidney may be in contact with the liver, and the left kidney is usually found several centimeters caudal to the liver. In dogs, the right kidney is relatively firmly attached by the renal fascia, but both kidneys are mobile in the cat.
- The renal arteries divide into dorsal and ventral branches after arising from the aorta. Each branch divides into five to seven interlobar arteries. The interlobar arteries branch into arcuate arteries at the corticomedullary junction and ultimately give rise to the radial interlobular arteries. Multiple renal arteries may occur on the left side in 13% of dogs and 10% of cats but are rare on the right side. The renal artery may give rise to the ovarian artery, and the left ovarian/testicular veins commonly drain into the renal vein. Multiple renal veins may be present in cats but are uncommon in dogs.

Ureter

- The ureter is a muscular tube that lies within the retroperitoneal space. The ureter carries urine to the bladder by coordinated peristaltic contractions and can dilate up to 17 times its resting diameter during diuresis or obstruction.
- The arterial blood supply of the ureter is longitudinal. Care must be taken not to disturb the arterial blood supply during dissection of the ureter.
- The ureter approaches the bladder at an oblique angle and passes submucosally within the bladder wall toward the neck of the bladder. A valve-like function is provided by the submucosal location of the ureters, which decreases vesicoureteral reflux of urine.

RENAL BIOPSY

Preoperative Considerations

- Platelet count and coagulation function must be normal prior to performing renal biopsy.

▼ ***Key Point*** Hemorrhage is a common complication after renal biopsy. Evaluate coagulation function before surgery. Apply pressure to the biopsy site until bleeding has stopped.

- If unilateral disease is present and a percutaneous biopsy is to be performed, identify the site of disease before performing the biopsy.

Surgical Procedure

Objectives

- Obtain a representative sample of renal tissue.
- Avoid damage to major vasculature or the renal pelvis.
- Control hemorrhage.

Equipment

- Standard surgical instruments and suture
- Vim-Silverman or Tru-Cut biopsy needle (or other biopsy needle of the surgeon's preference)
- Balfour self-retaining retractor for the celiotomy approach

Technique

Kidney biopsies can be performed through an ultrasound-guided percutaneous approach, through a "keyhole" approach, laparoscopically, or through a celiotomy. The celiotomy approach is described.

1. Place the patient in dorsal recumbency.
2. Aseptically prepare the ventral abdomen for a standard celiotomy incision.
3. Make a ventral midline approach to the abdominal cavity and extend the incision cranially to the xiphoid process to facilitate exposure of both kidneys.
4. Place a self-retaining Balfour retractor to maintain exposure of the abdominal cavity.
5. Examine and palpate the kidneys. If an isolated lesion is present, select an appropriate biopsy site.
6. Obtain single or multiple biopsy samples using a biopsy needle, or perform a nephrotomy to collect a wedge or slice of renal tissue. The technique for biopsy during nephrotomy is discussed in this chapter under Nephrotomy.
7. When a biopsy needle is used, direct the needle away from the pelvis through the cortical region to avoid damaging the pelvis and large vessels, and obtain at least two samples to be sure that a representative one has been taken. Apply pressure to the biopsy site for 5 minutes to promote hemostasis. If bleeding persists, tack the omentum onto the biopsy site with one or two sutures to act as a patch. Mattress or cruciate sutures can also be used in the renal capsule and superficial parenchyma. Tighten sutures just enough to stop bleeding, but avoid capsular tearing.

Postoperative Care and Complications

- Establish diuresis by IV administration of a balanced electrolyte solution at a rate of 90 ml/kg/24 hr for 8 to 12 hours. This helps prevent the formation of blood clots within the renal pelvis.
- Microscopic hematuria, gross hematuria, or both are often observed after renal biopsy and are usually self-limiting.
- Hemorrhage after renal biopsy can become life threatening. If this occurs during a limited approach procedure, surgically expose the kidneys via celiotomy, and place sutures in a mattress pattern through the renal capsule and superficial parenchyma to control hemorrhage. On rare occasions, uncontrollable hemorrhage necessitates nephrectomy.

NEPHROTOMY

Preoperative Considerations

- Nephrotomy is most often performed for removal of renal calculi. Investigate for other calculi within the urinary tract with excretory urography or ultrasonography before surgery.
- Remove large solitary calculi that result in extensive dilation of the renal pelvis by pyelolithotomy (described in other texts).
- Evaluate coagulation function before surgery. Abnormal coagulation may result in prolonged and possibly fatal hemorrhage after surgery. If possible, correct fluid deficits and serum electrolyte abnormalities before surgery.
- If bilateral renal calculi are present, perform nephrotomy as a staged procedure. Perform the second surgery 2 to 4 weeks after the first. Because transient decrease in renal function after nephrotomy is possible, absent or decreased function of the contralateral kidney may preclude nephrotomy. In these instances, pyelolithotomy is greatly preferred.

Surgical Procedure

Objectives

- Remove renal calculi.
- Obtain a renal biopsy or microbial culture specimen.
- Confirm patency of the ureter.

Equipment

- Standard surgical instruments and suture
- Balfour self-retaining retractor
- Catheters of appropriate diameter to pass into the ureter (3.5 Fr. or 5 Fr.)
- Vascular forceps or Rommel tourniquet

Technique

1–4. Refer to Renal Biopsy; Technique, Steps 1 to 4.

5. Examine and palpate the kidneys. Free the affected kidney of its peritoneal attachments, and identify and isolate the renal vasculature.
6. Apply a Rommel tourniquet or vascular forceps to the renal artery and vein. The time at which the vasculature is occluded is noted, and ischemia of the kidney is limited to 30 minutes or less.
7. Make a longitudinal incision through the renal capsule on the greater curvature of the kidney (Fig. 78-1*A*). Make the incision long enough to allow exposure of the renal pelvis after the renal parenchyma has been divided or incised. Sharply incise the renal parenchyma with a scalpel.
8. Remove calculi from the pelvis and diverticula of the kidney. Submit the calculi for analysis and culture.

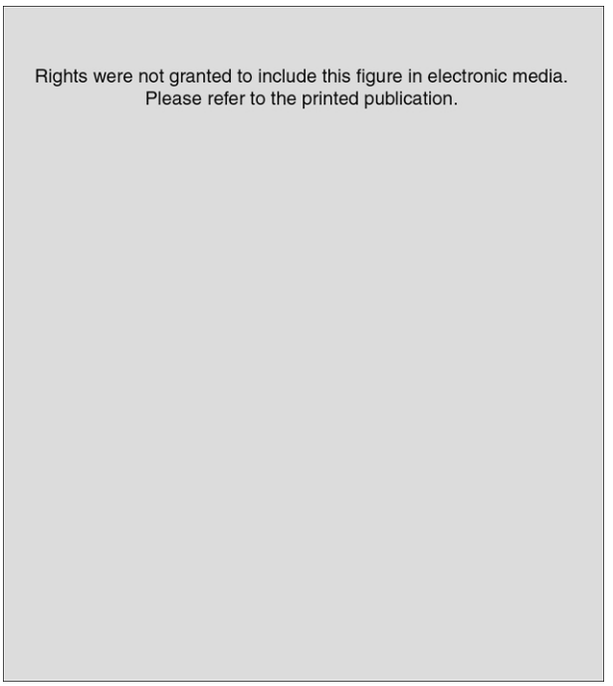

Figure 78-1. Nephrotomy. *A,* Make an incision through the renal capsule. Limit the length of the nephrotomy incision to the dimensions of the renal pelvis. *B,* Remove calculi from the renal pelvis, and pass a catheter through the ureter. *C,* Close the nephrotomy incision by placing sutures through the renal capsule and superficial parenchyma. (From Stone EA: Canine nephrotomy. Compend Contin Ed Pract Vet 9:883, 1987.)

▼ ***Key Point*** After removal of renal calculi, irrigate the renal pelvis and ensure that no calculi fragments are present in the ureter.

9. Pass a catheter through the ureter into the bladder to assess patency (Fig. 78-1*B*).
10. If a biopsy is to be done, remove a wedge or slice of parenchymal tissue 2 to 4 mm thick with a scalpel from the surface of the nephrotomy incision. Take care to avoid damaging the pelvis or diverticula.
11. Appose the exposed surfaces of the renal parenchyma, and hold them in this position with digital pressure as the tourniquet or vascular forceps is removed. Maintain pressure for 5 minutes to allow clotting to occur.
12. Close the nephrotomy incision by placing a single layer of absorbable suture in a simple continuous pattern through the renal capsule and superficial parenchyma (Fig. 78-1*C*).
13. If calculi are present in the bladder, perform a cystotomy to remove them.
14. Return the kidney to its normal position within the abdominal cavity. Close the body wall, subcutaneous tissues, and skin in a routine manner.

Postoperative Care and Complications

- Initiate and maintain diuresis by IV administration of a balanced electrolyte solution at a rate of 90 ml/kg/24 hr. Continue this for at least 12 to 24 hours. Monitor urine output to be sure that the kidneys are functioning satisfactorily.
- Hematuria is usually observed macroscopically for 1 to 3 days and microscopically for up to 1 week.
- Institute appropriate therapy to treat infection and prevent reformation of the calculi (see Chapters 77 and 79).

NEPHRECTOMY

Preoperative Considerations

▼ ***Key Point*** Function of the remaining kidney must be sufficient to support life.

- Preoperative evaluation of the function of a single kidney is often difficult. Common laboratory tests (determination of blood urea nitrogen, serum creatinine, serum potassium concentrations) are only relative indicators of renal function. Distinguish among prerenal, renal, and post-renal causes of azotemia. Concentration and excretion of a radiopaque dye (contrast agent) on excretory urography demonstrates that the vascular supply to the kidneys is intact and that the kidneys are capable of extracting the dye (contrast) from the blood and excreting it. This finding is only a relative indicator of renal function. Renal function is best evaluated by measuring the clearance of an indicator (e.g., creatinine, inulin, radioisotopes). Nuclear scintigraphy of the kidney allows determination of unilateral (differential) renal function, whereas determination of single kidney clearance of other indicators requires ureteral catheterization and collection of the urine from that kidney. See Chapter 77 for additional information on renal function testing. In general practice, excretory urography and standard clinical pathology testing are routinely done and usually provide adequate information.
- If possible, correct metabolic and hydration imbalances before performing surgery.

▼ ***Key Point*** If the kidney is functional, consider options for salvaging the kidney prior to performing a nephrectomy.

Surgical Procedure

- Indications for nephrectomy are listed in the introduction to this chapter.

Objectives

- Remove the diseased kidney and associated ureter.
- Control hemorrhage.

Equipment

- Standard surgical instruments and suture
- Balfour retractor
- Vascular forceps (optional)

Technique

1–4. Refer to Renal Biopsy; Technique, Steps 1 to 4.

5. Examine and palpate the kidneys. Obtain biopsy samples of the kidney to be preserved to be sure that it is free of disease.
6. Dissect the diseased kidney free of its attachments. Apply a vascular forceps or Rommel tourniquet to the renal vessels or ligate these vessels before dissection to minimize hemorrhage.
7. Ligate the renal vasculature with non-absorbable, monofilament (e.g., polypropylene) suture. Doubly ligate the renal vessels.
8. Ligate the ureter near the bladder with absorbable suture material, and remove the entire ureter. Leaving a segment of ureter may promote subsequent urinary tract infection by urine retention within the ureteral remnant.
9. Examine the renal bed for hemorrhage before closure of the abdominal wall.
10. Close the abdominal wall, subcutaneous tissues, and skin in a routine manner.
11. Submit the kidney and ureter for histopathology and culture if indicated.

Postoperative Care and Complications

- If the function of the remaining kidney is in doubt, initiate and maintain diuresis by IV administration of a balanced electrolyte solution at a rate of 90 ml/kg/24 hr until renal function and urine output appear satisfactory. (See Chapter 77 for more information on diuresis.)
- Observe the patient for 24 hours for hemorrhage due to displacement of ligatures.
- Warn the owner that continued renal disease in the patient may result in irreversible injury to the remaining kidney.

URETEROTOMY AND URETERAL ANASTOMOSIS

Preoperative Considerations

- Ureterotomy is most often performed for removal of calculi that have lodged within the ureter and cannot be dislodged by flushing and/or catheterization. Prolonged obstruction of the ureter by calculi results in necrosis of the ureteral wall and leakage of urine. Lesions of the distal ureter are best treated by ureteroneocystostomy.
- Ureteral obstruction or disruption most often is diagnosed by excretory urography, ultrasound evaluation, or contrast-enhanced computed tomography scan.
- When ureteral calculi are diagnosed, carefully examine the kidneys and bladder for additional calculi.
- Warn the owner of the potential for stricture formation after ureteral surgery.

Surgical Procedure

Objectives

- Relieve ureteral obstruction.
- Ensure patency and integrity of the ureter.

Equipment

- Standard surgical instruments and suture
- Balfour retractor
- Magnification loupes and microsurgical instrumentation (highly desirable); operating microscope (optional)
- Small (6-0 to 8-0) monofilament absorbable suture (polydioxanone [PDS], polyglyconate [Maxon], or poliglecaprone 25 [Monocryl])
- Catheters of appropriate size (3.5 or 5 Fr.)

Technique

1–4. Refer to Renal Biopsy; Technique, Steps 1 to 4. The incision is extended caudally to a few centimeters cranial to the pubis.

5. Examine and palpate the kidneys, ureters, and bladder.
6. Identify the site of the ureterotomy and make a longitudinal incision over the area of obstruction. Remove calculi, and pass a catheter through the ureterotomy site to the kidney and to the bladder to ensure patency of the ureter. In extremely small patients, use a large suture (1 or 0 polypropylene or nylon) instead of a catheter. Close the ureterotomy incision transversely with small (6-0 to 8-0) absorbable suture in an interrupted or continuous pattern. The transverse configuration of the closure increases the ureteral diameter at the site of the ureterotomy. This maneuver is achieved by initially opposing the midpoint of the proximal and distal ends of the ureterotomy incision with a single suture. To prevent misplacement of suture into the far wall of the ureter, close over a temporary stent.
7. If necessary, resect the devitalized portion of the ureter and identify the lumen of the proximal and distal remnants of the ureter. Make a linear incision 3 to 5 mm in length in the ends of the ureter to increase the circumference of the anastomosis. Perform the anastomosis with small, absorbable suture placed in an interrupted or a continuous pattern.

8. Pass a catheter through the urethra, bladder, and ureter to divert the flow of urine past the ureterotomy or anastomotic site for 10 to 14 days if leakage is considered a possibility. The placement of a catheter (stent) following surgery is controversial, and some believe this practice may predispose the patient to stricture formation in the ureter.
9. Close the abdominal wall, subcutaneous tissue, and skin in a routine manner.

Postoperative Care and Complications

- Stricture formation is common after ureteral surgery, particularly in cats and small dogs. Reevaluate the patient 3 to 4 weeks after surgery by excretory urography. If ureteral obstruction is observed, consider resecting the affected area of the ureter and performing an anastomosis or implanting the proximal portion of the ureter into the bladder (ureteroneocystostomy).

URETERONEOCYSTOSTOMY (URETERAL REIMPLANTATION)

Preoperative Considerations

- This procedure is performed most often for treatment of ectopic ureter (see Chapter 77 for diagnosis of ectopic ureter). Inform the owner that incontinence associated with an ectopic ureter may or may not resolve after ureteroneocystostomy. Incontinence that persists after this procedure may be the result of developmental abnormalities of the urethral sphincter or the presence of the remnant of the distal ureter within the sphincter mechanism.
- Ureteroneocystostomy may also be performed to treat disorders resulting in destruction or loss of function of the distal ureter and is preferable to resection and anastomosis of the distal ureter because a lower complication rate is observed after ureteroneocystostomy.

Surgical Procedure

Objectives

- Restore flow of urine from ureter into the bladder.
- Treat incontinence associated with ectopic ureter.

Equipment

- Standard surgical instruments and suture
- Balfour retractor
- Magnification—extremely helpful with small patients but optional with large patients
- Fine-gauge (5-0 to 7-0) absorbable suture

Technique

1–4. Refer to Renal Biopsy; Technique, Steps 1 to 4. Continue the incision caudally to the pubis.
5. Examine and palpate the kidneys, ureters, and bladder.
6. Identify the distal ureter and isolate it by dissection. Take care to preserve the longitudinal blood supply of the ureter. If the ureter is in an ectopic location, ligate and remove the distal continuation (Fig. 78-2*A*). Preserve a sufficient length of ureter to allow implantation into the bladder under minimal tension.
7. Perform a ventral cystotomy and create a circular defect 5 to 10 mm in diameter in the cranial aspect of the mucosa of the dorsal wall of the bladder (Fig. 78-2*B*). Pass a forceps from the lumen of the bladder at an oblique angle in a caudal-to-cranial direction. Grasp the distal end of the proximal

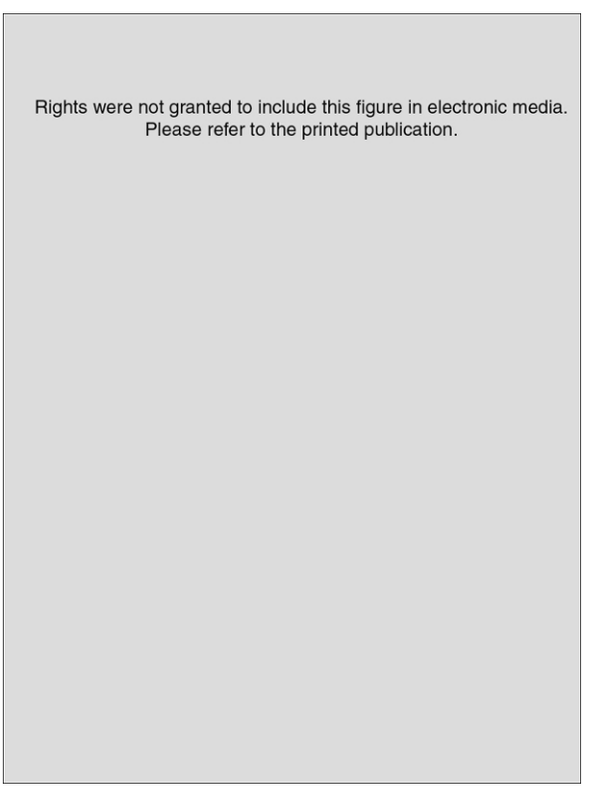

Figure 78-2. Ureteroneocystostomy. *A,* Isolate, ligate, and divide the distal ureter and perform a ventral cystotomy. *B,* Create a circular defect in the bladder mucosa, and pass forceps through the bladder wall to grasp the end of the ureter. *C,* Debride and spatulate the end of the ureter. *D,* Suture the ureter to the bladder mucosa. (From Rawlings CA: Repaired ectopic ureter. In Bojrab MJ [ed]: Current Techniques in Small Animal Surgery, 3rd ed. Philadelphia: Lea & Febiger, 1990, p 374.)

remnant of the ureter, or preferably a suture attached to this end of the ureter with the forceps, and draw the ureter through the bladder wall (Fig. 78-2*B*). As the ureter is drawn through the bladder wall, take care to avoid twisting the ureter, because this may obstruct the ureter or its blood supply.

8. Make a longitudinal incision 5 to 10 mm in length in the ventral aspect of the end of the ureter (Fig. 78-2*C*). Secure the ureter to the edge of the defect created in the bladder mucosa with small (5-0 to 7-0) synthetic absorbable sutures in an interrupted pattern (Fig. 78-2*D*). A ureteral catheter is not maintained after surgery.
9. Alternatively, create a new opening into the bladder by making an incision through the bladder mucosa overlying an intramural ectopic ureter into the lumen of the ureter (neoureterostomy). Suture the ureteral mucosa to the bladder mucosa with fine-gauge absorbable suture, and excise the distal ureter.
10. In addition to the above ureteral technique, some surgeons also prefer to remove the ectopic portion (remnant) of ureter that is present within the bladder neck and proximal urethra in dogs with ectopic ureter. This requires extension of the ventral cystotomy incision into the proximal urethra. From within the lumen, incise the bladder and urethral mucosa over the ureteral remnant, and carefully dissect the remnant from the urethral wall. Close the mucosal incision, and underlying urethral muscle layer, with 4-0 or 5-0 absorbable suture in a simple continuous pattern. Close the urethral and cystotomy incision with a simple continuous pattern of 4-0 absorbable suture. Consider placement of an indwelling urinary stent catheter in dogs undergoing this technique.
11. Close the cystotomy incision in a standard manner (see Chapter 80).
12. Close the abdominal wall, subcutaneous tissue, and skin in a routine manner.

Postoperative Care and Complications

- If an indwelling urinary catheter was placed, remove it 2 to 3 days postoperatively.
- Obstruction of the ureteroneocystostomy or leakage of urine from the site of ureteral reimplantation is uncommon.
- Treat urinary incontinence that persists after surgery with alpha-agonists in an attempt to increase urethral sphincter tone (see Chapter 83). If urinary incontinence persists with appropriate medical management, consider endoscopic submucosal implantation of collagen for urethral bulking to control urine outflow. Warn the owner that incontinence due to ectopic ureter may or may not improve in the patient after surgery and medical therapy.
- Perform excretory urography 4 weeks after surgery to assess the shape and function of the ureter.

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Chapter 79

Diseases of the Urinary Bladder

Jennifer A. Gieg / Dennis J. Chew / Mary A. McLoughlin

The bladder has a limited manner in which it can respond to a variety of diseases and insults. This accounts for the similarity in clinical signs of lower urinary tract disease despite the diverse spectrum of underlying bladder disorders. Signs of inflammation (urgency, pollakiuria, dysuria, and hematuria) are common with most diseases of the bladder. Some of the disease processes listed in Table 79-1 can be associated with obstruction to the outflow of urine. In these instances, systemic signs of uremia (anorexia, lethargy, vomiting, and dehydration), as well as decreased or absent urination, may be recognized. Inability to evacuate urine can be a manifestation of obstruction, decreased ability to contract the detrusor, or inability to coordinate detrusor contraction with urethral relaxation.

PRINCIPLES OF DIAGNOSTIC EVALUATION

Blood Tests

Complete blood count (CBC) and serum biochemical analysis are essential in patients with clinical signs referable to bladder disease that are also systemically ill (anorexia, vomiting, lethargy, weight loss, polyuria and polydipsia, anuria).

Urinalysis and Culture

Although voided urine samples may be adequate for evaluation of urine concentrating ability or presence of hematuria, obtain urine by cystocentesis for evaluation of most bladder diseases. If cystocentesis is not possible or is undesirable (e.g., suspected neoplasia), obtain samples by urethral catheterization.

- Use the dipstick part of the urinalysis to identify blood, glucose, protein, and ketones in the urine. Also perform microscopic analysis of the urine sediment. Evaluation of the urine sediment may reveal inflammatory cells (red and white blood cells), bacteria, epithelial cells, and casts or crystals that may be important indicators of the disease process.
- Perform quantitative urine culture on freshly collected urine to determine what role, if any, uropathogens are playing in a particular bladder disease.

▼ ***Key Point*** While a negative culture on voided urine can reliably rule out infection, a positive culture may represent contamination rather than true urinary tract infection (UTI). For this reason, quantitative cultures are much more easily interpreted when urine is collected by cystocentesis.

Diagnostic Imaging

- Lower urinary tract imaging can be used both to include and to exclude the various bladder disorders. Some combination of plain abdominal radiography, contrast urography, abdominal ultrasonography, and urinary endoscopy are required to establish a definitive bladder disease process (see Chapter 4).
- CT with and without contrast is useful in selected cases to more definitively define bladder disease. Imaging of the upper urinary tract (kidneys and ureters) in addition to the bladder is important for any disease process that could affect the upper urinary tract, such as bladder infection leading to pyelonephritis, or proliferative bladder disease that has caused obstruction of the ureteral openings or urethral outflow (see Chapter 4).

Measurement of Residual Urine Volume

Measurement of post-voiding urine volume from the bladder (residual volume testing) is occasionally helpful in the evaluation of dogs with recurrent UTI or patients suspected of partial urinary obstruction or voiding disorders. Methods to estimate residual urine volume using ultrasonography have been attempted, but we recommend passing a urinary catheter following voiding and measuring the actual urine volume.

- Normal residual volume is estimated to be 0.2 to 0.4 ml/kg in dogs.
- Normal female dogs may have up to 5 to 10 ml and normal male dogs may have up to 10 to 20 ml of residual urine.
- Cats may have up to 2 or 3 ml of residual volume that is considered normal.

Table 79-1. CAUSES OF BLADDER DISEASE

Cystitis
Bacterial—Most common in dogs
Polypoid
Fungal—Rare
Parasitic—Rare
Chemical—Cyclophosphamide, ifosfamide
Idiopathic feline lower urinary tract disease
Suture reaction
Emphysematous

Neoplasia
Transitional cell carcinoma
Rhabdomyosarcoma (botryoid sarcoma)
Lymphoma
Adenocarcinoma
Single polyps

Congenital
Persistent urachus
Urachal diverticulum
Pelvic bladder positioning
Abnormal trigone

Trauma
Bladder contusion
Ruptured bladder

Cystoscopy

Cystoscopy can be a useful diagnostic tool for a variety of conditions such as urolithiasis, mass lesions such as polyps and neoplasms, cystic diverticula, and ectopic ureters.

Biopsy

The gross and endoscopic appearance of several proliferative or inflammatory diseases of the bladder can be similar. Biopsy of abnormal bladder tissue is essential to differentiate among neoplastic, polypoid, and granulomatous changes. Samples can be obtained via cystoscopy or surgically by laparotomy (see Chapter 80).

CONGENITAL DISEASES

Patent Urachus

Etiology

The urachus is the fetal conduit that allows urine to pass from the developing urinary bladder to the placenta. It usually atrophies completely and is nonfunctional at birth. The atrophied urachus is typically seen as a fibrous connective tissue remnant at the bladder apex. If the urachus does not close normally, urine leakage may occur from the bladder to the cutaneous opening of the urachus. At its most extreme, bladder exstrophy exists in which the bladder opens directly to the outside in the area of the umbilicus.

Clinical Signs

Urine leakage is seen in the area of the umbilicus. This can range from visible dripping of urine to damp fur or skin in the area of the urachus. These signs are typically present since birth. As a result, this condition is generally diagnosed in young animals.

Diagnosis

- *Physical examination:* Urine may be observed to collect or leak on the ventral abdominal wall around the umbilicus. Dermatitis or urine scald may be present in the urine-soaked area.
- *Urinalysis and urine culture:* There is an increased risk of UTI because of the leakage of urine. The urinalysis is typically normal unless a UTI is present.
- *CBC and serum biochemical analysis:* These tests are usually unremarkable.
- *Radiography and ultrasonography:* Plain radiography is usually normal. Abdominal ultrasound may be suggestive in some cases. Contrast cystography is the preferred imaging method to reveal the patent urachus (see Chapter 4). Options include a contrast cystourethrogram, or if an orifice is identified, contrast may be introduced at the umbilical opening. In either case, it is essential that an adequate volume of the contrast agent is used to distend the bladder and patent urachus.

Treatment

Surgical resection of the patent urachus (partial cystectomy) is the only definitive treatment option (see Chapter 80).

Urachal Diverticulum (Vesicourachal Diverticulum)

Etiology

- An urachal diverticulum is a small outpouching of tissue at the bladder apex resulting from incomplete closure of the fetal urachus.
- The lesion may be undetectable in a healthy bladder, but it can become more obvious in association with bladder disease, such as urolithiasis or infection.
- A recent study indicates that urachal diverticula are common in normal dogs.
- In cats, urachal diverticula can be acquired following severe urethral obstruction and, in some cases, is a component of non-obstructive sterile idiopathic cystitis.

Clinical Signs

- No clinical signs are observed in dogs with urachal diverticula if no other bladder disease is present.
- The diagnosis may be an incidental finding on radiographs or abdominal ultrasound performed in association with other bladder disease.

- Some diverticula provide a source of urine retention that can serve as a nidus for infection. The recess makes it difficult to eradicate bacterial UTI. Over time, microscopic abscesses commonly develop around the diverticulum. Many patients have a history of lower urinary tract disease that is refractory to treatment.
- In cats, the role of urachal diverticula in creating sterile inflammation and clinical signs is controversial.

Diagnosis

- *Physical examination:* The diverticulum itself causes no clinical signs, but clinical signs related to secondary infection or urolithiasis may be noted.
- *Urinalysis and urine culture:* In the absence of infection, the urinalysis may be normal. Because of urine retention, crystalluria and UTI may be seen more frequently than in normal animals.
- *CBC and serum chemistry profile:* These tests are unremarkable.
- *Diagnostic imaging:* Diverticula are rarely observed on survey radiographs and ultrasound; usually, they are diagnosed with contrast cystography (see Chapter 4). Look for a small pouch or outpocketing of the bladder apex.

▼ ***Key Point*** If a small diverticulum is suspected, gradual distention of the urinary bladder with contrast may better elucidate the extent of the abnormality. Note that maximal bladder filling may distort the architecture of the bladder, making the diverticulum more difficult to identify.

- Confirmation of equivocal diverticula at surgery can sometimes be made by simple inspection, or it may require forceps to probe the region from the interior of the bladder following cystotomy (see Chapter 80).

Treatment

- If lower urinary tract disease has not occurred, the diverticulum may be an incidental finding and treatment is not necessary.
- For a documented urachal diverticulum with recurrent disease such as infection, perform surgical resection (partial cystectomy) (see Chapter 80).
- Despite the tenuous association with inflammation in cats, reduction or resolution of clinical signs of lower urinary tract inflammation has been seen in some cats following diverticulectomy. This would only be recommended in cats that have failed attempts at medical management of their disease.

Other Bladder Anomalies

- *Complete agenesis of the urinary bladder* is extremely rare. Bladder hypoplasia or excessively small bladder size has been reported most frequently in patients with persistent urinary incontinence. This is more likely to represent a failure to distend the bladder as a result of urethral incompetence rather than a true inability to distend the bladder.
- *Malformations of the bladder wall*, trigone, and vesicourethral junction resulting in a poor distinction between the bladder neck and the proximal urethra are frequently identified in patients with ectopic ureters (see Chapter 77).
- *Urinary bladder duplication and colo-urocystic fistula* have also been rarely observed.
- These congenital conditions often become symptomatic in younger animals. It is necessary to rule out ureteral or urethral abnormalities that do not allow the bladder to store urine normally.
- *Pelvic bladder* refers to caudal positioning of the bladder within the pelvic canal. The bladder often appears elongated with a shortened urethra and an indistinct vesico-urethral junction. Pelvic positioning of the bladder can exert effects in some dogs so that urethral function is compromised, resulting in urinary incontinence. Pelvic bladder can be found as an incidental finding in dogs without urinary tract signs.

Clinical Signs

- Any abnormality leading to poor urethral tone or abnormal placement of ureters may lead to incontinence.
- Recurrent or persistent UTI and associated lower urinary tract signs may be additional findings.

▼ ***Key Point*** Pelvic bladders may be identified in normal dogs and, thus, should not always be considered a pathologic abnormality.

Diagnosis

- *Physical examination:* Abdominal palpation may reveal a small bladder or a bladder that is difficult to palpate because of its positioning.
- *Urinalysis and urine culture:* These are normal unless UTI is present.
- *CBC and serum biochemical analysis:* These tests are unremarkable.
- *Radiography and ultrasonography:* Radiography or ultrasonography may confirm a small bladder, an abnormal bladder shape or wall thickness, or a widened and indistinct junction between the bladder neck and the proximal urethra. Radiography is needed to diagnose a pelvic bladder (see Chapter 4).
- *Cystoscopy:* Cystoscopy can confirm an abnormal urethra-to-bladder transition.

Treatment

Treatment of the primary disease is not always possible. Control of UTI may be beneficial. Patients with bladder hypoplasia and ectopic ureters may show improvement in bladder capacity as continence is restored following

surgical management of ectopic ureters (see Chapter 78).

Ureteral Ectopia or Trigone Abnormalities

See Chapter 77 for discussion of this topic.

INFLAMMATORY BLADDER DISEASE

Urolithiasis (Bladder Calculi)

Etiology

- Uroliths (calculi in the urinary tract) are concretions of minerals with a small portion of matrix proteins that form in the urinary tract. The urinary bladder is the most common site of urolith formation.
- Uroliths form when urine is oversaturated with minerals in susceptible individuals. Supersaturation occurs when the concentration of calculogenic minerals is increased.
- Factors such as urine pH and promoters or inhibitors of crystal formation may affect the solubility of the calculogenic minerals.
- Some types of uroliths form because of metabolic disease such as urate-containing calculi in dalmatians and calcium-containing uroliths in animals with hypercalcemia.
- Additional risk factors for urolith formation include breed, gender, age, and diet (Table 79-2). Once initiation of urolith formation has occurred, the nidus must be retained within the urinary tract, and conditions must favor continued precipitation of minerals to promote growth of the urolith.

Struvite Uroliths

- Struvite (triple phosphate) uroliths are most likely to form in alkaline urine. Struvite is the most common urolith in dogs. Although struvite once was the most common urolith in cats, currently calcium oxalate is the most common.
- In dogs, UTI with urease-producing bacteria predisposes the animal to struvite stone formation in the vast majority of cases. Urease-producing bacteria cause alkaline urine, increased levels of ammonium ion in the urine, and increased trivalent phosphate ions.

Table 79-2. UROLITH BREED PREDISPOSITIONS

Predominant Mineral Type	Canine Uroliths	Feline Uroliths
Struvite	Miniature schnauzer Shih Tzu Bichon frisé Lhasa apso Miniature poodle Cocker spaniel (sterile)	Ragdoll Foreign, domestic, and Oriental shorthair Chartreux Himalayan
Calcium oxalate	Miniature schnauzer Shih Tzu Bichon frisé Lhasa apso Yorkshire terrier Miniature poodle	Persian Himalayan British, foreign, and Oriental shorthair Havana Brown Scottish Fold Ragdoll
Calcium phosphate	Miniature schnauzer Bichon frisé Shih Tzu Yorkshire terrier	No breed predisposition
Urate	Dalmatian English bulldog Any breed predisposed to portosystemic shunt	No breed predisposition
Cystine	Newfoundland Mastiff English bulldog Dachshund Tibetan spaniel Basset hound	Siamese Domestic shorthair
Silica	German shepherd Old English sheepdog	No breed predisposition
Xanthine	Cavalier King Charles spaniel Dachshund	

- A urine culture positive for a urease-producing organism (usually *Staphylococcus* or *Proteus* species, occasionally *Streptococcus, Klebsiella,* or *Ureaplasma* species) is necessary for infection-induced struvite uroliths to develop.
- Canine breeds predisposed to struvite formation include miniature schnauzers, Shih Tzus, bichon frisés, Lhasa apsos, and miniature poodles. Cocker spaniels have been reported to develop sterile struvite urolithiasis. Feline breeds at increased risk include the Ragdoll, foreign shorthair, domestic shorthair, Oriental shorthair, Chartreux, and Himalayan. The Rex, Burmese, Abyssinian, Russian Blue, Siamese, and Birman cats are reported to be at decreased risk.

▼ ***Key Point*** Unlike dogs, 95% of struvite uroliths in cats are sterile and considered metabolic in origin.

Calcium Oxalate Uroliths

- Calcium oxalate crystalluria is more likely to occur in acidic urine. This is due to systemic acid-base effects and not the effects of urine pH favoring precipitation.
- Factors that contribute to calcium oxalate urolithiasis include hypercalcemia, administration of calciuretic substances (e.g., saline diuresis, furosemide, and glucocorticoids), and hyperadrenocorticism.
- Calcium oxalate uroliths are recognized more commonly in male dogs with the following breeds being predisposed: miniature schnauzers, Shih Tzus, bichon frisés, Lhasa apsos, Yorkshire terriers, and miniature poodles. Persian, Himalayan, Ragdoll, British shorthair, foreign shorthair, exotic shorthair, Havana Brown, and Scottish Fold cats are predisposed. Birman, Abyssinian, and Siamese cats are at decreased risk.

Ammonium Urate Uroliths

- Ammonium urate uroliths form when increased amounts of uric acid build up in the urine. This can occur if there is increased intake of purines, the precursors of uric acid. It is also more likely to occur in acidic urine.
- These calculi can also occur with impaired ability to convert uric acid to allantoin, the more soluble end product of purine metabolism.
- Breed predisposition to ammonium urate uroliths has been reported most often in the dalmatian. This appears to be due to both impaired conversion of uric acid to allantoin and increased uric acid resorption by the kidneys. English bulldogs are also predisposed to these calculi.
- Formation of ammonium urate uroliths can also be associated with hepatic disease, most notably with portosystemic shunts (PSSs) or microvascular dysplasia. The breeds predisposed to PSS formation include Maltese dogs, Yorkshire terriers, miniature schnauzers, and papillons (see Chapter 71).

Calcium Phosphate Uroliths

- Pure calcium phosphate (hydroxyapatite) uroliths occur infrequently in dogs and cats. Calcium phosphate is more commonly found as a component of other stones (such as struvite uroliths).
- Canine breeds predisposed to these calculi include miniature schnauzers, bichon frisés, Shih Tzus, and Yorkshire terriers.
- Alkaline urine causes increased precipitation of hydroxyapatite in the urine. Hyperparathyroidism is the most common clinical disorder associated with calcium phosphate urolithiasis.

Cystine Uroliths

- Cystine uroliths are found in both dogs and cats, although they are much less common than the types of urolith discussed previously.
- Acidic urine decreases the solubility of cystine crystals, increasing the likelihood of stone formation.
- Breeds that are predisposed to cystine urolithiasis include the mastiff, Newfoundland, English bulldog, dachshund, Tibetan spaniel, and basset hound. Siamese cats also appear to be predisposed. Male dogs and cats are more likely to develop cystine uroliths than females.

Xanthine Uroliths

- Primary xanthine urolithiasis is uncommon in both dogs and cats.
- Xanthine uroliths occur most commonly secondary to allopurinol administration in the treatment of urate calculi. This is particularly true in patients still consuming a high purine diet.
- Cavalier King Charles spaniels and dachshunds are at increased risk for primary xanthine urolithiasis. Overall occurrence of xanthine uroliths is most frequent in breeds, such as dalmatians, that are likely to be placed on allopurinol.

Silica Uroliths

- Silica uroliths occur rarely in dogs and cats.
- German shepherds and Old English sheepdogs have an increased incidence of silica urolithiasis. Males appear to be affected more frequently than females. There is no reported feline predisposition.

Clinical Signs

- Animals affected with urolithiasis of any type typically present with signs of lower urinary tract disease including dysuria, stranguria, pollakiuria, and hematuria.
- Bacterial UTI associated with uroliths may magnify clinical signs.

- A surprising number of animals with cystic calculi display no signs for protracted periods of time. Animals may have a history of passing uroliths or of previous urolith episodes.
- If uroliths are small enough to move out of the urinary bladder but too large to pass through the urethra, urethral obstruction can occur.
- In some animals, uroliths may not be associated with any clinical signs and diagnosis may be incidental.

▼ ***Key Point*** Diseases that predispose an animal to urolithiasis or recurrent UTI should raise the index of suspicion for uroliths.

Diagnosis

Physical Examination

The exam is often normal unless urethral obstruction is present. Uroliths may be palpated in approximately 20% of the cases. It is more difficult to palpate uroliths in dogs, particularly large breeds, than in cats.

- Animals that form ammonium urate uroliths in association with PSS may be stunted in growth or exhibit signs of hepatic encephalopathy (see Chapter 71).
- Dogs and cats with infection-induced struvite uroliths may exhibit more severe signs of lower urinary tract disease due to the bacterial UTI.

Urinalysis

- Examination of urine may reveal hematuria, pyuria, bacteriuria, and/or crystalluria.
- Urine pH may aid in predicting the possible mineral composition of the uroliths. If a UTI with urease-producing bacteria is present, the urine pH will be alkaline.

▼ ***Key Point*** Crystalluria may or may not be present with uroliths. If present, the type of crystalluria may be different from that of the urolith.

Culture and Sensitivity

- Urine cultures may be positive with any urolith because, once present, they serve as a nidus for infection and damage to the bladder mucosa, increasing the risk of bacterial UTI.

▼ ***Key Point*** Although struvite urolith formation is caused by a UTI in most dogs, the presence of a UTI does not prove that uroliths are composed of struvite.

- Consider culture of the bladder mucosa or a portion of the removed stone at the time of surgery if urine culture was negative.

Complete Blood Count and Serum Biochemical Analysis

CBC and serum biochemical analysis are usually normal.

- Hypercalcemia may be observed in approximately 4% of dogs and 35% of cats with calcium oxalate uroliths.
- A low blood urea nitrogen (BUN) concentration or hyperammonemia may be observed in animals with ammonium urate uroliths that form in association with liver diseases such as portosystemic shunting or microvascular dysplasia.

Diagnostic Imaging

- Survey radiography may reveal radiodense uroliths (e.g., struvite, calcium oxalate, and calcium phosphate) if they are of adequate size. Typically uroliths must be greater than 3 mm to be identified radiographically. Urate uroliths and some cystine uroliths may not be observed on plain radiographs because of their poor mineral density. Double-contrast cystography will reveal these uroliths (see Chapter 4).
- Ultrasonography may demonstrate uroliths. It can be difficult to distinguish very small uroliths from aggregates of sediment, for even experienced ultrasonographers. Only the proximal urethra may be evaluated by ultrasonography.
- Consider intravenous pyelography in animals with nephroliths or ureteroliths or in animals with recurrent bacterial UTI.

▼ ***Key Point*** It is essential that the entire urethra be included on radiographs of male cats and dogs with suspected urolithiasis. If necessary, obtain a separate film of the caudal abdomen to be sure that the entire urethra is evaluated.

Additional Laboratory Testing

A bile acids test or other indicator of liver function is indicated in animals with ammonium urate uroliths (other than in dalmatians or English bulldogs) to determine if hepatic disease is present (see Chapter 71).

Urolith Composition

Submit all uroliths that are retrieved for quantitative analysis, even in animals with crystalluria or history of formation of a particular type of urolith. Also, submit stones for analysis for each episode of urolithiasis to be sure that stone composition has not changed.

Treatment

- Uroliths can be treated either medically or surgically.
- Surgically remove uroliths that cause repeated urethral obstruction, that cause unacceptable clinical signs, or in which the owners do not wish to attempt medical dissolution.

- Uroliths that are smaller than the smallest diameter of the urethra may be retrieved using voiding urohydropropulsion or catheter-assisted retrieval technique.
- For all stones being treated with medical dissolution, continue therapy for 1 month after radiographic resolution of the uroliths. If no improvement is seen in size after 4 to 6 weeks of therapy, consider surgical removal.

▼ ***Key Point*** Because many types of uroliths are recurrent, surgical removal or medical dissolution of uroliths is not the end point of therapy. Institute appropriate preventive measures and follow-up evaluations. Lack of adequate patient surveillance is often associated with recurrent stone formation.

Struvite Uroliths (Table 79-3)

- *Infection induced:* Medical dissolution of infection-induced struvite uroliths is possible using appropriate antimicrobial therapy based on culture and sensitivity and a diet designed for struvite dissolution. A diet for struvite dissolution should be protein and magnesium restricted and should induce an acid urine pH (e.g., Prescription Diet s/d; Hills). The average time for dissolution of canine uroliths is 12 weeks.
- *Sterile:* Dissolution of sterile struvite uroliths is accomplished in a manner similar to infection-induced struvite uroliths except that antimicrobial therapy is not necessary. Average dissolution time for dogs and cats is 4 to 6 weeks.

Calcium Oxalate Uroliths (Table 79-4)

- There is no medical therapy available for dissolution of calcium oxalate uroliths; however, use medical therapy to prevent recurrence after urolith removal.
- Surgical removal, urohydropropulsion, and lithotripsy are the treatment options for uroliths that are causing clinical problems.

Ammonium Urate Uroliths (Table 79-5)

- *Associated with PSS:* Medical dissolution of ammonium urate uroliths in animals with hepatic disease has not been documented to be successful; therefore, surgical removal remains the treatment of choice if uroliths are causing clinical problems. Uroliths may be removed at the time of surgical ligation of the PSS. Theoretically, uroliths may dissolve after the shunt is corrected, but this has not been evaluated in clinical studies.
- *Not associated with PSS:* Urate uroliths may be dissolved using allopurinol and a diet low in purines (e.g., Hill's u/d). The canine dosage for allopurinol is 30 mg/kg/day PO divided into two or three doses every 24 hours. Although a published dosage of 9 mg/kg PO q24h is reported in cats, there is limited data on the safety and efficacy of this treatment in cats. As a result, use allopurinol cautiously in cats. The average dissolution time is 4 weeks. Medical dissolution is successful in approximately 50% of cases.

Calcium Phosphate Uroliths

- Surgically remove these uroliths.

Cystine Uroliths

- Dissolution can be achieved using a combination of medical and dietary therapy. For dogs, 2-mercaptopropionol glycine (2-MPG) (tiopronin, Thiola) can be given at a dosage of 15 to 20 mg/kg PO q12h. No feline dosage has been established. Feeding a low-

Table 79-3. PROTOCOL FOR DISSOLUTION OF STRUVITE UROLITHS IN ADULT DOGS AND CATS

1. Confirm the mineral composition of uroliths when a stone is available. If no stone is available, make the best estimate of its mineral content using results from a combination of urine pH, radiodensity, breed, sex, and diet history.
2. If uroliths are obstructive, recommend surgical removal to the owner (see Chapter 80).
3. In infection-associated stones, begin therapy for urinary tract infection with antibiotics based on cystocentesis, culture, and susceptibility. Maintain antimicrobial therapy during, and for 3 to 4 weeks following, urolith dissolution.
4. Dietary therapy includes use of a phosphorus- and magnesium-restricted diet that is highly acidifying. Dissolution of struvite stones has been achieved following the feeding of Prescription Diet s/d (Hills) (usually canned) in both dogs and cats and IVD Dissolution Diet in cats. Compliance with dietary recommendations is suggested by reduction in blood urea nitrogen concentration (usually <15 mg/dl). Other dietary formulations designed to undersaturate urine for struvite in prevention protocols are not useful in dissolution protocols.
5. Monitor efficacy of therapy:
   a. Perform serial radiographs at monthly intervals to evaluate stone location(s), number, size, density, and shape.
   b. If urinary tract infection was present, perform a quantitative urine culture 5 to 7 days after initiation of therapy to document sterile urine while on antibiotic therapy.
   c. Repeat urine culture several days after completion of antibiotic therapy to document sterile urine.
   d. Continue all therapy for 1 month after radiographic resolution of uroliths.
   e. If uroliths increase in size or have not decreased in size within 4 to 6 weeks of appropriate medical management, consider the following:
      (1) The wrong mineral component was identified
      (2) The nucleus of the uroliths is of different mineral composition than other portions of the urolith.
      (3) Relapsing urinary tract infection or reinfection is interfering with dissolution of the stones.
      (4) The owner or the patient is not complying with medical recommendations.
6. In dogs and cats with persistent urinary tract infection or stones despite appropriate medical therapy, surgical removal of the stones is recommended.

Table 79-4. PROTOCOL FOR PREVENTION OF CALCIUM OXALATE UROLITHS

1. Calcium oxalate stones cannot be dissolved medically. Recommend surgical removal, lithotripsy, or, for small enough stones, urohydropulsion.
2. Although urinary tract infection is not a cause of calcium oxalate urolithiasis, treat secondary urinary tract infection with antibiotics based on culture and sensitivity.
3. Perform complete blood count and biochemical profile on all patients with calcium oxalate urolithiasis to rule out hypercalcemia or any other diseases (e.g., hyperadrenocorticism) that could predispose to stone formation. Identify and treat the underlying cause of hypercalcemia. Persistent hypercalcemia greatly increases the risk of recurrence.
4. For normocalcemic patients with confirmed calcium oxalate urolithiasis take the following actions:
   a. Lower the dose or, if possible, discontinue medications that promote calciuresis (e.g., glucocorticoids and furosemide).
   b. Discontinue supplementation with calcium, vitamin D, and vitamin C.
   c. As with any type of urolith, increasing water intake is a critical part of preventative therapy.
      (1) Recommend transitioning pets to canned food or adding water to dry food.
   d. Diets that may help prevent calcium oxalate uroliths are less acidifying than other diets. Most are sodium restricted but are not magnesium restricted. Diets that may be effective include Prescription Diet canine u/d (Hills), Prescription Diet feline x/d (Hills), Eukanuba Moderate pH/O (Iams), and SO Diet (Waltham).
   e. In cases in which dietary therapy and control of metabolic disease alone have not prevented recurrence of calcium oxalate uroliths, addition of potassium citrate to the diet may be considered. Potassium citrate will help alkalinize the urine and may reduce precipitation of calcium oxalate crystals. The canine dosage is 50 to 75 mg/kg PO q12h. Similar dosages have been reported for cats. Eukanuba Moderate pH/O (Iams) and Prescription Diet feline x/d (Hills) contain increased amounts of potassium citrate.

Table 79-5. PROTOCOL FOR DISSOLUTION OF AMMONIUM URATE UROLITHIASIS*

1. Evaluate urolith(s) location(s), number, size, density, and shape in approximately monthly intervals. Intravenous urography may be utilized for radiolucent uroliths located in the kidneys, ureters, or urinary bladder. Double-contrast cystography may be required for radiolucent uroliths.
2. If the uroliths are obstructive, recommend surgical removal (see Chapter 80).
3. Initiate therapy with a low-protein, alkalinizing diet. In particular, it is important that the diet be low in purines. Purines are found primarily in animal protein, so diets that are based on vegetable proteins or diets that are low in protein will reduce the purine load. Examples of diets that could aid in dissolution of urate stones include Prescription Diet u/d (Hills).
4. If dietary therapy alone does not result in dissolution of stones, initiate therapy with allopurinol. The recommended canine dosage is 30 mg/kg q24h divided into two or three doses. The feline dosage is approximately 9 mg/kg PO q24h, but use it with caution because the safety of allopurinol in cats has not been determined.
5. If urine remains acidic, diet may be supplemented with potassium citrate to achieve a more alkaline urine pH (close to 7.0). The canine and feline dosages are similar, 50 to 75 mg/kg PO q12h.
6. If necessary, eradicate or control urinary tract infections with appropriate antimicrobial agents. Maintain antimicrobial therapy during, and for an appropriate period following, urate urolith dissolution.
7. Regularly monitor urolith size and number to evaluate whether the dissolution therapy is effective. If the stones become larger or have not dissolved within 4 to 6 weeks, consider surgical removal.
8. Continue calculolytic diet, allopurinol, and alkalinizing therapy for approximately 1 month following radiograph disappearance of uroliths.

*This protocol is not effective for ammonium urate uroliths associated with portosystemic shunts.

protein, alkalinizing diet (e.g., Hill's canine u/d) may also decrease cystinuria.
- Time for stone dissolution ranges from 4 to 12 weeks.

Xanthine Uroliths

- Dissolution of xanthine urolithiasis may be achieved with the use of a low purine diet. These include diets that are low in total protein and those composed primarily of plant-based proteins.
- If allopurinol is being given for treatment of urate uroliths, discontinue the drug while stone dissolution is being attempted.

Silica Uroliths

- No proven therapy for dissolution of silica urolithiasis has been reported. Perform surgical removal.

Prevention

- Most types of uroliths can reoccur; therefore, institute patient monitoring and preventive measures.
- Production of dilute urine is beneficial for all urolith types except for infection-induced struvite. Therefore, diet and environmental changes aimed at increasing water intake may help prevent recurrence of uroliths.
  - These changes may include transition from dry to wet diet or addition of water to dry food, placement of additional water bowls or different types of water sources in the home, and attention to water bowl hygiene.
- Dilute urine is a predisposing risk factor for UTI. Therefore, it may predispose an animal to infection-induced struvite urolith formation, although this has not been proven.

- Many uroliths are recurrent. Therefore, reexamine affected animals frequently and assess urine specific gravity, urine sediment, and perform diagnostic imaging if indicated.

Infection-Induced Struvite Uroliths

Because this type of struvite urolith forms as a result of a UTI with urease-producing bacteria, prevention is dependent upon preventing recurrence of the infection.

- Treat any underlying causes of recurrent UTI, such as hyperadrenocorticism and diabetes mellitus (see Chapters 33 and 34, respectively).
- Perform surgery to correct structural abnormalities such as perivulvar dermatitis and recessed vulva (see Chapter 54) that may predispose an animal to infection if untreated.
- If necessary, use low-dose antibiotic therapy as prophylaxis.
- Modification of the diet is not necessary, although increasing water intake and encouraging frequent voiding may assist urinary defenses.

Sterile Struvite Uroliths

Prevention of sterile struvite uroliths involves modification of the diet. Although the feeding of theses diets is logical, no evidence-based medicine studies exist to show long-term benefits to decrease stone formation.

- Because struvite is more soluble in acidic urine (pH <6.8), prevention usually involves feeding one of the several commercially available diets designed to acidify the urine. Excessive acidification of the urine (<6.0) should be avoided as this may indicate excessive effects on systemic acidosis.
- Dietary magnesium restriction may also be of benefit.

Calcium Oxalate Uroliths (See Table 79-4)

The cause of calcium oxalate urolith formation is not completely known. No treatment has been shown to be completely effective in prevention of recurrence. Question owners about any dietary supplements or medications (e.g., vitamin C, calcium, and glucocorticoids) that may increase calcium absorption or calciuresis. Any underlying disease such as hyperadrenocorticism that may predispose an animal to calcium oxalate stone formation should be controlled as well as possible.

- In dogs, feeding a protein- and sodium-restricted diet may delay recurrence. Less acidifying diets may decrease calciuresis. Choosing diets that promote a neutral pH or a pH between 6.5 and 7.0 may be of benefit. Strongly alkalinizing diets are not recommended because they may promote struvite urolithiasis.
- In dogs, if a neutral to slightly alkaline urine pH is not accomplished by diet alone, supplementation with potassium citrate (50–75 mg/kg PO q12h adjusted to alkalinize urine) may be of benefit, although the evidence for this is less convincing in veterinary literature than in human literature. A similar dose has been suggested for cats, but the efficacy of this is even less clear than in dogs.
- For cats with calcium oxalate uroliths, increasing water intake by feeding canned diets or diets with water added is our primary recommendation for prevention of recurrence. Several commercial feline diets are marketed for calcium oxalate prevention.
- Feeding high-fiber, protein-restricted, and phosphorus-restricted diets have been considered but are not documented to be successful.
- Other treatments that have been proposed for both dogs and cats include vitamin B_6 and hydrochlorothiazide (2 mg/kg PO q12h for dogs, 1 mg/kg PO q12–24h for cats). At present, no evidence-based medicine exists for these treatments. In animals with hypercalcemia, administration of hydrochlorothiazide or other thiazide diuretics is contraindicated because it may worsen the hypercalcemia. In these cases, treatment should be aimed at correcting the hypercalcemia rather than controlling the calciuresis.

▼ ***Key Point*** Because calcium oxalate uroliths are highly recurrent, frequently monitor urinalyses and survey abdominal radiographs in these patients.

Ammonium Urate Uroliths

Associated with Portosystemic Shunt

- If the vascular shunt can be repaired or attenuated (see Chapter 72), the risk of ammonium urate urolith formation should decrease. No further treatment may be indicated.
- If the shunt is not repairable, then a low-protein, alkalinizing diet may be beneficial (e.g., Prescription Diet i/d; Hills) in conjunction with appropriate medical therapy (see Chapter 71). The protein source may be of more importance than the amount of protein in the diet. Diets high in vegetable or dairy protein have a lower purine load than those derived from other protein sources.
- Dry formulations of low purine diets alone are much less effective in prevention of urate crystalluria compared with the canned version of the same formulation or the same dry diet mixed with an equal volume of added water.
- Allopurinol is not effective in animals with these calculi associated with PSS.

Not Associated with Portosystemic Shunt

- In dogs, feeding a low-protein, alkalinizing diet (e.g., Prescription Diet canine u/d; Hills) has been successful in preventing recurrence in approximately 80% of cases. As mentioned above, diets high in veg-

etable or dairy protein have a lower purine load than those derived from other protein sources.
- Canned formulations or dry diets with added water are more effective in controlling crystalluria than dry diets alone.
- If urate crystalluria persists despite feeding an appropriate preventive diet, administer allopurinol (10–20 mg/kg PO divided into two doses q24h for dogs). No preventative dose of allopurinol is published for cats.
- In cats, feeding a low-protein, alkalinizing diet alone may allow successful dissolution of urate stones.
- Dogs and cats being treated with allopurinol are at increased risk of developing xanthine uroliths, as well as other drug side effects. Monitor these patients closely during treatment.

Calcium Phosphate Uroliths

- Identify and treat of any predisposing factors, for example, hyperparathyroidism (see Chapter 32) or overly alkaline urine.
- If urine alkalinizers have been used to prevent calcium oxalate or other uroliths, discontinue or reduce the dose to establish a more neutral urine pH.

Cystine Uroliths

- A low-protein, alkalinizing diet is highly successful in preventing formation of cystine uroliths. Cystine solubility increases in alkaline urine; therefore, maintaining a urine pH of >7.5 is important.
- If the urine pH is not >7.5, administer potassium citrate (initial dosage of 50–75 mg/kg PO q12h; adjust the dosage to induce a urine pH >7.5).
- Alternatively, in dogs, 2-MPG (tiopronin, Thiola) (15–20 mg/kg PO q12h) can be given with alkalinization therapy without modifying diet. Occasionally, regenerative anemia and myopathy have been noted with use of this drug. One study also described altered behavior in the form of aggression of which owners should be made aware.

Xanthine Uroliths

- Primary xanthine urolithiasis is uncommon and, when present, is likely due to an inborn error of metabolism such as xanthine oxidase deficiency.
- Xanthine uroliths are most commonly associated with allopurinol administration. Occurrence of xanthine urolithiasis warrants dose reduction or discontinuation of allopurinol.
- Use of a low purine diet may help prevent xanthine, as well as urate, uroliths (e.g., Prescription Diet u/d; Hills).

Silica Uroliths

- Silica content is much higher in plant-based proteins than in animal proteins. Avoiding diets high in plant protein may reduce the recurrence of silica urolithiasis.
- Since there is a tenuous association between animals ingesting large amounts of soil and occurrence of silica urolithiasis, attempt to prevent this behavior in animals with these calculi.

Bladder Infection

Bacterial UTI is the most common infectious disease of the urinary bladder. Fungal cystitis is occasionally observed, particularly in animals that are immunosuppressed; however, many cases are self-limiting. Parasitic cystitis occurs rarely and is usually asymptomatic.

Etiology

Bacterial Cystitis

Bacterial cystitis is most often the result of ascending infection from bacterial contamination of the vulva, perivulvar skin, vestibule, or prepuce. This often results from fecal contamination of these areas, ascent of normal flora, or exposure to organisms in the environment (e.g., nosocomial infections). The body has many defense mechanisms to prevent bacterial invasion of the urinary bladder. Natural resistance factors, inherent to the urinary tract, include complete and frequent unidirectional voiding of urine, mucosal defense barriers, and antimicrobial properties of concentrated, normal urine. Therefore, any breach in these defense mechanisms may result in bacterial colonization of the urinary bladder.

- Bacterial cystitis is a common cause of lower urinary tract disease in dogs, with females affected more frequently than males.
- The most common organisms causing bacterial cystitis include *Escherichia coli* (40–50% of cases) and *Staphylococcus, Proteus, Streptococcus,* and *Enterobacter* species.
- Diseases that cause polyuria and polydipsia or those that affect host immunity may predispose an animal to development of UTI.
- Anatomic or functional abnormalities that affect the urethral tone or the integrity of the urethral and vulvar barriers to bacteria may also be predisposing factors. These include incontinence (of any cause), recessed vulva, perivulvar dermatitis, and urethral sphincter mechanism incompetence.

▼ ***Key Point*** In cats younger than 10 years, bacterial cystitis occurs in only 1% to 2% of cases of lower urinary tract disease. In cats older than 10 years, however, bacterial cystitis may occur in as many as 50% of cases.

- As in dogs, feline diseases that impair urine-concentrating ability predispose cats to UTI. Renal failure is

the most common disease associated with bacterial cystitis in older cats.
- Causative bacteria in cats are similar to those observed in dogs. Increased risk of bacterial UTI also occurs in cats following urethral catheterization (especially indwelling catheters) and perineal urethrostomy.

Fungal Cystitis

- Fungal cystitis is rare compared with bacterial cystitis and occurs mostly in patients that are immunocompromised. Yeast and fungi observed in urine usually represent contamination of the sample. Of organisms that represent true infections, *Candida* species is the most common.
- On occasion, other fungi and algae (e.g., *Blastomyces, Cryptococcus, Aspergillus,* and *Prototheca* and *Trichosporum domesticum*) may be observed in urine, but these have not been reported as isolated infections and instead represent one component of disseminated fungal infection (see Chapter 20).

Bladder or Urinary Tract Parasites

- Rarely, parasitic ova or adult worms are identified in urine samples or within the bladder.
- *Capillaria* and *Angiostrongylus* adults have both been identified within the urinary bladder. In most cases, however, clinical signs relate to infection elsewhere rather than aberrant bladder infection, although hemorrhagic cystitis has been reported with *Capillaria* infection.
- *Dioctophyma renale* is a parasite of the kidneys, but if a gravid female worm is present in the kidney, ova may be observed in urine. This would not be expected to cause lower urinary tract signs.

Clinical Signs

- Clinical signs of lower urinary tract disease are typically acute in onset if the UTI is the primary disease process.
- Clinical signs include gross hematuria, dysuria, and pollakiuria. Animals may also display inappropriate urination. A strong odor to the urine may be detected by the owner, but this is not a sensitive index for infection.
- Some patients with factors predisposing them to UTI may have a more protracted history with waxing and waning signs.

▼ ***Key Point*** Systemic signs are not expected with isolated lower UTI. If signs of systemic illness are present, perform further diagnostic evaluation for a predisposing primary disease or upper UTI.

- Polyuria and polydipsia may be observed with underlying renal failure, hyperthyroidism, diabetes mellitus, hyperadrenocorticism, pyelonephritis, or glucocorticoid therapy. Many of these patients lack the classic lower urinary tract signs seen with primary UTI.
- Skin, oral, or respiratory infections may be observed with immunosuppressive therapy or disease.
- Clinical signs are less likely to be observed when an infection occurs in association with polyuric states or immunosuppressive disease.
- Clinical signs of fungal cystitis are usually similar to those of bacterial cystitis.
- A surprising number of dogs presenting to referral hospitals have positive urine cultures without clinical signs referable to the urinary tract.

Diagnosis

Physical Examination

Physical examination may be normal. Abdominal palpation may reveal bladder pain or thickening of the bladder wall. Examination findings that relate to the predisposing cause may be observed (e.g., prostatic mass, hepatomegaly and alopecia with hyperadrenocorticism, and weight loss, uveitis, harsh lung sounds, and draining skin lesions with systemic mycosis).

Urinalysis

- The infectious agent (bacterium, fungus, yeast, or parasitic ova) is usually observed on urine sediment examination. Signs of inflammation are often present with bacterial cystitis but are usually not present with fungal or parasitic cystitis.
- Urine sediment may appear inactive if the animal is immunocompromised (e.g., hyperadrenocorticism, glucocorticoid therapy, feline leukemia virus, or immunodeficiency virus infection). For this reason, routine urine culture should be done in animals with these diseases.

▼ ***Key Point*** Nitrate and leukocyte pads on urinalysis strips are not accurate for use in dogs and cats. Examine urine sediment to identify inflammation and an infectious agent. Evaluate for glucosuria indicative of underlying diabetes mellitus.

Urine Culture

Perform aerobic bacterial culture of urine (collected by cystocentesis) in suspected cases of bacterial cystitis. Quantification of the number of bacterial colony-forming units per milliliter of urine is the gold standard for diagnosis of UTIs (Table 79-6).

▼ ***Key Point*** Confirmation of bacterial UTI is best made using quantitative culture of urine samples collected by cystocentesis.

- If immediate transport to a microbiology lab is not available, use a quantitative loop (usually 0.01 ml) to

Table 79-6. INTERPRETATION OF QUANTITATIVE URINE CULTURE RESULTS

Method of Collection	Results Indicative of Infection (CFU/ml)	Equivocal Results (CFU/ml)
Cystocentesis	>1000 (usually >10,000)	100–1000
Catheterization	>1000 in male and female cats and male dogs (usually >10,000) Unreliable in female dogs; 20% of normal female dogs have >100,000	100–1000
Voided	Cultures should be avoided (not useful unless no growth) Large quantitative growth is common	

CFU/ml, colony-forming unit per milliliter.

inoculate and streak out a blood agar plate. Incubate the plated urine at 35°C for 18 to 24 hours for most common uropathogens. Submit both a urine sample and the inoculated plate to a microbiology lab for evaluation. Fastidious organisms may require 3 to 5 days for isolation.

- Select antimicrobial agents on the basis of culture and sensitivity results. This is particularly important in patients with recurrent UTI and in those exposed to any antibiotic therapy within the past month.
- The agar-gel disc diffusion method is most commonly used. It is based on expected serum drug concentrations, not urine concentrations (which are higher by 10–100× for many drugs), and thus underestimates the effectiveness of some drugs.

▼ ***Key Point*** If sensitivities are established by determining the minimum inhibitory concentration (MIC), select antibiotics that reach urine concentrations 4 times the MIC.

- Alternatively, in first-time UTI without predisposing anatomic, metabolic, or functional issues, choose antibiotics based on known biologic behavior of uropathogens.
- Urine may be submitted for a fungal culture as well, although a diagnosis of mycotic infection is often made on the basis of sediment examination. Given the rarity of fungal UTI, be certain that the fungal elements are not contaminants from the stain or the environment. Confirm with a second positive sample.

Complete Blood Count and Serum Biochemical Analysis

Rule out cystitis associated with a systemic disease (such as renal failure or hyperadrenocorticism).

Diagnostic Imaging

Perform radiographs or ultrasound to rule out primary bladder or other urogenital diseases that create anatomic abnormalities that predispose the patient to UTI (see Chapter 4).

Additional Laboratory Testing

- Perform endocrine testing in dogs suspected of having hyperadrenocorticism or cats with hyperthyroidism (see Chapters 33 and 31, respectively).
- Perform a feline leukemia virus antigen test and a feline immunodeficiency virus antibody test in cats with UTI (see Chapters 8 and 9, respectively).

Treatment

Bacterial Cystitis

Always select antimicrobial agents on the basis of culture and sensitivity results.

- ***Uncomplicated infection:*** Treat uncomplicated cystitis with the appropriate antimicrobial for 10 to 14 days. If clinical signs resolve and this is a first-time infection, no follow-up is generally needed. However, consider reculture of the urine 3 to 7 days after completion of antibiotic therapy to document sterile urine.
- ***Complicated infection:*** Consider bacterial cystitis complicated if it is recurrent or associated with an underlying risk factor. Give antimicrobial therapy for 3 to 4 weeks. Obtain a urinalysis and urine culture 5 to 7 days after beginning therapy to ensure that there is no growth while on medication. Perform a final urine culture several days after cessation of therapy to document continued urine sterility.
- ***Relapsing infection:*** Relapsing infections (i.e., infection with the same bacteria following appropriate treatment) can occur if antibiotic choice, dose, or duration of therapy is inappropriate. Complicating factors or diseases that create a nidus for infection (e.g., urolithiasis or bladder diverticulum) may be present. Relapse of infection requires a reassessment of antimicrobial choice based on culture and sensitivity results and a search for and treatment of any

complicating factors. A deep-seated infection could require a second, longer course of therapy (Table 79-7).

- ***Reinfection:*** Reinfection (i.e., repeat infection with a different organism within a few weeks to months following documented eradication) generally indicates a predisposing anatomic, metabolic, or functional abnormality that increases the likelihood of development of UTI. Like relapsing infections, this necessitates reevaluation and treatment for complicating risk factors (Table 79-8). Documenting the organism responsible for infection and a negative culture following treatment is essential.
  - Consider long-term, low-dose antibiotic therapy to treat animals with frequent reinfections. This involves administering one-third to one-half of the recommended therapeutic dose of the antimicrobial once a day. This is best given at night to allow excretion and collection of the antimicrobial into the urine overnight, which maximizes contact of the antimicrobial with the bladder. Do not use this strategy for relapsing infection.
- ***Catheter-induced infection:*** Bacterial cystitis may occur as a result of urinary catheterization. If a catheter is passed only once into the urinary bladder, treatment

Table 79-7. DISORDERS TO CONSIDER FOR RECURRENT URINARY TRACT INFECTIONS

Functional/Anatomic Abnormalities
Deep-seated cystitis (chronic wall changes)
Pyelonephritis
Prostatitis
Metritis/pyometra
Neoplasia (bladder/urethra)
Small urinary calculi (previously undetected)
Urachal remnant (developmental)
Periurachal microabscesses
Ectopic ureters (developmental)
Urethral sphincter mechanism incompetence (incontinence)
Polypoid cystitis
Recessed vulva
Vestibulovaginal stenosis
Ureterocele
Bladder atony (abnormal residual urine volume)
Urethral stricture
Urethral fistula

Metabolic Conditions
Diabetes mellitus
Hyperadrenocorticism
Exogenous steroid administration
Renal failure (especially cats)
Hyperthyroidism
Immunosuppression/chemotherapy

Table 79-8. MANAGEMENT OF COMPLICATED AND RECURRENT URINARY TRACT INFECTIONS

Diagnostic Considerations
Are you certain that the disease is bacterial in origin?
Are there any predisposing anatomic abnormalities?
- Urolithiasis (upper or lower urinary tract)
- Ectopic ureters
- Neoplasia of bladder, urethra, or prostate
- Urachal diverticulum
- Polypoid cystitis
- Recessed vulva
- Chronic bladder thickening with extensive tissue changes
- Pyelonephritis
- Prostatitis

Has diagnostic imaging been adequate to exclude these problems?
Are there any underlying functional abnormalities?
- Can the animal completely evacuate the bladder such that a normal residual volume is left?
- Could primary sphincter mechanism incompetence or low urethral tone with urinary incontinence and subsequent wicking of bacteria be contributing? (See Chapter 83.)

Are there any underlying metabolic conditions (with or without obvious pyuria or bacteriuria)?
- Diabetes mellitus
- Hyperadrenocorticism
- Renal failure

Therapeutic Considerations
1. Identify and eliminate or control predisposing or complicating causes of the urinary tract infection (e.g., hyperadrenocorticism, diabetes mellitus, urolithiasis, and anatomic defects).
2. Identify causative pathogens by quantitative urine culture, and select antimicrobial drugs on the basis of antimicrobial susceptibility tests. Ideally, the agent chosen should have the narrowest possible spectrum of antimicrobial activity.
3. If signs of upper urinary tract infection are present (e.g., fever, leukocytosis, or polyuria and polydipsia), treat aggressively with appropriate dosages of antimicrobials. A longer duration of treatment (4 to 6 weeks) will be necessary for upper urinary tract or complicated lower urinary tract infections than for first-time lower urinary tract infections (10 to 14 days).
4. Reculture urine 5 to 7 days following initiation of therapy to check the efficacy of the antimicrobial agent in sterilizing urine.
5. Culture urine 3 to 5 days after the completion of therapy to confirm resolution of the infection.
6. Anticipate recurrence of infection in animals with underlying disease or anatomic abnormalities that cannot be corrected. Routine culture should be performed every 3 to 6 months in these patients even if they are asymptomatic. Counsel owners that any lower urinary tract signs should be evaluated promptly.
7. If recurrent infection continues despite routine screening and appropriate treatment, prophylactic therapy with constant low doses or pulse dosing of antibiotic therapy should be considered.

with amoxicillin or a cephalosporin should prevent infection. This can be given at the time of catheterization and for 2 to 3 days afterward. If an indwelling catheter is placed, do not administer antimicrobials while the catheter is in place. Instead, evaluate a urine sample when the catheter is removed. If bacterial cystitis is present at that time, treat appropriately based on culture and susceptibility.

Fungal Cystitis

- Treat a confirmed fungal infection whether or not the animal is symptomatic. Select the antifungal agent and dose based on the organism that is identified.
- Ketoconazole (10–20 mg/kg PO q24h or as a divided dose for dogs, 10 mg/kg PO q12h for cats), itraconazole (5 mg/kg PO q12–24h for dogs and cats), and amphotericin B (variable IV dosing) have been used successfully (see Chapter 20).
- Infusion of antifungal agents such as clotrimazole into the bladder has been reported for treatment of *Candida* spp. UTI. Altering urine pH as a means of treating fungal infection is not recommended as the sole therapy. If possible, treat any immunosuppressive disease or reduce or stop immunosuppressive medication.

Parasitic Cystitis

- Because many animals with parasitic cystitis are asymptomatic, treatment may not be warranted.
- For urinary capillariasis, give levamisole (2.5 mg/kg/d PO for 5 days). Use of fenbendazole (25 mg/kg PO q12h for 3–10 days) has been reported, but it does not appear to be as effective as levamisole.

▼ ***Key Point*** Albendazole is no longer recommended in dogs or cats because it can cause bone marrow aplasia.

Prevention

Prevention of infectious cystitis is dependent upon identifying and eliminating or controlling the underlying disease.

- Treat diseases such as diabetes mellitus or hyperadrenocorticism that may predispose the animal to infection as effectively as possible to minimize the risk of UTI.
- In patients with diseases such as renal failure, in which the predisposing factor (low urine specific gravity) cannot be corrected, regularly screen for UTI.
- Surgically correct anatomic abnormalities if they are present (e.g., bladder diverticulum or recessed vulva).

Emphysematous Cystitis

Emphysematous cystitis is a rare complication of bacterial UTI, particularly in patients with glucosuria.

Etiology

Emphysematous cystitis occurs when bacterial cystitis is caused by gas-producing bacteria such as *Clostridium* spp. These bacteria create pockets of gas within the wall of the bladder that are apparent on radiographs and ultrasound.

Clinical Signs

Clinical signs are similar to other forms of cystitis.

Diagnosis

- *History:* This type of bladder infection occurs almost exclusively in patients with glucosuria and UTI secondary to diabetes mellitus. It has also been associated with other immunosuppressive diseases such as hyperadrenocorticism.
- *Physical examination:* The urinary bladder is usually small and firm on palpation.
- *Urinalysis:* Urinalysis shows inflammation; the agent may not be observed. Perform cystocentesis carefully in these patients because the integrity of the bladder wall may be affected by gas within the bladder wall.
- *Urine culture:* Aerobic cultures may be negative if an anaerobic organism is responsible.
- *CBC and serum biochemical analysis:* These tests are usually normal unless associated with a metabolic disease such as diabetes mellitus or hyperadrenocorticism. Evidence for sepsis may be present. Evidence for bone marrow suppression may be present if associated with administration of chemotherapeutic agents.
- *Radiography and ultrasonography:* Radiography and ultrasonography show air trapped in the wall of the urinary bladder.

Treatment

- Administer an appropriate antimicrobial (e.g., ampicillin, amoxicillin, or amoxicillin-clavulanic acid) for 3 to 6 weeks.
- Treat the underlying predisposing disease, if possible. If the animal is receiving immunosuppressive or chemotherapeutic agents, consider temporarily stopping the drug or decreasing the dosage.

Prevention

- Identify animals at risk for infectious cystitis.
- Monitor for UTI periodically in animals known to have a disease that compromises their local or sys-

temic defenses and in animals receiving immunosuppressive or chemotherapeutic drugs.
- Many of these animals may not demonstrate clinical signs but may have evidence of UTI on urinalysis.

IDIOPATHIC FELINE LOWER URINARY TRACT DISEASE

Idiopathic feline lower urinary tract disease (IFLUTD) has also been called feline urologic syndrome (FUS) and feline interstitial cystitis (FIC) because of many similarities with human interstitial cystitis. Approximately 1% to 2% of cats in the United States are affected with lower urinary tract disease. In 50% to 70% of these cats that are less than 10 years of age, no definable cause can be found. In cats older than 10 years of age, IFLUTD is diagnosed in approximately 5% of the cases. Therefore, a thorough diagnostic workup should identify a primary disease in the older cats. IFLUTD can be associated with urethral obstruction, particularly in male cats. For information on diagnosis and treatment of urethral obstruction, see Chapter 81. The following discussion will emphasize non-obstructive IFLUTD.

Etiology

- The cause of IFLUTD is not known, but possibilities include viral cystitis, neurogenic inflammation, abnormal glycosaminoglycans lining the urinary bladder mucosa, unidentified bacterial infection, and mast cell–related disease.
- Since the cause of IFLUTD has not been identified, expect a variable clinical course.
- Activation of the sympathetic nervous system with enhanced norepinephrine outflow from the central nervous system appears to be a major factor in enhancing or activating inflammatory lesions. Enhanced sympathetic nervous system outflow at a time of suboptimal activation of glucocorticoids seems to be important in these cats. Studies documenting smaller adrenal glands in affected cats and a reduced response to adrenocorticotropic hormone during stress are supportive of this.
- Increased norepinephrine actively up-regulates the inflammatory response in the bladder, increases pain perception, increases mast cell degranulation, and increases detrusor muscle contraction. This may also change permeability of the bladder by effects on the mucosa.

Clinical Signs

- Clinical signs associated with IFLUTD include hematuria, dysuria, pollakiuria, and inappropriate urination, which often resolve spontaneously after 5 to 7 days. However, in some cats, signs may last for weeks or may wax and wane chronically.
- Urethral obstruction may occur in male cats (see Chapter 81).

▼ ***Key Point*** The clinical signs of IFLUTD can be identical to those seen with a bacterial UTI. UTI is rare in younger cats.

Diagnosis

- *History:* Clinical signs may be observed for a period of days before the cat is examined. There may or may not be a previous history of lower urinary tract disease.
- *Physical examination:* If urethral obstruction is absent, the urinary bladder will be small on palpation and may be painful.
- *Urinalysis and urine culture:* Hematuria and proteinuria are common, although pyuria is not a common finding. These findings can be episodic. Urine culture is negative. Crystalluria, if present, has little significance in the pathophysiology of the disease if urinary obstruction is not present.
- *CBC and serum chemistries:* These tests are normal.
- *Radiography and ultrasonography:* A small urinary bladder is observed on survey radiography. Contrast radiography and ultrasonography (see Chapter 4) may be normal or may reveal a thickened bladder wall. No uroliths or diverticula are identified.
- *Cystoscopy:* The hallmarks of IFLUTD are varying combinations of mucosal edema, glomerulations, and increased vascularity. Cystoscopy is valuable for ruling out other causes of lower urinary tract signs in cats with chronic or recurrent problems.

Treatment

Specific Treatment

- No specific treatment recommendations can be made because the cause of IFLUTD is unknown. There are few proven effective treatments for IFLUTD.
- Antibiotics are not warranted without evidence of bacterial cystitis (see previous discussion). In two placebo-controlled studies, antibiotics administered to cats with non-obstructive IFLUTD were no more effective than a placebo.
- Glucocorticoids administered to cats with IFLUTD have also not been more effective than placebo and therefore are not indicated.

Symptomatic Treatment

Environment

- Environmental enrichment may decrease baseline anxiety levels in cats prone to episodes of IFLUTD (see the Indoor Cat Initiative website for more information: http://www.indoorcat.org/index.php).
- One study of affected cats has shown an 80% decrease in recurrence of IFLUTD in cats given environmen-

tal enrichment relative to a control group whose environment was not changed.
- Providing both stimulation (e.g., toys and accessible windows to look outside) and safe areas (e.g., away from other pets and children) may be important in affected cats.

Diet and Water Intake

Increasing water intake encourages more frequent voiding. The dilution of urine may reduce noxious substances within the urine.

- Transition from dry to as much canned food as the cat will accept or add liquids (e.g., water, broth, or tuna juice) to the dry kibble.

▼ ***Key Point*** Transitioning to canned food may be the single most effective treatment of IFLUTD.

- Provide access to fresh water at all times.
  - Experiment with water bowl type, number, and location. Some cats prefer drinking from glasses rather than bowls. Most cats prefer a water container that is filled to the top.
  - Adding broth to the water bowl for flavoring may encourage water consumption.
  - Many cats prefer running water to standing water. Addition of a commercial pet fountain or a dripping faucet may encourage increased water intake.

Medical Therapy

Acute Crisis

- *Sedation or antianxiety:* Stress, or inability to cope with normal stressors, is thought to play an important role in this condition. For this reason, minimizing stress is essential in management of both acute and chronic recurrence of IFLUTD. In general, we recommend administering medications to relieve anxiety or sedatives in hospitalized patients as often as is necessary to produce visible sedation (e.g., presence of raised third eyelids in patients given acepromazine). This degree of sedation should only be necessary to control an acute episode and is not desired in patients once they are home.
  - Acepromazine (0.05–0.1 mg/kg SC q4–6h) may help reduce stress.
  - Because of the risk of acute hepatic necrosis, oral diazepam is no longer recommended in cats. In hospitalized animals, consider intravenous diazepam or intramuscular midazolam to provide sedation.
- *Analgesia:* Regardless of the underlying cause of IFLUTD, the inflammation in the bladder causes pain similar to that of any lower urinary tract inflammation. We recommend combining the antianxiety medications mentioned above with analgesics until clinical signs of cystitis resolve.
  - Butorphanol (Torbugesic) (0.2–0.4 mg/kg SC or PO q4–6h) or buprenorphine (Buprenex) (0.005–0.01 mg/kg SC or PO q6–8h) can be used. Buprenorphine may be preferable because of its prolonged duration of action (see Chapter 6).
- *Antispasmodics:* Although usually unnecessary, these drugs may be of benefit in refractory cases or in male cats for which obstruction is a concern. Options for antispasmodics include propantheline bromide (0.2–0.4 mg/kg PO q12–24h) and oxybutynin (0.5–1.0 mg/cat PO q8–12h).

Chronic Therapy

- Behavior modifying drugs such as amitriptyline, clomipramine (Clomicalm), and buspirone (Buspar) may be of benefit in cats whose signs are not controlled with environmental enrichment and increased water intake.
  - Tricyclic antidepressants (TCAs) may have powerful analgesic and anti-inflammatory effects.
  - Although results may be seen quickly, a minimum of 2 to 3 months of therapy is needed to decide if these drugs are helpful or not.
  - Never suddenly discontinue therapy with TCAs. Taper the drug slowly over 3 to 4 weeks.
- Glycosaminoglycan supplementation has been investigated, and no effect over placebo has been demonstrated.
- Anecdotal evidence suggests that pheromone therapy (e.g., Feliway) may be effective in some cases. This is most likely to be helpful in combination with environmental and dietary changes.

Prevention

The recommendations for treatment of IFLUTD (environmental enrichment, increased water intake, medical therapy) are the same as those for prevention. In general, we recommend trying environmental and dietary changes prior to chronic medical therapy, but in some refractory cases, medical management is needed.

POLYPOID CYSTITIS

Etiology

Polyps may be observed in animals with chronic urinary bladder disease. By definition, polypoid cystitis is a benign condition, but it must be differentiated from malignant neoplasia. Polyps typically represent an inflammatory response to an underlying condition such as chronic bacterial UTI or urolithiasis.

Clinical Signs

- Polyps may be subclinical or they may cause hematuria, dysuria, and pollakiuria.
- As with other inflammatory diseases of the lower urinary tract, they may cause inappropriate urination.

Diagnosis

- *History:* There may be a history of UTI because polyps are one cause of relapsing infection.
- *Physical examination:* This is usually normal. Check for evidence of neoplasia by doing careful abdominal and rectal palpation.
- *Urinalysis and urine culture:* Hematuria, pyuria, and bacteriuria are often observed. Urine cultures are usually positive.
- *CBC and serum chemistries:* These tests are usually normal.
- *Radiography and ultrasonography:* Survey radiography is usually normal unless radiodense uroliths are present. Contrast radiography and ultrasonography reveal the polyps associated with the bladder wall.
- *Cystoscopy:* Cystoscopy allows direct examination of the bladder mucosa. The endoscopic appearance of the polyps is typically different from that of malignancies, but obtain tissue samples for biopsies at the time of cystoscopy to confirm this.

Treatment

Treatment of the underlying disease sometimes results in resolution of the polyps if they are inflammatory in origin.

- It may be impossible to effectively treat an underlying UTI until the polyps are removed.
- Surgical excision is indicated if the polyps persist. Partial cystectomy or submucosal excision of the urinary bladder mucosa is indicated (see Chapter 80). Depending on the extent of the mucosal excision, reepithelization of the bladder lumen is complete between 10 and 28 days.
- Prevention of inflammatory polyps is dependent upon preventing the primary disease.

CYCLOPHOSPHAMIDE-INDUCED HEMORRHAGIC CYSTITIS

Etiology

Cyclophosphamide is an alkylating agent used frequently in the treatment of neoplasia (especially lymphoma) and occasionally in the treatment of immune-mediated diseases (see Chapter 26). Acrolein, a metabolite of cyclophosphamide that is excreted in urine, causes mucosal ulceration, necrosis of smooth muscle and small arteries, hemorrhage, and edema in some cases. The resulting sterile hemorrhagic cystitis can occur after months of treatment but has also been reported after a single dose.

Clinical Signs

The pollakiuria and stranguria that are seen are similar to other inflammatory diseases, but the degree of hematuria may be much more pronounced than in a typical UTI. Frank blood in the urine is often reported.

Diagnosis

- *Physical examination:* Pain may be elicited on bladder palpation. Blood or blood-tinged urine may be seen in the perivulvar or preputial areas.
- *Urinalysis and urine culture:* Hematuria, sometimes severe, is present; mild to moderate pyuria may be present. As indicated by the name *sterile hemorrhagic cystitis,* urine culture is usually negative.
- *CBC and serum chemistries:* These values are normal unless bone marrow suppression has occurred due to chemotherapy or unless changes secondary to the neoplasia are present.
- *Radiography and ultrasonography:* Radiographic changes will be similar to those seen with other causes of cystitis. The bladder may be small because of frequent voiding and may have thickened walls. Contrast radiography and ultrasonography reveal irregular mucosa. Blood clots may be present within the bladder lumen.

Treatment

- Discontinue administration of cyclophosphamide immediately.
- Inducing diuresis appears to be the only effective means of treating cyclophosphamide-induced cystitis, although serious necrosis and fibrosis may still occur.
- Systemic anti-inflammatory therapy has not been shown to be effective, although analgesia may help relieve some symptoms of inflammation. One report in the human literature showed resolution of clinical signs with pentosan polysulfate, a synthetic glycosaminoglycan. In this case, continuation of cyclophosphamide therapy was possible with continued use of the pentosan polysulfate.
- Infusion of dimethyl sulfoxide and formalin in the bladder has reportedly been effective, but these treatments have not been critically evaluated.

Prevention

- Once sterile hemorrhagic cystitis has occurred, the affected patient should never receive cyclophosphamide again.
- Another alkylating agent (typically chlorambucil) should be substituted if needed for continued chemotherapy or immunosuppressive therapy.
- Minimizing contact time of the acrolein with the bladder is the easiest way to prevent this complication from occurring. Administer the drug in the morning, counsel owners to take the animal out to void frequently, and encourage increased water intake (giving canned food or adding water to food).
- A recent report indicates that concurrent administration of furosemide with cyclophosphamide

decreases the risk of sterile hemorrhagic cystitis. This is likely due to furosemide-induced diuresis and may be a viable alternative to encouraging increased water consumption. Diuresis through parenteral fluid therapy is generally not needed, although it would be an effective preventative measure.

- The drug Mesna was designed to react with the acrolein in the urine, thus preventing hemorrhagic cystitis. This drug is highly effective and is routinely used in humans. It has been used safely in dogs, although infrequently because it is cost prohibitive in most cases.

URINARY BLADDER NEOPLASIA

Etiology

Neoplasms of the urinary bladder are the most frequently identified urinary tract tumor in dogs, but they account for <1% of all canine neoplasms. Bladder neoplasia is rare in cats. Bladder neoplasms tend to occur in older animals and are more frequently observed in female than in male dogs.

- The most common neoplasm of the urinary bladder is transitional cell carcinoma (TCC), a malignant epithelial tumor. Neoplasms of other types including lymphomas, fibromas, rhabdomyosarcomas, papillomas, squamous cell carcinoma, and adenocarcinomas occur less frequently.
- Rhabdomyosarcomas, although rare, are unique in their tendency to occur in younger animals (<2 years of age).
- For TCC, breed predisposition is most notable in Scottish terriers, but it is also reported in Shetland sheepdogs, collies, Airedales, and beagles. German shepherds are thought to be at reduced risk for the formation of bladder neoplasia. No breed predisposition is noted in cats.
- Previous exposure to certain lawn treatments (herbicides) and cyclophosphamide are shown to increase the risk of transitional cell carcinoma.

Clinical Signs

- Regardless of tumor type, clinical signs are similar and include hematuria, pollakiuria, and stranguria.
- Animals may not show any clinical signs in the early stages of the disease. Approximately two-thirds of bladder tumors involve the trigone region. Urethral or ureteral obstruction may occur, resulting in uremia.

▼ ***Key Point*** Bladder neoplasia is difficult to distinguish from other common urinary tract diseases such as infection or urinary calculi based on clinical signs alone.

Diagnosis

▼ ***Key Point*** Suspect bladder neoplasia in middle-aged and older dogs that present for hematuria or chronic or recurrent UTI.

- *Physical examination:* If large enough, the bladder tumor may be palpated. Perform rectal examination in all dogs with signs of urinary tract disease. This is particularly important in older dogs because extension of the mass into the urethra may be palpable. A large bladder, if the urethra is obstructed, or a large kidney, if a ureter is obstructed, may be palpated. In more advanced disease, cancer cachexia may be present. If lameness is present, consider associated hypertrophic osteopathy or bone metastasis.
- *Urinalysis and urine culture:* Hematuria and pyuria are common findings on evaluating the urine sediment. Often neoplastic cells may be observed in the urine sediment when examined by experienced personnel. Secondary UTIs are common with bladder tumors because of the inflammation and disruption of the normal mucosa that occur with neoplasia.

▼ ***Key Point*** If neoplasia is suspected, use catheterization or a voided sample instead of cystocentesis to collect urine. Cystocentesis and fine-needle aspirate of bladder masses can lead to seeding of the abdomen and skin with neoplastic cells. Ultrasonography of the bladder may be used to rule out neoplasia, making it safer to perform cystocentesis if necessary.

- *CBC and serum chemistries:* Usually normal. A mild normocytic, normochromic anemia consistent with chronic disease may be present. Azotemia may be present if the urethra or both ureters are obstructed.
- *Radiography and ultrasonography:* Survey radiography may be normal, although a large urinary bladder or a large kidney may be observed if there is urethral or ureteral obstruction secondary to the tumor. Sublumbar lymphadenopathy may be observed in cases of metastasis or severe local inflammation. Contrast cystography or ultrasonography is indicated if a tumor is suspected and survey radiographs appear normal (see Chapter 4). Lesions are most often seen as a mass or thickening in the bladder trigone. The proximal urethra is often affected as well.
- *Bladder biopsy:* Perform biopsy of the bladder mass by cystoscopy or laparotomy. Laparotomy may be the best option if resection or debulking of the mass is thought to be possible (see Chapter 80).
- *Bladder tumor antigen test:* The BTA stat test and V-BTA test (Polymedco) are urine tests designed to screen for the presence of bladder tumor antigen. Although these have a very high negative predictive value (98.6%), their positive predictive value is poor

(31%). False positives can be caused by proteinuria, pyuria, hematuria, and glucosuria, making this a poor test to distinguish neoplasia from other causes of lower urinary tract inflammation. Negative test results appear to be of value to help rule out neoplasia.

- *Traumatic catheterization:* If cystoscopy is not available to obtain a biopsy sample, tissue samples may be obtained via traumatic catheterization. Under heavy sedation with analgesia or general anesthesia, pass the largest urinary catheter possible through the urethra. Once urine is obtained, controlled, rapid movement of the catheter back and forth within the proximal urethra and bladder neck with suction will often produce small pieces of tissue that can be submitted for biopsy. Even if tissue samples are not large, neoplastic cells may be present in the sediment that will allow cytologic confirmation of neoplasia.

Treatment

- The long-term prognosis for most animals with bladder neoplasia is poor.
- Surgical excision is the treatment of choice for benign tumors and for malignant tumors that are not extensive and do not involve the trigone (see Chapter 80). Unfortunately, many bladder malignancies, especially transitional cell carcinoma, are found within the trigone, ureters, and/or urethra, making complete surgical resection difficult or impossible.
- Experience with urethrocystoscopy suggests that transitional cell carcinoma tumors are often found in multiple locations in the bladder and urethra even when only one mass is identified with contrast cystography or ultrasound.
- Transitional cell carcinomas do not respond well to most chemotherapy drugs. Administer piroxicam (0.3 mg/kg PO q48h for dogs; dosage undetermined for cats) in all cases both for its analgesic and for its antitumor properties.
- Neoplasms that are responsive to chemotherapy, such as lymphoma, should be treated accordingly (see Chapter 27).
- Investigation of intravesical infusion of chemotherapeutic agents is ongoing and may prove to be a viable treatment option.
- If urethral obstruction occurs, but the animal's quality of life is otherwise good, place a cystotomy tube to allow voiding (see Chapter 80). Monitoring for and treatment of secondary UTIs is an important component of therapy.

Prevention

Given recent evidence connecting herbicide exposure and transitional cell carcinoma, minimize contact with herbicide-treated lawns, particularly in predisposed breeds (e.g., Scottish terrier). In older animals, particularly female dogs, that have persistent or recurrent hematuria or UTI, perform a thorough diagnostic workup early in the course of disease.

BLADDER TRAUMA

Etiology

- The urinary bladder may be damaged or ruptured by any form of blunt or penetrating trauma.
- Acute or chronic bladder diseases, such as urolithiasis or urethral obstruction, may predispose the bladder to rupture.
- Iatrogenic trauma to the urinary bladder may occur secondary to problems with urethral catheterization or cystocentesis.

Clinical Signs

- Clinical signs may initially be limited to those of lower urinary tract inflammation such as hematuria, dysuria, and stranguria.
- Clinical signs of systemic illness (e.g., uremia and anuria) may be present if the bladder ruptures and urine leakage into the peritoneal cavity occurs.
- Bladder trauma can also occur as a result of displacement or entrapment, as in a perineal hernia. Investigate any abnormal swelling or protrusion in the area of perineum.

▼ ***Key Point*** Ability to urinate normally does not rule out a ruptured bladder.

Diagnosis

- *Physical examination:* Abdominal or inguinal bruising may be evident. Pain may be elicited on abdominal palpation. Fractures and other organ injury may be present. Perform rectal examination to help identify pelvic injury. Abdominal distention due to uroabdomen may be found. Even a ruptured bladder may be palpable, and ureteral rupture or small tears in the urinary bladder may still lead to uroabdomen or uroretroperitoneum. Examine the perineal area carefully as part of the physical exam for evidence of a perineal hernia (see Chapter 74).
- *Urinalysis and urine culture:* If urine can be collected, it may be hemorrhagic and may contain white blood cells. White blood cells may also be present secondary to urine in the peritoneal cavity if the sample is drawn from the abdomen rather than the bladder.
- *CBC and serum chemistries:* In cases of uroabdomen, initially all values related to the urinary system may be normal. Creatine phosphokinase and liver enzymes may be increased secondary to muscle and/or liver damage from trauma. Hyperkalemia is typically a late finding seen 2 to 4 days after uroabdomen develops. Azotemia typically takes 24 to 36 hours to develop with BUN increasing prior to crea-

tinine, although pre-renal azotemia secondary to hypovolemic or distributive shock may occur earlier than this. Hyperphosphatemia and metabolic acidosis due to uroabdomen occur after BUN and creatinine increase, although these may increase initially due to tissue trauma and shock (distributional or hypovolemic), respectively.

- *Radiography and ultrasonography:* On survey radiographs, the bladder may be small, may be present in the perineal region if herniated, or may not be visible. Abdominal fluid may be identified. Positive contrast cystography is the imaging procedure of choice for diagnosis of a ruptured bladder; perform this in all patients with pelvic fractures or a high index of suspicion for bladder rupture (see Chapter 4). Intravenous pyelography may be needed to identify ureteral rupture (see Chapter 4).
- *Abdominocentesis:* If abdominal fluid is present, perform abdominocentesis (see Chapter 3) and, along with blood samples, submit the fluid for biochemical analysis. The urea nitrogen and creatinine concentration of the abdominal fluid should then be compared with plasma to diagnose uroabdomen.

▼ ***Key Point*** The creatinine concentration will be higher in abdominal fluid than in blood if the fluid is urine. The concentration of BUN may be similar in fluid compared to plasma because smaller molecular size allows it to equilibrate more quickly than creatinine.

Treatment

- If a small rupture has occurred evidenced by minimal leakage on a positive contrast cystogram, place a urethral catheter and connect to a closed collection system for 3 to 7 days. Repeat the cystogram to confirm healing of the rent.
- If a large rupture has occurred, perform surgical repair (see Chapter 80).

Prevention

Iatrogenic trauma to the bladder is the only preventable form of bladder trauma.

- Use soft polyvinyl or Silastic catheters rather than rigid polypropylene catheters. Always lubricate the catheter well and pass the catheter slowly to minimize catheter-induced trauma. If rigid catheters are used for initial catheterization (as in blocked cats), replace them with softer catheters for indwelling use.
- If catheterization is difficult, consider flushing the catheter with sterile saline and/or water-soluble lubricant as the catheter is passed to help distend the urethra. Never force a catheter if an obstruction is encountered.
- Measure catheters prior to insertion to approximate the bladder location. Minimal advancement should be necessary once urine is observed to flow through the catheter.
- Obtain survey radiographs if there is any question about appropriate catheter placement.
- Although cystocentesis is an important diagnostic tool in veterinary medicine, it can result in bladder trauma. As with any technique, use adequate chemical or physical restraint to allow the urine sampling with minimal patient movement.
- If the bladder is friable and more susceptible to trauma (e.g., emphysematous cystitis), use extreme care in performing catheterization or cystocentesis and warn owners of the risk of bladder trauma.

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Chapter 80

Surgery of the Urinary Bladder

Gretchen K. Sicard / Roger B. Fingland

Cystotomy is the most common surgical procedure of the urinary bladder in small animals and is commonly performed for removal of urinary calculi. Subtotal or total cystectomy may be indicated for management of benign or malignant urinary bladder neoplasia. The incised bladder wall heals quickly and regains nearly 100% of original tissue strength after healing. The mucosal lining of the bladder is quite delicate and easily becomes edematous, necessitating meticulous tissue handling and proper suture placement.

ANATOMY

- The urinary bladder is divided into three regions: (1) the cranial portion is the apex, (2) the caudal portion that joins the urethra is the neck, and (3) the segment between the apex and neck is the body.
- The ureteral openings and the urethral orifice form a triangular area on the dorsal aspect of the bladder called the trigone.
- The three ligaments of the bladder are composed of double layers of peritoneum. The ventral ligament extends from the ventral surface of the bladder along the ventral midline of the abdominal wall to the umbilicus. The ventral peritoneal ligament contains the urachus in the fetus. The urachus is an embryologic structure that connects the urinary bladder and the allantoic sac. The urachus closes and atrophies soon after birth, leaving a small scar at the apex of the urinary bladder. The lateral ligaments connect the lateral aspects of the bladder to the pelvic canal and enclose the ureters, deferent ducts, and umbilical arteries.
- The major blood supply to the bladder comes from the caudal vesical artery, a branch of the internal pudendal artery that lies in the pelvic fascia. The cranial vesical artery, present in only 50% of adult dogs, supplies the cranial aspect of the bladder. Venous blood drains into the internal pudendal veins. Bladder lymphatics drain into the hypogastric, sublumbar, and median iliac lymph nodes.
- Sympathetic innervation to the bladder is via the hypogastric nerve, and parasympathetic innervation is via the pelvic nerves. The hypogastric and pelvic nerves reach the bladder through the lateral ligaments near the caudal vesical arteries.

ANOMALIES OF THE URACHUS

Preoperative Considerations

- Persistent urachus results when the entire urachal canal remains patent after birth. Urine is voided through the urachal opening at the umbilicus. Treatment consists of surgical excision of the entire urachal tube.
- Vesicourachal diverticulum results when the origin of the urachus at the bladder apex fails to close. The diverticulum forms a pocket of urine, predisposing the animal to recurrent bacterial urinary tract infections (UTIs).
- Vesicourachal diverticula may be diagnosed by contrast radiography or uroendoscopy. Diverticulectomy is indicated in animals with persistent UTI. Urachal scars commonly are observed at the dome of the bladder and seldom cause a problem. In contrast to a urachal scar, a diverticulum is a discrete pouch or sac that opens into the bladder lumen.
- Urachal cysts and urachal sinuses are uncommon urachal anomalies in small animals.

Surgical Procedure—Persistent Urachus

Objectives

- Remove the patent urachus.
- Obtain specimens for bacterial culture and histopathologic analysis.

Equipment

- Standard general surgery instrument pack and suture
- Balfour retractor
- Laparotomy sponges

Technique

1. Place the animal in dorsal recumbency.
2. Prepare the ventral abdominal region for aseptic surgery.

3. Perform a routine ventral midline celiotomy from approximately 3-cm cranial to 3-cm caudal to the umbilicus.
4. Make an elliptical incision around the umbilical opening. Dissect the urachus from the surrounding tissues.
5. Place a Balfour retractor and isolate the urinary bladder with moistened laparotomy sponges.
6. Place stay sutures in the bladder to facilitate retraction.
7. Create a full-thickness elliptical incision in the apex of the bladder around the origin of the patent urachus.
8. Submit the patent urachus for histologic analysis.

▼ ***Key Point*** Resect the entire urachus. Simply ligating the urachus at the bladder apex may result in a vesicourachal diverticulum, which can predispose the animal to persistent UTI.

9. Submit samples of the excised vesicourachal junction for bacterial culture and susceptibility testing.
10. Remove the stay sutures and laparotomy sponges. Close the bladder as described under "Cystotomy," "Technique."
11. Close the abdominal wall routinely.

Postoperative Care and Complications

- Postoperative complications are rare.
- Administer antibiotics based on the results of bacterial culture and susceptibility testing. Prolonged (>4 weeks) antibiotic therapy may be necessary to reduce the risk of recurrent UTI.
- See "Cystotomy," "Postoperative Care and Complications," for routine patient care.

Surgical Procedure—Vesicourachal Diverticulum Excision

Objectives

- Remove the vesicourachal diverticulum.
- Obtain samples for bacterial culture and susceptibility testing and histopathologic analysis.

Equipment

- Standard general surgery instrument pack and suture
- Balfour retractor
- Laparotomy sponges

Technique

1. Patient positioning and surgical approach are the same as those described under Persistent Urachus.
2. Do not make an elliptical incision around the umbilicus; instead, use the approach recommended for cystotomy.
3. Isolate the urinary bladder with moistened laparotomy sponges.
4. Place stay sutures to facilitate retraction.
5. Make a full-thickness elliptical incision in the bladder wall around and approximately 5 mm from the edge of the diverticulum.
6. Submit samples for histologic analysis and bacterial culture and susceptibility testing.
7. Remove stay sutures.
8. Close the bladder as described under "Cystotomy," "Technique."
9. Remove the laparotomy sponges, and close the abdominal incision routinely.

Postoperative Care and Complications

- Postoperative complications are rare. Recurrent infections after removal of the diverticulum are uncommon.
- Administer antibiotics based on the results of bacterial culture and susceptibility testing. Prolonged antibiotic therapy (>4 weeks) may be necessary. Reevaluate bacterial culture of the urine 1 week following the completion of antibiotic therapy.
- See "Cystotomy," "Postoperative Care and Complications," for routine patient care.

CYSTOTOMY

Preoperative Considerations

- Cystotomy in small animals is indicated most commonly for removal of cystic calculi.
- Neoplasia of the urinary bladder, polypoid cystitis, surgery involving the ureteral orifice(s) including neoureterostomy, and ureteral transposition require cystotomy.
- Antibiotics are not administered preoperatively unless prior urine culture indicates UTI. Otherwise, administer antibiotics intraoperatively after specimens for culture and susceptibility testing have been obtained.

Surgical Procedure

Objectives

- Open the urinary bladder to remove calculi, reimplant ureters, or explore the bladder lumen.
- Obtain samples for bacterial culture and susceptibility testing and histopathologic analysis.
- Prevent urine leakage into the peritoneal cavity.

Equipment

- Standard general surgery pack and suture
- Balfour retractor
- Laparotomy sponges
- Urinary catheter (male dogs)
- Human gallbladder scoop or sterile teaspoon to aid in stone removal
- 12-ml syringe

- 22-gauge needle
- Soft urethral catheter for patients with cystic calculi

Technique

1. Place the animal in dorsal recumbency.
2. Prepare the ventral abdominal region and vulvar or preputial area for aseptic surgery. Irrigate the prepuce with antiseptic solution and include it in the aseptic field to enable intraoperative urethral catheterization, if necessary.
3. Incise the skin and subcutaneous tissue on the ventral abdominal midline.
4. In male dogs, incise the skin and subcutaneous tissue parallel and adjacent to the prepuce. Identify and ligate the preputial branches of the caudal superficial epigastric vessels in the subcutis.
5. Incise the linea alba from the umbilicus to the pubis. (Incise from xyphoid to pubis if a full abdominal exploratory is necessary.) The paramedian approach can be used in male dogs.
6. Position the Balfour retractor. Explore the abdomen for associated abnormalities of the kidneys, ureters, prostate, urethra, and iliac lymph nodes.
7. Isolate the urinary bladder with moistened laparotomy sponges.
8. Place stay sutures at each end of the proposed cystotomy incision to facilitate retraction and atraumatic manipulation (Fig. 80-1*A*).
9. Remove urine from the bladder by cystocentesis.
10. Orient the cystotomy incision to avoid major vessels and provide optimal exposure for the procedure. A ventral incision is preferred for routine cystotomy and for exposure of the ureteral openings.

▼ ***Key Point*** A ventral cystotomy incision has no greater risk of leakage or adhesion formation than does a dorsal incision. In addition, the ureters are located well away from the ventral region, reducing inadvertent damage.

11. Plan the cystotomy incision to remove a vesicourachal diverticulum, if present.
12. Make a stab incision into the bladder with a scalpel (Fig. 80-1*B*).
13. Extend the incision proximally and distally with Metzenbaum scissors, avoiding the trigone and ureters.
14. Remove uroliths with the gallbladder scoop or sterile teaspoon.

▼ ***Key Point*** Always submit uroliths to the laboratory for stone analysis.

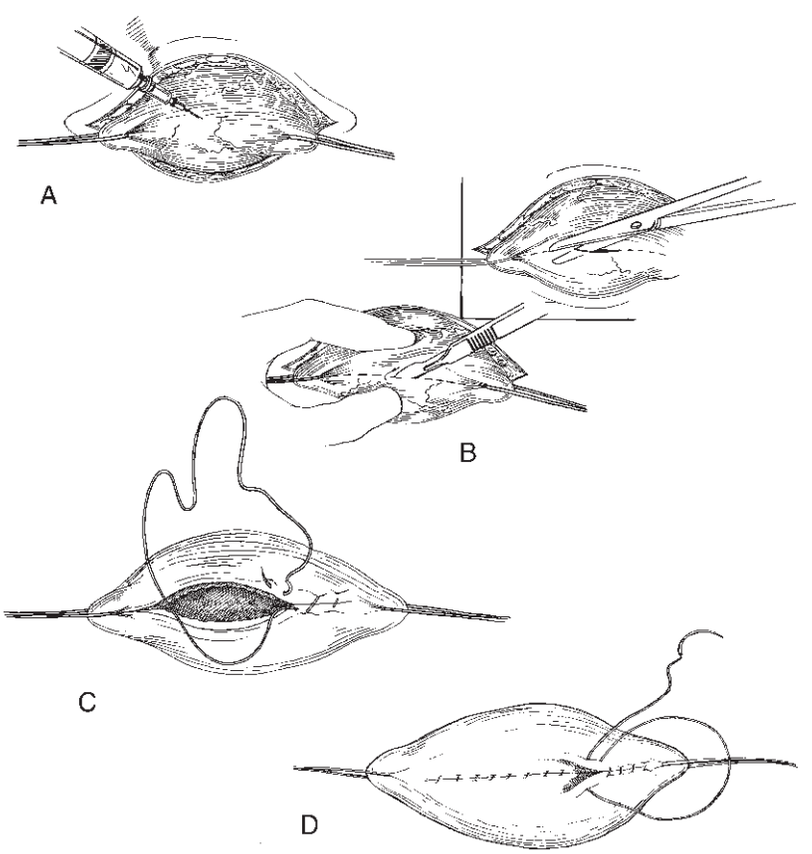

Figure 80-1. Cystotomy. *A,* With stay sutures in place, remove urine from bladder. *B,* Make stab incision with scalpel and extend with Metzenbaum scissors. *C,* After uroliths are removed and biopsy samples taken, place a Cushing pattern incorporating all tissue layers except the mucosa. *D,* Oversew the Cushing pattern with a Lembert pattern. If the bladder wall is inflamed or thickened, an appositional pattern may be used for closure.

15. Retrograde flushing may be required to remove small calculi from the proximal urethra in male dogs. Pass a sterile urinary catheter retrograde (from outside the penis) to the level of the os penis, occlude the end of the penis, and flush vigorously with sterile saline.
16. Pass a urinary catheter, both retrograde and antegrade, throughout the entire length of the urethra and feel for grit or roughness.
17. Do not close the bladder until all stones have been removed.
18. Incise a 4-mm × 1-cm full-thickness wedge of bladder wall from the edge of the cystotomy incision.
19. Submit half the wedge for histopathologic analysis and half for bacterial culture and susceptibility testing.

▼ ***Key Point*** If the animal has been on antibiotics, submit a full-thickness wedge of bladder wall for bacterial culture and susceptibility testing even if urine has been submitted for culture.

20. Remove stay sutures, and close the cystotomy (see subsequent description).

▼ ***Key Point*** Avoid incorporating the ureters in the bladder closure, especially with dorsal incisions.

21. Remove laparotomy sponges, and close the abdominal wall routinely.

Classically, cystotomy incisions are closed with a two-layer continuous inverting pattern. Synthetic absorbable suture material (3-0 to 4-0) with a swaged-on urogenital tapered needle is an ideal choice. A Cushing pattern, incorporating all tissue layers except the mucosa, is used for the first layer, followed by a Lembert pattern (Fig. 80-1 *C* and *D*).

The bladder wall may be quite thick in animals with chronic cystitis, making inversion of the wall difficult. In this situation, choose single-layer or double-layer continuous or interrupted appositional suture patterns. An appositional pattern is necessary when the cystotomy incision extends so far distally that inversion might result in occlusion of the ureters or narrowing of the urethra.

▼ ***Key Point*** The holding layer of the bladder is the submucosa.

Postoperative Care and Complications

- Hematuria for 12 to 36 hours after surgery is common.
- A transurethral catheter can be placed during surgery if necessary to maintain decompression of the bladder or to monitor urinary output. Connect to a closed collection system.
- Administer long-term (>4 weeks) antibiotic therapy based on results of bacterial culture and susceptibility testing. Based on the results of stone analysis dietary therapy may be indicated to medically manage animals with urolithiasis (see Chapter 79).
- Although rare, urine leakage from inadequate bladder closure may occur, particularly if obstruction develops distally. Monitor urine output.
- Observe for stranguria, which may occur secondary to inflammation.
- If multiple radiopaque stones were present, obtain abdominal radiographs after surgery to confirm complete stone removal.

BLADDER TRAUMA

Preoperative Considerations

- See Chapter 79, Diseases of the Urinary Bladder, for a discussion of etiology, pathophysiology, clinical signs, laboratory abnormalities, and diagnosis of ruptured bladder.
- Contusions, partial-thickness lacerations, and iatrogenic ruptures during catheterization usually heal spontaneously and are managed medically. Consider urinary diversion (transurethral catheterization or tube cystostomy) until healing is complete.
- Rupture of the urinary bladder may heal spontaneously; however, this outcome is inconsistent and unpredictable. Surgical repair is the treatment of choice.

▼ ***Key Point*** Fluid, electrolyte, and acid-base disorders (dehydration, hyperkalemia, acidosis, azotemia) must be managed prior to anesthetizing an animal for repair of a ruptured bladder.

- Animals with a ruptured bladder that cannot be anesthetized because of fluid, electrolyte, and acid-base abnormalities may be treated initially by temporary urinary diversion. Place a peritoneal dialysis catheter to drain urine from the peritoneal cavity (see Chapter 3). In addition, place a transurethral catheter to decrease the amount of urine leaking from the bladder into the abdominal cavity.
- Administer intravenous fluid therapy with isotonic saline and antibiotics. Also give sodium bicarbonate if necessary for acidosis.

Surgical Procedure

Objective

- Remove urine from the peritoneal cavity.
- Repair the ruptured bladder.
- Identify and treat other intra-abdominal injuries.

Equipment

- Standard general surgery instrument pack and suture
- Balfour retractor
- Laparotomy pads
- Suction device
- Foley catheter (if tube cystostomy is indicated).

Technique

1. Place the animal in dorsal recumbency.
2. Prepare the ventral abdominal region for aseptic surgery.
3. Perform a routine ventral midline celiotomy from the umbilicus to the pubis.
4. Perform an abdominal exploratory.
5. Isolate the urinary bladder with moistened laparotomy sponges.
6. Locate the rupture in the urinary bladder.
7. Place stay sutures to facilitate exposure of the rupture.
8. Liberally debride non-viable tissue from the edges of the rent.
9. Approximate the viable edges of the rent with 3-0 synthetic absorbable suture material using an inverting or approximating suture pattern.
10. Remove the stay sutures.
11. When the viability of the bladder wall is questionable, resect the non-viable region if possible. Alternatively, cover the area with omentum or a jejunal serosal patch.
12. Manage other intra-abdominal injuries.
13. Lavage the peritoneal cavity with copious amounts of warm, sterile, physiologic saline solution.
14. Remove residual abdominal fluid.
15. Submit samples of peritoneal fluid for bacteriologic culture and susceptibility testing.
16. Consider placing a sterile transurethral catheter to keep the bladder decompressed if the repair is tenuous or the viability of the bladder wall is questionable. Urinary diversion seldom is necessary following proper repair of ruptured bladder.
17. Close the abdominal wall routinely.

Postoperative Care and Complications

- Administer broad-spectrum antibiotics in animals with extensive tissue trauma until culture and susceptibility results can be used to direct antibiotic therapy.
- The animal may be hematuric and pollakiuric for 12 to 48 hours after surgery.
- Continue to monitor and manage fluid, electrolyte, and acid-base imbalances after surgery. Monitor urine output.
- If a transurethral catheter is in place to decompress the bladder when the repair is tenuous, remove it 2 to 3 days after surgery.
- See "Cystotomy, Postoperative Care and Complications," for routine patient care.

SUBTOTAL CYSTECTOMY

Preoperative Considerations

- Subtotal cystectomy is performed most commonly in an attempt to cure or palliate an animal with bladder neoplasia. Subtotal cystectomy may be indicated to remove benign lesions, such as traumatic or congenital diverticula (see under "Anomalies of the Urachus"), polyps, intramural granulomas, and devascularized areas of bladder wall.
- Therapeutic results are related to the size and location of the bladder neoplasm and the presence or absence of metastasis. Animals with bladder neoplasia must undergo thorough diagnostic testing, including thoracic and abdominal radiography, contrast radiographic studies, and cytologic evaluation prior to surgical intervention.
- Neoplasms located in accessible areas of the bladder (apex and body) can be removed by partial cystectomy. Subtotal cystectomy may require reimplantation of the ureter(s) when there is extensive involvement of the neck or trigone of the bladder. In this situation, the type of lesion and overall prognosis must be considered prior to performing a procedure with such a high rate of morbidity.

▼ ***Key Point*** A substantial portion of the non-trigone bladder, perhaps greater than 75%, can be excised with few untoward effects.

Surgical Procedure

Objective

- Remove abnormal section of bladder wall.
- Biopsy a bladder mass.
- Maintain reservoir function of bladder.

Equipment

- Standard general surgery instrument pack and suture
- Balfour retractor
- Sterile urinary catheter

Technique

1. Patient positioning, surgical approach, and isolation of the bladder are as described previously under "Cystotomy," "Technique."
2. If neoplasia is suspected, explore the entire abdomen for metastasis. Biopsy regional lymph nodes.
3. Locate the area to be removed by gentle palpation.
4. Isolate the bladder with moistened laparotomy sponges. Seeding of tumor cells from transition cell carcinoma into the abdominal cavity or surgical incision has been reported.
5. Excise the abnormal bladder wall, including at least 1 cm of normal-appearing tissue on all sides.

6. Ureteral transplantation may be necessary. Refer to Chapter 78.
7. If neoplasia is suspected, change gloves and obtain clean instruments prior to closure of the bladder to prevent tumor seeding.
8. Close the bladder with 3-0 or 4-0 synthetic absorbable suture material in an appositional or inverting pattern (see "Cystotomy," "Technique").
9. Remove the moistened laparotomy sponges.
10. Close the abdomen routinely.

Postoperative Care and Complications

- Adjunct radiotherapy or chemotherapy may be beneficial following subtotal cystectomy for bladder neoplasia.
- Hematuria and pollakiuria are commonly observed after subtotal cystectomy.
- Frequent voiding may persist due to loss of reservoir volume.
- The reservoir function of the bladder returns, at least partially, by 3 months.
- See "Cystotomy," "Postoperative Care and Complications," for routine patient care.

TUBE CYSTOSTOMY

Preoperative Considerations

- Tube cystostomy is indicated for temporary diversion of urine from the urethra.
- Dogs with metabolic alterations resulting from obstruction to urine outflow frequently are unable to tolerate general anesthesia.
- When transureteral catheterization is not possible or desired, diversion of urine via tube cystostomy permits delay of definitive repair of urethral trauma or removal of urethral calculi until metabolic alterations are corrected.
- Tube cystostomy is a practical means of temporary urine diversion when the bladder has lost contractile function.
- A permanent cystostomy catheter can be placed to relieve urine outflow obstruction in a dog with inoperable bladder neoplasia. Relatively long-term (months) palliation can be achieved with minimal complications.
- General anesthesia usually is not needed for tube cystostomy. Narcotic analgesics, such as oxymorphone, combined with local infiltration of lidocaine or bupivacaine, are adequate.

Surgical Procedure

Objective

- Divert the flow of urine from the urethra via a Foley or de Pezzer catheter placed into the bladder.

Equipment

- Standard general surgery instrument pack and suture
- Foley catheter with intact balloon or de Pezzer catheter (recommended for long-term use)
- Small Gelpi or Weitlaner retractor

Technique

1. Administer oxymorphone, 0.1 to 0.3 mg/kg intravenously, another appropriate analgesic, or inhalant anesthesia by mask (see Chapter 2).
2. Position the animal in dorsal recumbency.
3. Prepare the ventral abdominal region for aseptic surgery.
4. Infiltrate the abdominal wall with lidocaine or bupivacaine in the area of the planned paramedian incision—in the caudal ventral abdomen approximately 3 cm lateral to the midline.
5. Make a 4-cm incision in the caudal ventral abdomen on midline. Avoid incising the distended urinary bladder. Place the self-retaining retractor.
6. Pass the Foley or de Pezzer catheter through the abdominal wall via a paramedian stab incision made adjacent to the celiotomy incision.
7. Place a pursestring suture in the wall of the bladder on the ventral side near the apex. Use 3-0 synthetic absorbable suture material with a swaged-on taper needle.
8. Pass the Foley or de Pezzer catheter into the bladder through a stab incision in the center of the pursestring suture.
9. Tighten and tie the pursestring suture. Do not occlude the catheter.
10. Inflate the balloon of the Foley catheter with sterile saline.
11. Preplace four sutures of 2-0 or 3-0 synthetic absorbable material between the bladder and the abdominal wall, where the catheter exits.
12. Secure the bladder to the body wall by tying the preplaced sutures (Fig. 80-2).
13. Close the abdominal incision routinely.
14. Secure the Foley catheter to the skin using the Chinese finger trap knot (see Chapter 3).

Postoperative Care and Complications

- The catheter can be attached to a closed sterile urine collection system (preferred) or capped and drained intermittently.
- Place an Elizabethan collar on the animal to prevent mutilation of the system.
- Deflate the balloon and withdraw the catheter when it is no longer needed. If the catheter has been in place for approximately 7 days, the stoma will heal spontaneously. Earlier removal may require surgical closure of the bladder and abdominal wall.
- A low-profile gastrostomy tube can be placed at the time of surgery, or a Foley or de Pezzer tube can be

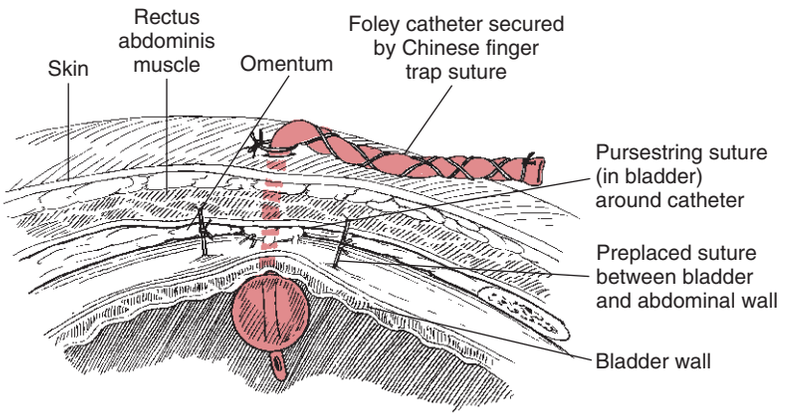

Figure 80-2. Suture and tube placement for tube cystotomy.

replaced with a low-profile tube after stoma formation. A low-profile tube can provide easier management and better cosmesis for longer-term use.

- Rarely, adhesions between the bladder and peritoneum from tube cystostomy can inhibit complete bladder emptying. Placement of the catheter in the body of the bladder rather than the apex helps prevent this problem.

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Chapter

81 Diseases of the Urethra

Hilary K. Matthews

CONGENITAL URETHRAL DISORDERS

Congenital diseases of the urethra are uncommon in both dogs and cats. The infrequency and small numbers have limited descriptions of congenital urethral diseases primarily to case reports. Puppies and kittens are often euthanized because of clinical symptoms associated with complete or partial urinary outflow obstruction or urinary or fecal incontinence before a definitive diagnosis is obtained. Many of these conditions have a poorly understood etiopathogenesis. Male puppies seem to be over represented in this class of disorders.

Etiology

- *Rectal urethral fistula* is due to incomplete division of the embryonic cloaca into the cranial ureterovesicular segment and the caudal rectal segment by the urorectal fold. This condition is thought to be heritable in the bulldog, but is thus far unproven.
- *Urethral hypoplasia* is often associated with uterine hypoplasia and vaginal aplasia with the uterine horns terminating in the dorsum of the urinary bladder. This is also called *congenital urethral sphincter mechanism incompetence*. Urinary incontinence occurs in almost all cases of this anomaly.
- *Urethral hypospadias* is often associated with pseudohermaphroditism, true hermaphroditism, in utero exposure to androgen inhibitors or estrogens, and inadequate production of androgens by the fetal testes. The result is incomplete fusion of the urethral groove resulting in the urethral opening occurring on the ventral aspect of the penis and prepuce. This defect occurs in combination with penile hypospadias and a bifid scrotum.
- *Epispadias* occurs in males and females and results in a dorsally displaced urethra.
- Other congenital urethral anomalies include urethral duplication, urethral agenesis, dilation/diverticulum of the pelvic urethra, urethral stricture and stenosis, urethral ectopia, accessory meatus, anterior or posterior urethra valves, and penile anomalies that secondarily affect the urethra such as apenia, megalopenis, and micropenis.

Clinical Signs

- In animals with a rectal urethral fistula, urine exits from the rectum, which may result in loose fecal material or diarrhea.
- Some urethral anomalies such as stricture and hypoplasia/aplasia result in signs of lower urinary tract outflow obstruction and potentially uremia.
- Other possible signs include urinary incontinence, urine scalding of the perineal region with resultant pyoderma, and persistent or recurrent urinary tract infections.

Diagnosis

- Many of the congenital urethral abnormalities are visible on physical examination or vaginal examination.
- Retrograde urethrogram or a vaginourethrogram can further locate and define the nature and extent of the abnormality. Voiding cystourethrography can also be a useful diagnostic modality (see Chapter 4).
- Vaginoscopy and urethroscopy may be useful as further defining tools. However, small patient size, and availability of an endoscope with a small diameter to provide visualization of the urethra, is sometimes a limiting factor.

Treatment

▼ ***Key Point*** Treatment of congenital urethral anomalies by surgical correction should only be attempted if the anomaly is causing clinical signs or husbandry problems.

- Correct urinary obstruction to stabilize the animal prior to additional diagnostics and treatment.
- Surgical correction of rectal urethral fistulas, hypospadias, strictures, urethral duplication, urethral dilation or diverticulum, and urethral hypoplasia can be attempted. Outcome of surgical intervention for these disorders is complicated and can be unrewarding or associated with a variety of complications, especially if not performed by a surgeon with advanced training.

- Medical treatment for incontinence may be necessary, especially in cases of urethral dilation or diverticulum formation, and urethral hypoplasia (see Chapter 83).

URETHRAL OBSTRUCTION

Etiology

- Complete or partial obstruction of the urethra is commonly encountered in veterinary practice. Almost any type of disease that affects the urethra can result in some degree of urethral obstruction. There are two classes of urethral obstruction: structural and functional.
  - *Structural urethral obstruction* is caused by anything that physically blocks the urethral lumen or compresses the urethral lumen from outside the urethra. Common examples include urethral calculi, neoplasia, mucous plugs, blood clots, and compression from external trauma to the pelvis area or lymphadenopathy. Strictures are also classified as a structural urethral obstruction. Inflammatory processes such as urethritis may result in swelling of the mucosa of the urethra that results in obstruction.
  - *Functional urethral obstruction* can be secondary to neurologic suprasacral spinal lesions, termed *reflex dyssynergia,* or may be idiopathic.

Clinical Signs

- Clinical signs are attributable to partial or complete urethral obstruction.
- With partial obstruction stranguria, pollakiuria, dysuria, hematuria, inappropriate urinations, and urine dribbling may occur.
- Complete urethral obstruction results in signs of uremia within a few days of the obstruction. The owners may note that the animal makes frequent attempts to urinate, but produces no urine.
- Functional urethral obstruction typically results in normal initiation of voiding, followed by a decrease in urine flow with the typical signs of partial urinary obstruction.

Diagnosis

Physical Examination

- On physical examination the urinary bladder may be by distended, turgid, and painful on palpation.
- It may or may not be possible to manually express the urinary bladder to determine urethral patency. Perform this procedure carefully to avoid urinary bladder rupture.
- Palpation of the urethra per rectum may reveal urethral thickening, calculi, or a mass.
- Exteriorize the penis to evaluate occlusion at the tip of the penis. Masses, calculi, and urethral plugs can be present in this location, causing obstruction, and are often overlooked on the initial examination.

▼ ***Key Point*** Carefully palpate the urethra at the base of the os penis in all male dogs as this is the most common site of urethral obstruction due to urolithiasis.

Complete Blood Count and Serum Chemistry Profile

- Blood should be submitted for a complete blood count and serum biochemical profile testing. Animals with complete urinary obstruction may have life-threatening metabolic abnormalities such as hyperkalemia, metabolic acidosis, and azotemia that require immediate attention.
- If complete obstruction has existed for approximately 2 to 3 days, signs of uremia may be present and reflected on the serum biochemical profile.

Electrocardiogram

- If the patient is bradycardic, monitor the electrocardiogram (ECG) to identify cardiac arrhythmias.

Urinalysis

- Submit a urine specimen obtained by cystocentesis for urinalysis and aerobic bacteriolgic culture.

Radiography

- Obtain abdominal radiographs including the perineal and preputial region to locate radiodense calculi in the urinary bladder or urethra.
- Consider contrast urethrography and/or urethroscopy after the patient is stable to further define the location and extent of the obstruction if necessary (see Chapter 4).

Treatment

▼ ***Key Point*** Regardless of the cause of urinary obstruction, the first step in patient treatment is stabilization.

Patient Stabilization Measures for Urinary Obstruction

- Place an indwelling intravenous catheter. Patient stabilization and treatment of metabolic abnormalities take precedence over decompression of the urinary bladder.
- Begin rehydrating the patient with a potassium-free fluid such as 0.9% NaCl until the serum potassium status is known. Animals that have complete urinary obstruction frequently have severe dehydration and

may experience hypovolemic shock. Adjust the fluid therapy to meet the patient needs.

- If bradyarrthymias and sinoatrial standstill secondary to hyperkalemia are present, use the following measures to drive the potassium back into the cells thereby lowering serum potassium:
  - Administer 0.9% NaCl. This will often normalize the serum potassium following relief of the obstruction if the serum potassium is 7 mEq/L or less.
  - Sodium bicarbonate given intravenously (IV) over 5 to 10 minutes at a dose of 0.5 to 1 mEq/kg. If necessary, then infuse an additional 1 to 2 mEq/kg slow IV over 30 to 60 minutes. This will rapidly decrease serum potassium and maintain it for several hours.
  - Consider 20% dextrose at 1 to 2 ml/kg IV over 30 to 60 minutes. This can be followed with regular insulin at 0.2 to 0.4 U/kg IV and 50% dextrose at 4 ml/unit of insulin slow IV. Dilute the 50% dextrose to a 2.5% to 5% solution.
  - Consider 10% calcium gluconate at 0.2 to 0.5 ml/kg IV over 15 minutes while monitoring an ECG to provide cardioprotective effects from the hyperkalemia. This treatment alone does not lower serum potassium; one of the above-listed treatments is additionally required.
  - Recheck serum electrolytes every 2 to 4 hours as needed.
- Provide aggressive thermal support as necessary.

Relief of the Urethral Obstruction

- After appropriate medical stabilization, place a urinary catheter to decompress the bladder and relieve the obstruction. If sedation or anesthesia is necessary for this procedure, care should be taken in drug selection as these patients are commonly volume depleted and have cardiovascular compromise.
- *Urethral hydropropulsion* is generally required to push urethral calculi back into the urinary bladder (see discussion later in this chapter). Rigid polypropylene catheters are most useful in the initial decompression of the urinary bladder, but should be replaced by softer and less reactive catheter material for indwelling use. Red rubber, Silastic, and silicone materials are superior for indwelling use. Place an Elizabethan collar on the animal after the indwelling urethral catheter has been placed and secured.
- Cats with urinary blockage due to urethral plugs or calculi do not commonly have associated urinary tract infection. Therefore, empirical use of antimicrobials in cats with urethral plugs is not warranted. Administer antimicrobial treatment if the urine culture is positive for bacteria. If urine was not obtained for culture at the time the cat was unobstructed, obtain samples for culture at the time the urinary catheter is removed. Use empirical or prophylactic antimicrobials only in cases of urinary obstruction that have clinical signs of urosepsis which are supported by findings on the urinalysis.
- Maintain a closed urinary system and measure urine output every 4 to 6 hours. Handle all connections to the urinary catheter and closed collection system in a sterile manner to prevent nosocomial infection. Measuring urine output is important since post-obstruction diuresis is common. Quantifying urine output will help determine intravenous fluid therapy dosages and alert the clinician if oliguria or anuria is a problem (see Chapter 5).
- To guard against reobstruction, maintain the indwelling urinary catheter until the animal is taken to surgery for surgical removal of the retropulsed calculi. In cases of feline urinary obstruction where a urethral plug is removed, maintain the catheter for 24 to 48 hours. Administer medications to relieve urethral spasm (acepromazine 0.05–0.1 mg/kg IM, IV, or SC q6–8h) and pain (butorphenol 0.2 mg/kg IM, IV, or SC q6–8h). If the cat can produce a good urine stream post obstruction, had not been obstructed for a prolonged period, and had minimal particulate matter flushed out of the urethra and/or bladder, an indwelling urinary catheter is not necessary.
- If post-obstructive diuresis occurs, potassium supplementation to the intravenous fluids and high fluid rates may be necessary to match the urine output.
- Recheck the serum biochemical profile and electrolytes in approximately 24 hours to ensure normalization of the values.
- Carefully monitor the urine stream diameter in cats with urethral plugs with attention to ease and frequency of urination for at least 12 hours prior to discharge from the hospital.

Technique for Urethral Hydropropulsion

- Sterile 0.9% NaCl mixed in a 25% to 50% combination with sterile water-soluble lubricant (e.g., K-Y jelly) can be used as the hydropropulsion fluid. Use a volume of 12 to 20 ml depending on patient size.
- Introduce the catheter in a sterile manner as far as possible into the urethra. When resistance is felt, gently dispense the fluid mixture into the urethra to flush the calculi or urethral plug into the bladder. If the calculi or plug is flushed out of the urethral orifice, submit it for analysis to aid in future medical management of the animal.
- In male cats urethral plugs are frequently lodged at the tip of the penis. Gently massage the tip of the penis to dislodge the plug and to make it easier to flush out.
- In male dogs urethral calculi are frequency lodged at the base of the os penis. When this occurs, hydropropulsion with fluid alone may not be enough to dislodge the calculus. Dilation of the urethra coupled with hydropropulsion is necessary.
  - Advance the catheter to the site of the blockage.

- With a gloved and lubricated finger, compress the pelvic urethra. At the same time occlude the tip of the penis and flush in the fluid under pressure. This is most easily done with one person compressing the urethra while the other person occludes the urethral opening and flushes in the fluid.
- Once dilation of the urethra is appreciated, stop the compression on the urethra and advance the catheter while continuing to flush in fluid.
- Several attempts are often necessary to move the calculi back into the urinary bladder.
- If it is not possible to relieve the urinary obstruction by passing a urinary catheter, perform intermittent therapeutic cystocentesis or placement of a temporary cystostomy tube until the patient is taken to surgery to relieve the obstruction.

URETHRITIS

Proliferative (Granulomatous) Urethritis

Etiology

- This condition is most common in middle-aged to older female dogs.
- Proliferative urethritis is an infiltrative inflammatory disease that is thought to be secondary to chronic bacterial urinary tract infection and/or an immune-mediated condition.
- This has previously been called *granulomatous urethritis,* but because a true granulomatous reaction is usually not identified on histopathology, *proliferative urethritis* is the preferred term.

Clinical Signs

- Clinical signs are associated with partial or total obstruction of the urethra and include pollakiuria, dysuria, hematuria, stranguria, and urinary incontinence.
- Symptoms attributable to uremia such as depression, anorexia, vomiting, and lethargy may occur if complete urinary obstruction occurs.

Diagnosis

- Palpation of the urethra per rectum may reveal a thickened and painful urethra.
- Obtain radiographs and/or abdominal ultrasound to evaluate the bladder and identify possible cystic calculi that may be a contributing factor to this disease.
- Submit a urine sample obtained by cystocentesis for bacteriologic culture and sensitivity testing.

Endoscopy and Biopsy

- Diagnosis is best accomplished via endoscopy and biopsy of the vaginal vault and urethra. Endoscopically the lesions appear as nodular masses with finger-like projections or cylindrical masses in the urethra and the vestibule.

▼ ***Key Point*** Histopathologic diagnosis of proliferative urethritis is critical to differentiate it from neoplasia.

- Traumatic urethral catheterization or blind urethral biopsy with the endoscopy biopsy forceps can be performed to obtain a tissue sample if an appropriate size endoscope is not available.
- Histopathology of biopsy specimens reveals primarily lymphoplasmacytic and neutrophilic inflammation.

Treatment

- If the process is so severe that urinary obstruction occurs, treat for the obstructive process first (see previous section in this chapter). Consider placing a urethral catheter or temporary urinary diversion procedure such as a tube cystostomy (see Chapter 80) to provide continuous urine drainage while treating the underlying condition.
- If infection is identified based on culture and sensitivity testing of the urine, treat with the appropriate antimicrobial(s) for 3 to 4 weeks. Reculture the urine via cystocentesis once the patient has been off all antimicrobials for 3 to 5 days to ensure that the infection is resolved.
- Identify and treat any predisposing causes to recurrent or relapsing urinary tract infections that may be correctable such as hypoplastic and/or recessed vulva with an excessive perivulvar skin fold (see Chapter 92).
- Treat cystic calculi, if present (see Chapter 79).
- Treat the inflammatory aspect of the proliferative urethritis with prednisone (0.5–2 mg/kg per day as a tapering dose over several weeks) and additional immunosuppresants (azathioprine 2 mg/kg PO daily for 10–14 days, then decrease to every other day) as needed.
- Despite clinical improvement, the endoscopic appearance of the urethra may continue to be abnormal.

Bacterial Urethritis

Etiology

- Bacterial infection of the urethra is often concomitant with bacterial cystitis.

Clinical Signs

- Clinical signs of bacterial urethritis include dysuria, stranguria, pollakiuria, hematuria, urinary accidents, and potentially urethral obstruction.

Diagnosis

- Because bacterial urethritis is almost always associated with bacterial cystitis, it is safe to assume that a bacterium cultured from the urine in the bladder is the same for the urethra.

▼ ***Key Point*** The best diagnostic test for bacterial urethritis is urine obtained via cystocentesis and submitted for identification and antimicrobial susceptibility testing.

Treatment

- Administer a systemic antimicrobial agent (or agents) based on urine culture and sensitivity testing for a minimum of 3 to 4 weeks. Reculture the urine via cystocentesis after the patient has been off antimicrobials for 3 to 5 days to ensure that the infection is cleared.
- Urethral obstruction may occur if significant urethral inflammation with resultant swelling and spasm has occurred secondary to the infection. These cases are treated by placing an indwelling urinary catheter for approximately 3 to 7 days until the inflammation has subsided. A soft red rubber silicone or Silastic catheter is preferable to a polypropylene catheter as it will be less irritating for indwelling use.
- Consider an anti-inflammatory dose of prednisone for the first 3 to 5 days to help decrease urethral inflammation.
- If urethral spasm is severe it may be helpful to treat the patient with drugs that relax the smooth and skeletal muscle of the urethra. Acepromazine (0.05–0.1 mg/kg IV, IM, or SC q8h), diazepam (0.2 mg/kg IV q8h), or phenoxybenzamine (5–15 mg PO q8h in the dog and 2.5–7.5 mg PO q8h in the cat) are reasonable choices in such cases.

URETHRAL TRAUMA

Etiology

- Anything that causes external trauma to the pelvic, perineal, or prepucial region of an animal may result in urethral trauma. Common causes are being hit by car, bite wounds, or any type of blunt or penetrating trauma.
- Iatrogenic trauma can be induced by urethral catheterization or uroendoscopy.

Clinical Signs

- Depending on the degree and location of the urethral trauma, a variety of clinical signs may occur.
- Trauma resulting in swelling, inflammation, and bruising may produce signs of partial to complete lower urinary obstruction. Dysuria, stranguria, pollakiuria, hematuria, and urine dribbling may be seen.
- A complete tear in the proximal urethra may result in uroabdomen and resultant signs of uremia.
- Complete urethral tears that result in urine leaking into the surrounding tissues produce severe inflammation and bruising. The skin may become necrotic secondary to the urine leakage. The affected area may extend from the perineal region to the inguinal area and down the rear thighs.

Diagnosis

- Suspect trauma to the urethra in all cases of trauma to the pelvic region. It is often difficult to distinguish if the swelling and bruising in the perineal region following trauma to the perineal region is due to the insult alone, or if concurrent urethral rupture has occurred.
- Carefully monitor the patient, including urea nitrogen and creatinine concentrations, electrolytes, and urinations. Post-renal azotemia will become evident if a full-thickness urethral tear has occurred.
- Palpate the abdomen and attempt to ballot a fluid wave.
- If abdominal distension occurs, perform a diagnostic abdominocentesis (see Chapter 3) to determine if urine and/or blood is accumulating in the peritoneal cavity. If urine is leaking into the peritoneal cavity, analysis of the concentrations of creatinine and potassium in the abdominal fluid will be greater than those levels in the serum.
- The concentration of urea nitrogen is typically increased in both the serum and abdominal fluid in patients with urine leakage into the peritoneal cavity.

Radiology

- Obtain plain abdominal radiographs and ultrasound (see Chapter 4).
- Perform positive contrast urethrography to definitively diagnose a urethral tear. Leakage of the contrast material is seen into the adjacent tissues and/or into the abdomen. Narrowing or attenuation of the contrast material may be seen in urethral stenosis or stricture secondary to urethral trauma.

Treatment

- Treat severe urethral swelling resulting in partial to complete urethral obstruction and partial urethral

tears by aseptic placement of an indwelling urinary catheter (red rubber, Teflon-coated, silicone, or Silastic). Use a urinary catheter size that approximates the normal urethral size so that urethral stenosis does not occur. Connect the catheter to a closed urinary collection system. Maintain the indwelling catheter for 1 to 4 weeks depending on the severity of the lesion.

- If necessary, administer urethral antispasmodic (acepromazine 0.05–0.1 mg/kg PO, SC, IM, or IV q8h or diazepam 0.2 mg/kg IV q6–8h), anti-inflammatory (prednisone/prednisolone 0.5–2 mg/kg PO or SC or dexamethasone 0.25–1 mg/kg IV or SC daily), and analgesic (butorphenol 0.2 mg/kg IV, SQ, or IM q6–8h) medications.
- Do not administer prophylactic antimicrobials for the sole reason that an indwelling urinary catheter has been placed. This may result in a urinary tract infection with resistant bacteria. Use antimicrobials to treat confirmed urinary infection. Bacterial culture of urinary catheter tips can be unreliable.
- Submit a cystocentesis urine sample for culture and sensitivity testing 3 to 5 days after the catheter is removed. The normal host defense mechanisms can clear many bacteria that are present in the urine at the time the urinary catheter is removed. Waiting to culture the urine 3 to 5 days after catheter removal allows time for this to occur.
- If necessary, perform surgical repair of complete urethral tears once the patient is medically stable (see Chapter 82). If primary repair is not possible, perform urethrostomy. Studies have shown that the urethral tear will usually heal using an indwelling urinary catheter if a section of mucosa that bridges the defect is still present.

URETHRAL STRICTURE

Etiology

- Urethral stricture may be acquired or congenital.
- Acquired stricture may be secondary to trauma, chronic inflammation or infection, neoplasia, or urethral calculi.
- Orphan puppies and kittens may suck on the external genitalia of littermates resulting in stricture formation.
- Iatrogenic stricture may result from traumatic or repeated urethral catheterization.

Clinical Signs

- Signs of lower urinary tract dysfunction, such as dysuria, stranguria, hematuria, and urine dribbling, are common.
- The owner may observe that the animal takes a long time to urinate, makes repeated attempts, and cannot produce a good urine stream.
- Lack of urine production may be noted if the stricture is complete.

Diagnosis

- The urinary bladder may feel enlarged, turgid, or painful if there is partial to complete urinary obstruction.
- If the urethra is completely occluded by the stricture, signs of uremia may be present and can be confirmed on a serum biochemical profile.
- Palpation of the urethra per rectum may be helpful in distal strictures. Dilation cranial to the stricture may be palpated.
- Perform positive contrast urethrography (see Chapter 4) or urethroscopy to make a definitive diagnosis.

Treatment

- Catheterize the urethra, if possible, to provide urine drainage.
- Determine if there are any underlying causes for the stricture and treat that process.
- Surgical intervention such as perineal, prepubic, or scrotal urethrostomy is required in many cases (see Chapter 82).
- Balloon dilation of the strictured area can be attempted. This is most likely to be of benefit in idiopathic or congenital cases.

URETHRAL PROLAPSE

Etiology

- Urethral prolapse occurs when mucosa of the urethra everts through the external urethral orifice.
- The cause of this condition is often unknown, but sexual excitement may play a role.
- Cystitis or urethritis may be predisposing or concomitant conditions.
- Young male brachycephalic breeds are predisposed, including bulldogs, Boston terriers, and Shar-Peis. Bulldogs between the ages of 9 and 13 months are commonly affected, and a genetic or congenital factor is speculated in this breed.

Clinical Signs

- Clinical signs are attributable to partial obstruction of the lower urinary tract or bleeding from the end of the prepuce. Stranguria, dysuria, urinary incontinence, and hematuria are common. Some owners may find that the dog is licking incessantly at the penis and discover a mushroom-shaped mucosal lesion associated with the tip of the penis.

Diagnosis

- Exteriorization of the penis is required to make a diagnosis. The everted urethral mucosa can easily be seen and commonly appears as a round or doughnut-shaped dark red mass at the tip of the penis.
- Obtain urine by cystocentesis for culture and susceptibility testing to rule out a bacterial infection as a predisposing cause.

Treatment

▼ ***Key Point*** Surgery is the treatment of choice for urethral prolapse.

- This condition rarely spontaneously resolves.
- Conservative management with sedation and subsequent manual reduction of the prolapse can be tried. The prolapse generally recurs with this form of treatment unless the prolapse is very minimal.
- Surgical resection of the prolapse is the best method of treatment (see Chapter 82). However, recurrence can occur postoperatively.
- If sexual excitement seems to play a role, recommend castration.
- Adjunctive treatments include anti-inflammatory and antispasmodic medications, antibiotics if bacterial urethritis is present, limiting trauma to the area by use of an Elizabethan collar and sedation.

URETHRAL NEOPLASIA

Etiology

- Tumors affecting the urethra include squamous cell carcinoma, transitional cell carcinoma, leiomyoma, rhabdomyosarcoma, adenocarcinoma, hemangiosarcoma, and undifferentiated sarcoma.

▼ ***Key Point*** Transitional cell carcinoma and squamous cell carcinoma are the most common tumor types of the urethra.

- Tumors of the urethra are relatively uncommon in dogs and more rare in cats. The most common signalment is middle-aged to older female dogs. Beagles are reportedly at an increased risk.
- Prostatic adenocarcinoma and transitional cell carcinoma may extend from the gland into the urethra in male dogs.
- In the male dog the most common tumor location is the prostatic urethra.
- These tumors tend to be slow growing. They commonly spread to the local surrounding tissue and the regional lymph nodes, especially the sublumbar lymph nodes. Metastasis to the lung and bone are not uncommon. There is often concurrent urinary bladder involvement.

Clinical Signs

- Signs of urethral neoplasia are attributed to partial or complete obstruction of the urinary tract. Stranguria, hematuria, pollakiuria, dysuria, urinary incontinence, and potentially urethral obstruction are possible.
- If urethral obstruction is complete, signs of uremia may also occur.

Diagnosis

- Palpation of the urethra per rectum may reveal a thickened and painful urethra.
- The urinary bladder may be distended and/or turgid if there is partial to complete urinary obstruction.
- Obtain a urine sample for culture since there is often concurrent urinary tract infection.

Radiology

- Abdominal radiographs or ultrasound may reveal a distended urinary bladder with sublumbar lymphadenopathy.
- If the patient is experiencing lameness or back pain, radiographs of the painful region are indicated to evaluate for the presence of bony metastasis.
- Three-view thoracic radiographs are recommended to evaluate for metastatic disease to the lungs.
- Positive contrast urethrography or vaginogram may show the location and extent of the disease/mass (see Chapter 4). The urethral mucosa appears irregular and thickened. A radiolucent filling defect may be seen when a mass is present.

Biopsy

- Obtain a tissue sample by traumatic catheterization, blind biopsy, or endoscopy. If a diagnosis cannot be obtained from these modalities, consider surgical exploration and biopsy.

Treatment

▼ ***Key Point*** Palliative treatment is the most realistic option for urethral neoplasia.

- If the patient is fully obstructed by tumor mass and associated inflammation, it may not be possible to pass a urinary catheter to relieve the obstruction. In such cases perform periodic cystocentesis or place a cystostomy tube (see Chapter 80) to provide drainage of the urinary bladder.
- In patients with distal urethral disease, surgical excision with permanent urethrostomy may be possible (see Chapter 82).
- With proximal urethral disease, perform permanent tube cystostomy to provide urinary drainage if surgical intervention is not possible (see Chapter 80).

- Palliative chemotherapy may be useful based on the tumor type. Piroxicam (0.3 mg/kg) daily to every other day is frequently a helpful palliative measure for transitional cell carcinoma. Monitor renal function every 2 to 4 months while on this drug. To minimize gastroenteritis, administer piroxicam with food. Consider giving misoprostol (1–5 mcg/kg PO q8h) for patients showing signs of gastroenteritis.
- If metastasis to the bone has occurred, administer analgesics. Nonsteroidal anti-inflammatory medications are generally inadequate to control pain associated with metastatic bone pain. Consider prescribing narcotics (transdermal fentanyl) or tramadol (1–4 mg/kg PO up to q6h in the dog and ¼ of a 50-mg tablet PO q12h in the cat).
- Newer modalities such as laser ablation of the tumor to reestablish the patency of the tumor-obstructed urethra have been tried with mixed success.
- Because most tumors are diagnosed when the disease is advanced, the prognosis is very poor. About 20% to 30% have already metastasized at the time of diagnosis, and surgical cure is rarely possible.

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Chapter

82 Surgery of the Urethra

Dale E. Bjorling / Támara M. Da Costa Gómez

Urethral disorders in dogs and cats frequently result in partial or complete obstruction. Emergency care may be required to restore the flow of urine and to treat metabolic imbalances. Calculi within the urethra are often accompanied by urinary tract infection (UTI) and cystic calculi. Aggressive medical and dietary management is required after surgery to prevent recurrence. Be careful during surgical manipulation of the urethra to minimize the potential for postoperative scar tissue formation and subsequent urethral obstruction.

▼ ***Key Point*** Correct metabolic imbalances in an animal with urethral obstruction prior to performing general anesthesia and prolonged operative procedures.

ANATOMY

Male Canine Urethra

- The urethra in the male canine is divided into three parts: the *prostatic, membranous,* and *cavernous* or penile portions.
- The urethral sphincter is not a discrete structure in the dog. Urethral pressure profiles demonstrate a zone of increased pressure that extends from the prostatic urethra into the membranous urethra. Of the components of the urethral sphincter closure mechanism (fibroelastic tissue, smooth muscle, striated muscle), smooth muscle is probably primarily responsible for maintaining tone in the resting state. Therefore, alpha-adrenergic agonists may be successful in the treatment of sphincter mechanism incompetence.
- The smooth muscle of the urethra is innervated by autonomic nerves arising from the pelvic plexus. The striated musculature receives innervation from branches of the pudendal nerve.
- The distal portion of the penile urethra lies within the os penis. Dilation of the urethra is limited within the os penis and in the perineal portion of the urethra, as it curves around the ischium. These are common locations for calculi to become lodged within the urethra.

▼ ***Key Point*** The most common sites of intraluminal urethral obstruction in male dogs are the base of the os penis, ischiatic arch, and prostate.

Male Feline Urethra

- The male feline urethra consists of three parts: (1) the *preprostatic,* which lies between the bladder and the prostate gland and is relatively longer than the corresponding portion of the male canine urethra; (2) the *prostatic* part, which extends from the prostate to the bulbourethral glands; and (3) the *penile* urethra. Immediately caudal to the bulbourethral glands, the urethral lumen rapidly narrows from approximately 4 mm in diameter to 1 mm. This diameter is maintained through the remainder of the penile urethra. When the penis is retracted, the prostatic and proximal penile urethra may assume the appearance of a flattened or gentle "s," which complicates urethral catheterization unless the penis is manually extended.
- An area of increased pressure thought to correspond to the sphincter mechanism is found in the urethra caudal to the prostate. Despite a decrease in intraurethral electromyographic activity after perineal urethrostomy (PU) in male cats, urinary incontinence is an uncommon occurrence. This may be due to the smooth muscle fibers as well as the remaining striated fibers of the urethral sphincter, which results in resting urethral pressure greater than intravesicular pressure during bladder distension.
- The urethra is innervated by branches of the pudendal nerve and receives autonomic fibers from the pelvic plexus.

Female Canine and Feline Urethra

- The urethra in the female dog and cat is relatively short in comparison to the male and corresponds to the portion of the male urethra found cranial to the level of the mid-prostate. The female urethra is also relatively larger in diameter and more distensible than the corresponding male urethra.
- It appears unlikely that a discrete urethral sphincter is present in either dogs or cats. The urethral pres-

sure profile does not demonstrate a discrete increase in pressure, but the major increase in urethral pressure develops in the mid-urethra of the female dog. A localized area of increase in urethral pressure has been observed in female cats associated with striated musculature near the external urethral orifice.
- The female urethra is innervated by autonomic fibers of the hypogastric and pelvic nerves and sensory and motor fibers from the pudendal nerve.
- Obstruction of the female urethra is extremely uncommon because of its short length, wide diameter, and relative distensibility.

URETHRAL ANASTOMOSIS

Preoperative Considerations

- Perform urethral anastomosis for treatment of urethral disruption, prostatectomy, stricture formation, or removal of granulomatous or neoplastic masses.
- Perform a retrograde positive contrast urethrocystography to identify the location of obstruction or disruption.
- Treat animals that are uremic or have other metabolic disorders as a result of urethral obstruction or leakage of urine into the periurethral tissues prior to inducing anesthesia and performing surgery.

▼ ***Key Point*** Treat incomplete lacerations or defects (discussed later in this chapter) by placing an indwelling urethral catheter to divert the flow of urine for 2 to 3 weeks. This form of treatment will be successful only when intact urethral mucosa bridges a portion of the injured area.

Surgical Procedure

Objectives

- Remove diseased or traumatized tissue.
- Restore urethral continuity.
- Minimize the potential for postoperative stricture formation.

Equipment

- Standard surgical instruments and suture
- Urethral catheters of appropriate diameter and length
- Gelpi or Weitlaner self-retaining retractors
- Monofilament non-absorbable suture (4-0 or 5-0) or synthetic absorbable suture (4-0 or 5-0)
- Delicate instruments for manipulation of the urethra (optional)
- Magnification (optional)
- Penrose drains, or closed suction drains if cellulitis or tissue necrosis due to extravasation of urine has occurred

Technique

1. The positioning of the animal (dorsal recumbency or ventral recumbency in a perineal stand) depends upon the portion of the urethra to be operated upon.
2. With the animal positioned appropriately, prepare the overlying skin for aseptic surgery.
3. Pass a sterile urethral catheter from the external urethral orifice in a retrograde direction to facilitate identification of the proximal end of the distal portion of the urethra.
4. If the distal end of the proximal portion of the urethra cannot be identified, perform a cystotomy and pass a urethral catheter in an antegrade direction.
5. Excise the damaged portions of the urethra. Although it is critical that a tension-free anastomosis be performed, do not be reluctant to debride and resect an adequate amount of urethra to properly treat the disease process.

▼ ***Key Point*** If the urethra cannot be reconstructed without undue tension across the anastomotic site, consider alternatives, such as prepubic urethrostomy.

6. With the urethral catheter in place, perform the anastomosis by placing full-thickness sutures in a simple interrupted pattern.
7. Place the first suture through the dorsal aspect of the urethra.
8. Cut the ends of the suture at a sufficient length so that they may be grasped by a forceps.
9. Gently rotate the urethra to facilitate placement of subsequent sutures. Placing the first two sutures 180 degrees apart facilitates appropriate apposition of the ends of the urethra and suture placement. Preplacement of sutures may help ensure accurate placement of sutures.
10. Place sutures evenly; six to eight sutures are usually sufficient to perform a satisfactory anastomosis.
11. Maintain a soft, preferably balloon-tipped catheter that approximates the diameter of the urethral lumen connected to a sterile urine collection bag for 7 to 10 days after surgery.
12. If necessary, use an Elizabethan collar to prevent catheter displacement. Alternatively, place a cystostomy catheter to divert the flow of urine from the urethra (see Chapter 80).
13. Close the incision routinely.
14. Submit calculi for analysis or culture, or submit tissue for histopathology if indicated.

Postoperative Care and Complications

- If the urethral catheter is removed prematurely, a decision must be made regarding whether or not to replace the catheter. If resistance is encountered

during attempts to pass the urethral catheter, replacement is abandoned.
  - Consider performing a retrograde positive contrast urethrocystogram to evaluate the integrity of the surgical site.
- Monitor the animal carefully for evidence of urine leakage.
- Warn the owners of the potential for postoperative stricture (most commonly observed 2–3 weeks after surgery), and advise them to carefully observe the animal during urination for evidence of urethral obstruction.
- Perform a retrograde positive contrast urethrocystogram 2 to 3 months after surgery to evaluate the urethral diameter at the anastomotic site.
- Treat infection or urinary calculi appropriately.

URETHROTOMY IN THE MALE DOG

Preoperative Considerations

- Perform this procedure to remove urethral calculi lodged proximal to the os penis or in the perineal urethra and to temporarily divert the flow of urine.
- If the animal is azotemic and depressed, this procedure can be performed without sedation by infiltrating the tissue overlying the urethra with local anesthetic.
- If calculi remain in the kidneys, ureters, bladder, or urethra after urethrotomy, perform definitive surgery to remove the calculi after the animal is stabilized.
- Perform urethrotomy only after attempts to pass a urethral catheter or to flush calculi in a retrograde direction into the bladder have failed.

Surgical Procedure

Objectives

- Relieve urethral obstruction.
- Remove urethral calculi.
- Pass urethral catheter.
- Allow patient stabilization prior to definitive repair.

Equipment

- Scalpel, hemostats, thumb forceps, Metzenbaum scissors
- Urethral catheter
- Suture to secure the urethral catheter

Technique

1. Restrain the dog in dorsal (prescrotal urethrotomy) or lateral recumbency (perineal urethrotomy). Prescrotal urethrotomy is the preferred technique.
2. If the procedure is not being performed under general anesthesia, infiltrate the skin and subcutaneous tissues overlying the urethra with local anesthetic.
3. Prepare the skin overlying the intended site of urethrotomy for aseptic surgery.
4. Make an incision 1 to 2 cm in length over the urethra at the level of obstruction.
5. Using a combination of blunt and sharp dissection, expose the appropriate area of the urethra.
6. In the prescrotal location, identify the retractor penis muscles and retract them laterally. The urethra appears as a purple structure on the midline flanked on either side by the white penile tunic.

▼ ***Key Point*** Take care to incise the urethra on the midline. The urethra is a highly vascular structure and will bleed briskly when incised.

7. Remove calculi from the urethra with forceps.
8. Pass a urethral catheter from the urethrotomy site into the bladder. Catheterize the distal urethra (retrograde and/or antegrade) to ensure patency.
9. Maintain the urethral catheter after surgery to monitor urine output and diminish the likelihood of subsequent urethral obstruction prior to surgical removal of cystic calculi.
10. Leave the urethrotomy open to heal by second intention or suture with 4-0 monofilament synthetic absorbable suture in a simple interrupted or simple continuous pattern.

Postoperative Care and Complications

- Hemorrhage may be observed intermittently, usually associated with urination, for 7 to 14 days after surgery. The flow of urine dislodges clots, and urokinase (a plasminogen activator found in urine) interferes with clot formation. This complication may be minimized by suturing the urethrotomy site.
- If the urethrotomy site is sutured, seroma or abscess formation may occur.
- On rare occasion, a stricture may form at the urethrotomy site. This is more likely when the urethral mucosa has sustained significant damage.
- Treat UTI and calculi with appropriate antibiotic and dietary therapy and other interventions to prevent reformation of calculi. Inform the owner that surgery will not cure this problem and appropriate medical therapy is critical to a satisfactory outcome.
- If calculi from the bladder pass into the urethra, urethral obstruction may recur despite the urethrotomy.
- If the skin incision is made too close to the scrotum, the testes may prolapse through the skin incision. Treat this prolapse by suturing the caudal aspect of the incision.
- Swelling and edema of the scrotum and testes may be observed because of inflammation associated with the urethrotomy or subcutaneous accumulation of urine. Subcutaneous accumulation of urine occurs infrequently if the urethrotomy incision is made near the proximal end of the os penis.

- Prolonged urethral obstruction and distension of the bladder may cause a loss of detrusor function of the bladder, resulting in loss of contractile function of the bladder (see Chapter 83 for treatment).

URETHROSTOMY IN THE MALE DOG

Preoperative Considerations

- Urethrostomy results in a permanent opening for the urethra and is performed proximal to the site of narrowing, obstruction, or destruction of the urethra. Perform urethrostomy in the male dog in the perineal, scrotal, prescrotal, or prepubic location.
- Urethrostomy is most often performed in the scrotal position, because the urethra is wide and superficial at this location. Minimal hemorrhage occurs, and a cosmetic result is achieved. Avoid urethrostomy in the perineal position because of the potential for urine scalding of the caudal surface of the thighs. Prepubic urethrostomy is discussed later in this chapter.

▼ ***Key Point*** Inform the owner that urethrostomy will not cure UTI or urinary calculi. In fact, urethrostomy may predispose the animal to UTI. However, the overall incidence of UTI after urethrostomy in male dogs is low.

- Urethrostomy decreases the potential for urethral obstruction due to passage of calculi but does not eliminate it. Calculi of sufficient diameter may still become lodged in the urethra proximal to the site of urethrostomy.

▼ ***Key Point*** Scrotal urethrostomy necessitates castration of the animal. Inform the owner prior to undertaking surgery.

- Stabilize azotemic animals prior to undertaking a prolonged anesthetic and operative procedure.

Surgical Procedure: Scrotal Urethrostomy

Objectives

- Allow discharge of urine proximal to the site of urethral obstruction or destruction.
- Diminish the possibility of urethral obstruction due to urinary calculi.

Equipment

- Standard surgical instruments and suture
- Monofilament non-absorbable suture (4-0 or 5-0) and synthetic absorbable suture (2-0 or 3-0) with swaged taper or taper-cut needle (preferred)
- Urethral catheter
- Delicate forceps for manipulation of the urethra (optional)
- Magnification (optional)

*Technique**

1. Place the dog in dorsal recumbency.
2. Prepare the caudal ventral abdomen, prepuce, scrotum, and ventral perineal region for aseptic surgery.
3. Make a circumferential incision around the scrotum at the point of reflection of the skin from the ventral body wall (Fig. 82-1*A*). Preserve enough skin to minimize tension on the suture line.
4. Isolate, ligate, and divide the spermatic cords and vessels by a combination of sharp and blunt dissection.
5. Free the scrotum and testes of their attachments to the ventral abdomen and penis and remove them (Fig. 82-1*B*).
6. Retract the paired retractor penis muscles laterally.
7. Secure the tunic of the penis to the subcutaneous tissues with four to six interrupted sutures of absorbable material (2-0 or 3-0) (Fig. 82-1*C*).
8. Place these sutures in such a manner that an adequate amount of skin is available to be sutured with minimal tension to the site of incision in the ventral urethra.
9. Make an incision in the ventral surface of the urethra for the length of the urethrostomy site (approximately 5 cm) (Fig. 82-1*D*).

▼ ***Key Point*** Make the urethral incision precisely on the ventral midline to facilitate urethrostomy closure.

10. If tension is encountered as the skin is drawn toward the edge of the urethra, adduct the stifles. This usually diminishes the amount of tension placed on the skin in this position.
11. Suture the urethral mucosa to skin with 4-0 or 5-0 monofilament non-absorbable suture in an interrupted or continuous pattern (Fig. 82-1*E* and *F*). Include a small bite of urethral tunic with the bite of mucosa, since the mucosa is friable and has poor suture-holding capacity. Place sutures from inside the urethral lumen (mucosa) to outside (skin) to improve apposition of mucosa to skin. The distal continuation of the urethra into the os penis remains open.

Postoperative Care and Complications

- Apply an Elizabethan collar to prevent postoperative self-mutilation.

*The procedure for scrotal urethrostomy is described. A similar technique is used to create urethrostomy in the perineal or prescrotal position.

Figure 82-1. Scrotal urethrostomy. *A,* Make an incision encircling the scrotum. *B,* Ligate and sever the spermatic cord and vessels and remove the scrotum and testes. *C,* The retractor penis muscles are drawn laterally; secure the subcutaneous tissues to the tunica albuginea. *D,* Make an incision on the ventral midline of the urethra. Placement of a catheter facilitates identification of the urethra. *E,* Suture the urethra to the skin. *F,* The cranial opening of the urethra at the urethrostomy site remains open. (From Smeak DD, Fingeroth JM: Scrotal urethrostomy. In Bojrab MJ (ed): Current Techniques in Small Animal Surgery, 3rd ed. Philadelphia: Lea & Febiger, 1990, p 381.)

- Hemorrhage may be observed intermittently from the urethrostomy site. This is particularly noticeable when the animal urinates. In the immediate postoperative period, treat this by applying pressure or a cold compress. Sedation of the animal, particularly with acepromazine (which may decrease the systemic blood pressure), may also decrease the incidence of hemorrhage. Warn the owner that hemorrhage may occur for up to 2 weeks after the surgery. Clinical studies have found decreased postoperative hemorrhage with the continuous suture pattern.
- Remove sutures 2 weeks after surgery. Sedate animals that are difficult to handle for suture removal.

▼ ***Key Point*** Inform the owner that the removal of the sutures may result in intermittent hemorrhage from the urethrostomy site for 2 to 3 days.

- Treat UTI and urinary calculi by appropriate antibiotic, dietary, and medical therapy (see Chapter 79). Inform the owner that urethrostomy will not treat UTI or prevent calculi formation and that urethral obstruction may recur if calculi form.
- Leakage of urine into the subcutaneous tissues is uncommon.
- Stricture formation is extremely uncommon but may occur. If this happens, reconstruct the urethrostomy

and carefully appose the mucosa to skin without tension.
- Scalding of the inner surface of the thighs by contact of the skin with urine is extremely uncommon. Apply petroleum jelly to the skin surrounding the stoma to reduce this problem until sutures are removed.
- Prolonged urethral obstruction and distention of the bladder may result in a loss of detrusor function of the bladder.
- Urinary incontinence due to surgery has not been reported.

PERINEAL URETHROSTOMY IN THE MALE CAT

Preoperative Considerations

- This procedure is performed most often in cats that suffer recurrent urethral obstruction because of idiopathic lower urinary tract disease, also referred to as feline interstitial cystitis (FIC) and feline urologic syndrome (FUS). Improved dietary management of this disorder has greatly decreased the need for urethrostomy in cats (see Chapter 79 for discussion of this disorder).

▼ ***Key Point*** Performance of PU will not cure FIC or FUS, and signs of this disorder may persist after surgery. Inform the owner that the surgery is performed to diminish the probability of urethral obstruction and not to cure FIC or FUS.

- This procedure can be used to treat any form of urethral obstruction due to lesions of the urethra distal to the bulbourethral glands.
- Castration and amputation of the distal penis are necessary for PU in cats. Inform the owner of these procedures.

Surgical Procedure

Objectives

- Create a cutaneous opening of the urethra of satisfactory diameter near the bulbourethral glands.
- Minimize tension across the suture line to decrease the potential for stricture formation.
- Preserve urethral sphincter function.

Equipment

- Standard surgical instruments and suture
- Delicate instruments for manipulation of the urethra
- 3.5 to 8 Fr. catheter
- Fine periosteal elevator (Freer)
- Monofilament suture (4-0 or 5-0), taper-cut needle
- Magnification (optional)

Technique (Fig. 82-2)

1. Place the cat in ventral recumbency with the hindquarters slightly elevated.
2. Secure the tail in a forward position.
3. Place a purse-string suture around the anus (Fig. 82-2*A*).
4. Completely evacuate urine from the bladder.
5. Prepare the perineal area surrounding the scrotum and prepuce for aseptic surgery.
6. If the cat is intact, make an incision at the reflection of the scrotum from the surrounding skin. This incision encircles the scrotum and continues ventrally along the line of reflection of the prepuce from the perineal skin.
7. If the cat has previously been castrated, make an incision encircling the prepuce and scrotal remnant. Ventrally, the incision comes to a point.
8. Isolate, ligate, and divide the spermatic cords and vessels.
9. Sharply divide the ventral attachments of the penis to the pelvic floor near their attachment to the penis.
10. Continue sharp and blunt dissection circumferentially adjacent to the penis until the ischiocavernosus muscles are identified. Take care to restrict dissection to the area immediately adjacent and ventral to the penis.
11. Divide or free the ischiocavernosus muscles and penile ligament of their attachments to the ischium to allow the penis to be drawn caudally. The muscles will bleed profusely if incised.
    a. Incise the fascia overlying the attachment of the ischiocavernosus muscles to the ischium.
    b. Sever the attachment of the ischiocavernosus muscles to the ischium with a periosteal elevator. This usually results in minimal hemorrhage.
12. Continue blunt dissection in a cranial direction until the penis is freed of its ventral attachments and the caudal aspect of the bulbourethral glands lies at the level of the skin incision.
13. Limit dorsal dissection to minimize the potential for postoperative incontinence. If exposure of the proximal, dorsal urethra is inadequate, careful dissection of dorsal urethra tissues may be necessary.
14. Retract the penis in a caudal direction, and pass a catheter into the urethra (Fig. 82-2*B*).
15. Identify the retractor penis muscle on the dorsal aspect of the penis and excise it as far proximally as possible (Fig. 82-2*C*).
16. Excise the distal penis and prepuce and discard, along with the scrotum and testes.
17. With the urethral catheter in place, make an incision in the dorsal aspect of the urethra to the level of the bulbourethral glands.

▼ ***Key Point*** Continue the incision cranially until the portion of the urethra that enlarges in diameter (typically at the level of the bulbourethral glands) is reached.

18. Secure the tunic of the penis distal to the bulbourethral glands to the subcutaneous tissues by a

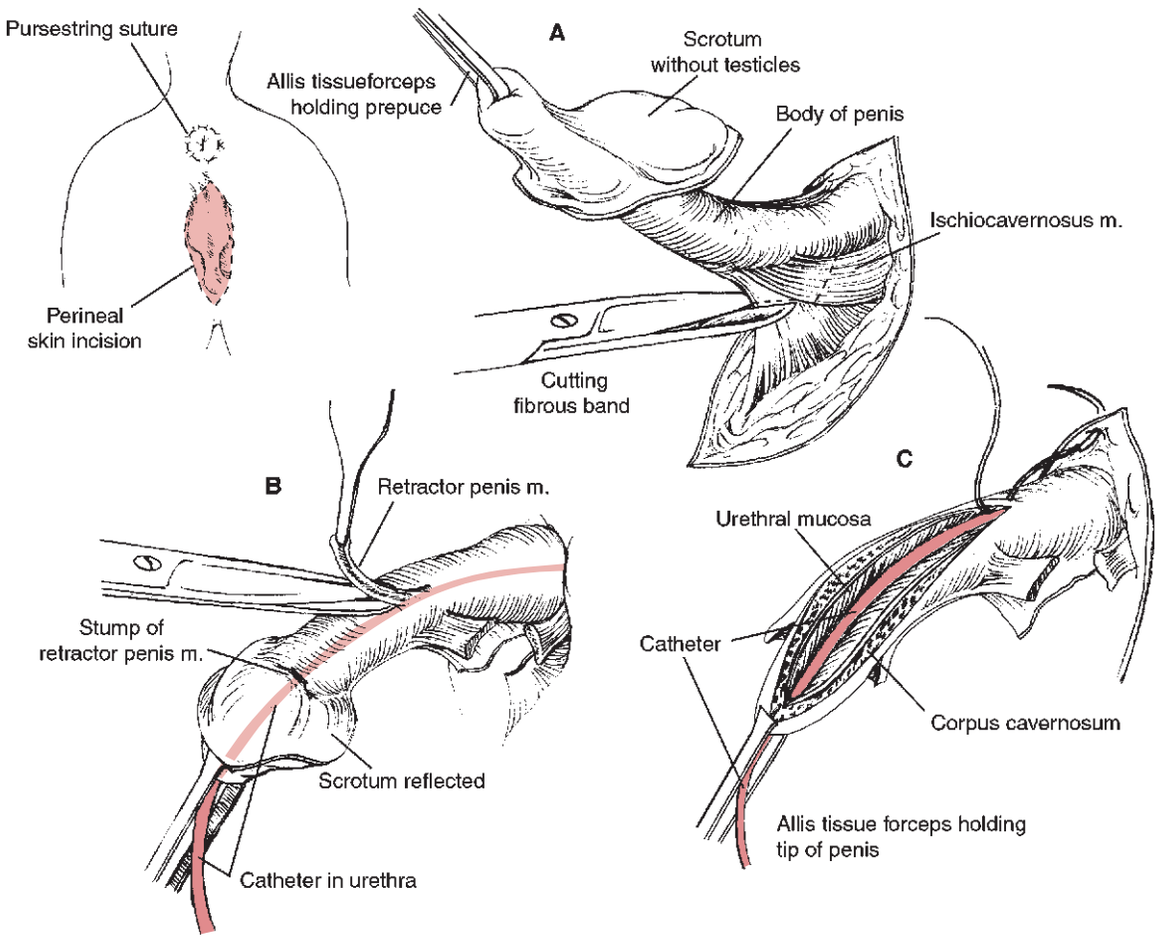

Figure 82-2. Perineal urethrostomy in the cat. *A*, Make an elliptical incision around the scrotal and prepuce (inset), and sharply incise the ventral fibrous attachments of the penis and the ischiocavernosus muscles. *B*, Carefully dissect and remove the retractor penis muscle from the dorsal aspect of the urethra. *C*, Incise the urethra exactly on the dorsal midline, and suture the urethra to skin using fine monofilament suture. Be sure to achieve accurate apposition of urethral mucosa to the skin.

few (two to four total) interrupted sutures of synthetic absorbable material (3-0 or 4-0). Place these sutures so that the skin may be brought to the edge of the urethral incision without tension across the suture line.

▼ ***Key Point*** Ensure that the urethral mucosa is well apposed to the skin to prevent stricture formation.

19. Suture the skin to the edge of the urethra. Place the first suture through the apex of the incision through the urethra and the most dorsal aspect of the skin incision.
20. Place interrupted sutures on either side from dorsal to ventral to create a satisfactory urethrostomy opening. Use monofilament non-absorbable suture (4-0 or 5-0).
21. After sutures have been placed along the urethra for a distance of approximately 1.5 cm, excise the remaining penis.

▼ ***Key Point*** Creation of a drain board distal to the urethrostomy will decrease the risk of urine scald of the perineum postoperatively.

22. Place and tighten an encircling absorbable suture submucosally around the exposed end of the penis. This will diminish hemorrhage from the body of the penis.
23. Close the remainder of the skin incision: subcutaneous tissue with absorbable suture in a continuous pattern skin with non-absorbable suture in an interrupted or continuous pattern.
24. Remove the urethral catheter upon completion of the surgery. Upon completion, a 5 to 8 Fr. catheter should pass into the bladder with ease.
25. Remove the purse-string suture around the anus.

Postoperative Care and Complications

- Place an Elizabethan collar to prevent self-inflicted damage of the urethrostomy site.

- Hemorrhage is frequently observed after surgery. In the early postoperative period, control this by applying pressure or cold compresses (ice packs). Tranquilization of the animal may be helpful in controlling prolonged hemorrhage.
- Stricture of the urethrostomy site is one of the most commonly observed complications.
- This complication most often results from failure to satisfactorily free the penis from its attachments within the pelvic canal, causing tension on the suture line; poor mucosa-to-skin apposition; or failure to continue the urethral incision far enough cranially.
- Subcutaneous leakage of urine may result in cellulites, abscessation, or dehiscence. This leakage usually results from poor mucosa-to-skin apposition, especially at the proximal aspect of the urethrostomy.
- Urinary or fecal incontinence is infrequently observed after PU in cats.
- The overall incidence of UTI in cats after PU is low; however, it is more commonly observed in these cats than in male cats that have not undergone the procedure.
- Perineal hernia has been reported after PU in male cats but is rare.
- Obstruction of the urethra may occur after PU because of the persistence of FIC/FUS or the development of urinary calculi.
- Prolonged urethral obstruction and bladder distension may result in a loss of detrusor function of the bladder (see Chapter 83).

PREPUBIC URETHROSTOMY

Preoperative Considerations

- Perform this procedure for treatment of diseases that cause a loss of urethral structure or function distal to the prostatic and pelvic portions of the urethra.
- This procedure can be performed in male or female animals.
- This can be performed as a salvage procedure following a failed PU in the cat.
- If a sufficient length of urethra and the associated innervation remain intact, the animal retains urinary continence.
- If this procedure is to be performed in a male dog with an enlarged prostate, a partial prostatectomy may also be necessary. This prevents the enlarged prostate within the subcutaneous tissues from interfering with the appropriate placement of the stoma.

Surgical Procedure

Objectives

- Create a new urethral opening on the ventral abdominal surface using the remaining length of urethra.
- Retain urinary continence.

Equipment

- Standard surgical instruments and suture
- Balfour retractors
- Monofilament non-absorbable suture (4-0 or 5-0)
- Urethral catheter
- Delicate instruments for manipulation of the urethra (optional)
- Magnification (optional)

Technique

1. Place the animal in dorsal recumbency.
2. Prepare the caudal surface of the ventral abdomen for aseptic surgery.
3. Make an incision on the ventral midline of the abdomen from the umbilicus to the pubis in female dogs and cats and male cats and in a parapreputial location in male dogs.
4. Examine the bladder, prostate (in male dogs), and urethra.
5. Identify the diseased portion of the urethra.
6. Transect the urethra, retaining the maximal amount of normal proximal urethra.
7. Resect the affected urethra if neoplasia is present.
8. Ligate vessels leading to the distal portion of the urethra and associated tissues.

▼ ***Key Point*** Take care during dissection to preserve the innervation and vascular supply of the bladder neck and proximal urethra located along the dorsolateral surface.

9. If difficulty is encountered in identifying the lumen of the proximal urethra, pass a catheter in a retrograde direction or perform a cystotomy to allow passage in an antegrade direction.
10. Bring the proximal urethra and adjacent structures to the level of the skin incision, and select an appropriate, tension-free site to create the stoma.
11. Create the stoma on the ventral midline in female dogs and cats and male cats and in a parapreputial position in male dogs. The stoma can be placed in the incision through which the abdominal cavity was entered. Position the stoma to allow the urethra to curve in a gentle arc through the ventral abdominal wall to avoid kinking or obstructing the urethra (Fig. 82-3).
12. Avoid twisting the urethra when passing it through the abdominal wall.
13. Close the abdominal wall in a standard manner, leaving 1.5 to 2.0 cm of the distal end of the proximal urethra exposed. The abdominal wall is not tightly closed in the area through which the urethra passes.
14. Secure the adventitia surrounding the urethra to the subcutaneous tissues with two absorbable sutures.

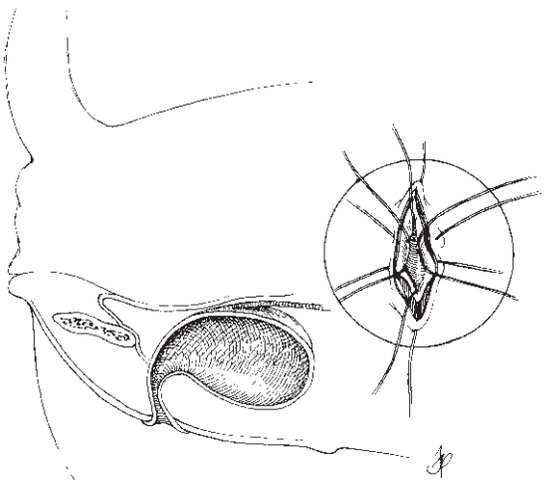

Figure 82-3. Prepubic urethrostomy. The urethra is brought across the body wall at a "gentle angle" to prevent urethral obstruction. Make an incision on the ventral surface of the urethra, and suture the urethra to the skin. (From Bjorling DE: Traumatic injuries of the urogenital system. Vet Clin North Am Small Anim Pract 14:61, 1984.)

15. Make an incision 1.5 to 2.0 cm in length on the ventral surface of the distal end of the proximal urethra. This is done to increase the diameter of the stoma.
16. Close the subcutaneous tissues in a standard manner.

▼ ***Key Point*** In obese animals or animals with redundant skin in the area of the urethral stomas, resection of skin and fat may be required to prevent obstruction of the stoma by adjacent skin folds.

17. Suture the cut edge of the urethra, including the mucosa, to the skin with monofilament non-absorbable suture (4-0 or 5-0) in an interrupted pattern to create the urethrostomy opening.
18. Close the remainder of the skin incision in a standard manner.
19. Catheterization of the urethra may facilitate accurate placement of sutures through the wall of the urethra.
20. Do not leave the catheter in place after surgery unless monitoring of urine output is necessary.

Postoperative Care and Complications

- Use an Elizabethan collar to prevent trauma after surgery.
- Leakage of urine into the subcutaneous space or abdominal cavity will result in cellulitis or peritonitis. Prevent this by accurate suture placement during the operative procedure.
- Stricture formation is an unusual complication of this procedure. When stricture occurs, revise the opening.
- If the procedure is performed appropriately and a satisfactory length of proximal urethra is available, urinary continence is retained. If urinary continence is lost, treat with alpha-agonists (see Chapter 83) to increase urethral tone. This therapy may or may not be successful if nerve or muscle function is lost.
- Prepubic urethrostomy predisposes an animal to ascending UTI. Frequent reevaluation and urine culture is recommended after the surgery.
- Loss of urinary continence predisposes to scalding of the ventral abdominal surface with urine.
- Urethral obstruction may occur if the position of the stoma results in an acute angle in the urethra relative to the bladder neck.

URETHRAL PROLAPSE IN THE MALE DOG

Preoperative Considerations

- Urethral prolapse occurs most often in young brachycephalic dogs.
- The most common complaint of the owner is that the dog develops hematuria or has bleeding from the penis when it becomes excited. Hemorrhage is usually self-limiting.
- After the exposed urethral tissue has been traumatized, hemorrhage may recur during or following urination because of dislodgement of blood clots by the flow of urine.
- Diagnose urethral prolapse by direct observation of exposed urethral tissue that appears as a fleshy ring surrounding the external urethral orifice. Extrude the penis from the prepuce to observe urethral prolapse.
- If the animal is not to be used for breeding, castration may help control urethral prolapse.

Surgical Procedure

Objectives

- Prevent hemorrhage from the tip of the penis.
- Excise exposed urethral tissue and prevent recurrence.
- Maintain an adequate urethral lumen.

Equipment

- Standard surgical instruments and suture
- Tourniquet or Penrose drain
- Urethral catheter
- Monofilament non-absorbable suture (4-0 or 5-0)

Technique

1. Place the dog in dorsal recumbency.
2. Prepare the interior of the prepuce and the penis for aseptic surgery.
3. Extrude the penis from the prepuce.

4. Pass a urethral catheter into the urethra until the tip lies approximately at the level of the scrotum.
5. Apply a tourniquet to the penis caudal to the os penis. The tourniquet will maintain the penis in an exteriorized position and minimize hemorrhage. Use a commercial tourniquet or a tourniquet created with a forceps and Penrose drain.
6. Partially excise the exposed urethral mucosa. Incise through the distal extent of the penile tunic and urethra, extending around half the circumference of the distal penis. This incision is proximal to damaged urethral mucosa and provides an exposed edge of the penile tunic, which is subsequently sutured to the urethra.
7. Suture the cut edge of the urethra to the tunic of the penis with monofilament non-absorbable suture (4-0 to 5-0) in an interrupted or continuous pattern. If a continuous pattern is used, avoid creating a "purse-string" effect.

▼ ***Key Point*** The purpose of initiating closure prior to complete excision of the urethral tissue is to prevent retraction of the urethral tissue within the penis and to facilitate accurate suture placement.

8. After the incision that has been made is partially closed, excise the remainder of the exposed urethral tissue by continuing the incision circumferentially.
9. Close the remainder of the defect with monofilament non-absorbable suture with a similar pattern.
10. Remove the tourniquet and urethral catheter.

Postoperative Care and Complications

- Intermittent hemorrhage may persist for 2 to 3 days (or longer) after surgery. This is usually associated with urination or excitement. If hemorrhage is excessive, re-examine the tip of the penis. Active bleeding from gaps in the closure may require placement of additional sutures. Tranquilization (e.g., with acepromazine) of the dog may decrease hemorrhage.
- Recurrence of urethral prolapse is uncommon. If this occurs, repeat the surgery and strongly recommend castration.
- Self-mutilation may occur and is discouraged by placing an Elizabethan collar or by using sedation.
- Sedate the dog for suture removal.
- Urethral prolapse rarely occurs in older animals. If observed in older animals, rule out a tumor at the tip of the penis. If there is concern that the tissue excised may be neoplastic, submit this tissue for histopathologic evaluation. Tumors of the distal urethra and penis are extremely uncommon.

SUPPLEMENTAL READING

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Chapter

83 Disorders of Micturition

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Micturition involves the passive storage and the active voiding of urine. Processes that interfere with the storage and voiding of urine are termed micturition disorders. The loss of voluntary control of micturition is defined as urinary incontinence.

Most cases of micturition disorders have been reported in middle-aged and geriatric dogs. The clinical importance of these disorders is twofold:

- Incontinence is unacceptable to most owners; if not adequately treated, this disorder may result in euthanasia of the pet.
- Micturition disorders may lead to unresponsive urinary tract infection, resulting in an ascending pyelonephritis.

▼ ***Key Point*** It is critical that the etiology of micturition disorders be diagnosed correctly in order to properly implement treatment.

NORMAL ANATOMY AND PHYSIOLOGY OF THE URINARY BLADDER

In order to recognize the many possible manifestations of micturition disorders it is imperative to understand the anatomy of the bladder, its functional composition, and the neurophysiology of micturition.

Bladder Function

Bladder function is primarily under the influence of smooth muscle. The body of the bladder contains smooth muscle, referred to as the detrusor muscle. The outlet conduit is composed of the trigone and proximal urethra. The smooth muscle fibers of the detrusor continue into the proximal urethra, forming a functional internal urethral sphincter mechanism. The distal urethra is composed of striated skeletal muscle and functions as an external sphincter.

During the storage phase of micturition, the bladder functions as a low-resistance, high-capacity reservoir. The urethra functions as a high-resistance barrier. The reverse is true during the voiding phase: The bladder acts as a muscular pump and the urethra is a low-resistance vessel.

The bladder functions like a compliant balloon as it fills, with pressure remaining lower than urethral resistance. With the initiation of normal urination, urethral resistance decreases and a phasic contraction of the detrusor muscle empties the bladder.

Nervous Control

Nervous control of the bladder and urethra is a combination of autonomic and somatic interactions. The micturition reflex is integrated by numerous interneurons and synapses between the sympathetic and the parasympathetic systems.

Parasympathetic Innervation

Parasympathetic innervation is supplied to the detrusor by the pelvic nerve, which arises from sacral spinal cord segments (S1–S3). Stimulation of the pelvic nerve results in detrusor contraction.

Sympathetic Innervation

Sympathetic innervation is supplied via the hypogastric nerve, which is composed of preganglionic fibers exiting the lumbar spinal cord (L1–L4) and synapses in the caudal mesenteric ganglion. Sympathetic innervation is supplied to both the detrusor and urethral smooth muscles and facilitates the storage phase of micturition. Alpha-adrenergic fibers synapse in smooth muscle in both the trigone and the urethra. Stimulation results in contraction of these muscles and forms a functional internal urethral sphincter mechanism. There are also alpha-adrenergic fibers that have a modulating effect on the external urethral sphincter. Beta-adrenergic fibers synapse in the detrusor muscle; stimulation results in relaxation.

Somatic Innervation

The pudendal nerve, which arises from sacral spinal cord segments (S1–S3), provides somatic stimulation to the striated urethral musculature.

Higher Centers of Innervation

For voluntary control of micturition to occur there must be integration among the cerebral cortex, the pons, and

the spinoreticular tract. A second pathway from the cerebral cortex to the sacral nuclei coordinates voluntary sphincter control. In addition, cerebellar neurons inhibit nervous transmission to the reticulospinal pathways in the pons.

ETIOLOGY OF MICTURITION DISORDERS AND INCONTINENCE

Disorders of micturition and continence can be divided broadly into two types: neurogenic and non-neurogenic (Table 83-1).

Neurogenic Disorders

There are three types of neurogenic disorders: lower motor neuron, upper motor neuron, and detrusor-urethral dyssynergia.

Lower Motor Neuron Bladder

Lower motor neuron, or atonic, bladder results from lesions involving the sacral spinal cord segments or pelvic nerve, including intervertebral disc disease, cauda equina syndrome, sacroiliac luxations, sacrococcygeal fracture or separation, and tumors (e.g., spinal lymphoma). This type of disorder causes both detrusor and sphincter areflexia. Dribbling of urine with the

Table 83-1. DISORDERS OF MICTURITION

Type of Disorder	Clinical Signs	Treatment
Neurogenic		
Lower motor neuron bladder	Distended, easily expressed Continuous incontinence No perineal or bulbospongiosus reflex No detrusor reflex	No effective therapy, Manual expression 3–4 times daily Trial with bethanechol chloride Concurrent antibiotics
Upper motor neuron bladder	Large, firm bladder Difficult manual expression initially Increased sphincter tone +/− detrusor reflex	Aseptic intermittent catheterization Concurrent antibiotics Antispasmodics or smooth muscle relaxants Long-term management usually frustrating
Detrusor-urethral dyssynergia	Large, non-expressible bladder Initiation of urine stream with abrupt disruption of urination Intact spinal reflexes Bladder easily catheterized	Prazosin Other alpha-antagonists Baclofen Diazepam Dantrolene
Non-neurogenic		
Hormone-responsive incontinence	Older, neutered animal Voluntary control of urination with intermittent incontinence Incontinence usually when relaxed or asleep	Diethylstilbestrol (females) Testosterone (males) Phenylpropanolamine
Urethral incompetence (stress incontinence)	Loss of voluntary control when placed in a stressful situation or at rest Ability to urinate voluntarily	Phenylpropanolamine Imipramine
Urge incontinence (detrusor hyperreflexia)	Frequent small urinations Hyperreflexive detrusor Urine spraying Stranguria	Flavoxate Oxybutynin Dicyclomine Propantheline bromide
Overdistension atony	Large flaccid bladder Continuous incontinence Large residual urine volume Intact perineal and bulbospongiosus reflex No detrusor reflex	Remove mechanical obstruction Indwelling bladder catheterization Bethanechol chloride
Paradoxical incontinence	Stranguria Persistent urine dribbling Large, turgid bladder that is difficult to express	Remove obstruction Indwelling catheterization Surgical exploration Cystoscopy
Ectopic ureter(s)	Continuous or intermittent dribbling of urine Ability to urinate voluntarily	Surgery Phenylpropanolamine
Pelvic bladder	Loss of voluntary control when placed in a stressful situation or at rest Ability to urinate voluntarily	Phenylpropanolamine Surgery

bladder remaining full is often referred to as overflow incontinence.

Upper Motor Neuron Bladder

Upper motor neuron, or automatic, bladder results from a lesion involving the spinal cord above the sacral spinal cord segments, such as intervertebral disc disease, tumor, or trauma. This disorder causes incomplete reflex detrusor contraction and spasticity of the urethral sphincter, with resulting incomplete emptying of the bladder.

Voluntary control is lost and manual expression is difficult if not impossible. After a period of days to weeks, the spinal reflexes resume. Non-voluntary micturition is initiated when the threshold capacity of the bladder is reached (automatic bladder).

Detrusor-Urethral Dyssynergia

In this condition, the initiation of the detrusor reflex resulting in voiding is followed by an involuntary contraction of the urethral sphincter. Detrusor-urethral dyssynergia refers to involuntary contraction of the external urethral sphincter in the postprostatic urethra (detrusor-striated muscle sphincter dyssynergia) or contraction of smooth muscle in the bladder neck and prostatic urethra (detrusor-smooth muscle sphincter dyssynergia) during detrusor contraction. It results from lesions or partial lesions (masses, degeneration) of the reticulospinal tract. Increased sympathetic activity of both the smooth and striated urethral musculatures may result from a lesion cranial to or involving the caudal mesenteric ganglion.

Non-Neurogenic Disorders

A number of disorders resulting in urinary incontinence are non-neurogenic in origin. A brief description of each disorder follows.

Hormone-Responsive Incontinence

Hormone-responsive incontinence is one of the most frequently diagnosed disorders. It is a disorder of older animals (mean age of occurrence is 8 years); however, it has been documented in animals as young as 8 to 9 months.

Hormone-responsive incontinence is seen primarily in spayed female dogs, which may be predisposed because of decreased sex hormone believed to contribute to normal urethral muscle tone and mucosal integrity.

Occasionally, hormone-responsive incontinence occurs in castrated male dogs, and it has been reported infrequently in neutered male and female cats.

Urethral Incompetence (Stress Incontinence)

This is the most common non-hormonal cause of urinary incontinence in small animals. Stress incontinence is a syndrome reported in women that consists of involuntary release of urine secondary to an increase in intra-abdominal pressure without detrusor atony or detrusor hyperreflexia. Urethral incompetence is the veterinary counterpart of stress incontinence. The cause is thought to be urethral smooth muscle incompetence or malposition of the vesicourethral junction or urethra.

Urge Incontinence (Detrusor Hyperreflexia)

Urge incontinence is due to involuntary detrusor contractions resulting in frequent voiding of small volumes of urine. The condition may result from an inflamed or irritated bladder or occasionally from partial spinal long tract or cerebellar involvement. The syndrome is commonly seen in cats that suffer from cystitis or idiopathic feline lower urinary tract disorders. An idiopathic form has been documented in cats and dogs without any evidence of cystitis.

Detrusor Atony from Overdistention

This results from a mechanical or functional outflow obstruction, causing separation of the tight junctions of the detrusor muscle. Subsequent contractions of the detrusor muscle are weak and ineffectual. A functional outflow obstruction may have a neurogenic component. It usually is the result of excessive sympathetic stimulation to the urethra, resulting in increased urethral tone. Common examples of mechanical obstruction are as follows:

- Urethral obstruction (especially in cats)
- Cystic and urethral calculi
- Neoplasia of the trigone or urethra
- Severe urethritis
- Stricture of the urethra
- Prostate disease

Obstruction causes an increase in urine volume until the intravesicular pressure can overcome the urethral resistance. Once the urethral pressure has been overcome, dribbling of urine occurs because of ineffectual detrusor contractions.

Paradoxical Incontinence

This is similar to overflow incontinence from detrusor atony. It is involuntary dribbling of urine associated with an outflow obstruction. It often results from a partial urethral obstruction caused by urethral calculi, neoplasia, or urethritis. The difference between the two conditions is a matter of duration and whether the atony is temporary or permanent. Paradoxical incontinence is of a shorter duration. When the partial obstruction is relieved, normal function returns, and the detrusor contracts effectively.

Ectopic Ureter(s)

Ectopic ureter and other congenital urethral malformations are a common cause of urinary incontinence.

The abnormal location of the ureteral orifice(s) within the bladder neck, urethra, or vagina results in continuous or intermittent leakage of urine (see Chapter 77).

Pelvic Bladder and Urethral Dysplasia

This is a condition in which the neck of the bladder is located extremely caudally in the pelvic canal and the urethra is shortened or displaced. It is most often associated with incontinence in young intact female dogs, but some dogs with pelvic bladder do not exhibit urinary incontinence.

Incontinence that accompanies a pelvic bladder is attributed to two components of the disorder:

- The extreme caudal displacement of the bladder into the pelvic canal, limiting the bladder distension.
- The abnormal position of the urethra in these animals. The dysplastic urethra may take on a variety of appearances, from short and dilated to S-shaped.

CLINICAL SIGNS

- *Incontinence:* Dribbling of urine, loss of voluntary control, and urine-scald dermatitis.
- *Abnormal micturition:* Inability to urinate, disruption of the urine stream, stranguria, dysuria, and abdominal pain or discomfort.
- *Lower motor neuron bladder:* Dribbling of urine and a large distended bladder that is easily expressed by manual compression.
- *Upper motor neuron bladder:* A full bladder that is difficult to express initially. Voluntary control of micturition is lost. After a period of days to weeks, the spinal reflexes resume and non-voluntary micturition is initiated when the threshold capacity of the bladder is reached. Incomplete and inappropriate urination is the result.
- *Detrusor-urethral dyssynergia* (differentiate from mechanical obstruction): Initiation of voiding, often after a period of hesitation, that then is abruptly disrupted; stranguria.
- *Hormone-responsive incontinence:* Normal voluntary urination with involuntary dribbling when the animal is relaxed or asleep.
- *Urethral incompetence (stress incontinence):* Signs similar to hormone-responsive incontinence; also involuntary loss of urine when placed in a stressful or new situation.
- *Detrusor hyperreflexia:* Frequent small urinations, stranguria, and urine spraying in cats; small bladder (compare with detrusor atony from overdistention).
- *Detrusor atony from overdistention:* Stranguria, dysuria, persistent urine dribbling; large distended bladder.
- *Paradoxical incontinence:* Same clinical signs as detrusor atony.
- *Ectopic ureter(s):* Continuous or intermittent dribbling of urine, usually with the ability to urinate appropriately and voluntarily. Most commonly diagnosed in young female dogs.
- *Pelvic bladder:* Same as urethral incompetence.

DIAGNOSIS

History

The history is of the utmost importance; include the following items:

- Reproductive status
- If animal was neutered, age at neutering
- Age at onset of problem
- Previous medical problems, especially those involving the urogenital system
- Previous history of trauma
- Description of the abnormality
- If the problem is incontinence, ask the following:
  - Is it continuous or intermittent?
  - What is the amount of urine passed?
  - Is the animal aware that urine is being passed?
- If the animal has difficulty urinating, ask the following:
  - How frequent is urination?
  - Is there nocturia, dysuria, or hematuria?

Physical Examination

Perform a general examination, with particular attention to the urogenital system, and perform a neurologic examination (see Chapter 125).

- Palpate the bladder carefully prior to and immediately following voiding to evaluate the extent of distention, tone, and ease with which the bladder may be manually expressed.
- Lower motor neuron lesions generally are associated with easy manual expression and reduced sphincter tone.
- Upper motor neuron lesions generally are associated with difficult manual expression and increased sphincter tone.
- In the neurologic examination, evaluate the innervation of the urogenital system.
- The perineal reflex evaluates the pudendal nerve. Pricking or pinching the skin of the perineum should result in anal sphincter contraction.
- The bulbospongiosus reflex evaluates the integrity of both the pudendal nerve and the sacral spinal segments. Squeezing the distal portion of the penis or vulva will cause anal sphincter contraction.
- Perform a rectal examination to evaluate the prostate gland, the pelvic diaphragm, and the anal tone.

▼ ***Key Point*** Observe the animal when urinating to verify the micturition abnormality.

- Measure the residual urine volume. Allow the animal to void until urine is no longer passed; catheterize the

bladder and collect and measure any residual urine. In a normal animal, the residual urine volume should not exceed 0.4 ml/kg.

Endoscopy

- Perform uroendoscopy if ectopic ureters are suspected.

▼ ***Key Point*** Uroendoscopy is considered the "gold standard" for the diagnosis of ectopic ureters but requires specialized equipment and skill.

Laboratory Evaluation

- Evaluate renal function by determining blood urea nitrogen (BUN) and serum creatinine concentration.
- To evaluate for associated urinary tract infection, perform cystocentesis and submit urine for urinalysis, culture, and sensitivity. If possible, do this before any bladder catheterization.

Radiographic Examination

Both survey and specialized studies may be useful.

- Use survey radiographs to evaluate any obvious abnormalities in the bladder, urethra, pelvis, or spine.
- Use contrast radiographic studies (intravenous urography, retrograde urethrocystography, and vaginourethrography) and contrast enhanced computed tomography (CT) (see Chapter 4) to evaluate for the following:
  - Ectopic ureters
  - Bladder wall thickening
  - Calculi
  - Urachal diverticulum
  - Prostatic enlargement
  - Urethral strictures
  - Pelvic bladder, urethral dysplasia
  - Skeletal abnormalities in the pelvis

Urodynamic Studies

Urodynamic studies to evaluate micturition disorders routinely consist of the cystometrogram and urethral pressure profile; electromyography also may be a part of the study. These specialized modalities are readily available at most veterinary institutions and are becoming increasingly common in private referral practices.

- The cystometrogram is a pressure-volume recording that measures bladder tone and volume, threshold volume and pressure, maximum contraction pressure, and the detrusor reflex.
- The urethral pressure profile measures intraurethral resistance and identifies and localizes areas of increased or decreased resistance.
- Electromyography can evaluate coordination of muscular activity between the detrusor and the urethral sphincter. Electromyography is usually performed on the anal sphincter; however, using specialized catheters that incorporate electrodes, it can be performed directly on the urethral sphincter.

Diagnosis of Individual Disorders

Lower Motor Neuron Bladder

- The bladder typically is large, distended, and easily expressed.
- The incontinence is continuous.
- There is a loss of perineal, bulbospongiosus, and detrusor reflexes.

Upper Motor Neuron Bladder

- The bladder is large, turgid, and initially extremely difficult to express.
- There is a history of an inability to urinate.
- Frequently there is concomitant hindquarter paresis or paralysis.

Detrusor-Urethral Dyssynergia

- Diagnosis is made by observation; commonly there is stranguria, initiation of voiding, and then abrupt disruption of the urine stream.
- Palpation often reveals a large, non-expressible bladder.
- The bladder is easily catheterized.
- There is no evidence of stricture or obstruction when a retrograde contrast cystourethrogram is performed. A cystometrogram reveals an intact pelvic nerve; however, the urethral pressure profile reveals increased resistance.

Hormone-Responsive Incontinence

- There is a history of neutering and subsequent intermittent incontinence.
- Palpation commonly reveals a small bladder.
- Urinalysis may or may not show evidence of cystitis.
- Typically there is response to sex hormone supplementation.

▼ ***Key Point*** Urinary tract infection results in an exaggeration of the incontinence; if infection is present, resolve it before making a diagnosis of hormone-responsive incontinence.

Urethral Incompetence (Stress Incontinence)

- There is a history of intermittent incontinence when the animal is at rest or placed in a stressful situation.
- Palpation reveals a small bladder.
- The animal is able to urinate voluntarily.
- There is no evidence of infection on urinalysis.
- There are no radiographic abnormalities.

Urge Incontinence or Detrusor Hyperreflexia

- The bladder is small on physical examination.
- Cystometrography reveals involuntary smooth muscle contractions during the filling phase of micturition.

Contractions can be spontaneous or provoked but cannot be suppressed.
- Urodynamically, detrusor instability usually appears as a rapid, involuntary increase of >15 cm of water pressure during the filling phase of the cystometrogram. However, there is voluntary control of urination.
- In cases associated with cystitis, there may be a history of urine spraying or infection, and there is evidence of inflammation on urinalysis. A urine culture may be positive or negative.
- With cystitis, the bladder may be thickened on palpation, and a contrast cystourethrogram may reveal bladder wall thickening.
- In idiopathic detrusor hyperreflexia, there is no evidence of cystitis and no abnormalities on contrast cystourethrograms.

Detrusor Atony from Overdistention

- There is a history of continuous incontinence and urine outflow obstruction.
- Abdominal palpation reveals a large, flaccid bladder.
- Neurologic examination reveals intact perineal and bulbospongiosus reflexes, yet there is an absent or weak detrusor reflex.
- There is a large residual urine volume.
- Urodynamic studies may help rule out a neurogenic component.

Paradoxical Incontinence

- Base the diagnosis on the results of a urinalysis and of plain, and often contrast, radiographs.

Ectopic Ureters

- Most common cause of urinary incontinence in young female dogs.
- Breeds of dogs most commonly affected include Labrador retriever, Golden retriever, Siberian husky, Newfoundland, standard poodle, toy poodle, soft-coated wheaten terrier, and Skye terrier.
- There usually is a history of continuous incontinence with ability to urinate voluntarily. Usually a small bladder is revealed on abdominal palpation.
- On the physical examination, urine-soaked fur often is seen along the rear legs.
- Make a definitive diagnosis by uroendoscopy or contrast radiography (intravenous urography, retrograde vaginocystography, or contrast-enhanced CT).
- Perform uroendoscopy to identify the locations of the abnormal ureteral orifice(s) and any other anatomic malformations.

Pelvic Bladder

- Incontinence is usually intermittent.
- There are voluntary urinations.
- Involuntary urine dribbles from vulva or prepuce.
- Urine "soiling" of the perineum, prepuce, tail, or caudal thigh.
- Urine spots or pools are present where dog has been lying down.
- Degree of incontinence caused by a pelvic bladder often exceeds that seen with urethral incompetence.
- Contrast cystourethrography may be required for full identification of caudally displaced bladder and may demonstrate a short, widened urethra or a urethra with a prominently convoluted appearance.

TREATMENT

Individual Disorders

Individual disorders are discussed in terms of their treatment modalities. See Table 83-2 for details of treatment, including drug dosages.

▼ ***Key Point*** Urocystitis commonly is associated with micturition disorders. Treat the underlying infection as well as the individual disorders.

Lower Motor Neuron Bladder

- Manually express the bladder 3 or 4 times daily.
- Long-term therapy for this disorder has not been successful.
- Bethanechol may be administered to increase detrusor contractions. Side effects such as vomiting, diarrhea, salivation, and anorexia may limit the drug's usefulness.
- Complications include urine scalding, decubital ulcers, and recurrent urinary tract infections.
- Agents that have been used experimentally to treat an atonic or hypocontractile bladder include metoclopramide, which has been reported to directly stimulate detrusor contractions in humans and dogs, and prostaglandins E_2 and F_2, which have been shown to stimulate both detrusor and urethral smooth muscle.

Upper Motor Neuron Bladder

- Initially, it is difficult to express the bladder manually. Because of the risk of bladder rupture, do not attempt this until manual evacuation of the bladder is tolerable.
- Instead, aseptically catheterize the patient at least 3 times daily to completely empty the bladder. Avoid using an indwelling catheter because of the risk of urinary tract infections.
- Perform frequent urinalyses with culture and sensitivity testing.
- Antibacterial agents may be indicated, especially with long-term intermittent catheterization.

Detrusor-Urethral Dyssynergia

Treat by decreasing sympathetic tone or with muscle relaxants (see Table 83-2).

Table 83-2. PHARMACOLOGIC MANAGEMENT OF MICTURITION DISORDERS

Drug	Class	Indications	Dosage	Side Effects	Contraindications
Baclofen (Lioresal, Ciba-Geigy)	Skeletal muscle relaxant	Detrusor-urethral dyssynergia	Dogs: 1–2 mg/kg q8h PO	General muscle weakness Gastrointestinal upset	
Bethanechol chloride (Urecholine, Merck Sharp and Dohme)	Parasympatho-mimetic	Detrusor atony	Dogs: 2.5–30 mg/dog q8h PO Cats: 2.5–5.0 mg/cat q8h PO	Vomiting Diarrhea Salivation Anorexia	Urethral obstruction
Dantrolene (Dantrium, Norwich Eaton)	Skeletal muscle relaxant	Functional urethral obstruction due to increased external urethral tone	Dogs: 3–15 mg divided q8–12h PO	Generalized muscle weakness Hepatotoxicity	
Diazepam (Valium, Roche Products)	Skeletal muscle relaxant	Functional urethral obstruction due to increased external urethral tone	Dogs: 2–10 mg q8h PO	Sedation	
Dicyclomine (Bentyl, Marion Merrill Dow)	Anticholinergic, direct-acting smooth muscle relaxant	Detrusor hyperreflexia Urge incontinence Obstructive uropathy	Dogs/cats: 10 mg q6–8h PO	Diarrhea Sedation	Hyperthyroidism Cardiac disease Prostatic hypertrophy
Ephedrine (various brand names and manufacturers)	Alpha-adrenergic agonist	Urethral sphincter incompetence	Dogs: 5–15 mg q8h PO Cats: 2–4 mg q8h PO	Restlessness Hypertension Excitability	Hypertension
Estrogen (Diethylstilbestrol, various veterinary compounding pharmacies)	Female sex hormone	Hormone-responsive incontinence	Dogs: 0.1–1.0 mg/day for 3 days, then 1.0 mg once weekly PO	Induces signs of estrus Bone marrow toxicity	
Flavoxate (Urispas, SmithKline & French)	Anticholinergic, smooth muscle relaxant	Detrusor hyperreflexia Urge incontinence	Dogs/cats: 100–200 mg q12–24h PO	Increased intraocular pressure Tachycardia	Glaucoma
Imipramine (Tofranil, Geigy)	Tricyclic antidepressant	Urethral incompetence	Dogs: 1 mg/kg q8h PO Cats: 2.5–5.0 mg q12h PO	Tachycardia Tremors Hyperexcitability Seizures	
Oxybutynin (Ditropan, Marion Merrell Dow)	Anticholinergic, smooth muscle relaxant	Detrusor hyperreflexia	Dogs/cats: 5 mg q8–12h PO	Diarrhea Sedation	Hyperthyroidism Cardiac disease Prostatic disease
Phenoxybenzamine (Dibenzyline, SmithKline & French)	Alpha-adrenergic blocker	Functional outflow obstruction	Dogs/cats: 0.25–0.5 mg/kg q8h PO Dogs (alternate): 2.5–20.0 mg/day PO	Nausea Hypotension Increased intraocular pressure	Glaucoma Diabetes mellitus
Phenylpropanolamine (various brand names and manufacturers)	Alpha-adrenergic agonist	Urethral sphincter incompetence Hormone-responsive incontinence	Dogs: 1–2 mg/kg q12h PO Cats: 1 mg/kg q12h PO	Restlessness Hypertension	Hypertension
Prazosin (Minipress, Pfizer)	Alpha-adrenergic blocker	Functional outflow obstruction	Dogs: 0.5–2.0 mg q12–24h PO Cats: 0.5–1.0 mg q12–24h PO	Hypotension Syncope Nausea/vomiting Diarrhea	Glaucoma Diabetes mellitus Caution with concurrent phenobarbital or sulfonamides

Table 83-2. PHARMACOLOGIC MANAGEMENT OF MICTURITION DISORDERS—cont'd

Drug	Class	Indications	Dosage	Side Effects	Contraindications
Propantheline bromide (Pro-Banthine, Schiapparelli Searle)	Anticholinergic	Detrusor hyperreflexia Urge incontinence	Dogs: 7.5–30.0 mg q8–24h PO; start low Cats: 7.5 mg q24–72h PO	Vomiting Xerostomia Sedation Constipation Increased intraocular pressure	Glaucoma
Testosterone cypionate (DEPO-testosterone, Upjohn)	Male sex hormone	Hormone-responsive incontinence	Dogs: 1–2 mg/kg q2–4wk IM	Prostatic enlargement Male sexual characteristics	
Testosterone propionate	Male sex hormone	Hormone-responsive incontinence	Dogs: 0.5–1.0 mg/kg 2–3 times per week SC or IM	Prostatic enlargement Male sexual characteristics	

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- Consider using alpha-adrenergic blocking agents, such as phenoxybenzamine, prazosin, and terazosin, to decrease internal sphincter resistance.
- In addition to its alpha-1 antagonism in urethral smooth muscle, prazosin can cause a centrally mediated decrease in somatic input to the external urethral sphincter.
- Consider diazepam and dantrolene as skeletal muscle relaxants to decrease external sphincter resistance.
- Baclofen is a skeletal muscle relaxant that decreases muscle tone by a depressive effect on the central nervous system (CNS). The drug inhibits medullary interneurons and spinal reflexes. Baclofen decreases muscle spasticity by reducing the activity of gamma-efferent neurons, which decrease the sensitivity of muscle spindles that initiate striated muscle stretch reflexes.

Hormone-Responsive Incontinence

Replacement of the sex hormone is necessary for successful treatment (see Table 83-2).

- Treat female dogs with diethylstilbestrol or an alpha-adrenergic agonist.

▼ ***Key Point*** Do not use estradiol cypionate because of the potential for bone marrow suppression.

- Testosterone cypionate may be used in male dogs. Minimal side effects have been noted except for prostatic enlargement.
- In some instances, animals develop a tolerance for hormonal replacement. Additional therapy with a sympathetic alpha-agonist that increases urethral tone is then indicated (see Table 83-2).

Urethral Incompetence (Stress Incontinence)

Treat with drugs that increase urethral tone (see Table 83-2).

- The most successful drugs are the sympathomimetic alpha-adrenergic agonists, which directly increase urethral smooth muscle tone. The drug of choice is phenylpropanolamine; an alternate drug is ephedrine.
- Imipramine is a tricyclic antidepressant agent that causes inhibition of norepinephrine reuptake at the synaptic level and results in increased urethral tone.

Urge Incontinence (Detrusor Hyperreflexia)

Treat with drugs that reduce detrusor hyperspasticity and relax smooth muscle (see Table 83-2).

- Flavoxate is an anticholinergic drug that decreases detrusor hyperspasticity. Start with the lowest possible dosage and slowly increase until signs are alleviated or side effects are encountered.
- Direct-acting smooth muscle relaxants are promising in the treatment of this syndrome. These drugs also have a mild anticholinergic effect. Recommended drugs include oxybutynin, dicyclomine, and propantheline bromide (marked anticholinergic effects).

Detrusor Atony from Overdistention

This is the single disorder in which indwelling urinary catheterization for up to 7 to 14 days is indicated to keep the bladder as small as possible in order to re-establish tight junction connections in the detrusor muscle. When indwelling catheterization cannot be accomplished, tube cystostomy is an alternative (see Chapter 80).

- Remove the obstruction or primary cause. Occasionally anti-inflammatory therapy is indicated.
- Perform frequent urinalyses and administer appropriate antibiotics based upon susceptibility results.
- The cholinergic drug bethanechol has been used successfully to stimulate detrusor contractions in both neurogenic and non-neurogenic atonic bladders (see Table 83-2). It is effective for postobstructive atony; however, be careful to ensure urethral patency.
- When the overdistension is caused by increased urethral resistance, administer an alpha-adrenergic blocker prior to giving the bethanechol.

Paradoxical Incontinence

Treat by relieving the obstruction. Retropulsion of calculi or urethrostomy or surgical exploration (e.g., for neoplasia) may be required (see Chapter 82).

- In some instances, indwelling catheterization may be indicated (e.g., severe urethritis) until the inflammation resolves.

Ectopic Ureter(s)

Treat by surgically re-establishing urine drainage into the bladder lumen (ureteral transposition or neoureterostomy (see Chapter 78).

- Ectopic ureters are often associated with other urinary tract abnormalities (urethral incompetence) that may be treated with alpha-adrenergic agonists.

Endoscopic Injections

Teflon

Teflon injections have been used clinically and experimentally for the treatment of urethral sphincter incompetence in dogs. A Teflon paste is injected endoscopically into urethral and periurethral tissues. This procedure inflates the tissues and compresses the urethral lumen at the site of injection.

Collagen

Collagen-based agents have supplanted Teflon products. Submucosal implantation of glutaraldehyde cross-linked collagen has had good results. One study found 75% of collagen-treated dogs becoming continent after one or two injections, with no complications.

▼ ***Key Point*** Consider collagen implantation for dogs that are not responsive to pharmacologic treatment. Also consider collagen implantation for dogs that continue to be incontinent after surgical correction of ectopic ureters.

Surgical Techniques

Several surgical treatments for incontinence have been described in the veterinary literature and include sling urethroplasty, colposuspension, and urethral compression (cystourethropexy or urethral banding). Surgery for disorders of the urinary system and micturition are discussed elsewhere in this text (see Chapters 78, 80, and 82).

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Chapter

84 Diseases of the Prostate Gland

Nancy D. Kay

Diseases of the prostate gland are common in middle-aged and older dogs. Medium- and large-breed dogs (especially Doberman pinschers) are more commonly affected. Although cats have prostate glands, for unknown reasons feline prostatic disease is extremely rare. This chapter discusses canine prostatic disease only.

ETIOLOGY

Several types of prostatic disease exist and some may occur simultaneously (e.g., prostatic cyst with abscessation or prostatic neoplasia with bacterial prostatitis).

Benign Prostatic Hyperplasia

To some degree, both hypertrophy (increased size) and hyperplasia (increased numbers) of prostatic cells account for enlargement of the gland in all middle-aged and older non-castrated dogs.

▼ ***Key Point*** Benign prostatic hyperplasia is the most common disorder of the prostate gland.

- Causes of benign prostatic hyperplasia include an imbalance in the ratio of androgens to estrogens, increased numbers of androgen receptors, and increased tissue sensitivity to androgens.
- Dihydrotestosterone is the main androgen that promotes prostatic hyperplasia.

Squamous Metaplasia

This morphologic alteration of prostatic epithelial cells is caused by estrogen stimulation arising from an exogenous or endogenous (e.g., Sertoli cell tumor) source.

Cystic Hyperplasia

This condition refers to multiple fluid-filled cavities within the prostatic parenchyma that result from the obstruction of glandular excretory ducts.

- Cystic hyperplasia commonly is associated with benign prostatic hyperplasia and squamous metaplasia.

Paraprostatic Cyst

These fluid-filled structures develop adjacent to the prostate gland and result from fluid accumulation within embryologic vestiges (uterus masculinus). The cystic lining may become calcified.

Prostatic Infection

- Bacterial prostatitis occurs when normal host resistance is altered.
- Predisposing causes include disruption of normal glandular architecture (benign hyperplasia, squamous metaplasia, neoplasia, parenchymal cysts), urethral diseases, urinary tract infections, alterations in urine flow, altered prostatic secretions, and host immune dysfunction.
- Infection usually occurs by an ascending route, although hematogenous spread of bacteria also may occur.
- The most common pathogens are *Escherichia coli, Staphylococcus, Proteus mirabilis, Streptococcus,* and *Mycoplasma.* Less common isolates include *Klebsiella, Brucella canis, Pseudomonas,* and *Ureaplasma.* Anaerobic infections are rare.
- In rare cases, disseminated (systemic) mycotic infections, such as *Blastomyces, Cryptococcus,* or *Coccidioides,* can cause prostatitis (see Chapter 20).

Idiopathic Prostatitis

Idiopathic (non-bacterial) prostatitis has been documented in dogs.

- Clinical signs are similar to those associated with chronic bacterial prostatitis.
- The etiology of the inflammation is uncertain.

Prostatic Abscess

Prostatic abscesses are either extensions of bacterial prostatitis in which obstruction of an excretory duct has occurred or secondary infection of a preexisting cyst.

Prostatic Neoplasia

Neoplasia is relatively rare compared with other forms of canine prostatic disease.

- Prostatic adenocarcinoma and transitional cell carcinoma are most common.
- Previously, castration was thought to prevent the development of prostatic cancer. In one study, 19 of 43 dogs had been castrated at least 3 years before the development of prostatic disease. More recent studies have also concluded that castration at any age has no sparing effect on the development of prostate cancer. Tumors from neutered dogs tend to be more highly undifferentiated and often metastasize to the lung. This may reflect a more aggressive neoplastic process or delayed detection of the disease.
- Development of prostatic cancer in dogs may not be hormonally mediated or may be influenced by hormones of non-testicular origin. Hormones produced by the adrenal and pituitary glands may play a significant role.
- Metastasis is common. Frequent sites of metastasis include lymph nodes (regional and distant), bones (near and distant), and visceral organs.

CLINICAL SIGNS

Clinical signs associated with canine prostatic disease are variable. Depression, anorexia, and vomiting are systemic manifestations of bacterial prostatitis or prostatic abscessation. Other clinical signs do not correlate well with etiology (Table 84-1). Hematuria and blood dripping from the prepuce are the most frequent signs seen with most types of prostatic disease. In animals with uncomplicated benign prostatic hyperplasia, however, clinical signs frequently are absent until prostatomegaly becomes severe.

- *Hematuria* is caused by reflux of blood from the prostatic urethra into the bladder. It also may be associated with a concurrent bacterial cystitis.
- *Urethral discharge* results from the exudation of blood, pus, and/or prostatic fluid into the prostatic urethra. This fluid drips passively from the penile urethra and is often blood tinged.
- *Stranguria* is present if partial or complete urethral obstruction results from prostatic enlargement.
- *Fecal tenesmus* or a *change in stool diameter* occurs when prostatic gland enlargement encroaches on the rectum. *Constipation* may be secondary to avoidance of pain associated with defecation.
- *Fever, depression, anorexia, vomiting,* and *diarrhea* are signs of systemic involvement and are most commonly associated with bacterial prostatitis or prostatic abscessation.
- *Recurrent urinary tract infection* in a male dog may be associated with non-resolving or recurrent bacterial prostatitis.
- *Abdominal distention* may be caused by a paraprostatic cyst or prostatic abscess.
- *Caudal abdominal pain, lumbar pain,* and/or *hind limb stiffness* may be associated with metastasis of prostatic neoplasia to bone or muscle or with peritonitis associated with prostatic abscess.
- *Hypertrophic osteopathy* may occur secondary to prostatic disease such as tumors.
- *Hind limb pitting edema* may occur secondary to lymphatic invasion by metastatic tumors.
- *Urinary incontinence* can be caused by impingement on the pelvic nerves by an adjacent prostatic mass (tumor or abscess) or from inflammation of the urethra from urinary tract infection.
- Other clinical conditions that may be associated with prostatic disease include *impaired libido, infertility, sepsis, ketoacidotic diabetes mellitus, perineal hernia,* and *testicular tumor.*

DIAGNOSIS

Localizing and defining the etiology of diseases of the prostate gland can be a challenging task. Until recently, few diagnostic techniques have combined reliability and

Table 84-1. INCIDENCE OF CLINICAL SIGNS ASSOCIATED WITH PROSTATIC DISEASE

Prostatic Disease (No. of Cases)*	Hematuria	Blood Dripping from Prepuce	Stranguria	Tenesmus	Depression/ Anorexia	Vomiting	Diarrhea	Abdominal Pain	Hind Limb Deficit	Chronic UTI
Bacterial prostatitis (12)	4	3	2	2	3	2	2	1	0	2
Nonbacterial prostatitis (7)	1	2	0	0	0	0	0	1	0	3
Hyperplasia (16)	7	6	1	1	0	0	1	0	0	4
Neoplasia (4)	3	3	2	3	0	0	0	0	1	0
Squamous metaplasia (2)	2	0	1	0	0	0	0	0	0	1

*Some prostate glands were affected by more than one disease process.
UTI, urinary tract infection.
Kay ND, Ling GV, Johnson DL: Clinical diagnosis of canine prostatic disease using a urethral brush technique. J Am Anim Hosp Assoc 25:517–526, 1989.

specificity of results with safety and ease of application. The ideal method for the diagnosis of prostatic disease should localize the disease to the prostate gland and eliminate other parts of the urinary and reproductive tracts as sources of the disease.

Physical Examination

Abdominal palpation in dogs with prostatic disease may reveal abdominal pain, abdominal distention, or the presence of an abdominal mass.

▼ ***Key Point*** A rectal examination is essential in the diagnosis of prostatic disease.

- In rectal examination, palpate ventrally for the prostate gland and dorsally for iliac lymph node enlargement or lumbar pain.
- Evaluate the prostate gland for location, size, symmetry, surface contour, consistency, movability, and pain. The normal prostate gland is bilobed, intrapelvic, symmetric, smooth, movable, and non-painful.
- As the prostate gland enlarges with disease, it may move cranially over the pelvic brim. Therefore, simultaneous rectal and caudal abdominal palpation may be helpful.

▼ ***Key Point*** The prostate gland of a normal Scottish terrier may be up to 4 times larger than those of other breeds.

Imaging Studies

Abdominal Radiography

Abdominal radiography rarely determines the specific etiology of prostatic disease, but it can reveal various associated abnormalities, including the following:

- Prostatomegaly
- Prostate gland asymmetry
- Abnormal fluid-filled mass in the caudal abdomen
- Prostate gland mineralization
- Iliac lymph node enlargement
- Vertebral or pelvic bone periosteal reactions
- Decreased soft tissue detail in the caudal abdomen due to tissue inflammation
- Urine or fecal retention

▼ ***Key Point*** Prostate gland mineralization and iliac lymph node enlargement are often but not always associated with prostatic neoplasia.

Urethrography

Positive-contrast retrograde urethrography may help localize the disease process. However, there is no correlation between the urethroprostatic reflux and the type of prostatic disease. Reflux may be observed in some dogs without prostatic disease.

Ultrasonography

Ultrasonography can be used to evaluate the prostate location, size, and architecture and to guide percutaneous needle aspiration or needle core biopsy. Ultrasound observations may include the following:

- Prostatomegaly
- Intraprostatic cyst or abscess (appears as focally hypoechoic or anechoic)
- Paraprostatic cyst
- Focal or multifocal areas of increased echogenicity (may represent bacterial prostatitis or neoplasia)
- Shadowing (may represent bacterial prostatitis or neoplasia)
- Prostatic calculi
- Iliac lymphadenopathy

Laboratory Studies

Complete Blood Count and Serum Biochemistry

- Hemogram abnormalities do not consistently correlate with the occurrence of infectious or noninfectious prostatic diseases. An exception is neutrophilic leukocytosis, which is consistently associated with acute, fulminant bacterial prostatitis.
- A mild to moderate nonregenerative anemia may occur in chronic inflammatory or neoplastic prostatic disease.
- An increase in serum alkaline phosphatase commonly accompanies bacterial prostatitis and prostatic neoplasia. It is not known which alkaline phosphatase isoenzyme is responsible.

Urinalysis and Urine Culture

- Bacterial cystitis and bacterial prostatitis may occur independently.
- Urinalysis and urine culture are always indicated for animals with signs of urinary tract disease. However, they may not be useful in the diagnosis of prostatic disease.
  - For example, urine sediment examination is not reliable for the diagnosis of prostatic neoplasia, and urine cultures can be negative in dogs with bacterial prostatitis or prostatic abscess.
  - For this reason, in addition to urine, evaluate prostatic fluid, prostatic tissue, or both in dogs suspected of prostatic disease.

Prostatic Fluid or Tissue Culture

This procedure is necessary for documentation of bacterial prostatitis. *Mycoplasma* organisms require specialized culture media (pleuropneumonia-like organism [PPLO] agar); therefore, specifically request this culture (see "Specimen Collection" for techniques for collection of microbiology specimens).

Prostatic Fluid Cytology

Cytologic studies may identify benign prostatic hyperplasia, squamous metaplasia, bacterial prostatitis, nonbacterial prostatitis, and prostatic neoplasia (see "Specimen Collection" for techniques for collection of cytology specimens).

Serum and Seminal Plasma Markers

- Prostate-specific antigen is not detected in canine serum or seminal plasma.
- Serum and seminal acid phosphatase activities do not differ between normal and diseased dogs.
- Serum canine prostate–specific esterase activity is higher in dogs with benign prostatic hyperplasia than in normal dogs.

Specimen Collection

Ejaculate Specimen

For ejaculate collection, handle the dog in a quiet environment. Many dogs are more responsive if exposed to a female in estrus or to vaginal swabs obtained from a female in estrus (Table 84-2).

Advantages

- It is relatively easy to perform.
- It is safe.
- It can be done without chemical restraint.
- It is inexpensive.
- It provides specimens for bacterial culture.

Disadvantages

- Success depends on the animal's compliance, which may be diminished if the animal is old, ill, weak, nervous, overexcited, or in pain.
- It is difficult to effectively separate the prostatic fluid component from the presperm and sperm components.
- A positive bacterial culture fails to localize the disease process. Potential sources of infection include the testes, epididymides, deferent ducts, prostate gland, and urethra. A distal urethral culture with quantitation of organisms collected before ejaculation is useful in interpreting ejaculate specimen culture results.
- The ejaculate specimen is not useful for cytology.

Table 84-2. TECHNIQUE FOR COLLECTION OF EJACULATE SPECIMEN

1. Retract the prepuce and gently cleanse the tip of the glans penis with a sterile gauze sponge.
2. Apply digital pressure with one hand at the base of the penis proximal to the bulbus glandis.
3. With the other hand, manipulate the penis within the sheath.
4. Collect the specimen in a sterile container.
5. The first two components of the ejaculate (presperm and sperm) are milky in appearance. Separate these from the third component, which is clear prostatic fluid, by collecting into two different sterile containers.
6. Perform a bacterial culture on the prostatic fluid.

Prostatic Wash Specimen

A prostatic wash specimen has potential microbiologic and cytologic applications (Table 84-3).

Advantages

Advantages of this technique are similar to those of ejaculate specimen collection.

Disadvantages

- Results may be inaccurate due to urine and urethral contamination, as well as volume dilution by urine. Microbiology results are non-interpretable in cases with concurrent bacterial cystitis.
- The prostate gland may not be within reach for effective rectal massage (abdominal prostatic massage may be effective).
- Overzealous massage can rupture a prostatic abscess or cause sepsis in dogs with acute bacterial prostatitis.

Urethral Brush Specimen (Figs. 84-1 and 84-2)

This technique uses a 90-cm microbiology specimen brush designed for bronchoscopic use (Microbiology Specimen Brush, Microvasive; Watertown, MA) (Table 84-4).

Advantages

Advantages of this technique are similar to those of ejaculate specimen collection and prostate wash, *plus the following:*

- The disease process is localized to the prostate gland; urethral contamination is minimized because of the plug in the tip of the catheter.

Table 84-3. TECHNIQUE FOR PERFORMING PROSTATIC WASH

1. Pass a urethral catheter into the bladder and remove all urine.
2. Flush the bladder with 5 ml of sterile physiologic saline solution and save the fluid. Label this specimen Sample 1.
3. Retract the catheter tip and align it with the caudal pole of the prostate gland (positioning is determined via rectal palpation).
4. Massage the prostate gland for 1 minute.
5. Flush 5 ml of sterile physiologic saline solution slowly through the catheter while the urethral orifice is occluded around the catheter to prevent retrograde loss of sample.
6. Advance the catheter into the bladder as the fluid is aspirated. Save the fluid and label it Sample 2.
7. Quantitate bacterial numbers in both specimens to ascertain the significance of bacterial growth in the prostatic fluid specimen (Sample 2).

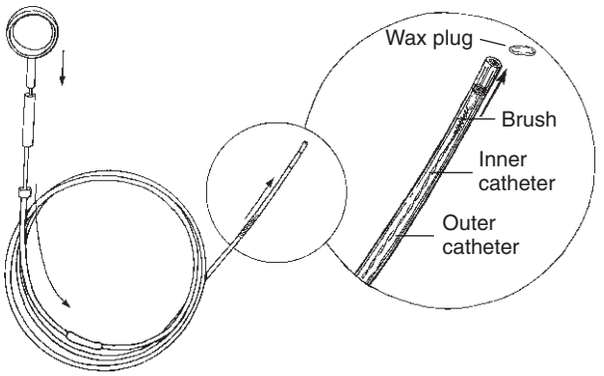

Figure 84-1. The microbiologic specimen brush used for obtaining prostatic urethral specimens.

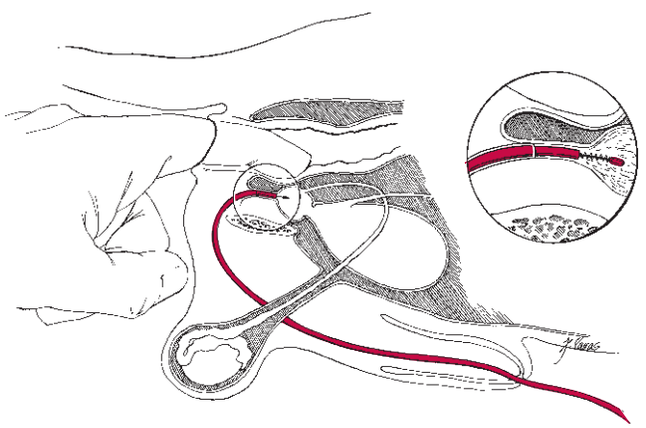

Figure 84-2. With the catheter positioned in the prostatic urethra, advance and retract the brush 5 or 6 times *(inset)*.

Table 84-4. TECHNIQUE FOR OBTAINING URETHRAL BRUSH SPECIMEN

1. Place the animal in lateral recumbency.
2. Retract the prepuce and cleanse the end of the glans penis with a sterile swab.
3. Advance a sterile, 90-cm microbiologic specimen brush (Microbiology Specimen Brush, Microvasive; Watertown, MA) into the urethra (see Fig. 84-1).
4. Direct an assistant to use rectal palpation to align the tip of the catheter with the caudal pole of the prostate gland (see Fig. 84-2). The catheter is then held in this position.
5. Have the assistant massage the prostate gland per rectum for 1 minute.
6. Advance the inner catheter approximately 1 cm within the urethra, thereby dislodging the absorbable catheter plug (see Fig. 84-1).
7. Advance and retract the microbiologic brush 5 or 6 times within the prostatic urethra for sample collection (see Fig. 84-2).
8. Following sample collection, retract the brush and inner catheter and remove the apparatus from the urethra.
9. Expel any fluid within the catheter into a test tube containing 3 ml of sterile lactated Ringer's solution.
10. Extend the brush, remove with sterile scissors, and drop into the same test tube.

- Useful cytologic and microbiologic information is obtained.

Disadvantages

- The specimen brush cannot be reused, which makes the procedure relatively expensive.
- The prostate gland may not be within reach for effective rectal massage (prostate massage through the abdominal wall is typically not effective).
- Overzealous massage can rupture a prostatic abscess or cause sepsis in dogs with acute bacterial prostatitis.

Ultrasound-Guided Prostatic Aspirate

This technique uses ultrasonography to guide the insertion of a needle into the prostate gland. Its documented use is for the diagnosis of bacterial infection and possibly neoplasia.

Advantages

- It is a safe procedure in non-infectious conditions.
- It accurately localizes the source of bacterial infection to the prostate gland.

Disadvantages

- Specialized equipment and skills are required.
- Chemical restraint usually is necessary.
- Aspiration of a prostatic abscess has the potential to result in peritonitis; seeding of the abdomen with neoplastic cells may occur with prostatic neoplasia.

Prostate Gland Biopsy

- Before performing biopsy, evaluate the animal for normal coagulation status.
- Several techniques have been described for prostate biopsy, including transperineal, transrectal, transabdominal, and ultrasound-guided biopsy and biopsy via laparotomy or laparoscopy (see Chapter 85).
- Ultrasound-guided prostate gland biopsy uses ultrasonography to assist in directing the biopsy instrument into the gland.
- The frequency of complications is less than with some other biopsy techniques, and the success of obtaining a definitive diagnosis is enhanced because focal lesions can be identified ultrasonographically.
- Chemical restraint, as well as specialized skill and equipment, are necessary.
- If ultrasonography is not available, biopsy via laparotomy is the most accurate, although the most invasive, technique.

- Several complications from prostate gland biopsy are possible (Table 84-5).

TREATMENT

Treatment of canine prostatic disease is based on the specific diagnosis. Conservative management (castration and drug therapy) of canine prostatic disease is discussed in this chapter. Surgical management of prostatic disease is discussed in Chapter 85.

Benign Prostatic Hyperplasia and Sterile Cystic Hyperplasia

Therapy may not be indicated if clinical signs are absent. However, it is advisable to caution owners that problems associated with prostatomegaly may develop.

Descriptions of various treatment modalities follow.

Castration

- Castration (see Chapter 87) is the treatment of choice in dogs not intended for breeding.
- A significant decrease in prostate gland size occurs within 1 to 4 weeks following castration.

Estrogen Therapy

- Theoretically, estrogen acts to decrease prostatic tissue mass by decreasing the concentration of gonadotropin-releasing hormone, which, in turn, decreases the concentration of testosterone. However, estrogen may act directly on the prostate gland to cause stromal hypertrophy and squamous metaplasia.
- It also may alter prostatic secretions and increase the gland's susceptibility to infection.
- Bone marrow suppression is a potential serious side effect.

▼ ***Key Point*** Because of potentially serious side effects, estrogen is contraindicated for the treatment of benign prostatic hyperplasia.

Megestrol Acetate

- Megestrol acetate interferes with the conversion of testosterone to dihydrotestosterone, the main androgen that promotes prostatic hyperplasia. This drug is also thought to increase metabolic clearance of androgens, as well as cause direct pituitary suppression.

▼ ***Key Point*** Megestrol acetate effectively decreases the size of the prostate gland without impairing fertility in cases of benign prostatic hyperplasia.

- Administer 0.55 mg/kg q24h PO for 4 weeks; then give the same dosage once a week. Do not use for longer than 32 consecutive days.
- This drug reportedly produces a decrease in the size of the prostate gland without decreasing the number of spermatozoa. Thus, a treated animal subsequently may be used for breeding purposes.

Finasteride

- Finasteride is an azasteroid that inhibits activity of the enzyme 5-alpha-reductase, which therefore prohibits the conversion of testosterone to dihydrotestosterone.
- Finasteride is reported to cause a decrease in prostatic size of 48% to 70% by 8 to 12 weeks of treatment.
- Administer 0.1 to 1 mg/kg/day (one 5-mg tablet daily for dogs weighing 5–50 kg). The optimum duration of therapy is unknown.
- Neither side effects nor decreased fertility have been reported.

▼ ***Key Point*** Finasteride has been reported to effectively decrease the size of the prostate gland without impairing fertility in cases of benign prostatic hyperplasia.

Delmadinone Acetate

- Delmadinone acetate (Tardak, Pfizer) is an androgen inhibitor licensed for use in dogs in some countries other than the United States and Canada.
- It is recommended for the treatment of benign prostatic hyperplasia, perianal tumors, and hypersexuality.
- Delmadinone acetate is administered SC or IM at doses of 1.5 to 2.0 mg/kg for dogs less than 10 kg, 1.0 to 1.5 mg/kg for dogs 10 to 20 kg, and 1.0 mg/kg for dogs greater than 20 kg; subsequent doses in 3- to 4-week intervals usually are necessary.
- Effects are observed within 2 to 4 days. A second treatment is recommended at 8 days if no improvement is noted.
- Concurrent use of other steroid drugs should be avoided, and this drug is contraindicated in dogs with a history of decreased fertility or lack of libido if they are to be used for breeding.

Other Hormone-Manipulating Drugs

New drugs, which work either by lowering serum testosterone (flutamide), blocking conversion of testosterone

Table 84-5. COMPLICATIONS ASSOCIATED WITH PROSTATE GLAND BIOPSY

Periprostatic hemorrhage	Hematuria
Perineal hematoma	Septicemia
Urethral perforation	Fever
Perineal abscessation	Peritonitis
Dissemination of neoplastic cells	Urethral fistula formation

to dihydrotestosterone (finasteride), or decreasing gonadotropin-releasing hormone (leuprolide) may show promise in the future for treating benign prostatic hypertrophy. However, minimal information is currently available regarding use of these drugs in dogs.

Squamous Metaplasia

- Discontinue any source of exogenous estrogen.
- Castration is the treatment of choice. Examine the testicles histopathologically for the presence of an estrogen-secreting Sertoli cell tumor.

Bacterial Prostatitis

Principles of Antibiotic Therapy

See Table 84-6 for specific drugs and dosages.

- Select an antibiotic based on urine or prostatic fluid culture and susceptibility results.

▼ ***Key Point*** The ideal antibiotic for bacterial prostatitis is lipid soluble and therefore capable of penetrating the blood-prostate barrier. Antibiotics of choice include erythromycin, chloramphenicol, trimethoprim-sulfa, clindamycin, oleandomycin, and enrofloxacin.

- The ideal antibiotic has a relatively low degree of protein binding, which allows greater drug availability for diffusion into the prostate gland. Chloramphenicol is highly protein bound; therefore, it should be used at the higher end of the recommended dosage range (see Table 84-6).
- In cases of bacterial prostatitis, the pH of the prostatic fluid is usually acidic. Antibiotics that work best in an acidic environment are erythromycin, enrofloxacin, clindamycin, trimethoprim-sulfa, and chloramphenicol. Ciprofloxacin and norfloxacin do not appear to penetrate into the prostate gland as readily as enrofloxacin.
- Continue antibiotic therapy for a minimum of 4 weeks. Reculture the prostatic fluid 5 to 7 days after the onset of therapy to document the in vivo effectiveness of the antibiotic and again in 2 to 3 weeks following discontinuation of therapy.
- If initial culture and susceptibility results cannot be obtained, a good initial treatment choice is trimethoprim-sulfa, chloramphenicol, or enrofloxacin.

Table 84-6. ANTIBIOTICS RECOMMENDED FOR THE TREATMENT OF BACTERIAL PROSTATITIS

Drug	Dosage
Trimethoprim-sulfa (multiple manufacturers)	15 mg/kg q12h PO or SC
Chloramphenicol (multiple manufacturers)	50 mg/kg q8h PO, IV, SC, or IM
Erythromycin (multiple manufacturers)	10 mg/kg q8h PO
Clindamycin (Antirobe, Upjohn)	5–10 mg/kg q8h PO, IV, or IM
Enrofloxacin (Baytril, Bayer)	5 mg/kg q12h PO*

*This is twice the manufacturer's current recommended dosage.

Treatment of Concurrent Septicemia or Peritonitis

- Evaluate the patient for abdominal effusion.
- Obtain abdominal fluid and/or blood for bacterial culture and susceptibility testing and select an appropriate antibiotic.
- Obtain a blood specimen for bacterial culture and susceptibility.
- Monitor the patient for hypoglycemia.
- Administer IV fluids and parenteral antibiotics.
- If a prostatic abscess is thought to be the source of septicemia, surgical drainage of the abdomen and treatment of the prostate is indicated (see Chapter 85).
- Treat peritonitis as described in Chapter 76.

Castration

Castration diminishes the potential for recurrence of bacterial prostatitis, but do not perform castration until the patient is clinically stable and has been on antibiotic therapy for at least 1 to 2 weeks. Rule out a prostatic abscess or paraprostatic cyst, because castration alone typically is not curative for these conditions.

Idiopathic Prostatitis

- Because idiopathic prostatitis in dogs has only recently been described and the etiology is unknown, effective therapy has not been reported. Castration is likely to be beneficial.
- Treatment of idiopathic prostatitis in humans has included tetracycline, corticosteroids, anticholinergic drugs, and muscle relaxants. No consistently positive results have been reported.

Paraprostatic Cysts and Prostatic Abscesses

- Medical therapy consists of antibiotics if infection is present and treatment of concurrent septicemia, peritonitis, or hypoglycemia.
- Paraprostatic cysts and prostatic abscesses are indications for surgical therapy (see Chapter 85).

Prostatic Neoplasia

Multiple therapeutic modalities exist; however, the prognosis in cases of prostatic neoplasia is poor.

Radiation Therapy

- Intraoperative radiation therapy is currently the treatment of choice. It is well tolerated by the patient and has few side effects.
- Radiation therapy is not indicated if metastasis is detected. The most common site for metastasis is the iliac lymph nodes. Other sites include lungs, omentum, mesentery, pelvis, and lumbar vertebrae.

Prostatectomy

Prostatectomy (see Chapter 85) is associated with a high rate of complications including urinary incontinence and urethral stricture and is typically not offered as a treatment.

Noninvasive Ultrasonic Subtotal Ablation

This experimental technique uses high-intensity, focused ultrasound to ablate the prostate gland without damaging surrounding tissues.

Chemotherapy

No known protocols have any documented efficacy.

Castration

Castration is of questionable benefit. The cancer growth may not be hormonally mediated, or it may be affected by non-testicular hormones (adrenal androgens or estrogens, luteinizing hormone [LH], follicle-stimulating hormone [FSH], prolactin, or growth hormone).

Estrogen Therapy

Estrogen therapy suppresses gonadotropin secretion by the pituitary gland, which, in turn, decreases the level of testicular testosterone secretion. As with castration, non-testicular hormones are unaffected.

Total Androgen Blockade

The advantage of a total androgen blockade over castration is that all sources of androgen production are affected rather than just testicular androgens.

- Luteinizing hormone-releasing hormone (LH-RH) agonists cause a transient rise followed by a paradoxical decrease in FSH, LH, and testosterone release. This decrease may be due to down-regulation of, or a decrease in, the number of pituitary LH-RH receptors. There is minimal information about use of these drugs in veterinary medicine.
- Ketoconazole (see Chapters 20 and 33 for details of ketoconazole therapy) inhibits testicular and adrenal testosterone synthesis and decreases the testosterone level to that of a castrated dog in 24 to 48 hours. The dosage range in humans is 400 to 1200 mg/day. Currently, a dosage for the treatment of canine prostatic neoplasia has not been determined, but dosages reported in limited studies vary from 20 to 30 mg/kg/day PO.
  - Ketoconazole has been shown to have a significant effect on hormonal production by the adrenal gland in the treatment of canine hyperadrenocorticism at an oral dose of 30 mg/kg once daily or divided twice daily. A similar dosage may be effective in the treatment of canine prostatic neoplasia.
  - Dosages of 10 to 30 mg/kg/day are tolerated by most dogs when used for antifungal therapy.

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Chapter 85

Surgery of the Prostate Gland

Harry W. Boothe

Surgical procedures of the prostate gland include biopsy, drainage procedures (including ultrasound-guided percutaneous needle drainage, drain tube placement, omentalization, and marsupialization), and resection procedures (partial or complete resection of prostatic cysts and partial or complete prostatectomy). Perform orchidectomy of the patient with prostatic disease either before or at the time of prostatic surgery (see Chapter 87 for castration technique). Prostatic disorders that may require surgery include hyperplasia, trauma, infection (abscess), cyst formation, and neoplasia. A thorough understanding of prostatic anatomy is necessary before performing surgery. Information in this chapter refers only to the dog because prostatic disease is extremely rare in cats. See Chapter 84 for additional information on prostatic diseases.

ANATOMY

- The prostate gland completely encompasses the proximal portion of the male urethra at the neck of the bladder.
- The position of the prostate is age dependent; the prostate is confined to the pelvic cavity until about 4 years of age and is essentially totally within the abdomen by 10 years of age.
- The dorsal prostatic surface is flattened and has a mid-dorsal sulcus. The gland has a relatively thick capsule and is divided into right and left lobes by a prominent median septum.
- The two deferent ducts enter the craniodorsal surface of the prostate.
- The blood supply is closely allied to the nerve supply, with both being located in the lateral pedicles and entering the prostate dorsolaterally. The prostatic artery gives off branches to the ductus deferens, urethra, urinary bladder, ureters, and rectum. Damage to branches of the prostatic artery may result in devascularization of surrounding structures.
- The hypogastric (sympathetic) and pelvic (parasympathetic) nerves follow the vasculature.

▼ ***Key Point*** The hypogastric and pelvic nerves are required for micturition and continence. Avoid iatrogenic trauma to these structures.

- The prostatic lymph vessels empty into the median iliac lymph nodes.

BIOPSY

Preoperative Considerations

- Accurate preoperative assessment of prostatic size, consistency, and location is important. Palpation (both rectal and abdominal), radiography (including contrast radiography), and ultrasonography are helpful in gaining this information. Ultrasound can also be used to assist in obtaining fine needle aspirates of the prostate (see Chapter 84).
- Adequate immobilization of the prostate gland during biopsy is indicated, particularly when using needle biopsy techniques.

▼ ***Key Point*** Perform aspiration of the prostate before needle biopsy to exclude abscessation.

Procedure for Percutaneous Needle (Punch) Biopsy

Objectives

- Obtain a representative sample of the prostate gland for histologic and microbiologic evaluation.
- Avoid entering the prostatic urethra.
- Minimize blood loss and potential dissemination of infection.

Equipment

- Tru-Cut or similar type of biopsy needle (one-handed model) or Franklin-Silverman needle
- Scalpel blade and handle

Technique

1. Place the dog in sternal recumbency with the tail positioned over the back.
2. Prepare the perineal region from the base of the tail to ventral to the level of the ischial tuberosities.
3. Direct an assistant to exert gentle pressure on the caudal abdomen to move the prostate gland into the pelvic inlet.

4. Perform rectal examination to define the position of the prostate gland.
5. Incise the perineal skin (5 mm long) just off the midline midway between the anus and the ischial tuberosity.
6. Insert the biopsy needle in the closed position through the prostatic capsule under digital control within the rectum by the other hand.
7. Fully insert the inner cannula into the prostate gland and, while holding the inner cannula stationary in its extended position, sharply advance the outer cannula over the inner rod.
8. Remove the biopsy needle in a closed position.
9. Verify that an adequate biopsy has been obtained by seeing prostatic tissue in the specimen notch.
10. Place the biopsy sample in the appropriate containers for histologic and microbiologic testing.

Surgical Procedure: Wedge Biopsy

Equipment

- Standard general surgical pack and suture
- Laparotomy sponges
- Balfour retractors

Technique

1. Place the dog in dorsal recumbency on a level surgery table.
2. Aseptically prepare the ventral abdominal region from the xiphoid process to caudal to the pubic brim.
3. Incise the skin and ventral abdominal wall from the umbilicus to the pubis while avoiding the prepuce. Use a midline abdominal approach. Alternately, a paramedian approach to the caudal abdomen can be used.
4. Gently retract the urinary bladder cranially using a stay suture. Isolate the prostate gland with moistened laparotomy sponges.
5. Excise a representative wedge of prostatic tissue, while avoiding the urethra on the midline and the dorsolateral aspect of the prostate gland, using a scalpel blade.
6. Close the prostatic defect (simple interrupted or continuous pattern, absorbable suture).
7. Routinely close the ventral abdominal incision in three layers.

Postoperative Care and Complications

Short Term

- Closely monitor for hemorrhage, including hematuria, infection, and urine leakage.
- Monitor for postoperative orchitis and scrotal edema.

Prognosis

- The prognosis depends on the disease process(es) present.
- Prostatic biopsy is usually associated with minimal patient morbidity.

DRAINAGE PROCEDURES

Preoperative Considerations

- Perform ultrasonography to determine the degree and location of cavitation within the prostatic parenchyma.
- Distinguish between infectious and non-infectious causes of fluid retention within or near the prostate gland.
- Perform microbiologic testing of prostatic fluid to assist in selection of an antimicrobial agent.
- When prostatic abscessation is present, drainage, omentalization, or resection of diseased parenchyma is indicated.
- Perform orchidectomy before or at the time of a prostatic drainage procedure.

▼ ***Key Point*** Always biopsy and obtain culture samples from the prostate as part of the drainage procedure.

- Choice of drainage procedure (i.e., ultrasound-guided percutaneous needle drainage, placement of drain tubes, omentalization, or marsupialization) depends on the size and location of prostatic cavitation. Large cystic lesions may be more amenable to partial resection and omentalization.

Objectives

- Thoroughly evacuate cavitary lesion(s).
- Create a common cavity to provide ventral drainage (surgical drainage).
- Thoroughly lavage the cavity at the time of drainage (surgical drainage).
- Avoid entering the prostatic urethra if possible.
- Minimize blood loss and dissemination of infection.

Procedure for Ultrasound-Guided Percutaneous Drainage

Equipment

- Ultrasound unit with a 7.5- or 8.5-MHz transducer (see Chapter 4)
- 22-gauge spinal needle, extension set, and syringe

Technique

1. Place the dog in dorsal or lateral recumbency (use sedation or anesthesia).
2. Aseptically prepare the abdominal region.
3. Examine the prostate ultrasonographically in both sagittal and transverse planes using a prepubic approach.
4. Measure and record prostatic size and appearance and any cavitary lesions.

5. Insert the needle using ultrasound guidance and completely drain the cavitary lesion(s).
6. Submit fluid samples for cytologic and microbiologic testing.

Surgical Procedure: Omentalization

Equipment

- Standard general surgical pack and suture
- Penrose drain(s)
- Suction apparatus, tubing, and tip
- Laparotomy sponges
- Balfour retractors

Technique

1. Place the dog in dorsal recumbency. Catheterize the urethra.
2. Aseptically prepare the ventral abdominal region from the xiphoid process to caudal to the pubic brim.
3. Incise the skin and ventral abdominal wall from the umbilicus to the pubis while avoiding the prepuce.
4. Isolate the prostate from the rest of the peritoneal cavity, using laparotomy sponges.
5. Incise the lateral aspects of each prostatic lobe.
6. Temporarily position a Penrose drain around the prostatic urethra within the parenchyma.
7. Remove fluid, using suction and lavage after digitally creating a common cavity. Obtain biopsy and culture samples.
8. Introduce the greater omentum through one capsulotomy wound by using forceps, which is placed through the contralateral prostatic wound (Fig. 85-1).
9. Pass the omentum around the prostatic urethra and exit it through the same capsulotomy wound through which it was introduced.
10. Suture the omentum to itself (horizontal mattress pattern, absorbable suture; see Fig. 85-2).
11. Routinely close the ventral abdominal incision.

Surgical Procedure: Placement of Drain Tube(s)

Equipment

- Same as for omentalization, plus red rubber urethral catheter

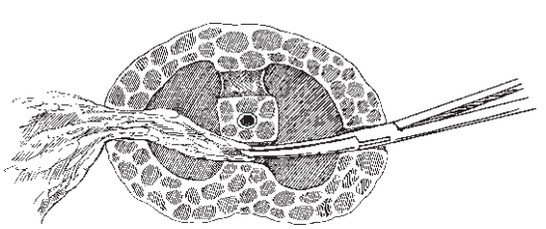

Figure 85-1. Intracapsular omentalization procedure. The greater omentum is introduced into the dorsal abscess cavities by using a forceps. (From White RAS, Williams JM: Intracapsular prostatic omentalization: A new technique for management of prostatic abscesses in dogs. Vet Surg 24:392, 1995.)

Technique

1. Refer to steps 1 to 4 under "Surgical Procedure: Omentalization."
2. Incise the ventrolateral aspect of the prostatic lobe(s) containing the fluid. Avoid vessels and nerves contained in the lateral pedicles.
3. Remove fluid, using suction and lavage after digitally creating a common cavity. Obtain biopsy and culture samples.

▼ ***Key Point*** Creation of a common prostatic cavity during any drainage procedure improves drainage and decreases the probability of recurrence.

4. Place one or more drains into the prostatic cavity while avoiding the urethra using one of the following methods:
   a. Pass Penrose drain(s) ($\frac{1}{4}$ inch) through the cavity to exit on the ventrolateral aspect of each lobe (Fig. 85-3).

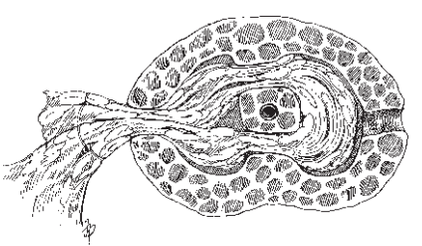

Figure 85-2. The omentum has been packed in the prostate gland encircling the urethra and has been sutured to itself. (From White RAS, Williams JM: Intracapsular prostatic omentalization: A new technique for management of prostatic abscesses in dogs. Vet Surg 24:393, 1995.)

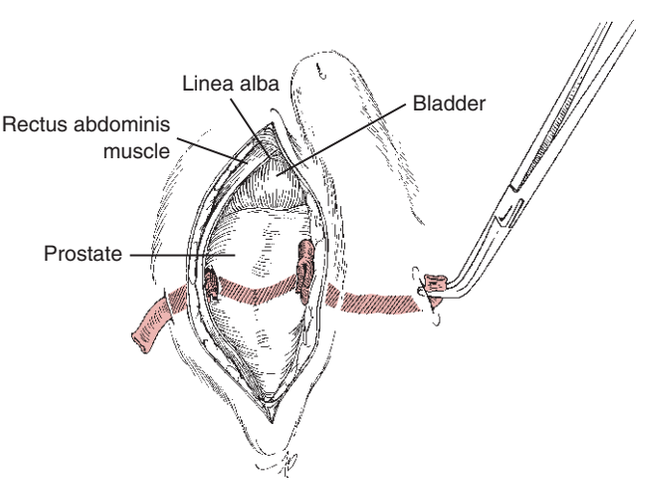

Figure 85-3. Prostatic drainage procedure. A single Penrose drain has been placed within the abscess cavity of the prostate and exits on the ventrolateral aspects of the gland. The ends of the drain are placed through the body wall and skin on each side of the prepuce.

b. Position a single red rubber catheter to permit continuous drainage of the prostatic cavity.
5. Exteriorize the end(s) of the drain tube(s) through the body wall approximately 2 cm lateral to the prepuce, and suture the drain to the skin.
6. Routinely close the ventral abdominal incision.

Surgical Procedure: Marsupialization

Equipment

- Same as for omentalization.

Technique

1. Refer to steps 1 to 4 under "Surgical Procedure: Omentalization."
2. Incise the ventrolateral aspect of the fluid-filled prostate and evacuate fluid, using suction and lavage after digitally creating a common cavity. Obtain biopsy and culture samples.
3. Incise the skin (5 cm long), subcutaneous tissue, and abdominal musculature just lateral to the prepuce on the side opposite the original skin incision.
4. Place the walls of the prostatic cavity near the skin incision and appose the wall adjacent to the prostatic incision to the external rectus fascia (simple continuous pattern, absorbable suture) and the incised prostatic edges to the skin (simple interrupted pattern, non-absorbable suture).

▼ ***Key Point*** If a paraprostatic cyst is present and can be dissected free from surrounding tissues, resection of all or most of the cyst is indicated. Pack the cyst remnant with omentum. This eliminates the complications associated with marsupialization.

5. Routinely close the ventral abdominal incision.

Postoperative Care and Complications

Short Term

- Closely monitor for hemorrhage, peritonitis, and septicemia.
- Prevent self-inflicted trauma to the drain(s) or the stoma site (marsupialization) or drain tubes by using a side brace or Elizabethan collar until the drains are removed.
- Continuous suction drainage using a single red rubber catheter and a suction reservoir may be more effective in evacuating prostatic cavities than simple gravity drainage; however, such drainage requires more conscientious postoperative patient observation and care.
- Passage of urine through the drainage tubes may occur but usually resolves in a few days.
- Prostatic abscessation requires aggressive medical therapy to eliminate infection and usually responds better to omentalization or drain tube placement than to marsupialization.
- Remove drains about 3 weeks postoperatively.
- Administer an appropriate antibiotic (see Chapter 84) to patients with prostatic abscessation for 2 to 4 weeks after the hospitalized period.

Long Term

- Long-term complications of prostatic tube drainage procedures include urinary incontinence (46% incidence), recurrent urinary tract infection (30% incidence), recurrence of prostatic abscessation (18% incidence), and urethrocutaneous fistula formation (2% incidence).
- Carefully monitor response to therapy through urine or prostatic fluid culture and susceptibility testing, as well as ultrasonography, if available, after discontinuing antibiotics.

Prognosis

▼ ***Key Point*** Paraprostatic cysts respond best to complete or partial surgical removal, because recurrence following drainage may occur and require additional drainage procedure(s), usually within 6 weeks of the initial drainage procedure.

- Prostatic abscessation has the potential for significant morbidity and mortality, and immediate postoperative mortality may approach 25%.
- The incidence of postoperative sepsis and shock approximates 33%. Rupture of a prostatic abscess results in a mortality rate of approximately 50%.
- Patients with prostatic abscessation that survive the initial 2 weeks after surgery will likely make a satisfactory recovery.

PARTIAL (SUBTOTAL) PROSTATECTOMY

Preoperative Considerations

- Be familiar with the vascular and regional anatomy of the prostate and surrounding structures.
- Perform partial prostatectomy for stable patients with recurrent abscessation and for dogs with cystic disease that have not responded to more conservative methods (i.e., orchidectomy and drainage).

▼ ***Key Point*** Complete rather than partial prostatectomy is indicated for prostatic neoplasia.

- Pass a urethral catheter to the urinary bladder to aid in identification of the urethra.

Surgical Procedure

Objectives

- Remove as much diseased prostatic tissue as possible while maintaining urinary continence.

- Avoid traumatizing the prostatic urethra.
- Maintain the blood supply to the prostatic urethra and adjacent organs.

Equipment

- Standard general surgical pack and suture
- Electrocoagulation unit with both coagulation and cutting capabilities
- Laparotomy sponges
- Balfour retractors

Technique

1. Refer to steps 1 to 4 under "Surgical Procedure: Omentalization."
2. Isolate and ligate all major vessels leading to the prostate, while staying immediately adjacent to the prostate gland.
3. Incise and remove the prostate to within approximately 5 mm of the lateral aspect of the prostatic urethra, using scissors and electrocoagulation, cutting electrocoagulation, or an ultrasonic surgical aspirator (Fig. 85-4).
4. Routinely close the ventral abdominal incision.

Postoperative Care and Complications

Short Term

- Submit excised tissue for histologic and microbiologic evaluation.
- Maintain urinary diversion (i.e., indwelling urethral catheter) for approximately 5 days.
- Prevent self-inflicted trauma to the urinary catheter by using either an Elizabethan collar or side brace until the catheter is removed.
- Shock, urine leakage, and urinary incontinence are potential short-term complications of partial prostatectomy.

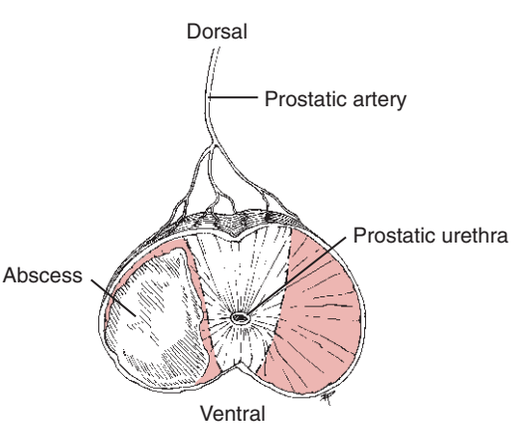

Figure 85-4. Partial (subtotal) prostatectomy technique. The shaded area denotes the prostatic parenchyma to be removed to within approximately 5 mm of the prostatic urethra using sharp dissection and/or an ultrasonic surgical aspirator.

Long Term

- Nocturnal urinary incontinence has been identified as a long-term complication of partial prostatectomy in approximately 50% of patients.

Prognosis

- The prognosis depends on the disease process(es) present.
- Resolution of prostatic and urinary tract infection is likely following partial prostatectomy and appropriate antimicrobial therapy.

TOTAL PROSTATECTOMY

Preoperative Considerations

- Indications for total prostatectomy include severe trauma, localized neoplasia with no apparent metastasis, and recurrent prostatic abscessation unresponsive to other, less invasive surgical procedures.

▼ ***Key Point*** Urinary incontinence is a common complication of total prostatectomy.

Surgical Procedure

Objectives

- Remove the entire prostate gland.
- Preserve the blood supply to the urinary bladder and urethra.
- Preserve as much urethra as possible.
- Perform an accurate urethral anastomosis.

Equipment

- Standard general surgical pack and suture
- Electrocoagulation unit
- Laparotomy sponges
- Urethral catheter
- Balfour retractors

Technique

1. See steps 1 to 4 under "Surgical Procedure: Omentalization."
2. Expose the prostate by careful dissection through the periprostatic fat as close to the prostate as possible.
3. Ligate and divide the prostatic vessels and ductus deferens close to the gland.
4. Carefully dissect the prostatic tissue from the urinary bladder and urethra, using sharp and blunt dissection.
5. Transect the urethra as close to the prostate and as far from the bladder neck as possible.
6. Transect the urethra as close to the caudal extent of the prostate as possible.

7. Remove the prostate by slipping it off the urinary catheter, and reposition the catheter into the urinary bladder. Submit the gland for histologic and microbiologic evaluation.
8. Approximate the urethral ends in an end-to-end fashion (simple interrupted pattern, synthetic absorbable suture), starting at the dorsal aspect of the urethra. Temporarily leave suture tags long and use them to help rotate the urethra to facilitate the anastomosis.
9. Thoroughly lavage the abdomen before closure.
10. Provide urinary diversion by performing a prepubic tube cystostomy (see Chapter 80) or by maintaining placement of the urethral catheter for approximately 2 weeks (longer if delayed healing is expected).
11. Routinely close the ventral abdominal incision.

Postoperative Care and Complications

Short Term

- Prevent self-inflicted trauma to the catheter by using a side brace or Elizabethan collar.
- Complications include urinary incontinence, urine leakage at the urethral anastomosis, and urethral stricture.

Long Term

- Urinary incontinence may be a long-term complication. Treat incontinence using drugs to increase proximal urethral tone (see Chapter 83).

Prognosis

- Prostatic neoplasia in the dog is most commonly malignant (adenocarcinoma or transitional cell carcinoma); metastasis is most common to the median iliac lymph nodes, periprostatic tissue, urinary bladder, pelvic structures, and lung (see Chapter 84).
- Successful treatment of prostatic neoplasia is difficult because of its aggressive biologic behavior; micrometastasis to adjacent tissues is probable, even when no gross evidence of metastasis exists.

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Chapter 86

Diseases of the Testes and Scrotum

Thomas K. Graves

A number of congenital and acquired diseases affecting the testes and scrotum are commonly recognized in small animal patients. Traumatic, infectious, and inflammatory diseases of the testes or scrotum are less common but may result in discomfort to the patient warranting presentation. Most dogs with testicular diseases have no clinical signs with the exception of infertility in breeding dogs.

DISEASES OF THE TESTES

Etiology

Congenital Disorders

Cryptorchidism

- Cryptorchidism is a common hereditary disorder in which one or both testicles fail to descend to the normal scrotal position. The disorder is recognized in both dogs and cats and is a sex-linked autosomal recessive trait.
- In dogs, toy breeds, boxers, and German shepherds are predisposed; in cats, the Persian breed is predisposed.
- In dogs, testicular descent occurs by 10 days of age, but it may be delayed 8 weeks or longer.
- Cryptorchid testes may be located within the abdominal cavity, within the inguinal ring, or subcutaneously in the prescrotal region.
- Unilateral cryptorchidism is more common than bilateral (75%).
- Dogs with bilateral cryptorchidism are sterile, whereas those with unilateral cryptorchidism are fertile. Undescended testicles are abnormal and have abnormal spermatogenesis because of the exposure to high body temperature.
- Even sterile dogs with cryptorchidism have normal libido, and male characteristics because testosterone secretion from interstitial cells is preserved.

▼ ***Key Point*** Perform bilateral orchiectomy (see Chapter 87) for all cryptorchid animals to eliminate the potential risk of testicular neoplasia, male feminizing syndrome, and testicular torsion and because it is a hereditary disorder.

Male Pseudohermaphroditism

- Affected dogs have testes, and XY chromosomes, but have external or internal female genitalia.
- The testes are hypoplastic and cryptorchidism is common.
- Abnormalities in the development of the prepuce and penis may also be noted.

Testicular Feminization Syndromes

- These dogs or cats have XY chromosomes but have partial or complete failure of masculinization.
- The syndrome is due to X-linked mutations in the androgen receptor gene.
- There can be a certain degree of testicular development in some animals. Others, although male, can be phenotypically female with no noticeable testicular development.

XX Sex Reversal

This chromosomal abnormality is associated with testicular abnormalities, as well as other genital malformations in dogs. (See Chapter 88.)

Acquired Disorders of the Testes

Orchitis-Epididymitis

Infectious Orchitis-Epididymitis

- Infection of the testes and epididymis can come from penetrating wounds, can be acquired hematogenously, or can come from spread of infections of the urogenital tract, including the prostate.
- Aerobic bacteria are most common.
- *Brucella canis* is an important cause of orchitis-epididymitis.
- *Mycoplasma* organisms have been implicated.
- Viral causes of orchitis-epididymitis include canine distemper virus and feline infectious peritonitis.
- *Blastomyces* organisms can be implicated in endemic areas.

- *Rickettsial* infections such as ehrlichiosis and Rocky Mountain spotted fever can be associated with testicular or epididymal infection.

Immune-Mediated Orchitis

- Normally, the blood-testis barrier prevents immune responses to spermatozoal antigens.
- When this barrier is disrupted, orchitis can ensue, and it is associated with lymphocytic infiltration of the testes and infertility.

Testicular Neoplasia

- Testicular tumors are relatively common in dogs and uncommon in cats.
- Primary testicular tumors include Sertoli cell and interstitial cell tumors and seminoma.
- Testicular neoplasia is 9.6% to 13.6% more likely in cryptorchid patients due to prolonged exposure of the retained testicle to normal body temperatures.
  - The contralateral descended testicle demonstrates the same neoplastic cells in 40% of the cryptorchid dogs.
  - Testicular neoplasia is rarely seen in cryptorchid cats.
- Most testicular tumors in dogs are so slowly metastatic as to be considered benign.
- Most testicular tumors in non-cryptorchid dogs are incidental findings in older patients. Intra-abdominal testicular tumors are usually suspected based on age, signs of hyperestrogenism or hypertestosteronism, and history of cryptorchidism.
- Sertoli cell tumors can result in male feminizing syndrome including hair loss (see Chapter 51), gynecomastia, hematologic abnormalities, testicular atrophy, and squamous metaplasia of the prostate.

Trauma

- Trauma to the testes and scrotum can lead to chronic orchitis-epididymitis or ischemia, so prompt attention to testicular trauma is necessary.

Testicular Torsion

- Testicular torsion can occur in cryptorchid or normal testes and is associated with acute onset of pain.
- Torsion results in swelling of the testicle and spermatic cord due to complete or partial obstruction of arterial blood flow and venous drainage.

Secondary Testicular Disorders

- Testicular dysfunction and infertility can occur secondary to endocrine diseases such as hyperadrenocorticism, diabetes mellitus, and hypothyroidism.
- A full metabolic evaluation is useful for dogs presenting for infertility.

Other Testicular Diseases

- Sperm granuloma can develop when sperm cells accumulate in the spermatic ducts, and a chronic inflammatory response ensues.
- Spermatocele is a sperm-containing dilation of the duct system and is considered a benign lesion.
- Varicocele is a dilation of the spermatic vein, which can lead to thrombosis but may also be a benign lesion.

Clinical Signs

- In some animals with testicular diseases, no clinical signs are noticed by the owner.
- Infertility is a common clinical sign.

Orchitis-Epididymitis

- Infection, trauma, or immune-mediated disease can cause pain and inflammation of the testes.
  - Animals may have scrotal swelling and a stiff gait. Frequent licking of the scrotum may be observed.
- Infectious disease of the testes can involve other components of the urogenital system, so clinical signs of prostatic disease (e.g., straining to urinate or defecate) can be present, as can signs of lower urinary tract infections (hematuria, stranguria, pollakiuria).
- Testicular inflammation can be associated with systemic signs of inflammation (e.g., depression, anorexia, and fever).

Neoplasia

- Estrogen from Sertoli cell tumors can result in feminization (testicular atrophy, infertility, gynecomastia), bone marrow suppression, alopecia (see Chapter 51), and squamous metaplasia of the prostate. Testosterone from interstitial cell tumors can result in prostatic hypertrophy, perianal adenoma, and other androgen-dependent changes. Seminoma has also been associated with hyperestrogenism.

Torsion

- Dogs with testicular torsion can present with acute, severe pain and swelling of the scrotal testicle. Testicular torsion occurring in cryptorchid patients may present with clinical signs of acute abdominal pain and vomiting.

Secondary Testicular Diseases

- Testicular diseases occurring secondary to endocrine and metabolic disorders are accompanied by clinical signs of the underlying primary disease.

Diagnosis

Physical Examination

- Perform a complete physical examination for all animals presented for testicular diseases or infertility (Fig. 86-1).

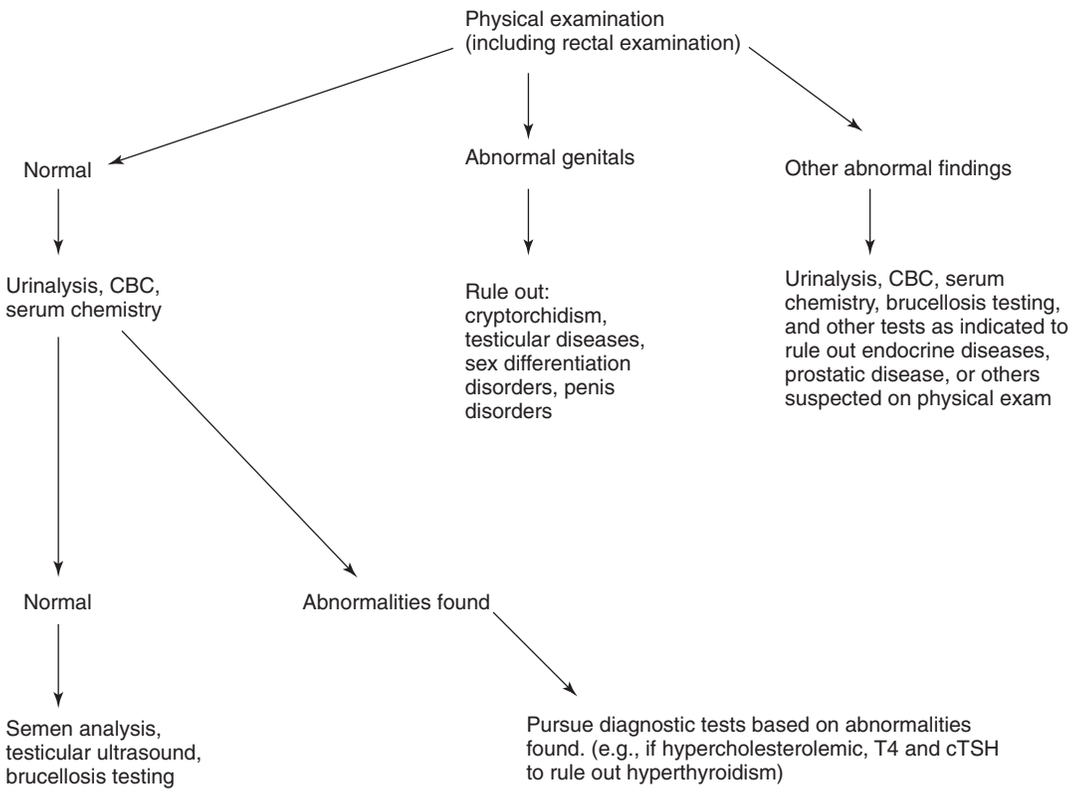

Figure 86-1. Algorithm for diagnosis of male infertility.

- Normally, the scrotum should contain two testicles of approximately equal size and shape. Testicles should be freely moveable within the scrotum.
- There is variability in testicular size among breeds of dogs and among individuals of the same breed.
- Cryptorchidism is diagnosed on physical exam, often as an incidental finding. Non-scrotal testes are found most commonly lateral to the prepuce or in the inguinal area. Abdominal testes usually cannot be palpated unless a neoplasm is present.
- The presence of one enlarged testicle indicates possible neoplasia, granuloma, spermatocele, varicocele, inflammation, or torsion. Assess for pain and the consistency of the testis, and distinguish the epididymis from the testis.

▼ ***Key Point*** An enlarged, firm testicle suggests neoplasia, whereas an enlarged, painful testicle is more consistent with orchitis.

- One abnormally small or irregular testicle in the presence of one normal testicle suggests a degenerative process due to local disease (e.g., chronic inflammation).
- Two small, soft testicles are consistent with testicular degeneration due to chronic inflammation, systemic conditions that cause testicular degeneration (e.g., some endocrine disorders), failure of normal testicular development, or normal aging.
- Perform rectal examination to assess the prostate gland and pelvic urethra in inflammatory disorders of the testes.
- Perform complete examination of the penis and prepuce because congenital developmental disorders of the testes are often associated with penis/prepuce malformations.

Routine Laboratory Tests

- Since many testicular disorders can be associated with systemic illness, perform complete blood count, serum biochemistry, and urinalysis as part of the diagnostic evaluation. These tests will aid in the diagnosis of inflammatory diseases, infectious diseases, neoplasia, and infertility.

Brucellosis Testing

- Brucellosis serology is first evaluated by the rapid slide agglutination test done in a hospital.
  - Because this test can have false-positive results, confirm a positive result with serology performed in a commercial diagnostic laboratory (see Chapter 19).

Diagnostic Imaging

- Ultrasonography can be used to detect undescended testicles.
- Ultrasonography can be used to detect testicular tumors. It can also help differentiate testicular lesions from epididymal lesions and can be used to guide fine-needle aspirates of the testes.
- Evaluate the prostate with ultrasonography in animals with testicular disorders since a variety of prostatic changes can occur.
- Although most testicular tumors are slow to metastasize, consider thoracic radiography to evaluate for metastatic tumors.

Semen Evaluation

Semen collection and evaluation is commonly performed to evaluate testicular abnormalities in breeding dogs. However, this procedure is technically difficult and not routinely performed in cats. In cases of infertility or inflammatory diseases, semen evaluation is indicated (see Chapter 94).

Technique

- Collect semen by retracting the prepuce caudally and manually stimulating the penis.
- If an artificial vagina is used, sterilize it before use to minimize contamination from penile and preputial mucosa commensal organisms. Alternatively, collect semen into a sterile cup placed at the tip of the penis. Most dogs ejaculate willingly and with minimal stimulation.
- Canine sperm is ejaculated in three fractions:
  - The first is a clear pre-sperm fraction of very small volume, composed of prostatic fluid.
  - The second is the sperm-rich fraction and is milky white in a volume ranging from 0.5 to 5 ml.
  - The third fraction is again clear, is composed of prostatic fluid, and can have very large volumes.

▼ ***Key Point*** The third fraction is not useful for semen analysis; separate it from the first two fractions. The third fraction may be useful to detect prostatic disorders.

  - Do not collect semen from an animal with obvious, overt inflammation of the testes. Collection of semen in these cases will not likely be possible, and testicular samples can be collected by fine-needle aspiration instead.

Semen Color and Consistency

- Blood-tinged semen can be the result of traumatic collection or prostatic disease.
- A non-opaque second fraction is consistent with oligospermia.
- Dogs with orchitis-epididymitis may have flecks or clumps of discolored debris in the semen consistent with purulent material.

Sperm Count

- Use a hemocytometer, using either the white or the red blood cell method, for determining the number of sperm per milliliter of ejaculate. Multiply this number by the volume of the ejaculate to determine the total sperm count.
- A normal canine ejaculate contains more than 200 million sperm cells.

Motility

- More than 70% of canine sperm should be progressively motile.
- To assess motility, place a drop of ejaculate on a warmed microscope slide covered with a warmed cover slip. Use microscope objectives of both 40× and 100×.

Morphology

- Abnormalities of morphology should not be seen in more than 20% of spermatozoa.
- Primary abnormalities are the result of abnormal spermatogenesis and include cytoplasmic droplets in the proximal midpiece, thickened midpiece, or misshaped heads.
- Distal cytoplasmic droplets can indicate epididymal disease.
- Secondary abnormalities occur in the epididymis and distally, so they are not due to abnormal spermatogenesis but can be due to post-testicle disorders or poor sample handling. These abnormalities include coiled or bent tails and detached heads.

Semen Cytology

Air-dried slides of semen samples can be stained and examined for inflammatory cells and infectious organisms.

Semen Alkaline Phosphatase

- Azoospermia can be the result of blockage of the epididymis. Because the canine epididymis produces alkaline phosphatase, the finding of a low activity of alkaline phosphatase in a semen sample indicates the absence of epididymal fluid.
- The normal range of alkaline phosphatase activity in canine semen is above 4,000 IU/L.

- Semen alkaline phosphatase activity is measured by the same methods as serum alkaline phosphatase activity.

Semen Culture

- Perform bacterial culture of the semen to diagnose infectious orchitis-epididymitis.
- Samples for culture include manually collected semen samples or testicular fine-needle aspirates.
- Culture results must be interpreted carefully in light of possible contamination from urogenital tract infections and from normal flora of the penis and prepuce.
- In general, semen culture from a dog with active bacterial infection should yield more than 10^5 colony-forming units per milliliter.
- Dogs with chronic infections can have false negative bacterial cultures.

Fine-Needle Aspiration

- Cytology of testicular/epididymal aspirates can reveal infectious organisms, inflammatory cells, or neoplastic cells.
- Normal testicular aspirates should contain sperm cells in their various stages of development.
- Chronic inflammation resulting in testicular atrophy and azoospermia can make collection of diagnostic fine-needle aspirates of the testes difficult.

Testicular Biopsy

- Surgical biopsy of the testicle is indicated to investigate azoospermia when no cause has been found by other diagnostic methods (see Chapter 87).
- Immune-mediated orchitis is an uncommon complication of testicular biopsy.

Diagnosis of Testicular Feminization Syndromes

- Diagnosis depends on demonstration of bilateral testes (although they may be intra-abdominal and minimally developed), XY chromosomal status, and positive response to a human chorionic gonadotropin (hCG) or gonadotropin challenge test to demonstrate that androgens are present.
  - Challenge testing is done by measuring testosterone in the serum 4 hours after hCG administration or 1 hour after gonadotropin-releasing hormone (GnRH) administration. The dose for hCG is 40 µg/kg IM in dogs and 250 µg total dose per cat IM in cats. GnRH is given at 2 µg/kg IM in dogs and 25 µg total dose per cat IM in cats.

Treatment

Cryptorchidism

- Because undescended testicles are at a highly increased risk for neoplasia, and to prevent promulgation of an undesirable hereditary trait, perform bilateral castration for cryptorchidism (see Chapter 87).

Orchitis-Epididymitis

- Castration, in combination with antibiotic therapy, is curative in most cases of bacterial orchitis-epididymitis (see Chapter 87). Assess the entire urogenital tract for sources of infection, and treat as necessary. Treat immune-mediated orchitis by castration.

Brucellosis

- Treatment of brucellosis is difficult. The infection is not always eradicated despite long-term antibiotic therapy. Combinations of a tetracycline antibiotic (doxycycline at 10 mg/kg PO bid, or tetracycline hydrochloride at 25 mg/kg PO tid) given for 4 weeks and dihydrostreptomycin (10 mg/kg IM tid during weeks 1 and 4 of tetracycline treatment) may be effective. (See also Chapter 19.)

▼ ***Key Point*** Do not breed dogs with brucellosis. Castrate these dogs to prevent spread of infection.

Testicular Neoplasia

- Perform castration for all testicular tumors (see Chapter 87). Adjunctive treatments are determined by results of histopathology and tumor staging.

Inherited Testicular Feminization Syndromes

- Perform castration (see Chapter 87).
- Because of the X-linked mode of inheritance, 50% of male offspring of a female carrier are affected, and 50% of female offspring are carriers. Care should be taken to identify carrier animals and remove them from breeding programs to prevent the disorder.

DISEASES OF THE SCROTUM

Primary diseases of the scrotum are uncommon, although changes in the scrotum are often seen in conjunction with other multisystemic diseases. In addition, generalized dermatopathies, such as those caused by dermatophytes, pyoderma, lupoid syndromes, keratinization defects, food hypersensitivities, and many others, can cause scrotal lesions.

Etiology

- *Contact dermatitis* through exposure of the scrotum to chemical irritants such as soaps or dips can cause local irritation and erythema.
- *Neoplasia* of the scrotum can occur such as cutaneous mast cell tumor, squamous cell carcinoma, and malignant histiocytic disease.

- *Environmental injury* can occur to the scrotum, such as frostbite or sunburn.
- *Drug eruption* can occur from drugs such as diethylcarbamazine, 5-fluorocytosine, and aurothioglucose.
- *Trauma,* such as abrasions, penetrating injuries, or blunt trauma causing hematoma.
- *Scrotal self-mutilation* associated with sperm granuloma, orchitis, or drug-induced pruritus or as a complication of castration.
- *Scrotal hernia* can cause abdominal contents to herniate through the inguinal canal and protrude into the vaginal process next to the spermatic cord in intact dogs. When this occurs, a scrotal swelling is noted. Strangulation of displaced contents within a scrotal hernia can cause acute severe pain and systemic illness and is a surgical emergency.

Diagnosis and Treatment

Diagnosis and treatment of primary scrotal disorders requires identification of the underlying cause. A thorough medical history aids in the diagnosis of environmentally induced scrotal injury or drug exposure. For diagnosis and treatment of specific skin disorders, see relevant chapters in Section 5.

- *Cytology* of scrotal skin can support a diagnosis of infectious or inflammatory disease (see Chapter 37).
- *Ultrasound* of the scrotum can help identify tumors, testicular adhesions, and scrotal hernia. Fine-needle aspiration and cytology of scrotal masses can identify tumor types.

▼ ***Key Point*** With severe lesions, perform scrotal ablation (with castration of intact animals) and histopathology to confirm a diagnosis, indicate treatment options, and provide prognostic information (see Chapter 87).

- Scrotal hernia repair involves castration and suture closure of the defect in the inguinal ring.

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Chapter 87

Surgery of the Testes and Scrotum

Harry W. Boothe

Orchidectomy is the most commonly performed surgical procedure of the testis. The technique depends, in part, on species and location of the testes (i.e., ectopic or scrotal). Indications for performing orchidectomy are listed in Table 87-1. Testicular biopsy may be part of a fertility examination. Scrotal ablation may be part of a routine orchidectomy or for neoplasia resection, especially in older dogs. It is also performed at the time of scrotal urethrostomy and feline perineal urethrostomy.

▼ ***Key Point*** Obtain owner consent before performing orchidectomy as a primary procedure or concurrent with another surgical procedure.

ANATOMY

- The testes are positioned obliquely within the scrotum, with their long axis directed dorsocaudally.
- The scrotal testis is covered by peritoneum (parietal and visceral vaginal tunics) and a dense, white, fibrous capsule (tunica albuginea).
- The testis and epididymis are connected to the parietal vaginal tunic by the caudal ligament of the epididymis.
- The arterial and venous patterns are similar, with the right testicular artery originating from the abdominal aorta cranial to the left and the veins forming an extensive pampiniform plexus in the spermatic cord.
- The right testicular vein empties into the caudal vena cava, whereas the left terminates in the left renal vein; testicular lymphatics drain to the median iliac lymph nodes.
- The canine scrotum is located more ventrally than the feline.
- The scrotal wall consists of the skin and dartos, a layer of smooth muscle and elastic fibers.
- The external spermatic fascia attaches to the caudal aspect of the scrotum as the scrotal ligament.
- Blood supply to the scrotum is principally via branches of the external pudendal artery; lymphatic drainage is to the inguinal lymph nodes.

TESTICULAR BIOPSY

See Chapters 86 and 94 for indications.

Preoperative Considerations

- Usually only one testis is sampled.
- Incisional techniques usually provide the best tissue samples for analysis.
- Fixation of specimens in Bouin's, Zenker's, or Stieve's fixative is preferable to formalin fixation because of better preservation of architectural detail.

Surgical Procedure

Objectives

- Obtain a representative sample of the testis for histologic evaluation.
- Minimally disrupt the testicular architecture.

Equipment

- Standard general surgical pack and suture
- Sterile, thin razor blade
- Bouin's, Zenker's, or Stieve's fixative

Technique

1. Place the animal in dorsal recumbency and aseptically prepare the prescrotal area.
2. Incise the skin just cranial to the scrotum and place the testis with the epididymis away from the incision.
3. Incise the tunics with a scalpel blade and the tunica albuginea with a sterile, thin razor blade, while avoiding blood vessels.
4. Excise the bulging testicular tissue using the razor blade or, if testicular tissue does not bulge, excise a wedge of testicular parenchyma. The razor blade's sharp, flat blade makes it ideal for this procedure.
5. Close the tunica albuginea and the tunics separately (simple interrupted pattern, 4-0 absorbable suture).
6. Routinely close the skin (simple interrupted pattern, non-absorbable suture).

Table 87-1. INDICATIONS FOR PERFORMING ORCHIDECTOMY IN THE DOG AND CAT

Sterilization	Prostatic cyst
Modification of behavior patterns	Perineal adenoma
Testicular neoplasia	Perineal hernia
Severe testicular or scrotal trauma	Scrotal urethrostomy (canine)
Refractory orchitis-epididymitis	Perineal urethrostomy (feline)
Benign prostatic hyperplasia	
Suppurative prostatitis	

Postoperative Care and Complications

- Uncommon complications include hemorrhage, infection, scarring, adhesions, and atrophy.
- A temporary slight decrease in sperm count may occur.

Prognosis

- The prognosis depends on the disease process(es) present (see Chapters 86 and 94).
- Minimal patient morbidity is expected.

ORCHIDECTOMY IN THE DOG

Preoperative Considerations

- Determine the location of the testes before surgery.

Cryptorchidism

- If the animal is a unilateral cryptorchid, determine which testicle has descended and therefore which one is retained.
  - Push the normal testicle dorsally and cranially to determine which inguinal canal (right or left) it slides into.
  - Carefully palpate the inguinal canal(s) to determine if the retained testicle is located there or in the abdominal cavity.
- In a cryptorchid animal, approach an abdominal testis through a paraprepucial skin incision and an extra-abdominal ectopic testis by incising directly over the testis (usually in the inguinal region).
- Histologically examine all ectopic and grossly abnormal testes.

Surgical Procedures

Objectives

- Remove both testes.
- Remove scrotal testes using either the closed or the open method (choice of technique is the surgeon's preference).
- Minimize postoperative complications and patient morbidity.

Equipment

- Standard general surgical pack and suture

Technique for Scrotal Testis (Closed Technique)

1. Place the dog in dorsal recumbency and aseptically prepare the prescrotal area. Avoid clipping and scrubbing the scrotal skin to minimize dermal irritation.
2. Incise the prescrotal skin on the midline while gently pushing one testis toward the skin incision.
3. Incise the subcutaneous tissue and spermatic fascia over the testis to expose the parietal vaginal tunic.
4. Exteriorize the tunic-covered testis and, using scissors, incise the spermatic fascia and scrotal ligament close to the testis.
5. Reflect the fat and fascia surrounding the parietal vaginal tunic using a gauze sponge to enable maximal exteriorization of the spermatic cord.
6. Double-ligate the intact spermatic cord and vaginal tunics using transfixation ligatures of absorbable suture material (Fig. 87-1).
7. Transect the spermatic cord and cremaster muscle distal to the ligatures and return them to the inguinal region.
8. Routinely close the subcutaneous tissue (simple interrupted pattern, absorbable suture) and skin (simple continuous intradermal pattern, absorbable suture).

Technique for Scrotal Testis (Open Technique)

1. Exteriorize the testis as described for the closed technique.
2. Incise the parietal vaginal tunic where ligatures are to be placed on the spermatic cord.
3. Double-ligate the spermatic cord using transfixation ligatures of absorbable material.

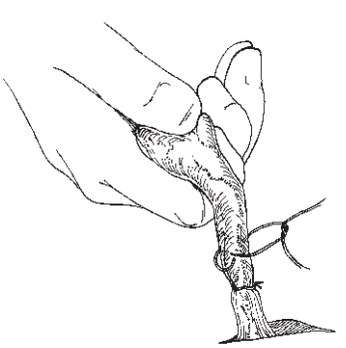

Figure 87-1. Transfixation (double) ligation of the intact spermatic cord. The suture needle is carefully passed through the ductus deferens of the spermatic cord. The entire spermatic cord, vaginal tunics, and cremaster muscle are enclosed in the ligature.

4. Alternatively, incise the parietal vaginal tunic over the testis and then double-ligate the spermatic cord using transfixation ligatures of absorbable material.
5. Ligate the parietal vaginal tunic and cremaster muscle using a transfixation ligature; transect the spermatic cord and cremaster muscle, and return them to the inguinal region.
6. Routinely close the subcutaneous tissue (simple interrupted pattern, absorbable suture) and skin (simple continuous intradermal pattern, absorbable suture or routine skin closure with monofilament non-absorbable suture).

Technique for Abdominal Ectopic Testis

1. Place the dog in dorsal recumbency and aseptically prepare the ventral abdominal region from the xiphoid process to caudal to the pubic brim.
2. Incise the skin and ventral abdominal wall from the umbilicus to the pubis while avoiding the prepuce. A midline abdominal approach is used. In a unilateral cryptorchid dog, a paramedian abdominal approach can be used on the side of the retained testicle.
3. Locate the ectopic testis by tracing one of the following:
   - Ductus deferens from its prostatic termination
   - Testicular artery from its aortic origin
   - Testicular vein from its termination in the caudal vena cava (or left renal vein)
   - Gubernaculum testis to the testis
4. Double-ligate the testicular vessels and ductus deferens.
5. Transect the vessels and ductus deferens; remove the testis and submit it for biopsy.
6. Routinely close the ventral abdominal incision in three layers.

Technique for Extra-Abdominal Ectopic Testis

1. Place the dog in dorsal recumbency and prepare the pubic region.
2. Incise the skin and subcutaneous tissue directly over the testis. Remove any loose connective tissue to expose the spermatic cord.
3. Double-ligate and transect the spermatic cord.
4. If the testis is not found subcutaneously, extend the incision into a paramedian approach to the abdomen and find the testis, as previously described.
5. Routinely close the subcutaneous tissue (simple interrupted pattern, absorbable suture) and skin (simple interrupted pattern, non-absorbable suture).

Postoperative Care and Complications

Short Term

- Use an Elizabethan collar to help prevent self-inflicted trauma. Intradermal skin closure also helps prevent self-trauma to the incision.
- Consider postoperative analgesic administration (see Chapter 6).
- Scrotal bruising and inflammation may occur, particularly following the open technique.
- Hemorrhage may occur and can be serious. Severe scrotal swelling from hemorrhage may necessitate scrotal ablation.
- Scrotal infection may require drainage or scrotal ablation.
- Inadvertent prostatectomy has been reported as a complication of removal of abdominal ectopic testes.

Prognosis

- Prognosis following orchidectomy of the cryptorchid dog is generally favorable even with testicular neoplasia, which usually is benign.

ORCHIDECTOMY IN THE CAT

Preoperative Considerations

See "Orchidectomy in the Dog."

Surgical Procedure

Objectives

See "Orchidectomy in the Dog."

Equipment

- Standard minor surgical pack

Technique

1. Position the cat in dorsal recumbency with the rear limbs pulled cranially, and aseptically prepare the perineal region.
2. Incise the scrotum over each testis and expose the testis.
3. Grasp the parietal vaginal tunic with hemostats, separate it from the testis, and excise it.
4. Separate the ductus deferens from the rest of the spermatic cord and separate it from the testis.
5. Tie two square knots in the spermatic cord, using the ductus deferens and spermatic vessels as separate strands, and transect the spermatic cord distal to the knots.
6. Alternatively, ligate the spermatic cord using an instrument-tied overhand knot with absorbable suture material or by tying the spermatic cord on itself.
7. Do not suture the scrotal incision.

▼ ***Key Point*** Do not perform the traction avulsion technique of feline orchidectomy because of the potential for significant postoperative complications, including hemorrhage and urethral avulsion.

Postoperative Care and Complications

See "Orchidectomy in the Dog."

Prognosis

See "Orchidectomy in the Dog."

SCROTAL ABLATION

Preoperative Considerations

- Indications include severe trauma, neoplasia, ischemia, scrotal abscess, orchidectomy in old dogs with pendulous scrotums, scrotal urethrostomy, and feline perineal urethrostomy.

▼ ***Key Point*** Plan the skin incisions to leave sufficient skin for tension-free closure.

Surgical Procedure

Objectives

- Reduce postoperative problems following orchidectomy in the dog.
- Allow incision into the urethra and subsequent urethrostomy.
- Remove redundant scrotal tissue.

Equipment

- Standard general surgical pack and suture

Technique

1. Place the animal in dorsal recumbency and prepare the periscrotal region.
2. Incise the skin in an elliptical, curvilinear fashion near the base of the scrotum, with the incisions curved toward the scrotum (Fig. 87-2).
3. Transect the scrotal septum after orchidectomy and routinely close the subcutaneous tissue (simple interrupted pattern, absorbable suture) and skin (simple interrupted pattern, non-absorbable suture).

Postoperative Care and Complications

Short Term

- Consider postoperative analgesic administration (see Chapter 6).
- Prevent self-inflicted trauma to the incision. This may require an Elizabethan collar.

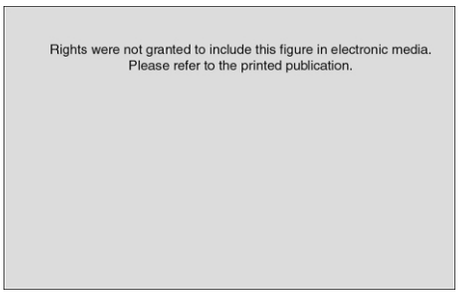

Figure 87-2. Ablation of the scrotum in the dog. The curved scrotal skin incision curves toward the scrotum to ensure tension-free closure of the incision. (From Harvey CE: Scrotal ablation and castration in the dog. J Am Anim Hosp Assoc 9:170, 1973.)

- Common complications include hemorrhage, particularly associated with urethrostomy procedures (see Chapter 82), infection, and dehiscence.

Prognosis

- Minimal patient morbidity is expected.

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Chapter 88

Diseases of the Penis and Prepuce

Thomas K. Graves

Animals with diseases of the penis and prepuce can be presented for a variety of clinical signs. Commonly, discharge or hemorrhage from the prepuce is the presenting complaint. Other clinical problems associated with penis and prepuce disorders are abnormal urination, neoplasia, inability to mate, or persistent penile erection. Urethral diseases are discussed in Chapter 81.

ETIOLOGY

Congenital Disorders of the Penis and Prepuce

Congenital disorders of the penis and prepuce are uncommon in dogs and cats. Congenital malformations of the penis are often associated with preputial malformations. Clinical signs may result from either the inability to retract the penis into the prepuce or the inability to extend the penis from the preputial orifice.

Persistent Penile Frenulum

- During the perinatal period, the surface of the glans penis and the preputial mucosa separate. When this separation fails, abnormal connective tissue, most commonly joining the ventral midline of the distal penis and prepuce, persists, resulting in the inability of the penis to extrude fully from the prepuce.

Hypospadia

- Hypospadia results from abnormal closure of the urethral tube during development and can cause one or more abnormal urethral orifices located anywhere along the length of the urethra.
- Most commonly, the abnormal orifice is located along the ventral aspect of the penis and prepuce, but it may extend through the scrotal region to the perineal region. The condition is due to incomplete masculinization during development, and it can be associated with an underdeveloped penis and/or with preputial malformations.
- An androgen receptor defect is responsible for lack of normal penile development under the influence of dihydrotestosterone.
- Familial hypospadia has been recognized in Boston terriers.
- Teratogens have been implicated in hypospadia in other species but not in dogs and cats.

Penile Hypoplasia

- Hypoplasia can occur with failure of masculinization, as seen in androgen receptor defects, and has been observed in both dogs and cats.
- Ambiguous genitalia can be found in XX sex reversal syndromes. Affected dogs can exhibit multiple penile and preputial abnormalities and are sterile.
  - Breeds reported with XX sex reversal include English cocker spaniel, American cocker spaniel, Weimaraner, beagle, Doberman pinscher, pug, Kerry blue terrier, soft-coated wheaten terrier, German shorthaired pointer, and Pomeranian.
- Female pseudohermaphroditism, in which the chromosomal sex is XX and ovaries are present, results from the presence of androgens during fetal development. Affected animals can exhibit clitoral enlargement or any degree of penile development, which can mimic penile hypoplasia.
- Penile hypoplasia can result in urine pooling, causing irritation and inflammation of the preputial lining.

Phimosis

- Phimosis occurs when the preputial opening is too small (preputial stenosis) to allow extrusion of the penis. Pooling of urine within the prepuce can result in inflammation and infection (balanoposthitis).

Os Penis Deformity

- Deformity of the os penis can result in deviation of the penis.
- Copulation may be impaired due to excessive flaccidity of the penile tip.

Acquired Penile Disorders

Priapism

- Priapism is defined as persistent, abnormal penile erection and is due to failure of venous outflow of blood from the erect penis.
- The causes are often not well understood. A persistent erection that is associated with hyperactive behavior or sexual arousal is not considered priapism. Also, priapism must be differentiated from other disorders that cause persistent swelling of the penis, such as hematomas that can be observed in association with trauma or coagulopathies.

▼ ***Key Point*** Priapism is considered a medical emergency. Stasis of blood in the engorged penis can lead to thrombosis and ischemia.

- In men, priapism can be drug-associated, caused by use of alpha-adrenergic antagonists, antidepressants, and phosphodiesterase inhibitors used to treat erectile dysfunction (e.g., sildenafil). With more widespread use of these drugs in people, animal toxicities causing priapism are likely.

Trauma

- There are numerous causes of blunt or penetrating trauma that can affect the preputial region and possibly the penis in small animal patients.
- Penile damage may be clearly evident in some animals presented as trauma emergencies. In other animals, trauma to the penis, due to such causes as animal bites, mating mishaps, human malice, or iatrogenic trauma from repeated catheterizations, can present with preputial discharge and swelling, pain, fever, or other signs of inflammation.
- Penile hematoma resulting from trauma may mimic priapism.

Foreign Body

- Foreign bodies can become lodged within the prepuce surrounding the penis and can create significant damage and inflammation.
- Grass awns, mulch, other plant materials, or small particulate materials can lodge with the prepuce, creating significant inflammation and resultant balanoposthitis.
- Circular constricting lesions from preputial hair rings or other foreign objects within the prepuce can result in constriction of the penis, venous stasis, swelling, and paraphimosis.

Neoplasia

- Benign and malignant neoplasms involving the prepuce and penis are relatively uncommon in dogs and cats.

Transmissible Venereal Tumor

- This tumor is usually seen in young dogs and presents as a reddened, irregular mass on the mucosa of the penis.
- It is transmitted sexually and can affect either sex.

Preputial Tumors

- The most commonly seen preputial tumors are cutaneous mast cell tumors, affecting the skin of the prepuce, and transmissible venereal tumors.

Other Tumors

- Urethral tumors can involve the penis. Examples of such tumors include transitional cell carcinoma and squamous cell carcinoma.
- Osteosarcoma of the os penis has been reported in the dog.

Balanoposthitis

- Balanoposthitis is inflammation of the prepuce and penis. The most common cause is bacterial infection, which can occur secondary to preputial or penile malformation, trauma, a lodged foreign body, or spontaneously.
- Non-bacterial causes of balanoposthitis, such as herpesvirus and *Blastomyces dermatitidis*, have been seen but are uncommon.
- Balanoposthitis is common in dogs but extremely uncommon in cats.
- Because of the abundance of normal flora in the prepuce, balanoposthitis can be associated with many different bacteria.

Paraphimosis

- Paraphimosis is a disorder in which the penis, following extrusion during an erection, is unable to retract back into the prepuce.
- The condition occurs when the penile mucosa adheres to the skin, mucosa, or hair of the prepuce.
- When retraction of the penis is attempted, the prepuce rolls in on itself, creating an inadequate opening to allow retraction of the penis.
- Paraphimosis can lead to edema of the penis, and chronic paraphimosis can result in ischemic damage and necrosis.

CLINICAL SIGNS

- *Purulent preputial discharge* can be seen with balanoposthitis, a foreign body, trauma, or any penile malformation that results in abnormal urine flow and infection.

- *Hemorrhagic discharge* is seen in some cases of balanoposthitis, trauma, or a lodged foreign body.
- With *abnormal urination,* the urine stream may be misdirected, urine dribbling may occur after urine pooling in the prepuce, and urine scalding can be seen on the perineal and abdominal skin.
- A *persistent erection* is a clinical sign of priapism and, in some cases, paraphimosis.
- *Pain, swelling, and inflammation* may occur in animals with penile and/or preputial trauma, inflammation, or foreign bodies. Fever and other systemic signs may also occur with these disorders.
  - If the urethra is damaged or obstructed by penile or preputial swelling, the animal may be unable to urinate.
- *Inability to copulate* may be the only sign of a penile or preputial disease.

▼ ***Key Point*** Unwillingness to breed a bitch can be a sign of penile or preputial pain due to inflammation or trauma, or it can be due to pain associated with a persistent penile frenulum.

DIAGNOSIS

History

- Obtain a thorough history of breeding attempts, urinary patterns, presence of preputial discharge, and traumatic events to help with diagnosis of penis and prepuce disorders.

▼ ***Key Point*** Dogs with penile and preputial disorders will often have a history of excessive licking of the affected area.

Physical Examination

- Perform a complete physical examination, including rectal examination to evaluate the prostate, pelvic urethra, and sublumbar lymph nodes. Thoroughly examine the penis and prepuce.
- A small amount of greenish discharge is a normal finding in dogs, especially in sexually intact dogs, but is abnormal in cats.

Prepuce

- The prepuce should be pain free and should move easily over the surface of the penis as the penis is extruded from the prepuce.
- Examine the preputial orifice to detect phimosis. The orifice should be a longitudinal slit located slightly ventrally at the tip of the prepuce. The opening should be large enough to allow the penis to be extruded fully.

Penis

- The penis should be light pink in color and moist, with a palpable os penis (in dogs) and the urethral orifice located at the tip.
- The feline penis is difficult to examine without sedation. In a sedated cat, the penis has an elongated conical tip with small barbs (in intact males), and the urethral orifice located at the tip.
- Fractures of the os penis can be palpable, and there is typically local swelling.
- In cases of penile trauma, gently pass a urethral catheter, with sterile lubrication, to assess the patency of the urethra.
- Thoroughly investigate any swelling. Swelling may be associated with trauma, neoplasia, hematoma, or foreign bodies.
- If an erect penis is evident, examine it carefully to differentiate priapism from paraphimosis. With paraphimosis, there is often an inverted roll of preputial skin strangulating the penis and preventing retraction back into the prepuce. Paraphimosis can also be from a hair ring encircling the shaft of the penis. Erection can be mimicked by a severe penile hematoma.
  - A persistent erection can be due to prolonged sexual arousal in a dog. Remove the dog from premises in which semen was collected or in which an estrual bitch has been. An erection caused by sexual stimulus may also subside if a cold compress is applied gently.

Laboratory Tests

Complete Blood Count

- Complete blood count is indicated in severe trauma, inflammation, or if hematomas of the penis or prepuce are found. Hematomas can be due to thrombocytopenia or other bleeding disorders.

Serum Chemistry

- Serum chemistry is indicated in the staging of any possible neoplastic disorder or if an animal has signs of systemic illness, inflammation, or severe trauma.

Urinalysis

- Urinalysis is important in the workup of any patient with abnormal urination. Urethral neoplasia can extend to the penis, and urine sediment examination may reveal neoplastic cells. Preputial and penile abnormalities can be associated with urinary tract infection.

Cytology

- Cytology of preputial discharge can be helpful in the diagnosis of balanoposthitis. In balanoposthitis, large numbers of bacteria and toxic neutrophils are seen.

In balanoposthitis due to blastomycosis, fungal organisms can be seen on cytology. Preputial cytology can also reveal neoplastic cells.
- Because of the many bacteria that make up the normal flora of the prepuce, bacterial culture is usually not helpful.

Diagnostic Imaging

- *Radiography* of the penis can reveal fractures of the os penis.
- *Contrast retrograde urethrography* is indicated in penile trauma to evaluate the patency of the urethra and to rule out rupture of the urethra (see Chapter 4).
- *Ultrasound* of the prepuce and penis may be indicated if adhesions prevent extrusion of the penis in chronic inflammatory or neoplastic conditions.
- *Computed tomography or magnetic resonance imaging* of the spinal cord, lumbosacral region, and lower urinary tract may be indicated as part of a complete evaluation in neutered male dogs presented with priapism.

Karyotype Analysis

- Sex differentiation disorders can be investigated by determining which sex chromosomes are present on cytogenetic evaluation.
  - This test is not done commonly, and it requires a fresh, cooled (not frozen) blood sample submitted in a lithium heparin tube (green top) to allow culture of leukocytes needed for karyotyping.

TREATMENT

▼ ***Key Point*** Keep the penis moist and protected from environmental damage or preputial adhesions during therapy for many penile/preputial diseases.

Surgical Treatment of Congenital Disorders

- Phimosis and persistent penile frenulum can be treated surgically (see Chapter 89).

Priapism

- Protect the penis against environmental exposure and damage. Frequently apply sterile lubricant jelly.
- If possible, replace the penis within the prepuce. If necessary, place a temporary purse-string suture at the preputial orifice to maintain the penis within the prepuce.
- If there has been significant trauma or drying of the penile mucosa, apply topical antibiotic ointments.
- Non-ischemic priapism can respond to medical therapy with antihistamines or anticholinergic drugs if used within the first few hours of priapism. Administer diphenhydramine (25–50 mg/dog IV) and atropine (0.02–0.04 mg/kg IV). Benztropine, a compound drug containing diphenhydramine and atropine, can be used (0.015 mg/kg IV).
- Alpha-adrenergic agonists have been used successfully to treat priapism in men; consider using in dogs with priapism. Examples of these drugs include phenylephrine, pseudoephedrine, and metaraminol.
- Advanced ischemia will result in necrosis and may require amputation of the penis and scrotal urethrostomy (see Chapter 89).

Trauma

- Clean, debride, and suture penile wounds as necessary.
- Use systemic antibiotics (e.g., amoxicillin-clavulanic acid) for open wounds.
- If open wounds are present, extrude the penis from the prepuce and clean 2 to 3 times daily with a dilute chlorhexidine solution to prevent penis-to-prepuce adhesions.
- Treatment of urethral damage depends on severity, but maintenance of urethral patency by placement of an indwelling urinary catheter is usually necessary (see Chapters 81 and 82).
- Fractures of the os penis may be treated conservatively or surgically, depending on the degree of displacement.

Neoplasms of the Penis

- Treatment of penile neoplasia is surgical excision. The surgical decision to perform a complete or partial penile amputation is based on location and extent of the lesion, determination of malignancy, and presence of urethral obstruction.
- Complete penile amputation requires diversion of the urinary outflow (see Chapter 89).

Transmissible Venereal Tumor

- Spontaneous remission is possible but not predictable.
- Medical treatment with vincristine once weekly (0.5–0.7 mg/m^2 IV) given for 2 weeks beyond apparent remission is usually curative (see Chapter 26 for more information on chemotherapy).
- Radiation therapy can be curative.

Balanoposthitis

- Clean the preputial cavity with antiseptic solutions (e.g., dilute chlorhexidine solution).
- Topical antibiotic creams (e.g., a neomycin, polymyxin, and bacitracin combination) can be helpful.
- Apply an Elizabethan collar to prevent licking of the prepuce.
- Treat underlying disorders.
- See Chapter 20 for treatment of blastomycosis.

- Castration usually results in diminished preputial discharge (see Chapter 87).

Paraphimosis

- Restore the normal anatomic position of the penis in the prepuce. This usually relieves edema and inflammation.
  - Sedate or anesthetize the animal if necessary.
  - Cleanse and lubricate the penis to facilitate replacement into the prepuce. Apply cool saline soaks or hypertonic dextrose solution if necessary to reduce edema.
  - Remove constricting preputial hair or foreign material.
- If mucosal damage to the penis is evident, cleanse and apply topical antibiotic cream.
- Consider surgery to cranially advance the prepuce in dogs with incomplete preputial coverage of the penis (see Chapter 89).
- In severe, long-standing cases, damage to the penis is extensive enough to necessitate amputation (see Chapter 89).

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Chapter 89

Surgery of the Penis and Prepuce

Harry W. Boothe

Surgical procedures of the penis and prepuce include the following:

- Penile amputation to treat traumatic or neoplastic lesions
- Enlargement of the preputial orifice to treat phimosis or paraphimosis
- Cranial advancement of the prepuce to treat minor deficiency in preputial length
- Severance of persistent penile frenulum

Diagnosis and medical treatment of penile problems are discussed in Chapter 88.

ANATOMY

Penis

- The feline penis is shorter, directed caudally, and covered with small papillae compared with its canine counterpart, but both species have three principal penile divisions: root, body, and distal portion (glans).
- The penile corpora contain enlarged venous spaces and have two principal divisions: the corpora cavernosa and the corpus spongiosum.
- Each corpus cavernosum (right and left) arises from the ischial tuberosity, continues distally in the dorsolateral part of the penile body as far as the os penis, and is covered by the tunica albuginea.
- The corpus spongiosum originates within the pelvic cavity, surrounds the penile urethra throughout its course, and supplies both the bulbus glandis and the pars longa glandis in the distal penis.
- The os penis is located in the penile body and is attached to the bulbus glandis, pars longa glandis, and tunica albuginea.
- The four paired extrinsic penile muscles in the dog are the retractor penis, ischiocavernosus, bulbospongiosus, and ischiourethralis.
- The principal blood supply to the penis is from three branches of the artery of the penis, which are continuations of the internal pudendal artery: artery of the bulb, deep artery of the penis, and dorsal artery of the penis.
- Venous drainage occurs via the internal and external pudendal veins. Lymphatic drainage is to the inguinal lymph nodes.
- See Chapter 82 for penile anatomy associated with perineal urethrostomy in cats.

Prepuce

- The canine and feline prepuce covers the non-erect penis.
- Paired preputial muscles extend from the xiphoid cartilage to the dorsal preputial wall.
- Blood supply is via the caudal superficial epigastric artery and the dorsal artery of the penis; lymphatic drainage is to the inguinal lymph nodes.

PENILE AMPUTATION

Preoperative Considerations

- The location and extensiveness of traumatic or neoplastic penile lesions determine the site of penile amputation. Animals with urethral prolapse that recurs after attempts to resect urethral mucosa may require partial penile amputation. Non-surgical management of certain neoplasms of the penis (e.g., transmissible venereal tumor) may be preferable (see Chapter 88).
- Preputial shortening may be indicated after partial penile amputation.
- Bilateral orchidectomy, scrotal ablation, and scrotal (preferred) or perineal urethrostomy are indicated following extensive penile amputation.

Surgical Procedure

Objectives

- Provide hemostasis by ligation of blood vessels and closure of the tunica albuginea.
- Create a permanent urethrostomy by suturing urethral mucosa to either penile mucosa or skin.
- Avoid an osteotomy by positioning the amputation site either cranial or caudal to the os penis.

Equipment

- Standard general surgical pack and suture
- Penrose drain tubing for temporary tourniquet application

Technique for Partial Amputation

1. Place the dog in dorsal recumbency, prepare the preputial cavity by multiple flushes with chlorhexidine solution (Nolvasan, Fort Dodge), and catheterize the urethra.
2. Maintain penile exteriorization from the prepuce by placing Penrose drain tubing in tourniquet fashion around the penis as far caudally as possible.
3. Create bilateral flaps of the tunic and cavernous tissue, using sharp dissection, proximal to the os penis while leaving the urethra intact (Fig. 89-1*A*).
4. Dissect the urethra and transect it just distal to the proposed amputation site.
5. Transect the os penis, if necessary, with bone-cutting forceps at the base of the flap.
6. Identify and ligate blood vessels after loosening the tourniquet, and appose the tunica albuginea and flaps of erectile tissue (simple interrupted pattern, absorbable suture).
7. Suture urethral mucosa to penile mucosa over the ventral portion of the end of the penile stump (simple interrupted, absorbable suture) after incising the urethra along its ventral midline (Fig. 89-1*B,C*).

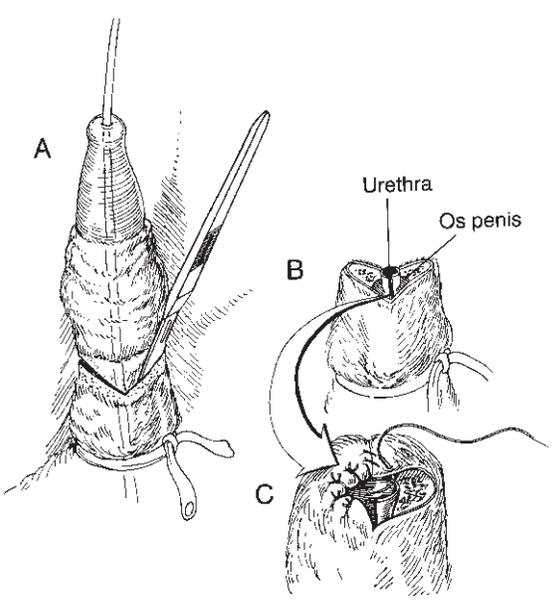

Figure 89-1. Closure of the end of the penis following partial penile amputation. The urethral mucosa is sutured to penile mucosa near the ventrum of the incision, while the remainder of the end of the penis is closed.

Technique for Subtotal Penile Amputation

1. Place the dog in dorsal recumbency and prepare the ventral abdominal and perineal regions.
2. Incise the skin in a curvilinear fashion from just cranial to the prepuce, along each side of the prepuce, to an appropriate level on the perineal midline.
3. Isolate and temporarily encircle the penis cranial to the scrotum, using a heavy ligature proximal to the initial transection site.
4. Transect and remove the penis, prepuce, testes, and scrotum.
5. Exteriorize the proximal portion of the penis through a separate midline perineal skin incision or through the caudal aspect of the original skin incision. Remove the temporary ligature, provide definitive hemostasis, and close the tunica albuginea over the end of the penis (simple interrupted pattern, absorbable suture).
6. Perform a scrotal or perineal urethrostomy (depending on how much of the penis is amputated) proximal to the penile amputation site (simple interrupted or continuous pattern, non-absorbable sutures) (see Chapter 82).
7. An alternative sequence of steps is to perform the urethrostomy first, followed by penile amputation. This allows having a urethral catheter in place while performing the urethrostomy.
8. Routinely close the ventral abdominal incision.

Postoperative Care and Complications

- Administer postoperative analgesics (see Chapter 6).
- Prevent self-inflicted trauma with an Elizabethan collar or a side brace.
- See Chapter 82 for postoperative care and complications of urethrostomy.
- Hemorrhage and/or hematoma formation may occur at the penile amputation or urethrostomy site.

Prognosis

- The prognosis depends on the disease process(es) present.
- Urethral stricture may occur if healing is complicated (e.g., urethral mucosal dehiscence occurs).
- Minimal long-term patient morbidity is expected.

ENLARGEMENT OF THE PREPUTIAL ORIFICE

Preoperative Considerations

- Use this procedure to correct phimosis (multiple attempts may be necessary in the young dog) or paraphimosis. Position the incision on the dorsal aspect of the prepuce to avoid persistent exposure of the glans penis.

- Perform castration of the patient (see Chapter 87), as well as preputial orifice reconstruction, to reduce the possibility of paraphimosis recurrence following erection.

Surgical Procedure

Objectives

- Enlarge the preputial orifice to allow unrestricted movement of the penis in and out of the prepuce.
- Minimize fibrous tissue formation by accurately apposing tissues.
- Completely excise neoplasms, if present.

Equipment

- Standard general surgical pack and suture.

Technique

1. Position the dog in dorsal recumbency and aseptically prepare the paraprepuital area.
2. Depending on the degree of phimosis, either excise a wedge-shaped segment of skin or make an incision through the subcutaneous tissue and preputial mucosa on the dorsal surface of the prepuce to enable exteriorization of the end of the penis.
3. Appose the preputial mucosa to the skin (simple interrupted pattern, non-absorbable sutures).

Postoperative Care and Complications

- Administer postoperative analgesics (see Chapter 6).
- Prevent self-inflicted trauma to the surgical site (an Elizabethan collar may be necessary).
- Postoperative fibrosis may create an insufficient preputial orifice.
- Patient growth may necessitate another surgical procedure.

Prognosis

- If a tumor was present, the prognosis generally is good, provided there was a complete excision.

CRANIAL ADVANCEMENT OF THE PREPUCE

Preoperative Consideration

- This procedure is indicated in dogs with incomplete preputial coverage of the penis to prevent penile desiccation and irritation. Only minor deficiencies (<1–2 cm) in preputial length can be corrected by advancing the prepuce cranially along the abdominal wall.

Surgical Procedure

Objective

- Achieve complete coverage of the distal penis.

Equipment

- Standard general surgical pack and suture.

Technique

1. Place the dog in dorsal recumbency and aseptically prepare the ventral abdomen.
2. Make a U-shaped incision in the skin immediately cranial to the prepuce.
3. Dissect this part of the prepuce from the abdominal skin, advance the prepuce cranially until the penis is covered, and mark this point on the skin.
4. Make a similar U-shaped incision in the skin at the mark and excise the skin between the two incisions.
5. Suture the prepuce to its cranial position (two-layer closure: subcutaneous tissue with simple interrupted, absorbable suture and skin with simple interrupted, non-absorbable suture).

Postoperative Care and Complications

- Administer postoperative analgesics (see Chapter 6).
- Although adequate penile coverage may be achieved at surgery, exposure of the distal penis may recur postoperatively.
- Prevent self-inflicted trauma with an Elizabethan collar.

Prognosis

- Repair of congenital preputial defects has a guarded prognosis.
- An extensive preputial deficiency may require partial or subtotal penile amputation (preferred) or preputial reconstruction.

CORRECTION OF PERSISTENT PENILE FRENULUM

Preoperative Considerations

- The penile frenulum normally ruptures by puberty.
- The persistent penile frenulum usually is composed of minimally vascular connective tissue.

▼ ***Key Point*** Diagnose persistent frenulum by extruding the penis manually or by observing penile deviation during erection.

Surgical Procedure

Objective

- Sever the persistent penile frenulum to enable painless extrusion of the penis from the prepuce.

Equipment

- Standard minor surgical pack.

Technique

1. Place the dog in lateral recumbency and aseptically prepare the preputial cavity.
2. Exteriorize the penis and excise the penile frenulum with scissors. Control hemorrhage with local pressure.

Postoperative Care and Complications

- Prevent self-inflicted trauma.

Prognosis

- The prognosis is good.

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Chapter 90

Diseases of the Ovaries and Uterus

Thomas K. Graves

DISEASES OF THE OVARIES

Disorders of the Ovarian Cycle

Etiology

Disorders of the ovarian cycle are seen when ovarian secretion of estrogen and/or progesterone are abnormal. Hormonal abnormalities can be associated with cystic ovarian disease, ovarian dysgenesis, ovarian neoplasia, ovarian remnants, and secondary conditions that affect ovarian function. Ovarian cycle abnormalities usually manifest as abnormalities in reproductive events. The hormonal, physiologic, cytologic, and behavioral events of the normal estrus cycle are presented in Table 90-1.

Clinical Signs

Failure to Cycle or Persistent Anestrus

- Primary anestrus in bitches is defined as failure to enter an estrous cycle by 24 months of age.
- Prolonged anestrus is defined as interestrous intervals of greater than 1 year in the bitch and 1 month in the cycling queen.
- Failure to cycle should be differentiated from "silent heat," in which outward manifestations of estrus are not observed. This happens especially in young bitches in their first cycle.
- If clinical signs of endocrine disorders (hypothyroidism or hyperadrenocorticism) are present, these conditions should be pursued as an underlying cause (see Chapters 31 and 33).
- Basenji, Tibetan mastiff, and dingo breeds can have long interestrous intervals as a normal breed variation.
- Failure to cycle can be associated with intersex conditions (see Chapter 94).
- Luteal cysts that persistently secrete progesterone can delay estrus.

Short Interestrous Intervals

- Four months or less between ovarian cycles is considered abnormal as the uterus requires an adequate amount of time to repair and regenerate, permitting normal implantation on subsequent breedings.
- The most common clinical manifestation is failure to conceive.
- The German shepherd sometimes has short interestrous intervals (4–5 months) that are not associated with infertility.

Prolonged Estrus

- Estrus is considered prolonged if the signs persist greater than 35 days in the bitch and greater than 16 days in the queen.
- The most common cause is follicular ovarian cyst.
- "Split heat" can be confused with prolonged estrus. In a split heat, proestrus ends and estrus does not begin until 2 to 4 weeks later, giving the false impression of prolonged estrus.
- Functional ovarian tumors can secrete estrogen and cause clinical signs of prolonged estrus, but these are uncommon.

Diagnosis

Physical Examination

Careful physical examination can yield findings consistent with secondary causes of ovarian disease (e.g., dermatologic findings in endocrine diseases).

Examine the vulva to determine degrees of swelling and types of discharge that suggest various stages of the estrous cycle (see Table 90-1).

Vaginal Cytology Technique

- Insert a saline moistened cotton-tipped swab into the cranial vagina. Direct the swab dorsally through the vestibule, then redirect to advance the swab cranially. Avoid contact with the floor of the vestibule and vagina so that the clitoral fossa or urethra is not entered.
- Once removed from the vagina, roll the swab several times across the surface of a glass slide and allow to air dry.
- Stain slides with various stains such as Diff-Quick.
- The stage of the estrous cycle is determined by the cells present (see Table 90-1).

Table 90-1. EVENTS OF THE CANINE ESTRUS CYCLE

	Proestrus	Estrus	Diestrus	Anestrus
Duration	0–17 days	3–21 days	2 months	4 months or more
Behavior	Receptivity to male increases Male interest increases	Receptive to male "flagging" Male very interested	Refuses to mate Male may still be attracted	Will not mate Males not attracted
Vulva	Swelling begins and increases	Vulva is large and turgid	Swelling subsides	Normal
Vaginal Discharge	Sanguineous	Sanguineous progressing to clear	Mostly clear, sometimes a little blood during early diestrus	No discharge
Vaginal Cytology	Mostly parabasal and intermediate cells Some superficial cells	Mostly superficial and anuclear squamous cells	Dramatic shift to parabasal and intermediate cells with superficial cells disappearing	No superficial cells No anuclear squamous cells Rare intermediate cell Mostly parabasal cells
Hormonal Events	Estradiol steadily rises Progesterone remains low	Estradiol declines LH surge at onset of estrus Progesterone begins to rise, followed by ovulation	Estradiol remains low Progesterone stays above 15 ng/ml and drops as diestrus ends	Progesterone low Estradiol variable FSH elevated

FSH, follicle-stimulating hormone; LH, luteinizing hormone.

Hormonal Analysis

Estradiol

- Typical serum concentrations are 5 to 10 pg/ml during anestrus, 10 to 100 pg/ml during proestrus. During estrus and diestrus, serum estrogen concentrations are often undetectable.
- Elevated serum estrogen concentrations are sometimes found in cystic ovarian disease, but this is not consistent.

▼ ***Key Point*** Estrogen concentrations fluctuate widely and are unreliable indicators of estrous stages.

Progesterone

- Serum concentrations of progesterone greater than 8 ng/ml are consistent with ovulation.
- Parturition occurs at the end of diestrus when the serum concentration of progesterone falls below 1 to 2 ng/ml.
- The finding of increased progesterone concentrations in an animal suspected of prolonged anestrus indicates that a luteal cyst may be present, or that a normal estrus cycle occurred and was not clinically observed.
- A low concentration of serum progesterone during diestrus indicates inadequate luteal function, and may be an underlying reason for infertility.

Ultrasound

Abdominal ultrasonography can be useful for identifying cystic structures on the ovary, but it is difficult to differentiate normal from abnormal follicular structures.

Laparoscopy and Exploratory Surgery

Ovarian disease is definitively diagnosed by visual examination of the ovaries using laparoscopic or an open celiotomy approach.

Treatment

Failure to Cycle or Persistent Anestrus

- Induction of estrus can be attempted, but success in inducing a fertile estrous cycle is unpredictable at best.
- The GnRH analogue, d-Trp^{6}-GnRH (Decapeptyl), has been used to induce estrus in bitches and queens by giving 1 µg/kg subcutaneously every 8 hours until estrus begins, and then half the dose q8h for an additional 3 days.
- Diethylstilbestrol has been used to induce estrus at 5 mg PO daily until 2 days after the onset of estrus.
- Estrus can be induced in the queen by exposure to 12 continuous hours of bright light per day. This results in estrus within 1 to 2 months.
- Porcine follicle-stimulating hormone given at 2 mg/cat IM daily has been used to stimulate estrus in cats.

▼ ***Key Point*** Clinicians using hormonal induction of estrus should be aware that gonadotropins can predispose to the development of cystic ovaries.

Prolonged Estrus

- The most reliable means of treating follicular ovarian cysts is to rupture them manually during exploratory laparotomy, or to remove the ovaries completely.

- Medical induction of ovulation has been reported using GnRH (Cystorelin) at 2.2µg/kg IM once daily for 3 days.
- In the queen, ovulation can be induced mechanically. Insert a lubricated small rectal thermometer (or another similar probe) into the vagina and manipulate in a pulsatile fashion for about 5 seconds at 15-minute intervals 4 to 5 times. This mimics copulation and causes a surge in luteinizing hormone (LH) that results in ovulation in most queens.

Ovarian Remnant Syndrome

Etiology

- Ovariohysterectomized dogs and cats exhibiting clinical signs of estrous are likely to have ovarian remnant syndrome, which is due to incomplete removal of all ovarian tissue at the time of ovariohysterectomy.
- Cats are more likely to have ovarian remnants than are dogs.

Clinical Signs

Clinical signs of estrus typically reoccur between 1 and 3 years following ovariohysterectomy.

Diagnosis

- Diagnosis can be confirmed by vaginal cytology and hormonal assay.
- The finding of increased serum progesterone concentrations that are consistent with diestrus in a female with clinical signs of estrus indicates the presence of ovarian tissue.
- Evaluation of LH levels will also confirm the presence of ovarian tissue in a spayed female. High serum concentrations of LH are normal in a spayed female due to lack of negative feedback from the ovaries. A low LH level is an excellent indicator that a spayed female has ovarian tissue present.
- Definitive diagnosis is made by exploratory laparotomy and biopsy of the remnant tissue.

Treatment

- Treatment is by abdominal exploratory and removal of the ovarian remnants (see Chapter 91 for a description of ovariohysterectomy).

▼ ***Key Point*** Perform the exploratory when the animal is in estrus since the ovarian tissue will be more vascular and easier to identify.

- Ovarian remnant tissue is found in its normal anatomic location near the caudal pole of each kidney.
- Nearly half of cases have bilateral remnants.

Ovarian Neoplasia

Etiology

- Ovarian neoplasia is uncommon in small animals, but several types have been reported.
- The more commonly reported tumors in dogs include granulosa cell tumors (which can cause hyperestrogenism), adenoma, adenocarcinoma, and germ cell tumors such as teratoma and dysgerminoma.
- In cats, granulosa cell tumors, which are more often malignant than in the dog, are most common. Teratoma has also been reported.
- Granulosa cell tumors can occur in ovarian remnants.

Clinical Signs

- Ovarian tumors often cause no clinical signs.
- Functional granulosa cell tumors can cause signs of hyperestrogenism (persistent estrus, gynecomastia, anemia, bone marrow suppression, dermatologic signs) or can underlie infertility in the bitch or queen.
- Granulosa cell tumors can be large enough to cause abdominal distention.
- Malignant ovarian tumors can cause abdominal effusions, systemic illness, and signs of metastatic disease involving any number of organ systems.

Diagnosis

- Clinical signs of hyperestrogenism, palpable abdominal mass, or abdominal effusion aid in the diagnosis.
- Perform a complete blood count, serum chemistry profile, and urinalysis to investigate effects of hormonal imbalances.
- Measurement of serum concentrations of estradiol are not always reliable due to fluctuations in hormone secretion and cannot effectively differentiate between a functional ovarian neoplasm and ovarian remnant syndrome.
- Abdominal radiography can reveal a mass effect in the region of the kidneys. Also perform thoracic radiography to evaluate for metastasis.
- Perform abdominal ultrasound to identify ovarian tumors.
- Ovariectomy and histopathologic examination provide a definitive diagnosis (see Chapter 91). Examine regional lymph nodes and obtain tissue samples for histopathology at the time of exploratory laparotomy.

Treatment

Ovariohysterectomy is the recommended treatment for ovarian neoplasia (see Chapter 91). Surgery may not be curative in animals with malignant disease. Consider adjunctive therapy (e.g., chemotherapy) in these animals.

DISEASES OF THE NON-PREGNANT UTERUS

Pyometra

Etiology

- Progesterone normally causes endometrial gland growth and fluid secretion, as well as decreased myometrial contractility and retention of uterine contents. These hormonal effects are necessary to sustain pregnancy, and serum progesterone concentrations are normally elevated throughout diestrus, finally decreasing to below 1 to 2 ng/ml just prior to parturition.
- The non-pregnant uterus typically goes through the same hormonal cycle as a gravid one, and cystic endometrial hyperplasia (CEH) can occur.
- Bacteria from the lower genital tract can colonize the uterus leading to infection. The most commonly isolated bacteria from pyometra are *Escherichia coli*.

Risk Factors for Pyometra

- Previous treatment with progestins such as megestrol acetate predisposes the patient to the development of pyometra. Progestins are sometimes used in bitches to suppress estrus and are used for dermatologic and behavioral conditions, although their use should be minimized.
- Pyometra may also be more common in bitches treated with estrogens, as is sometimes done to prevent pregnancy in mismating incidents. Estrogens potentiate the uterine effects of progesterone.
- A genetic component to pyometra has not been identified.
- Nulliparous bitches (which have had no puppies) have a highly increased risk of pyometra compared with multiparous bitches.

Clinical Signs

- Because the disorder is progesterone dependent, clinical signs should begin sometime after the onset of diestrus. Therefore, a history of estrus within the preceding weeks is common. Although progesterone is needed to initiate CEH and pyometra, the condition can persist after diestrus has ended, and some cases are diagnosed several weeks after progesterone would be expected to be elevated.
- Vaginal discharge is a common clinical sign. When vaginal discharge is observed, the pyometra is said to be "open," referring to patency of the cervix.
- Pyometra in the absence of vaginal discharge is referred to as "closed," meaning that uterine contents are unable to drain through a closed cervix. Whether the cervix is actually patent or not in a given case of pyometra is usually not investigated, and a true difference between these two classifications may not exist.
- The vaginal discharge of pyometra is usually purulent but can be a combination of pus and blood.
- Dehydration and depression are common in pyometra.
- Polyuria is a common finding in dogs with pyometra and is thought to be a bacterial endotoxin effect on the renal urine concentrating mechanism. Polyuria is not noted in cats with pyometra.
- Vomiting, inappetence, and general signs of systemic illness are often present.
- Fever may be noted but, surprisingly, is not common.
- The clinical signs of pyometra can be nonspecific, especially in cats.

Diagnosis

Diagnostic tests in suspected cases of pyometra are essential to differentiate between pyometra and pregnancy.

History and Physical Examination

- Obtain a thorough breeding history and timing of clinical signs in relation to the estrous cycle.
- Physical examination may or may not reveal vaginal discharge. Cats and some dogs may keep themselves clean enough that discharge goes unnoticed, but gentle opening of the vulva may reveal residual discharge in the vestibule.
- Abdominal palpation may reveal an enlarged fluid-filled uterus or tubular mass.
- In severe cases, animals can be in septic shock and can present in circulatory collapse.

Laboratory Tests

- Complete blood count commonly shows neutrophilia with toxic changes and/or a left shift. Neutrophil counts can be extremely high, sometimes over 100,000 cells/μl. A mild nonregenerative anemia is usually present, which can be masked by severe dehydration. In septic patients, there may be a leukopenia with a high percentage of band neutrophils (degenerative left shift).
- Serum biochemistry abnormalities can include azotemia and hyperproteinemia (from dehydration), as well as liver enzyme elevations.
- Perform urinalysis to investigate causes of polyuria and polydipsia. Do not obtain the urine by blind cystocentesis because of the risk of penetrating the uterus. Common urinalysis findings included isosthenuria, bacteriuria, and proteinuria.

Vaginal Cytology and Culture

- Cytology of a vaginal swab reveals a septic exudate with endometrial cells present.
- Bacterial culture of the exudates can be performed to identify a bacterial pathogen.

- Obtain samples for culture through a sterile vaginal speculum or use a guarded swab to prevent contamination from normal vaginal flora.
- Culture and antimicrobial drug sensitivity results can aid in the selection of antibiotics.

Diagnostic Imaging

- Radiographs of the abdomen may reveal an enlarged, fluid-dense tubular structure that is consistent with pyometra, but this is not always seen. Fetal calcification is not seen until roughly 45 days of gestation, so care must be taken to differentiate a fluid-filled uterus from a gravid one.
- Abdominal ultrasound is extremely useful in diagnosis of pyometra and can also detect the presence of a fetus (see Chapter 4).

Treatment

Fluid Therapy

- Aggressive fluid therapy is especially important in septic or dehydrated animals. Lactated Ringer's solution is a good choice for correction of dehydration and management of septic shock (see Chapter 5).
- Administer fluid therapy to even relatively stable animals prior to treatment of the pyometra itself.

Antibiotic Therapy

- Due to the wide range of possible bacterial pathogens in pyometra, administer broad-spectrum antibiotics. Because *E. coli* is a common pathogen, choose an antibiotic that is effective against this organism.
- Dehydrated, inappetent, vomiting, or severely depressed animals or those for whom surgery is planned should be given parenteral antibiotics. Oral antibiotics can be given if appropriate for the individual patient.

Recommended Antibiotics

- Combination of ampicillin (20 mg/kg q8h) and enrofloxacin (2.5 mg/kg q12h)
- Combination of cephalothin (20 mg/kg q8h) and amikacin (5 mg/kg q12h)
  - Because of potential nephrotoxicity, avoid amikacin in animals with questionable or documented impaired renal function.
- Amoxicillin/clavulanate (12.5–25 mg/kg q12h)

Medical Management

Prostaglandins

- When pyometra is encountered in valuable breeding bitches, in which ovariohysterectomy is not preferred, medical therapy with prostaglandin F2-alpha ($PGF_{2\alpha}$) can be used.
- It is commonly recommended that $PGF_{2\alpha}$ therapy only be used in young bitches without signs of systemic illness and that treatment be reserved for open-cervix pyometra. There is little evidence, however, to support these recommendations, and, in my experience, $PGF_{2\alpha}$ therapy can be successful regardless of the clinical presentation.
- $PGF_{2\alpha}$ causes uterine contraction, relaxation of the cervix, and expulsion of uterine contents.
- Closed-cervix pyometra patients are thought to be at risk for uterine rupture or pressure-driven expulsion of uterine contents through the oviduct, both resulting in peritonitis, but this is not well established.
- Several synthetic analogues of $PGF_{2\alpha}$ have been investigated in the dog, but most clinicians have used the natural product (Lutalyse), and it is the preferred drug.
- $PGF_{2\alpha}$ can cause adverse reactions including nausea, abdominal pain, panting, mydriasis, defecation, salivation, fever, and nesting behavior. These side effects are less pronounced with lower doses of the drug.
  - Adverse reactions develop quickly after drug administration and are anecdotally less severe if the patient is exercised (e.g., walked briskly) for 20 minutes following $PGF_{2\alpha}$ administration. Adverse reactions also become milder as the course of therapy progresses.
- Bitches undergoing successful $PGF_{2\alpha}$ therapy have subsequent conception rates and litter sizes similar to those of bitches not having pyometra.
- Once having undergone $PGF_{2\alpha}$ therapy, redevelopment of pyometra on subsequent estrous cycles is a risk. For this reason, bitches should be bred on each subsequent estrous cycle if possible.

▼ ***Key Point*** Carefully calculate the dose of $PGF_{2\alpha}$ because the drug can be very toxic.

Protocol for Prostaglandin F2-alpha Therapy

- Begin fluid and antibiotic therapy, and continue antibiotics for 2 weeks past the end of $PGF_{2\alpha}$ therapy.
- Administer $PGF_{2\alpha}$ at a dosage of 0.1 to 0.2 mg/kg subcutaneously bid for 3 to 5 days or more.
- Little effect on vaginal discharge is seen on the first day of treatment.
- On subsequent days, $PGF_{2\alpha}$ therapy often results in an increase in vaginal discharge as the uterus is evacuated.
- Monitor uterine contents by ultrasound, and continue treatment until evidence of uterine fluid is no longer seen and vaginal discharge has stopped.
- Treatment for more than 5 to 6 days is said to be associated with a poor prognosis, but this is not well established and bitches treated for considerably longer periods can be fertile.

Surgical Management

- Ovariohysterectomy is the most definitive treatment of pyometra, especially for dogs not intended for future breeding (see Chapter 91).
- Administer fluid therapy and antibiotics as discussed under "Medical Management" in this section.

- Consider placement of closed suction drains or open peritoneal drainage if uterine rupture and gross peritonitis is present (see Chapter 76).

DISEASES OF THE PREGNANT UTERUS

Etiology

Uterine diseases that occur during pregnancy can result in abortion. Abortion is not always due to uterine disease per se but can also be caused by fetal genetic or developmental abnormalities, by toxic drugs or teratogens, by hormonal influences that result in a shortened diestrus (e.g., luteal failure or glucocorticoid excess), or by non-uterine disorders of the bitch or queen that result in the inability to carry a pregnancy to term.

Infectious Diseases

- In dogs, *Brucella canis* and herpesvirus are probably the most important pathogens causing abortion.
- Other pathogens associated with abortion included canine distemper virus, canine parvovirus, *Toxoplasma gondii, Neospora caninum,* and various bacteria.

▼ ***Key Point*** The association between *Mycoplasma canis* and reproductive disorders has not been proven. *Mycoplasma* and *Ureaplasma* organisms are found in normal canine reproductive tract, as well as in bitches with reproductive disorders, so a cause-and-effect relationship is not established. Experimental infection with *Mycoplasma* can cause metritis in the bitch.

- In cats, feline panleukopenia virus and feline herpesvirus are most commonly associated with abortion.
- Feline retroviral infections can also result in pregnancy loss.
- *Mycoplasma* infections, as in dogs, have not been established as a cause of abortion in cats.

Brucellosis

B. canis is a small, gram-negative, intracellular parasite that grows in placental tissue (and others) and infects the uterus and fetus (see also Chapter 19).

Herpesvirus

Herpesvirus infections can cause abortion in both dogs and cats (see also Chapter 16). Prevalence of infection is very high in both dogs and cats. In kennels, infection rates may be as high as 85%.

Clinical Signs

- Most affected bitches have no clinical signs other than abortion. Abortion can occur at any time during pregnancy.
- Lymphadenopathy may be found.
- Non-reproductive tissues can be affected in brucellosis, causing clinical signs of uveitis, discospondylitis, lymphadenitis, and dermatitis.
- The most common clinical signs of herpesvirus infections are upper respiratory signs.

Diagnosis of Brucellosis

- The rapid slide agglutination test (RSAT) detects cell wall antigens of *B. canis* that are also components of some other bacteria, so this test is not specific and false-positive results can occur. The RSAT is, however, highly sensitive and is easily performed as a cage-side test. A positive RSAT must be confirmed with further serologic testing.
- Agar-gel immunodiffusion (AGID) tests to detect *Brucella* species cytoplasmic antigens are very specific and are used to confirm a diagnosis of brucellosis.
- Stillbirth and neonatal death are more common sequelae to infection than abortion.

Treatment

Brucellosis

- Treatment of brucellosis is difficult. The infection is not always eradicated despite long-term antibiotic therapy. Combinations of a tetracycline antibiotic (doxycycline at 10 mg/kg PO q12h or tetracycline hydrochloride at 25 mg/kg PO q8h) given for 4 weeks and dihydrostreptomycin (10 mg/kg IM q8h during weeks 1 and 4 of tetracycline treatment) may be most effective (see Chapter 19).
- Results of serologic tests and blood cultures for *B. canis* will become negative after treatment, even if a chronic infection persists. Eradication of *B. canis* may not be possible.

▼ ***Key Point*** Bitches with brucellosis should never be used for breeding and must be spayed to prevent spread of infection.

- *B. canis* infections are uncommon in human brucellosis, but zoonotic infections have been reported. For this reason, and because of the difficulty in treating an infection, dogs with brucellosis are sometimes euthanized.
- There is no vaccine available to prevent brucellosis in dogs.

Herpesvirus

Most herpesvirus infections in dogs are subclinical, and abortion, stillbirth, and neonatal death usually occur only if the initial infection occurs during gestation. A bitch aborting a litter due to herpesvirus infection is unlikely to abort the next litter due to the same infectious cause. Treatment is not effective or needed.

DISORDERS OF PARTURITION AND DYSTOCIA

- Dystocia is common in dogs. It can occur because conformation of the birth canal is inadequate to allow parturition, because of a relatively oversized fetus, or because of factors that affect the normal contractile function of the uterus.
- Toy-breed dogs with large heads and relatively small pelvic canals are predisposed to dystocia.
- In breeds such as bulldogs and Pekingese, dystocia is so common that breeders typically request cesarean sections without allowing bitches to progress past the initial stage of labor.
- Brachycephalic cat breeds and the Devon Rex are also predisposed.
- Uterine inertia is common in many breeds and the cause is not known.

Normal Labor

Traditionally, the labor process is divided into three stages. In stage 1, dilation of the cervix and uterine contractions occur. In stage 2, the offspring is delivered, and in stage 3, the placenta is delivered. The terminology used in dogs and cats is borrowed from the human terminology but is less appropriate for animals with multiple births. The lines between these stages are not obvious, and dogs and cats can alternate between delivery of pups and kittens and delivery of placentas. For these reasons, the traditional stages of labor are not presented here, but a description of the process is given in a stepwise fashion.

Events of Normal Parturition

- Prior to the onset of labor, a transient temperature drop (usually below 100°F) occurs in the dog. For this reason, owners of pregnant bitches are instructed to monitor the temperature twice daily during the last week of gestation. In cats, monitoring of rectal temperature during late gestation is not typically done.
- During or following the temperature drop the cervix dilates and uterine contractions begin. This step can go unnoticed by pet owners.
- During cervical dilation and initial contractions, bitches typically refuse food and may vomit, shiver, and become restless. Queens are consistently anorectic before and during parturition.
- Nesting behavior can be evident at this point.
- Typically, after 6 to 12 hours, active contractions and straining to deliver a fetus begin. At this point, the cervix is fully dilated and a fetus enters the birth canal.
- The chorioallantoic membranes are sometimes first seen as a bubble protruding from the vulva, and amniotic fluid may be passed.
- Although the time is highly variable, delivery of the first pup or kitten typically occurs in less than 4 hours. Toy breeds or breeds predisposed to dystocia should not be allowed to strain for more than 2 hours before delivery of a first fetus.
- Once a fetus is within the birth canal and is evident externally, it should pass easily from the dam within seconds. A pup or kitten easily palpated in the vagina or protruding from the vulva without being fully delivered is a cause for concern; use gentle traction to help the delivery. It is common for the attendant to manually assist the delivery of each pup or kitten.
- Variability on fetal position during delivery is common in dogs and cats. Both cranial and caudal presentations are normal. Fetal posture can be with the neck flexed or extended. The fetal position in the vagina is almost always dorsal.
- Immediately following delivery, fetal membranes are removed manually from the head to allow breathing. The umbilical cord should be clamped about 2 cm from the body wall, severed, and ligated.
- Inspect the oral cavity of the newborn and remove excess fluid by gentle suction. Check for cleft palates.
- Place the newborn in a clean towel. Stimulate and dry by rubbing. Do not swing newborn puppies between the attendant's legs, as is commonly practiced, because this can result in injury and can remove surfactant from the airways. Also, it has no benefit over safer methods to remove fluids and stimulate respiration.
- Subsequent deliveries can happen rapidly or can be delayed for considerable periods of time. Bitches will often rest, sometimes for up to 2 hours between deliveries.
- Intense straining should produce a pup or kitten within less than 20 minutes.
- Passage of placentas is variable. Sometimes delivery of each fetus is followed by delivery of a placenta. Sometimes they are delivered simultaneously. Sometimes entire litters can be delivered before placentas are passed.
- A dark green or brown discharge is common during and following labor. It occurs because a placenta has been detached from the uterine wall. The appearance of this discharge without delivery of a pup is cause for concern because placental detachment results in fetal oxygen deprivation.

Etiology

Maternal Causes

Uterine Inertia

Possible causes of uterine inertia (lack of uterine contractions) include fatigue, hypoglycemia, and hypocalcemia, but in most cases the cause is unknown. Uterine inertia can be classified as primary (inherent problem with the uterus or underlying systemic disorder) or secondary (persistent straining against an obstruction).

Anatomic Abnormality

- The pelvic canal may be abnormally small due to previous pelvic fractures or as a developmental abnormality in brachycephalic breeds and others.
- Uterine malposition from uterine torsion or prolapse can occur.
- Vaginal or vulvar hypoplasia, persistent bands of tissue in the vagina, or strictures can be present (see Chapter 92).

Fetal Causes

Oversized Fetus

- Single-fetus pregnancies can produce an abnormally large fetus.
- Hydrops fetalis is a condition of fetal edema, referred to by dog breeders as "water puppies." The cause is usually undiagnosed but can be from conditions such as immune-mediated vasculitis and congestive heart failure in other species.
- Hydrocephalus can result in a relatively oversized fetus.

Fetal Death

Fetal death can cause metritis, resulting in dystocia.

Diagnosis

- Obtain a thorough history to determine length of gestation and events of parturition.
- Normal gestation in the dog averages 66 days (range of 64–71 days) and in the cat averages 64 days (range of 59–70 days).

Physical Examination

- Examine the perineum first for evidence of a partially delivered fetus. If no partially delivered fetus is present, perform a full physical examination to investigate signs of systemic illness that may cause dystocia and to assess the uterus by abdominal palpation.
- Digitally examine the vagina using sterile technique. When the cranial vaginal wall is stroked with a fingertip, vaginal and abdominal contractions can be felt.
  - The absence of contraction is consistent with, but not diagnostic for, uterine inertia.

Diagnostic Imaging

- Obtain abdominal radiographs to assess fetal size and health, as well as to determine the number of fetuses.
- Radiographic signs of fetal death include intrafetal gas, overlap or misalignment of bones (especially skull bone overlap), or fetal demineralization.
- Perform abdominal ultrasound to assess fetal heart rate. Normal canine fetuses have heart rates greater than 200 bpm. If the fetal heart rate is less than 180 bpm, severe fetal stress is present and immediate cesarean section is indicated.

Laboratory Tests

- Obtain blood for a complete blood count and serum biochemistry.
  - Hypoglycemia and/or hypocalcemia may be present.
- Mild anemia is normal in full-term bitches and queens.

▼ ***Key Point*** If possible, measure the serum progesterone concentration. If it is greater than 2 ng/ml, the pregnancy is not at full term.

Criteria for Diagnosing Dystocia

- If it has been more than 24 hours since the rectal temperature dropped in a bitch, and labor has not begun
- A full-term queen that has been anorectic for more than 24 hours
- Prolonged gestation (>70 days from breeding)
- Active straining for >30 to 60 minutes without expulsion of a fetus
- Resting phase between delivery of a fetus >4 hours with known retained fetuses
- Intermittent weak contractions for >2 hours without delivery of a fetus
- Systemic signs of illness (e.g., fever, severe weakness, and vomiting)
- Signs of severe pain during parturition
- Purulent or hemorrhagic vaginal discharge
- Evidence of fetal death

Treatment

Medical Management

- If both mother and offspring appear healthy, and there is no obstruction, consider oxytocin therapy. Oxytocin (0.25 U/dog IM or SC) increases the frequency of uterine contractions.
- A pup should be delivered within 30 minutes of oxytocin administration.
- Animals not responding to oxytocin within 30 minutes are candidates for cesarean section.

▼ ***Key Point*** Repeated doses of oxytocin are usually not helpful and are not recommended because the hormone can cause placental separation and fetal death. Sustained uterine contractions induced by oxytocin can also cause decreased fetal blood supply.

- *Calcium gluconate* is sometimes given prior to oxytocin because calcium is necessary for muscle contraction, and calcium administration can increase uterine contraction even if the measured serum calcium concentration is normal.

- 10% Calcium gluconate is given as a very slow intravenous bonus (through an indwelling catheter to avoid the risk of extravasation) at a dosage of 0.2 ml/kg.

▼ ***Key Point*** Do not administer calcium salts subcutaneously because they are irritating and can cause tissue necrosis and subcutaneous calcium deposition.

Indications for Caesarian Section (see Chapter 91)

- No response to medical management
- Uterine inertia
- Maternal pelvic or vaginal abnormality or systemic illness
- Oversized fetus
- Evidence of fetal death
- Owners concerned about loss of newborns during a difficult parturition (e.g., brachycephalic dog)
- Hypocalcemia or hypoglycemia in the bitch or queen; parturition rarely resumes following correction of these biochemical abnormalities, so perform cesarean section along with treatment for hypoglycemia or hypocalcemia

POSTPARTUM UTERINE DISORDERS

Bacterial Metritis

Etiology

Bacteria can ascend into the uterus and cause severe, life-threatening infection following normal parturition, prolonged dystocia, parturition with retained fetus or placenta, or abortion.

Clinical Signs

- History of recent parturition (usually within a week).
- Hemorrhagic, fetid, mucopurulent vaginal discharge is common.
- Depression, lethargy, anorexia, vomiting, and any sign of systemic illness can be present.
- The abdomen can be painful on palpation, and a turgid uterus can be palpated. Uterine involution in a normal postpartum period is not complete by this time, so palpation findings are subjective.
- Patients can present in septic shock.

Diagnosis

- Urinalysis, complete blood count, and serum chemistry can show results consistent with sepsis, dehydration, and, if advanced, multiple organ failure.
- Vaginal cytology yields degenerate neutrophils and bacteria.
- Bacterial culture of the vaginal discharge is useful in selecting an antibiotic.
- Perform abdominal ultrasound to detect a dead fetus, retained placenta, uterine enlargement, and abdominal effusions associated with peritonitis.
- Obtain abdominal radiographs to detect retained dead fetuses.

Treatment

- Fluid therapy is essential, and shock doses of intravenous fluids are often needed.
- Add potassium and glucose to the fluids as needed (indicated by serum chemistry profile results).
- Administer broad-spectrum antibiotics (see under "Pyometra"). Choose antibiotics based on antimicrobial sensitivity testing if possible.
- Oxytocin therapy has been recommended to evacuate uterine contents, but this hormone is not effective more than 48 hours after parturition. Endogenous oxytocin should have already maximally stimulated its receptors, so there is little rationale for its use.
- Because of the risk of sepsis and death, exploratory laparotomy and ovariohysterectomy are necessary (see Chapter 91).

Uterine Prolapse

- Rarely, the uterus can prolapse immediately following parturition.
- The condition is diagnosed by the finding of tissue protruding from the vulva following parturition.
- Treatment involves manual reduction of the prolapsed tissue, or, if tissue is devitalized, amputation. For a discussion of surgical treatment of uterine prolapse, see Chapter 91.

Subinvolution of Placental Sites

Etiology

- The process of uterine involution occurs for up to 3 months postpartum but is usually essentially complete by 6 weeks. During that period, a hemorrhagic, sometimes brownish, and mucoid discharge from the vagina is normal. Early in the process of uterine involution, the discharge can seem quite copious.
- In some bitches, placental attachment sites are invaded by trophoblastic cells, these sites fail to regress normally, and hemorrhage persists.
- Subinvolution of placental sites (SIPS) is most common in younger bitches.
- SIPS is not known to occur in the cat.

Clinical Signs

Persistent vaginal bleeding for more than 6 weeks postpartum in an otherwise normal bitch is the typical clinical sign of SIPS.

Diagnosis

- Examination of a vaginal smear from a bitch with SIPS reveals hemorrhage, parabasal cells, and, sometimes, the presence of trophoblastic cells.
- Blood loss due to SIPS is rarely clinically significant. Monitor red blood cell count or packed cell volume if indicated.
- If clinical anemia develops, other causes of blood loss should be investigated.

Treatment

- SIPS eventually resolves without treatment.
- Bitches are commonly fertile following an episode SIPS, and the condition does not necessarily develop following subsequent pregnancies.

UTERINE NEOPLASIA

Etiology

- Tumors of the uterus are rare in dogs and cats, probably because of the high prevalence of ovariohysterectomy.
- Endometrial adenocarcinoma is the most common uterine tumor of the queen, and leiomyoma and leiomyosarcoma are the most common uterine tumors of the bitch.
- A variety of other tumors have been reported in dogs and cats, but they are very uncommon.

Clinical Signs

- Uterine tumors are most often found incidentally at ovariohysterectomy.
- Vaginal discharge may be present in some animals with invasive uterine tumors. Tumors of the cervix may cause bleeding.
- In cats, endometrial adenocarcinoma is typically associated with local and distant metastases to many different organs, and clinical signs referable to any organ system can be seen.

Diagnosis

- Uterine masses may be detected by abdominal palpation.
- In rare cases, cytology of vaginal discharge may yield tumor cells.
- A suspected uterine mass can be confirmed by abdominal ultrasound, whereas it is difficult to localize a mass to the uterus on plain abdominal radiographs.
- Ultrasound-guided fine-needle aspiration of a uterine mass may yield a cytopathologic diagnosis.
- Perform preoperative evaluation consisting of urinalysis, complete blood count, serum chemistry, three-view thoracic radiographs, and abdominal ultrasound to evaluate for metastatic disease.
- Definitive diagnosis is made by histopathology of surgically obtained tissues.

Treatment

- Ovariohysterectomy is the recommended treatment (see Chapter 91).
- Most bitches can be cured by complete excision of a uterine mass.

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Chapter

91 Surgery of the Ovaries and Uterus

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Surgical procedures performed on the uterus and ovaries include ovariohysterectomy, cesarean section, uterine biopsy, and rarely, ovariectomy. Uterine surgery usually is straightforward but requires sound basic surgery skills and a thorough understanding of the anatomy and physiology of the reproductive tract.

ANATOMY (Fig. 91-1)

Ovaries

- The ovaries are located 1 to 3 cm caudal to the kidneys.
- The ovaries are attached to the abdominal wall by the mesovarium, a part of the broad ligament.
- The suspensory ligament is the cranial continuation of the broad ligament and extends between the ventral third of the last two ribs and the ventral surface of the ovary.
- The proper ligament is a continuation of the suspensory ligament and extends from the caudal end of the ovary to the cranial end of the uterine horn.
- The ovarian arteriovenous complex (OAVC) lies on the medial side of the broad ligament and supplies the ovaries and the cranial portion of the uterine tube. The distal two-thirds of the OAVC is convoluted in the dog, similar to the pampiniform plexus in males.
- The left ovarian vein drains into the left renal vein; the right ovarian vein drains into the caudal vena cava.

Uterus

- The uterus consists of the cervix, body, and two uterine horns. Oviducts (uterine tubes) connect the uterine horns and ovaries.
- The uterus is attached to the dorsolateral wall of the abdominal cavity and the lateral wall of the pelvic cavity by paired double folds of peritoneum called broad ligaments.
- The round ligament is the caudal continuation of the proper ligament. The round ligament extends caudally and ventrally in the broad ligament and passes through the inguinal canal, terminating subcutaneously near the vulva.
- The uterine branch of the internal iliac artery is the main artery to the uterus. The uterine branch of the urogenital artery supplies the caudal portion of the uterus, the cervix, and part of the vagina. The uterine branch of the ovarian artery supplies the cranial part of the uterine horns.

OVARIOHYSTERECTOMY

Preoperative Considerations

- Elective sterilization is the most common indication for ovariohysterectomy. Ovariohysterectomy is the treatment of choice for most uterine diseases including pyometra, uterine torsion, cystic endometrial hyperplasia, uterine rupture, and uterine neoplasia (see Chapter 90 for a description of these diseases).

▼ ***Key Point*** Ovariohysterectomy before the first or second estrus provides a definitive protective factor against development of mammary neoplasia. After the third estrus (or approximately 2.5 years), there is no significant effect of ovariohysterectomy for the prevention of mammary neoplasia.

- An alternative method of sterilization of a female dog or cat is ovariectomy without hysterectomy. Studies have shown no difference in long-term results, or complications, between ovariectomy and ovariohysterectomy. Ovariectomy may also be considered for the surgical treatment of small animal patients with a mass lesion involving the ovary, particularly if the owner wishes to maintain the reproductive status of the animal. However, if ovarian neoplasia is suspected, ovariohysterectomy coupled with a complete abdominal exploratory is indicated to ensure complete resection of the neoplasm and examination of all abdominal viscera for evidence of metastasis.
- Whether the procedure is elective or not, perform an appropriate preoperative evaluation, including a complete history, physical examination, and appropriate blood work.

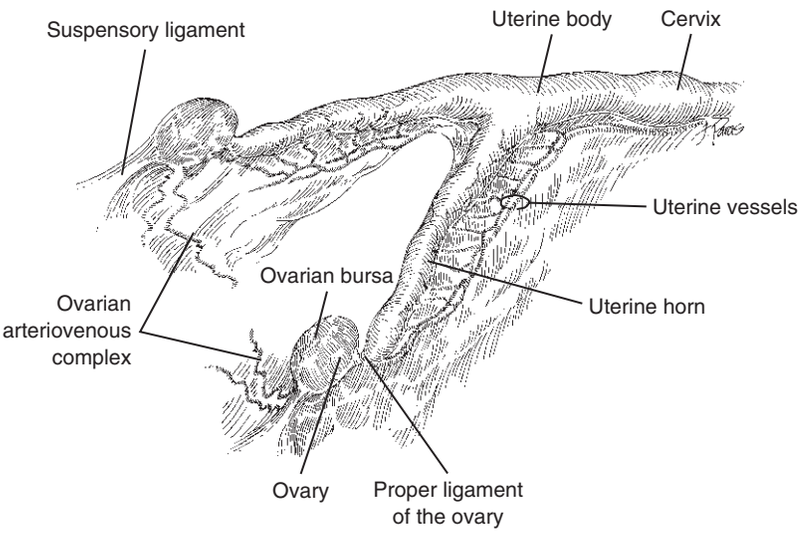

Figure 91-1. Anatomy of the uterus and ovaries.

Surgical Procedure

Objective

- To remove the uterus and ovaries

Equipment

- Standard general surgery instrument pack and suture
- Ovariohysterectomy (Snook) hook (optional)

Technique

1. After anesthetizing the animal, manually express the urinary bladder.
2. Position the animal in dorsal recumbency.
3. Prepare the entire ventral abdominal region for aseptic surgery.
4. Skin incision:
   a. *Dog:* Make a ventral midline incision extending from the umbilicus to a point halfway between the umbilicus and the brim of the pubis.
   b. *Cat:* Begin the ventral midline incision approximately 1 to 2 cm caudal to the umbilicus and extend the incision caudally 3 to 5 cm.
   c. A longer abdominal incision is required to remove an enlarged uterus (e.g., pyometra).
   d. Attempt to incise exactly on midline in lactating bitches to avoid trauma to the mammary glands.
5. Enter the abdominal cavity through the linea alba.
6. Locate the left uterine horn using the ovariohysterectomy hook or index finger. Displace the omentum and bowel cranially if necessary to find the uterus.
7. Place a small hemostat across the proper ligament to aid in caudal retraction of the ovary.
8. Grasp the ovary between the thumb and the middle fingers. Place the index finger as far proximal as possible on the suspensory ligament (Fig. 91-2*A*).
9. Place tension on the suspensory ligament by rotating the index finger caudally. Gradually increase tension on the suspensory ligament until the ligament stretches or ruptures.

▼ ***Key Point*** Avoid placing tension on the OAVC during manipulation of the suspensory ligament or when placing ligatures.

10. Identify the OAVC. Using a Rochester-Carmalt hemostatic forceps (clamp), make an opening in the mesovarium immediately caudal to the OAVC in an area clear of vessels and fat (Fig. 91-2*B*).
11. Triple-clamp and transect the OAVC (Fig. 91-2*C*).
    a. Double-clamp the OAVC with Rochester-Carmalt hemostatic forceps. Place the first clamp immediately proximal (toward the aorta) to the ovary and the second clamp approximately 5 mm proximal to the first. Place a third clamp across the proper ligament between the ovary and the uterine horn. Transect the OAVC between the middle clamp and the ovary (Fig. 91-2*D*).
    b. Alternatively, place all three clamps across the OAVC proximal to the ovary. Transect the OAVC between the middle clamp and the clamp adjacent to the ovary (Fig. 91-2*E*).

▼ ***Key Point*** Place the hemostatic forceps on the OAVC as close as possible to the ovary to prevent accidental inclusion of the ureter, but be sure to remove all of the ovarian tissue.

12. Loosely place a circumferential ligature around the proximal clamp (Fig. 91-2*F*). Tighten the ligature as the clamp is removed. In this manner, the circumferential ligature is tightened in the groove of crushed tissue created by the clamp (Fig. 91-2*G*).

▼ ***Key Point*** The clamp adjacent to the ligature may need to be loosened before knotting to ensure proper tightness of the knot.

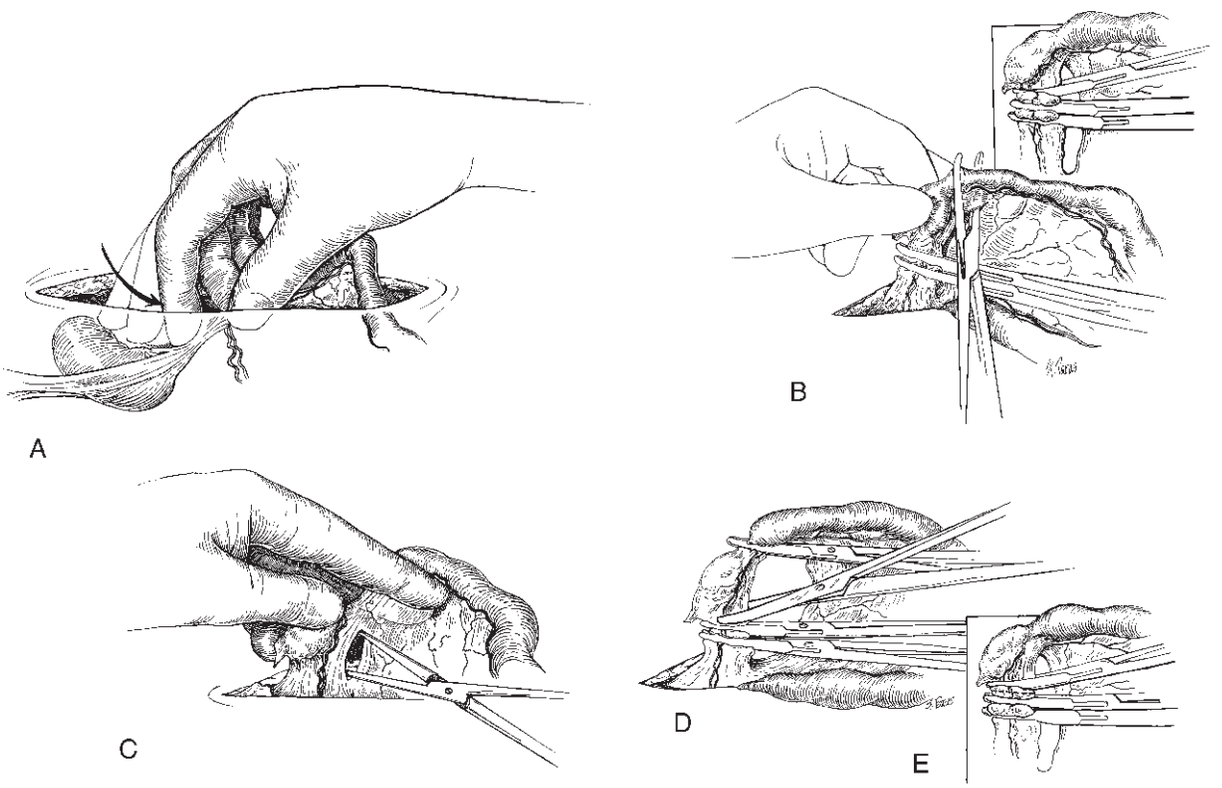

Figure 91-2. Ovariohysterectomy. *A,* Separate the suspensory ligament. *B,* Open the mesovarium immediately caudal to the ovarian arteriovenous complex (OAVC). *C,* Triple-clamp the OAVC. *D,* Transect the OAVC between the ovary and the clamp. *E,* Alternative clamp and transection method.

13. Place a transfixing ligature between the circumferential ligature and the transected end of the OAVC (Fig. 91-2*H* and *I*). A full ligature (circumferential) may be used instead of a transfixing ligature in young cats or small dogs.

▼ ***Key Point*** Never include ovarian tissue in the ligatures.

14. Grasp the OAVC distal to the ligature (without grasping the ligature) with thumb forceps, remove the middle clamp, and inspect the OAVC for bleeding. If bleeding occurs, place a second circumferential ligature on the OAVC proximal to the first.
15. Follow the left uterine horn distally to the bifurcation, locate the right uterine horn, and follow the right uterine horn proximally to the right OAVC.
16. Ligate and transect the right OAVC, as described previously.
17. Transect the broad ligament.
    a. In most preparturient animals, the broad ligament can be manually separated. Make an opening in the broad ligament adjacent to the uterine artery and vein close to the cervix (Fig. 91-2*J*). Place four fingers through the opening in the broad ligament and grasp the entire broad ligament, including the round ligament (Fig. 91-2*K*). Pull the broad ligament cranially (not ventrally) until the broad ligament and the round ligament are free (Fig. 91-2*L*).
    b. If the broad ligament is highly vascular, large vessels may be ligated individually or mass ligation of the broad ligament or portions of the ligament may be ligated.
18. Exteriorize the uterine body and locate the cervix.
19. Divide the uterine body after two ligatures are placed (Fig. 91-2*M* through *O*). Remove the entire uterus proximal to the cervix.
20. Evaluate the OAVC pedicles and the uterine body for bleeding prior to abdominal closure. The left and right OAVC are located immediately caudal to the caudal pole of each respective kidney.
    a. Locate the left OAVC pedicle by retracting the descending colon medially, exposing the left paralumbar gutter.
    b. Locate the right OAVC pedicle by retracting the duodenum medially, exposing the right paralumbar gutter.
    c. Retroflex the bladder. The ligated uterine body lies ventral to the descending colon and dorsal to the bladder.
21. Close the abdominal incision routinely.

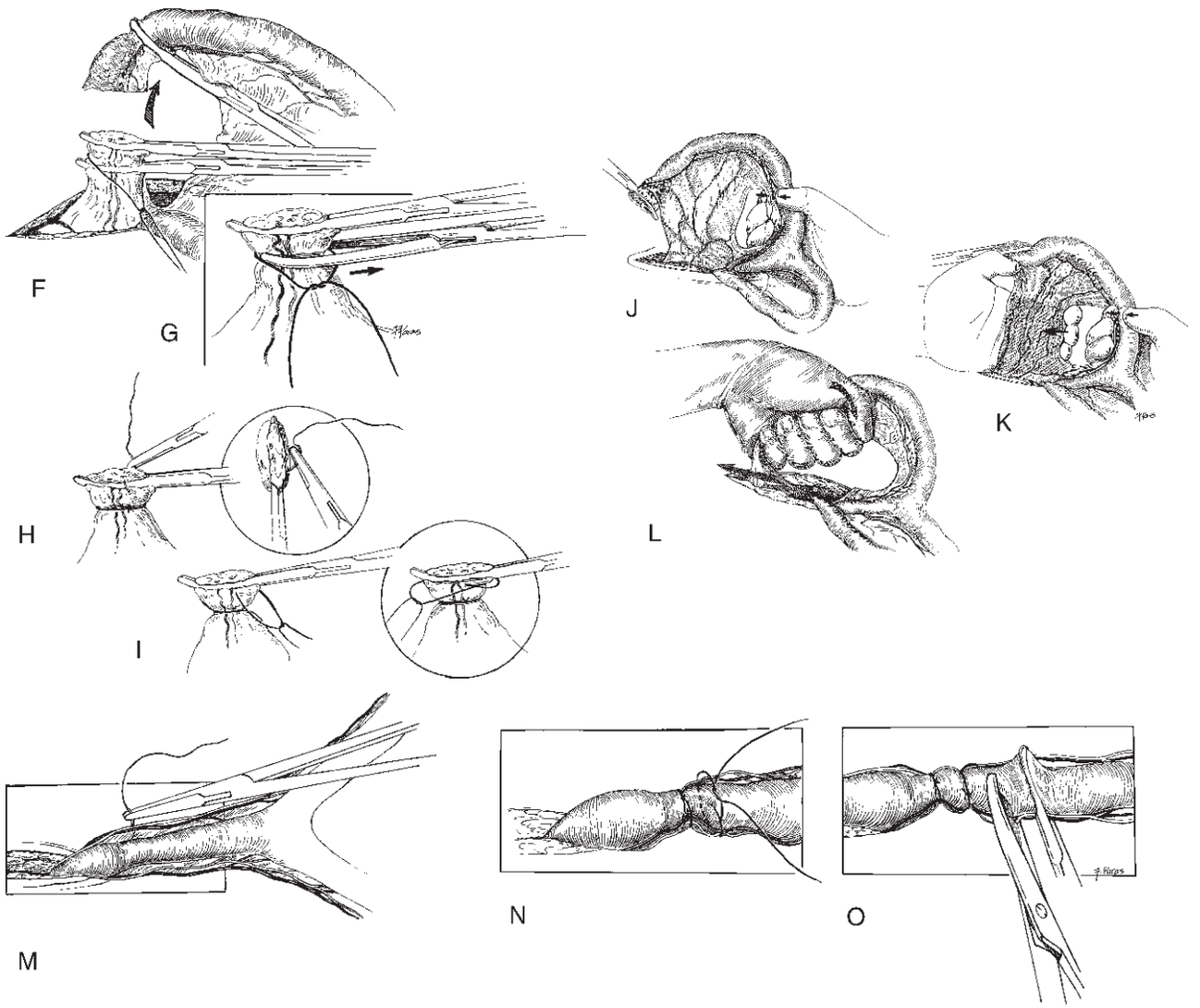

Figure 91-2. ***Continued*** *F,* Place circumferential suture around the proximal clamp. *G,* Tighten the suture in the groove of crushed tissue. *H* and *I,* Ligature pattern for transfixing ligature. *J,* Open the broad ligament adjacent to the uterine artery and vein close to the cervix. *K,* Grasp the broad ligament. *L,* Pull the broad ligament cranially until it and the round ligament are free. *M,* Place the first transfixing suture. *N,* Place the second transfixing suture. *O,* Transect the uterine body.

Postoperative Care

- Administer postoperative analgesics as needed (see Chapter 6).
- Restrict exercise and monitor for wound complications or hemorrhage after ovariohysterectomy.
- Postoperative care following ovariohysterectomy for pyometra:
  - Dogs with pyometra frequently have renal dysfunction without associated morphologic abnormalities, and they may be azotemic, oliguric, or anuric. Monitor renal function and maintain hydration after surgery. Diuresis with crystalloid fluids administered intravenously for at least 24 to 36 hours after surgery is advisable. Placement of a urinary catheter will assist with monitoring urine output (see Chapter 90 for more information on pyometra).
  - Dogs with pyometra may be toxemic or septicemic (see Chapter 90). Administer broad-spectrum antibiotics during surgery, and continue antibiotics after surgery if the animal is toxemic or septicemic or if peritonitis was present at surgery.

Postoperative Complications

Complications following elective ovariohysterectomy are rare and may include the following.

Hemorrhage

- Hemorrhage is the most common complication following ovariohysterectomy in dogs weighing more than 25 kg.
- Common causes of hemorrhage include failure to adequately tighten circumferential or transfixion

ligatures, tearing of the OAVC while breaking the suspensory ligament, failure to ligate large vessels in the broad ligament, tearing of the uterine artery due to excessive traction on the uterine body and premature removal of a clamp during ligation. In addition, persistent hemorrhage after surgery can occur in patients with undiagnosed or untreated coagulation disorders such as von Willebrand disease or specific coagulation factor deficiency (see Chapter 23).

- The incidence of hemorrhage can be reduced by maintaining meticulous surgical technique. Avoid becoming complacent during routine ovariohysterectomy.

Uterine Stump Pyometra

Uterine stump pyometra can occur if a portion of the uterine body or uterine horn is not removed and the animal has increased serum progesterone. The source of the increased serum progesterone can be endogenous from residual ovarian tissue or exogenous from progestational compounds administered for treatment of dermatitis.

▼ ***Key Point*** Complete excision of the uterine body and ovaries reduces the incidence of uterine stump pyometra.

Ovarian Remnant Syndrome (Recurrent Estrus)

- This condition results from retained functional residual ovarian tissue.
- Treatment is removal of residual ovarian tissue.

▼ ***Key Point*** To increase the likelihood of identifying residual ovarian tissue, perform exploratory celiotomy to find ovarian remnants when the dog is showing signs of recurrent estrus.

- If ovarian tissue is not located, identify both ureters and resect remnants of the OAVC pedicles bilaterally. Submit the tissue for histopathologic analysis.

Ligation of Ureter

- This complication is more likely to occur when ovariohysterectomy is associated with hemorrhage, pyometra, or cesarean section. It may also occur when the urinary bladder is distended and the trigone and ureterovesical junction are displaced cranially.
- Hydronephrosis and occasionally pyelonephritis can result.
- Ureteronephrectomy may be required.
- Avoid by careful placement of ligatures on the OAVC and uterine body.

Urinary Incontinence

- Urinary incontinence after ovariohysterectomy can occur in susceptible individuals (approximately 20% of canine patients) due to a combination of low systemic estrogen levels and increase production and secretion of follicle-stimulating hormone and luteinizing hormone.
- Additional structural causes of urinary incontinence may include adhesions or granulomas of the uterine stump that interfere with urinary bladder sphincter function and, rarely, vaginoureteral fistula from common ligation of the vagina and ureter.
- Prudent administration of exogenous estrogens or alpha-adrenergic drugs may be indicated for estrogen-responsive urinary incontinence (see Chapter 83).

Fistulous Tracts and Granulomas

- Sublumbar draining sinus tracts in spayed female dogs may develop when non-absorbable multifilament suture material, such as polymerized caprolactam (Braunamid, B. Braun Melsungen) used for ligating the OAVC or uterine body becomes contaminated.
- Treatment is exploratory celiotomy and removal of suture material.

▼ ***Key Point*** Do not use non-absorbable multifilament suture material for ligation of the OAVC or uterine body.

Body Weight Gain

Weight gain may occur after ovariohysterectomy; the cause is poorly understood.

Eunuchoid Syndrome

This is a rare complication identified in working dogs after ovariohysterectomy. Clinical signs include decreased aggression, loss of interest in work, and decreased stamina.

Complications Related to Celiotomy

The most common complications associated with celiotomy are the following:

- Self-mutilation of the abdominal wound
- Seroma formation
- Dehiscence
- Failure to remove gauze sponges from the abdominal cavity
- Laceration of the spleen or urinary bladder

CESAREAN SECTION

Preoperative Considerations

Indications for Cesarean Section

- Dystocia from primary uterine inertia
- Protracted dystocia resulting in secondary uterine inertia

- Obstructive dystocia (oversized fetus or narrow pelvic canal)
- Prolonged gestation
- Dystocia from fetal malpositioning
- Fetal death with putrefaction

Certain breeds (Chihuahuas, English bulldogs) frequently require cesarean section because of a high incidence of dystocia. (See Chapter 90 for further discussion of dystocia.)

Anesthesia

- Animals that require cesarean section may have fluid and metabolic disturbances that place them at greater risk for general anesthesia.
- Correction of fluid and metabolic abnormalities should be well under way prior to induction of anesthesia. Administer intravenous fluid therapy and a prophylactic broad-spectrum antibiotic such as cefazolin, 22 mg/kg IV.
- Various regimens for induction and maintenance of anesthesia (see Chapter 2 for general principles of anesthesia) have been recommended. The objective is to administer an appropriate level of anesthesia and analgesia to the dog or cat without causing excessive depression of the puppies or kittens.
- Epidural anesthesia using a local anesthetic with or without an opioid can be attempted in dogs.
- Intravenous narcotics or propofol combined with local anesthesia may be used in dogs.
- Ketamine and local anesthesia may be used in cats.
- Administer standard inhalation anesthesia after the puppies or kittens are removed.

▼ ***Key Point*** Minimize time from induction to delivery by fully preparing the surgical site prior to anesthesia.

- Induce anesthesia and intubate the animal on the surgery table, preferably after the initial skin preparation.

▼ ***Key Point*** Inform the owner prior to surgery that ovariohysterectomy may be necessary if the uterus is not viable.

Surgical Procedure

Objective

- To remove all fetuses from the gravid uterus as quickly and safely as possible

Equipment

- Standard general surgery instrument pack and suture
- Laparotomy sponges
- Clean towels
- Doxapram (Dopram, Robins) and naloxone (Narcan, Elkins-Sinn) (if narcotics are used for induction)
- Incubator or heat lamp

Technique

1. Position the animal in standard dorsal recumbency.
2. Perform the final skin preparation and place surgical drapes.
3. Incise skin, subcutaneous tissue, and linea alba on the ventral midline beginning cranial to the umbilicus and extending as far caudally as necessary to exteriorize the uterus.

▼ ***Key Point*** Avoid incising mammary tissue when making the initial skin incision. Enter the abdominal cavity cautiously to avoid lacerating the gravid uterus.

4. Exteriorize the uterus.
5. Isolate the uterus from the abdominal viscera with moist laparotomy sponges.
6. Identify an avascular area on the dorsal or ventral midline of the uterine body. Make a small incision in the uterine body with a scalpel by tenting the tissue of the uterine wall to avoid inadvertently lacerating a fetus with the scalpel.
   a. Extend the incision with Metzenbaum scissors to a sufficient length to accommodate the largest fetus. The uterus may tear during extraction of a fetus if the length of the incision is not adequate.
7. Move a fetus to the incision by gently squeezing the uterine horn (Fig. 91-3*A*).
8. Grasp the fetus and gently remove it from the uterus.
9. Open the amniotic sac as the fetus is removed (Fig. 91-3*B*). Direct fetal fluids away from the operative field to minimize contamination.
10. Clamp and transect the umbilical vessels approximately 2 cm from the fetal abdominal wall (Fig. 91-3*C*).
11. Place the neonate on a sterile towel and pass it to an assistant. Alternatively, the neonate can be passed to the assistant before the umbilical vessels are transected, leaving this responsibility to nonsterile operating room assistants.
12. Remove the placenta by separating the placental attachment from the endometrium using gentle traction. To decrease the potential for severe postoperative uterine hemorrhage, do not remove the placenta if placental separation is difficult.
13. Extract the remaining fetuses by gently manipulating them toward the site of the uterine incision.
14. Palpate the uterus from the pelvic canal to the ovaries to make certain that no fetuses remain.
15. The uterus will contract rapidly after all fetuses have been removed and occasionally during extraction of the last few fetuses. Administration of oxytocin rarely is necessary to initiate uterine involution.
16. Close the uterus with 2-0 or 3-0 absorbable suture material in a one- or two-layer inverting suture pattern (e.g., Cushing and Lembert).

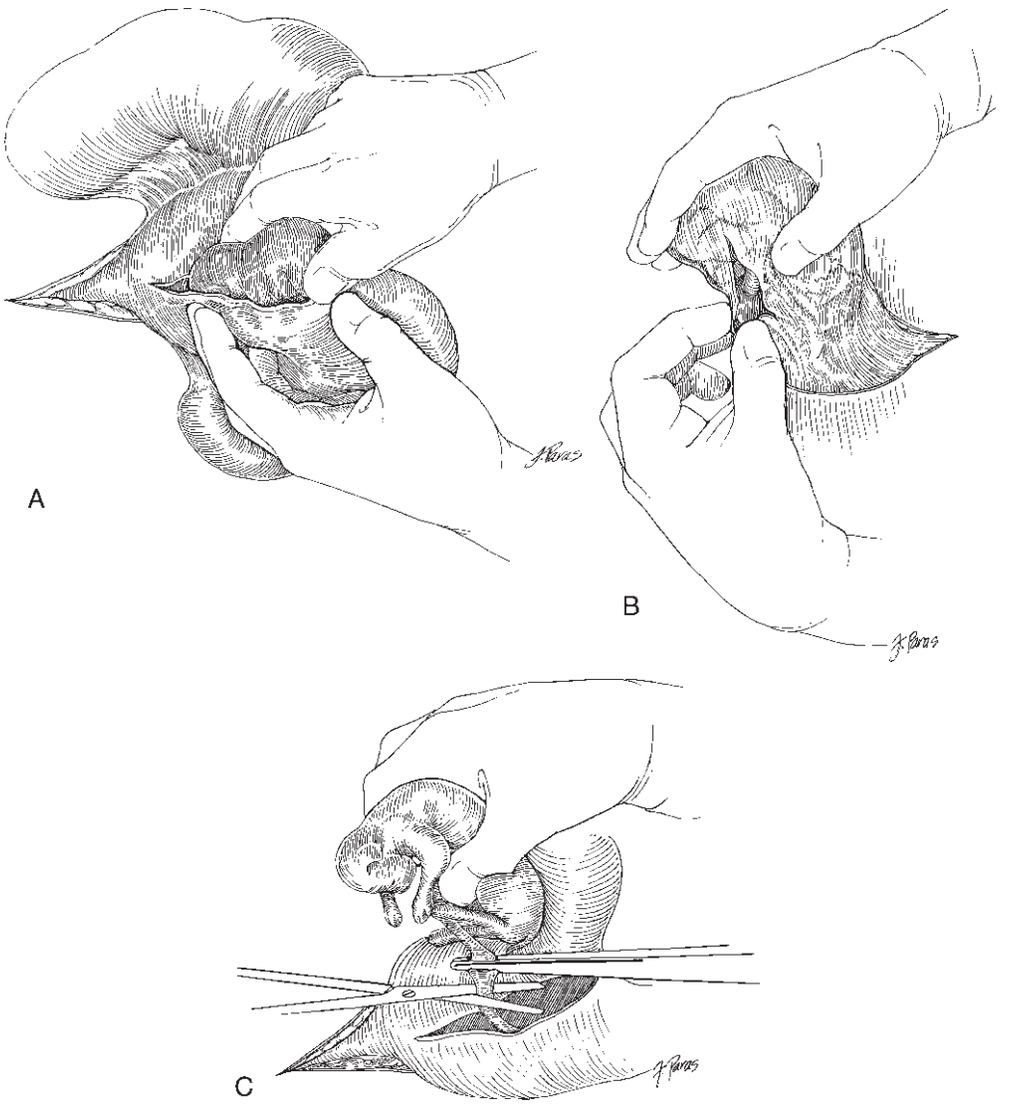

Figure 91-3. Cesarean section. *A,* Move the fetus toward the incision. *B,* Break the amniotic sac as the fetus is removed. *C,* Clamp and transect the umbilical vessels.

17. Locally lavage the uterus with warm physiologic saline solution prior to returning it to the abdominal cavity.
18. Lavage the abdominal cavity with warm physiologic saline solution and aspirate all lavage fluid if contamination or spillage of uterine contents occurred.

▼ ***Key Point*** En bloc ovariohysterectomy (rapid removal of the uterus and ovaries before hysterotomy and removal of the neonates) is associated with a neonatal survival rate that is similar to other techniques for medical and surgical management of dystocia.

Postoperative Care and Complications

Care of Neonates

▼ ***Key Point*** Remove the fetal membranes from the neonate's mouth and nose immediately after delivery.

- Clamp the umbilical vessels and remove the fetal membranes if this was not done by the surgeon.
- Clear mucus from the mouth and nares with gentle suction or cotton swabs.
- Assess the viability of the neonate. Neonates often are bradycardic and apneic.

- Dry the neonate briskly with a soft towel because skin stimulation reflexly stimulates respiration.
- Mucus can be cleared from the upper airway by grasping the neonate firmly and slowly swinging it downward.
- Administer a respiratory stimulant such as doxapram (Dopram, Robins), 0.5 to 2.0 mg/kg PO or IM, if the neonate does not respond to mechanical stimulation.
- Poor neonatal viability can be due to anesthetic agents administered to the dam for induction of anesthesia. Administer a narcotic antagonist such as naloxone (Narcan, Elkins-Sinn), 0.01 mg/kg PO or IM, if the dam was given a narcotic for induction of anesthesia.
- Alternately, medications can be given topically on the neonate's tongue to be absorbed through the mucous membranes.
- Some neonates may not breathe spontaneously for 30 to 60 minutes after delivery. Be persistent with resuscitation efforts. Neonates that do not breathe spontaneously can be intubated with a sterile puppy feeding tube for assisted ventilation.
- Place neonates in an environmental temperature of approximately 32°C.
- Examine neonates for congenital abnormalities such as cleft palate, imperforate anus, hernias, and limb deformities.

Care of the Dam

- Clean residual antiseptic solution, blood, and fetal fluids from the dam's mammary glands prior to allowing the neonates to nurse.
- Place the dam with neonates after anesthetic recovery so that neonates receive colostrum as soon as possible after birth.
- Make certain that the dam has adequate milk and that each neonate nurses.
  - Oxytocin (0.5 U/kg IM or SC) can be administered to stimulate milk letdown.

▼ ***Key Point*** Ovariohysterectomy performed in conjunction with cesarean section should not interfere with the dam's mothering instincts or ability to produce milk. Ovarian hormones are not important for maintenance of lactation.

- Consider discharging the dam and neonates as soon as the dam has recovered from anesthesia and has demonstrated appropriate behavior toward the neonates.

Complications

Short Term

- These include hemorrhage, hypovolemia, and hypothermia.
- Place the dam in a warm, quiet environment and administer intravenous crystalloid or colloid fluids as needed.

Long Term

- Potential long-term complications include peritonitis, wound dehiscence, agalactia, and uterine hemorrhage.
- Prolonged severe endometrial hemorrhage may require administration of oxytocin or, in nonresponsive cases, emergency ovariohysterectomy.
- Monitor serum calcium levels if hypocalcemia is suspected. See Chapter 32 for diagnosis and treatment of eclampsia.
- Although multiple cesarean sections can be performed on a dam, uterine scarring may prevent future placentation, and peritoneal adhesions may complicate subsequent celiotomies.

UTERINE PROLAPSE

Preoperative Considerations

- Uterine prolapse is a rare condition that can occur anytime during or up to several days after parturition.
- Animals presented with uterine prolapse may be clinically stable or may have mild to severe metabolic imbalances. Treat disturbances in fluid, electrolyte, or acid-base balance before managing the uterine prolapse.
- Assess the viability of the prolapsed uterus.
- Treatment options include manual reduction, manual reduction with immediate ovariohysterectomy, internal reduction via celiotomy, and amputation of the uterus externally.
- Manual reduction of the prolapsed uterus is the treatment of choice, although an episiotomy may be required.
- Ovariohysterectomy may be necessary after manual reduction if the uterus is devitalized.
- Consider external amputation only if the uterus cannot be reduced. Then remove ovaries through a celiotomy incision.

Manual Reduction

Technique

1. Epidural anesthesia is preferred, but standard general anesthesia can be used.
2. Clean the uterus and wrap it with sterile gauze sponges soaked in physiologic saline. Soaking the sponges with a hypertonic dextrose solution may help reduce swelling.
3. Apply sterile water-soluble lubricating jelly to the uterus and attempt gentle reduction with a gloved finger or with a sterile, smooth syringe case.
4. If manual reduction is unsuccessful, prepare the perineum and the prolapsed uterus for aseptic surgery and perform an episiotomy (see Chapter 93 for technique). Reduction is facilitated by episiotomy. If manual reduction still is not possible,

consider internal reduction via celiotomy or external amputation.

Surgical Procedure for External Amputation of Prolapsed Uterus

Objectives

- To resect the prolapsed uterine horns and, if possible, the ovaries
- To avoid contamination of the abdominal cavity
- To minimize uterine hemorrhage

Equipment

- Standard general surgical instrument pack

Technique

1. Administer epidural or general anesthesia.
2. Position the animal in dorsal recumbency with the rear limbs tied forward.
3. Prepare the ventral abdominal and perineal areas for aseptic surgery. Place a purse-string suture in the anus.
4. Incise the uterine body near the vulva. Place stay sutures in the incised proximal wall of the uterine body to prevent retraction into the vagina. Be careful not to damage the urethra if the vagina has prolapsed with the uterus.
5. Identify the uterine horns.
6. Apply gentle caudal traction on the uterine horns to expose the ovaries. Ligate the right and left OAVC.
7. If the ovaries cannot be exposed, place two circumferential ligatures around each uterine horn as far cranial as possible. Transect the uterine horns between the two ligatures.
8. Double-ligate and transect the uterine vessels.
9. Close the proximal stump of the uterine body with synthetic absorbable suture material in a simple interrupted pattern and reduce the remaining tissue into the abdomen.
10. If the ovaries remain, perform a ventral midline celiotomy and bilateral ovariectomy.

Postoperative Care and Complications

- Recurrence after successful manual reduction of a uterine prolapse is rare. However, warn owners that recurrence is possible with subsequent whelping, particularly if dystocia occurs.
- Complications seldom occur after manual reduction or external amputation of the uterus. Life-threatening hemorrhage can occur rarely after external amputation.

UTERINE BIOPSY

Uterine biopsy and culture is most commonly indicated in female patients of breeding age with a clinical history of reproductive failure or persistent vaginal discharge arising from the uterus. Uterine biopsy is performed for the purposes of diagnosis and prognosis.

Surgical Procedure for Uterine Biopsy

Objectives

- To obtain a full thickness tissue sample and culture sample from the uterus
- To minimize contamination of the peritoneal cavity

Equipment

- Standard general surgical instrument pack

Technique

1. Follow the surgical technique described under "Cesarean Section," steps 1 to 5, to expose the uterus.
2. Palpate the uterus for abnormalities such as mass lesions, cystic areas, or fluid accumulation.
3. Use a 4- to 6-mm skin biopsy punch to obtain a full thickness biopsy sample of either one of the uterine horns or the uterine body.
4. Insert a small sterile swab into the uterine lumen to obtain a sterile culture sample.
5. Close the biopsy site using 4-0 or 5-0 synthetic absorbable monofilament suture (Monocryl, PDS) in an interrupted or cruciate pattern.

▼ ***Key Point*** The submucosa is the holding layer of the uterus. Avoid placing suture material within the lumen of the uterus.

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Chapter 92

Diseases of the Vagina and Vulva

Mary A. McLoughlin

Small animals with diseases of the vulva and vagina can present with clinical signs of lower urinary tract disease (urgency, pollakiuria, stranguria, and hematuria), intermittent or continuous urinary incontinence, vaginal discharge, perivulvar dermatitis, excessive licking, and foul odor. Because the vulva and the vestibule form a common orifice for the lower urinary and reproductive systems, careful examination of associated diseases is warranted. See Chapter 93 for discussion of the anatomy of the vagina and vulva.

DISEASES OF THE VULVA

Congenital Abnormalities

Congenital abnormalities of the vulva are uncommon and are often detected because of the secondary problems they cause. Abnormalities of the anatomic structure, size, or positioning of the vulva have been shown to be contributing factors to the development several disorders, including chronic or recurrent urinary tract infections, cystitis, vaginitis, vestibulitis, urine pooling or urinary incontinence, perivulvar dermatitis, and difficulty with natural mating. Diagnosis of vulvar disorders is made by physical examination of the vulva and perivulvar region, as well as digital palpation and vaginoscopy.

Vulvar Hypoplasia or "Juvenile" Vulva

Etiology

- Vulvar hypoplasia has been described as a small or infantile vulva, which is frequently retracted and obscured by the perivulvar skin folds. The patient's weight or body condition score should not bias the diagnosis of vulvar hypoplasia.
- The vulva should not be covered or obscured by regional skin folds dorsally or laterally. It should not be necessary to pull upward on the perineal skin between the anus and the vulva to expose the complete extent of the vulva.
- Tremendous variation in size, structure, and position of the vulva exists among various breeds of dogs, as well as within specific breed standards. The vulva should be located on the perineal midline directly ventral to the anus. Although the size of the vulva varies among dogs, it should be readily visible in the standing dog when viewed from behind. The vulva should not be positioned ventrally between the rear legs so that it is no longer visible.
- Perivulvar skin folds may obscure both hypoplastic and normal-sized vulvas. There are a number of breeds of dogs that appear to be conformationally predisposed to perivulvar skin folds as young dogs without being overweight, including Newfoundland, Labrador retriever, mastiff, German shepherd, Akita, basset hound, Staffordshire terrier, and bull terrier.
- It is well recognized that the anatomic characteristics of the vulva are altered due to the hormonal influence of the estrus cycle in unspayed females. The vulva becomes swollen and enlarged during proestrus and estrus. As the vulva enlarges, it is generally assumes a more dorsal position in the perineal region to facilitate mating.
- The size of the vulva generally does not change in spayed female dogs. It has been theorized that vulvar hypoplasia results from ovariohysterectomy at an early age prior to development of secondary sex characteristics. However, there is no scientific literature to support this statement.

Clinical Signs

- A small or hypoplastic vulva is common and frequently not associated with any clinical abnormalities. However if the vulva is small and recessed by the surrounding perivulvar skin folds, body heat and moisture from vaginal secretions or urine can accumulate between local skin folds, creating an environment conducive to skin maceration, inflammation, and bacterial overgrowth. Microtrauma to the skin surfaces from friction between the opposing skin folds, combined with tissue maceration and inflammation, causes normal skin defense mechanisms to be overwhelmed, allowing secondary bacterial infections to occur.

- Superficial dermatitis in the perivulvar region can result in a foul odor and discharge.
- Secondary clinical signs of chronic vestibulitis, vaginitis, cystitis, and ascending urinary tract infection have also been reported.

Treatment

- Medical management of perivulvar dermatitis with systemic antibiotics or topical therapies such as antimicrobials, antiseptic, cleansing, or drying agents can be performed (see Chapter 38). However, this approach is typically only palliative and often unrewarding for long-term resolution.
- Episioplasty, the surgical excision of the excessive perivulvar skin folds to expose and reposition a small or recessed vulva, is the treatment of choice for perivulvar dermatitis, chronic or recurrent urinary tract infections, or vestibulitis secondary to ascending infection or chronic local inflammation (see Chapter 54).

Vulvar Stenosis

Etiology

- Abnormal fusion of the genital folds and genital swellings can result in narrowing or stenosis of the vulva, vestibule, or vestibulovaginal junction.
- Vulvar stenosis has been most frequently reported in the collie and Shetland sheepdog breeds.

Clinical Signs

- There are frequently no clinical signs if the affected animal has been spayed.
- This abnormality may be overlooked unless the affected female is intended for breeding or a digital examination of the vulva, vestibule, and vestibulovaginal junction is indicated.
- Affected females may experience pain when mating is attempted, requiring the deposition of semen by artificial insemination.
- If pregnancy does occur, vulvar stenosis can result in dystocia. A planned cesarean section can be performed to avoid this complication, or an episiotomy can be performed at the time of delivery of the first fetus.

Treatment

- Enlargement of the vulvar orifice, rima vulvae, by permanent episiotomy (episiostomy) can be performed (see Chapter 93).
- Increasing the size of the vulvar orifice may result in an increased exposure of the vestibule, vagina, and lower urinary tract to ascending environmental contaminants, resulting in secondary vestibulitis, vaginitis, and urinary tract infection.

Clitoral Hypertrophy

The clitoris is located on the ventral floor of the vulva, normally recessed within the clitoral fossa. The clitoral fossa demarcates the cranial edge of the vulva at the transition of the vulva to the vestibule. The clitoris is described as the female homologue to the penis and may contain an os clitidoris.

Etiology

- Clitoral enlargement is typically associated with any one of a number of developmental or acquired etiologies, including disorders of sexual differentiation (see Chapter 90), exposure to anabolic steroids, or hyperadrenocorticism (see Chapter 33).
- Enlargement of the clitoris may result in exposure of the clitoris by its protrusion through the vulvar cleft.
- Clitoral enlargement has been documented in normal female dogs.

Clinical Signs

- The clinical signs associated with clitoral hypertrophy are variable. Animals may be presented for purely cosmetic reasons rather than specific health concerns.
- Enlargement of the clitoris and exposure through the vulvar cleft can result in clitoritis from environmental exposure, drying, and mechanical irritation.
- Inflammation of the clitoris can also result in secondary urinary tract infection, vestibulitis, or vaginitis with discharge due to drainage around the enlarged clitoris.

Treatment

- Symptomatic therapy with systemic antimicrobials, anti-inflammatory drugs, or local treatment with topical therapies is typically unrewarding for long-term resolution of clinical signs.
- Determination of an underlying etiology is essential to direct treatment at an inciting cause. Withdrawal of all anabolic steroids or treatment of hyperadrenocorticism may result in regression of the clitoral enlargement.

▼ ***Key Point*** Surgical treatment of clitoral hypertrophy is not indicated if a patient does not have any associated clinical signs.

- Perform clitoral resection for patients with persistent clinical signs associated with clitoral enlargement.

Surgical Procedure: Clitoral Resection

Technique

1. Perform an episiotomy to expose the clitoris and clitoral fossa. The external urethral orifice is identified and catheterized (see Chapter 93).

2. Dissect the base of the clitoris, which may include an os, from the fossa and surrounding vulvar and vestibular mucosa using sharp dissection.
3. Control hemorrhage with electrocautery or a laser. Larger "phalluses" present in dogs with intersex disorders may bleed profusely. Control of local hemorrhage is essential.
4. Close the incised edges of the vulvar and vestibular mucosa with a monofilament absorbable suture, eliminating the clitoral fossa.
5. Close the episiotomy in a routine manner (see Chapter 93).

Postoperative Care

- Place an Elizabethan collar to prevent self-trauma.
- Consider administration of nonsteroidal anti-inflammatory drugs after surgery for swelling, pain, and discomfort (see Chapter 6).

Vulvar Enlargement

Etiology

- Edema or swelling of the vulva is a normal response to estrogenic stimulation during the follicular stages of the estrus cycle in intact dogs and cats. Typically, vulvar swelling resolves on its own as the female enters diestrus.
- Persistent or prolonged swelling of the vulva in cycling females may represent prolonged estrogenic stimulation from cystic ovaries or an estrogen-producing ovarian neoplasm, such as a granulosa cell tumor (see Chapter 90).
- Vulvar swelling in a spayed female dog is also associated with estrogenic stimulation and may be a result from the presence of functional ovarian tissue after ovariohysterectomy (ovarian remnant syndrome; see Chapter 90).
  - Ovarian remnants are reported more frequently in cats than in dogs, with remnant ovarian tissue more frequently retained at the site of the right ovarian pedicle.

Clinical Signs

The vulvar lips appear edematous and turgid on physical examination. A serosanguineous discharge may be noted.

Diagnosis

- *Vaginal cytology:* Evidence of estrogenic stimulation. Smears should contain mostly superficial and anuclear squamous cells.
- *Hormonal evaluation:* Evaluation of serum concentrations of estradiol and progesterone may be warranted (see Chapter 90).
- *Abdominal ultrasound examination:* Cystic ovarian tissue, ovarian remnants, and ovarian neoplasia may be evident in the region of the ovaries at the caudal pole of either kidney.

Treatment

Exploratory laparotomy and biopsy: Direct identification, excision, and biopsy of a mass lesion in the region of either or both ovarian pedicles will definitively diagnose the presence of estrogen-secreting ovarian tissue and distinguish among ovarian remnant syndrome, neoplasia, and cystic ovaries (see Chapter 91). Surgical identification of ovarian remnants is easier if the exploratory is performed while the animal is in estrus.

Vulvar Trauma

Etiology. Injury to the vulva is relatively uncommon but can occur as a result of blunt or penetrating trauma, dog fights, injury during breeding, attempts to disrupt a mating, or difficulty whelping.

Diagnosis

- Evaluation of the injury requires a complete physical examination, digital vulvar and vestibular examination, episiotomy, or vaginoscopy.
- Complete examination of the vulva to determine the extent of the injury may require sedation or general anesthesia when the patient is stable.
- Placement of a urethral catheter and closed urinary collection system may be necessary with severe trauma or swelling of the vulvar or perivulvar region.

Treatment

- Standard care and treatment of local wounds is indicated. Flushing of the wounds and surgical debridement may be necessary (see Chapter 56).
- Primary closure or reconstruction of the vulva may be necessary to prevent narrowing or stenosis as a result of second-intention healing.
- Placement of a urinary catheter attached to a closed collection system will aid management of wounds in this location.

DISEASES OF THE VESTIBULE AND VAGINA

Congenital Abnormalities

Abnormalities in the embryologic development of the urogenital sinus may result in structural malformations affecting the vagina and vestibule, including vaginal septum, persistent hymen, septal remnants, or persistent paramesonephric remnant and vestibulovaginal stenosis. Any of these conditions may prohibit or prevent natural mating or may contribute to the susceptibility of the local environment to chronic or recur-

rent ascending infections of the urinary or reproductive tracts.

Persistent Hymen, Septal Remnants, Paramesonephric Remnants, and Vestibulovaginal Stenosis

Many names are currently being used to describe the persistent vertical bands of tissue located at the opening of the vestibulovaginal junction, including persistent hymen, septal remnants, paramesonephric remnants, and vaginal septum.

Etiology

- If the paramesonephric ducts fail to unite with each other or fail to fuse or cannulate with the urogenital sinus, it can result in a vertical septum or annular fibrous stricture at the vestibulovaginal opening.
- Incomplete fusion of the caudal paramesonephric ducts with retention of a medial partition results in an elongated vertical vaginal band, a vaginal septum, or rarely a bifid vagina.
- Vertical bands of tissue of varying width are commonly identified at the cingulum, which is the circular opening at the vestibulovaginal junction. These bands can be found in normal female dogs and those with developmental abnormalities of the lower urinary and reproductive tracts.
- Vertical bands of tissue at the cingulum of the vestibulovaginal junction are seen in almost all patients diagnosed with ureteral ectopia.
- Vertical or annular bands that narrow or partition the vestibulovaginal junction result in clinical signs associated with mating difficulties.

Clinical Signs

Clinical signs of chronic vaginitis, vestibulitis, vaginal discharge, urine pooling, chronic cystitis, or urinary tract infection have been attributed to narrowing of the vestibulovaginal junction in dogs. However, no cause and effect has been clearly identified.

Diagnosis

- A number of diagnostic techniques can be used to evaluate the vestibulovaginal anatomy, including digital vaginal examination, urogenital endoscopy, and positive-contrast retrograde vaginourethrography.
- *Digital examination* can be performed with the patient awake or sedated.
  - Diagnosis of a hymen or persistent septal remnant is made when two small openings are identified on either side of a centrally oriented band.
  - For female dogs with an annular or stenotic opening at the vestibulovaginal junction, digital penetration of the cranial vaginal vault is not possible. If vestibular or vaginal stenosis is of concern, the bitch should be evaluated under the effects of sedation during estrus, when this opening should be at it widest.
- *Rigid or flexible endoscopy* allows examination of the vestibule, vestibulovaginal junction, and cranial vaginal vault region. Fluid insufflation will provide an optically clear environment and provide distension of the local tissues to improve visualization.
  - Definitive diagnosis of a septum, septal remnant, or annular narrowing at the vestibulovaginal junction is made by endoscopic examination.
- *Positive-contrast retrograde vaginourethrography* has recently been advocated as a method to diagnosis vestibulovaginal stenosis in dogs. Controversy exists regarding the specific radiographic measurements necessary to accurately make this diagnosis. No effort has been made to correlate clinical signs and endoscopic and radiographic findings in female dogs with suspected vestibulovaginal stenosis.

Treatment

Persistent Hymen or Septal Remnant. Surgical correction of persistent vertical bands of tissue located at the vestibulovaginal junction is indicated in bitches with persistent clinical signs or failure to successfully breed or whelp.

▼ ***Key Point*** Surgical excision of the vertical band of tissue at the vestibulovaginal junction is not indicated in asymptomatic patients.

Surgical Procedure: Removal of Persistent Hymen or Septal Remnant

1. Thin and moderately thick bands of tissue can be easily removed using cupped biopsy forceps while examining the area through a rigid or flexible endoscope.
2. Grasp the band with the forceps at its base and separate it from its attachment along the vestibulovaginal junction.
3. Separate the tissue remnant from the opposite base of attachment and remove.
4. Remove thick or broad-based septa via a direct surgical approach using an episiotomy (see Chapter 93) or using a surgical laser.

Annular Bands or Vestibulovaginal Stenosis

Complete resection of an annular stricture at the vestibulovaginal junction and anastomosis of the remaining vagina and vestibule is an extremely difficult and time-consuming surgery. A short (<1.5 cm) narrowed region of the vagina or vestibulovaginal junction can be opened or widened using a vestibulovaginoplasty procedure (see Chapter 93).

Vaginal Edema (Vaginal Hyperplasia)

Etiology

An edematous thickening of the vaginal and vestibular mucosa occurs during the follicular phase of the estrous cycle. This broad-based mucosal proliferation originates cranial to the external urethral orifice.

Clinical Signs

- The proliferative vaginal tissues may protrude through the vulvar orifice as a smooth, fleshy mass. Exposure of the vaginal mucosa to the environment quickly results in drying, inflammation, congestion, edema, ulceration, and potential necrosis.
- Vaginal edema is most commonly recognized in young female dogs during their first estrus cycle. It is reported with an increased frequency in several breeds, including bulldogs, boxers, and Labrador retrievers.
- The edematous tissue will spontaneously regress during diestrus. Affected females may experience recurrence of the condition with each successive estrus cycle.

Diagnosis

- Determine recent history and physical examination findings of estrus.
- Digital examination of the vulva and vestibule and vaginoscopy reveals a broad-based mass arising from the cranial vaginal vault. The external urethral orifice is caudal to the base of the protruding mass.
- Differentiate vaginal edema from benign or malignant neoplasia of the vestibule or vagina. If vaginal neoplasia is suspected, obtain tissue samples for histopathology.

Treatment

- Ovariohysterectomy is the surgical treatment of choice and appropriate for females that were not intended for breeding purposes (see Chapter 91).
- Attempts can be made to reduce the edema of the exposed tissues by applying gentle manual compression and topical application of a hyperosmotic solution such as 50% dextrose. As the edema subsides, attempts can be made to reduce the exposed tissues through the vulvar orifice into the vestibule.
- If the proliferative vaginal tissue cannot be reduced, it must be kept moist and well lubricated until it regresses following the spay procedure. It is essential that the patient be fitted with an Elizabethan collar or cage muzzle to prevent self-trauma.
- Vaginal edema in dogs intended for breeding poses a number of issues to consider.
  - The heritable nature of this disorder is unknown.
  - Although breeding can be accomplished via artificial insemination, the protruding mucosa must be managed until it regresses during diestrus.
  - As the concentration of progesterone decreases at the end of diestrus, with impending whelping, recurrence of the vaginal edema can occur.
  - If the redundant vaginal tissue remains regressed, ability to whelp should not be affected. It is unknown whether affected bitches may be predisposed to vaginal prolapse.
- Surgical treatment of vaginal edema should only be considered in patients with devitalized or necrotic tissues. Surgical treatment involves resection of the redundant mucosa (see Chapter 93).

▼ ***Key Point*** Surgical resection of redundant vaginal mucosa does not prevent reoccurrence of vaginal edema at the next estrus cycle.

Vaginal Prolapse

Etiology

- Vaginal prolapse is relatively uncommon in small animals and should not be confused with vaginal edema. Like vaginal edema, vaginal prolapse is also recognized during the estrus phase of the reproductive cycle or periods of hyperestrogenism.
- Complete or partial vaginal prolapses can occur. If the cervix protrudes from the vulva, a complete vaginal prolapse has occurred.
- The underlying etiology remains unknown in most cases.
- Brachycephalic breeds including Boston terrier and boxer appear to have an increased predisposition compared with other breeds of dogs for the development of vaginal prolapse.
- Vaginal prolapse can result from dystocia.

Clinical Signs

- The animal presents with a protrusion of the complete vaginal circumference including the external urethral orifice, which is positioned ventrally.
- Swelling and protrusion of the vaginal mucosa rapidly results in venous congestion and discoloration of the tissues with a “doughnut” appearance. These tissues are friable and ulcerate readily.

Diagnosis

- Physical examination reveals a tubular or doughnut-shaped structure protruding from the vulva.
- Differential diagnoses are vaginal edema or vaginal neoplasia.
  - Differentiate vaginal prolapse from these other lesions by passing a sterile probe between the mass and the vaginal wall. Whereas with a tumor or edema the probe will travel well into the vagina without obstruction, with vaginal prolapse the probe will hit a blind “pouch” and not be able to penetrate further.

Treatment

- A mild or partial prolapse may resolve during diestrus.
- Keep exposed tissues clean, moist, and lubricated.
- If possible, manually reduce the exposed tissues to a more normal anatomic position.
- If necessary, apply a hyperosmotic solution such as 50% dextrose to the exposed tissue after cleaning to assist in reducing some of the edema.
- Episiotomy may also aid the manual reduction of the displaced vaginal tissues.
- If manual reduction is successful, a sterile, balloon-tipped catheter should be placed through the urethra into the bladder and attached to a closed urinary collection system.
- The labia of the vulva can be sutured closed using a non-absorbable monofilament suture until the swelling resolves.
- Perform ovariohysterectomy in females that are not intended for breeding purposes (see Chapter 91). Owners wanting to salvage a potential breeding female should be counseled that the heritable nature of this trait is unknown and that reoccurrence is possible.
- Surgical pexy of the uterine body or horns to the dorsolateral body wall can be performed to help prevent future prolapse in a breeding female. Objective evaluation of uterine pexy on future reproduction status is unknown.
- Severe or devitalized vaginal prolapse may present as an acute or chronic condition with congestion, ulceration, infection, and necrosis of the affected tissues.
  - Attempts at reduction and replacement of the devitalized tissues are contraindicated. Evaluate the patient for systemic infection.
  - Surgical resection of devitalized tissue may be necessary on an emergency basis (see Chapter 93).
  - Reevaluate the surgical site via digital vaginal examination at 2 weeks and again before the next estrus cycle to evaluate continuity of healing and to be sure that a stricture has not occurred.

Neoplasia of Vagina, Vestibule, and Vulva

The most common neoplasms of the vulva, vestibule, and vagina are benign and include leiomyoma, fibromas, and lipoma. The most common malignant neoplasms of this region include leiomyosarcoma, squamous cell carcinoma, adenocarcinoma, mast cell tumor, and transmissible venereal tumor (TVT).

Benign Neoplasia

Etiology

Leiomyoma

- Leiomyoma is the most frequently reported neoplasm affecting the cervix, vagina, or vestibule arising from the smooth muscle of these structures.
- Leiomyomas can be intraluminal or extraluminal.
  - Intraluminal leiomyomas appear as a smooth fleshy mass pedunculated on a stalk arising from the vestibular wall.
- When the initial mass is small, it may go unnoticed for an extended period of time as it is contained within the vestibule. The tumor may remain unnoticed until it is large enough to protrude through the vulvar cleft.
  - Extraluminal leiomyomas arise from the wall of the vestibule or vagina and may expand into the perineal space. Extraluminal leiomyomas may present because of perineal swelling or impingement on surrounding structures such as the rectum. Complete surgical resection is typically curative. Local recurrence can be a problem if surgical resection is incomplete.

Lipoma

Benign fatty masses located in the perineal region, vagina, or vestibule can occur but are less common than leiomyoma.

Clinical Signs

- Clinical signs are extremely variable and are dependent on the location and size of the mass.
- Signs may range from none to perineal swelling, vaginal discharge, mass protrusion through the vulvar cleft, bloody vaginal discharge or hematuria, excessive licking, foul odor, constipation, dysuria, or dystocia.

Diagnosis

- Most vestibular or vaginal masses are diagnosed by examination of the vulva, digital examination of the vagina and rectum, or vaginoscopy.
- Although vaginal cytology is not typically helpful to obtain a specific diagnosis of the mass lesion, fine-needle aspiration of the mass itself may provide cytologic information for diagnosis.
- Incisional biopsy samples may be obtained surgically using a local anesthetic if the mass is assessable.
- Biopsy samples may be obtained from a mass that cannot be exteriorized (within the vestibule or vagina) using a biopsy instrument with a rigid or flexible endoscope.

Treatment

- Complete surgical resection is the treatment of choice for benign masses located within the vestibule and vagina (see Chapter 93).
- Extremely large masses may require complete vulvovaginectomy and urinary diversion for complete excision. Refer these patients to a surgical specialist.
- Consider ovariohysterectomy as an adjunct surgical treatment for all vestibular and vaginal tumors (see Chapter 91).

Malignant Neoplasia

Etiology

Leiomyosarcoma

- Leiomyosarcoma is the most common malignant tumor affecting the vestibule and vagina. Other malignant tumors that have been reported affecting the vulva, vestibule, or vagina include squamous cell carcinoma, adenocarcinoma, mast cell tumor, hemangiosarcoma, and hemangiopericytoma.
- It may be difficult to distinguish between benign and malignant neoplasia in this region without biopsy results.

Transmissible Venereal Tumor

- Canine TVT is a proliferative tumor of the vulva, vestibule, or vagina that is transmitted by sexual or social contact between animals. Cells of this tumor directly transplant, resulting in proliferative or cauliflower-like lesions (see Chapters 30 and 88).
- TVT is noted in younger sexually active male and female dogs, often in crowded urban areas.
- Metastasis is rare but can occur in the regional lymph node.

Clinical Signs

- TVT may present as a solitary lesion or as multiple friable, hemorrhagic, or cauliflower-like lesions.
- Extragenital sites include oral and nasal mucosa, skin, and perineum.

Diagnosis

See the previous discussion under "Benign Neoplasia" of the vagina.

Treatment

- Staging of the patient prior to surgery is essential.
- Complete surgical resection of malignant tumors with adequate margins is the treatment of choice.
- Complete resection of malignant masses in this region may require vulvovaginectomy and urinary diversion. Refer the animal to a surgical specialist.
- Small, isolated lesions can be removed surgically. Large or multiple lesions can be treated with radiation therapy or chemotherapy.
  - Chemotherapy is the treatment of choice for multiple or metastatic TVT. Either a single-agent or a combination protocol is effective in controlling this tumor (see Chapters 30 and 88).

▼ ***Key Point*** Vincristine is highly effective for the treatment of TVT.

Vaginitis

Etiology

Juvenile Vaginitis

Inflammation of the vestibule and vagina can occur in female dogs prior to their first estrus cycle (generally less than 1 year of age). The cause of the inflammation is nonspecific and usually resolves without treatment after the first estrus cycle. This type of vaginitis is not a result of bacterial overgrowth.

Bacterial Vaginitis

Bacterial infection of the vagina or vestibule is uncommon as a primary disorder in small animals. The vagina contains a mixed population of bacteria considered normal flora, including *Staphylococcus aureus, Streptococcus, Escherichia coli, Pasteurella, Klebsiella, Mycoplasma,* and *Ureaplasma.* Bacterial vaginitis typically occurs secondary to diseases of the lower urinary system, reproductive system, neoplasia, clitoral hypertrophy, and trauma.

Viral Vaginitis

- In addition to causing fatal infections in newborn puppies, canine herpesvirus infection causes vesicular mucosal lesions in the vagina and vestibule of affected females (see Chapter 16).
- These vesicular lesions are usually transient but often recur during proestrus.
- The raised mucosal lesions identified with canine herpesvirus can look similar to the more commonly diagnosed lymphoid hyperplasia in the vestibule, which occurs secondary to inflammation or bacterial infections associated with either the genital or the urinary system.
- Canine herpesvirus infection can result in infertility, abortion, and neonatal death.

Diagnosis

- *Physical examination:* Perform a complete examination of the external genitalia and surrounding perivulvar region. Determine vulvar size, position, and degree of recession by surrounding skin folds. Carefully examine the perivulvar region for ulceration, maceration, or hyperpigmentation commonly seen with perivulvar skin fold dermatitis.
- *Digital examination of the vulva and vestibule:* Examine for any underlying anatomic abnormalities such as vulvar or vestibular stenosis, presence of a vaginal septum, or septal remnant. Digital examination may reveal mass lesions within the vagina or vestibule that are not visible.
- *Vaginal cytology:* Microscopic examination of exfoliated cells from the vaginal vault will aid in differen-

tiating vaginitis from a vaginal discharge associated with any one of the stages of the estrus cycle. Examination of the vaginal cytology will also determine the general type and number of bacteria and the characterization of neutrophils and other cell types.

- *Urinalysis:* Obtain a urine sample by cystocentesis for urinalysis and aerobic bacteriologic culture of the urine to rule out urinary pathogens as a predisposing or secondary cause of the vaginitis.
- *Endoscopic examination of the vestibule, vagina, and lower urinary tract:* Rigid or flexible endoscopy will confirm the presence of suspected anatomic abnormalities or mass lesions and will permit biopsy.
- *Bacteriologic culture and susceptibility testing*
- *Abdominal ultrasound:* Completely evaluate the urinary and reproductive organs within the abdominal cavity.

Treatment

Juvenile Vaginitis

- This disorder is self-limiting and will resolve after the first estrus; therefore, no treatment is indicated.
- Systemic or local symptomatic treatment typically does not cause resolution of the clinical signs.
- Be sure to examine the external anatomy of the vulva to rule out perivulvar skin folds as a possible underlying cause, even in a young female.
- If the vaginitis persists after the first estrus, further diagnostic evaluation as described above is warranted.

Bacterial Vaginitis

- Identify and treat the underlying primary genital or urinary abnormality, including correction of developmental abnormalities and excision of mass lesions within the vagina, vestibule, clitoral fossa, and vulva.
- Secondary bacterial vaginitis commonly resolves with no therapy or medical treatment once the underlying cause is resolved or eliminated.
- Medical treatment consists of appropriate antibiotics based on results of culture and sensitivity testing.
- In dogs, trimethoprim-sulfonamide, erythromycin, norfloxacin, and ciprofloxacin have been shown to achieve concentrations in the urethra and vaginal secretions several times higher than the minimal inhibitory concentration against common urinary pathogens.

Viral Vaginitis

- No specific therapy is currently available to treat canine herpesvirus infections in affected bitches.
- Symptoms can be transient and commonly recurrent.
- Isolate affected females and counsel breeders not to use affected individuals in the breeding program.
- See Chapter 16 for more information on prevention of transmission of canine herpesvirus.

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Chapter 93

Surgery of the Vagina and Vulva

Gretchen K. Sicard / Roger B. Fingland

The surgical procedures performed most commonly on the vagina and vulva are episiotomy, episioplasty, and excision of devitalized hyperplastic vaginal tissue. Episiotomy is performed to increase exposure for excision of vaginal or vestibular masses. Vaginal neoplasia is uncommon, and the majority of vaginal tumors are benign. Vaginal edema (previously referred to as vaginal hyperplasia) and vaginal prolapse occur only in intact females during estrus. Diseases of the external genitalia that require surgical intervention are rare in neutered females. See Chapter 92 for discussion of diseases of the vagina and vulva.

ANATOMY

Vagina

- The vagina is a musculomembranous distensible canal that extends from the uterus to the vulva.
- The caudal boundary of the vagina is located cranial to the urethral opening, a point demarcated from the vestibule by a transverse mucosal ridge. A hymen normally is not present at the vestibulovaginal junction in the adult, although a vestige is retained in some females.
- The vagina is quite long in dogs, necessitating episiotomy for adequate surgical exposure. Caudal abdominal celiotomy may be necessary to gain surgical exposure to the cranial aspect of the vagina.
- The longitudinal folds (rugae) of the vaginal mucosa allow significant expansion in diameter during pregnancy and whelping.
- The dorsal median postcervical fold extends from the cervix and terminates caudally by blending with longitudinal folds of vaginal mucosa. This fold can be mistaken for the cervical os during vaginoscopy.
- Blood supply to the vagina is via the vaginal artery, a branch of the urogenital artery.

Vulva

The vulva (external genitalia) consists of three parts:

- The *vestibule* is the space between the vagina and the labia.
  - The urethral tubercle (papilla), a ridgelike projection on the ventral floor of the vestibule caudal to the vestibulovaginal junction, contains the external urethral orifice.
  - The vestibulovaginal junction is readily identified because the vestibular mucosa is smooth, unlike the vaginal mucosa, which is thrown into distinct ridges.
- The *labia* form the external boundary of the vulva.
  - The right and left labia join dorsally and ventrally at the commissures.
  - The labia open to form the vulvar cleft.
- The *clitoris* is the homologue of the penis.
  - The clitoris normally does not contain structures comparable to the os penis or the urethra of the male.
  - An os clitoris may develop in response to altered hormone balance.
- The vulva is surrounded by two striated circular muscles.
- The constrictor vestibule muscle fuses along its caudal surface to the external anal sphincter.
- The thinner constrictor vulvae muscle lies immediately caudal to the constrictor vestibule muscle.
- Blood supply to the vestibule, labia, and clitoris is via branches of the urogenital arteries and the internal and external pudendal arteries.

EPISIOTOMY

Indications

- Resect benign or malignant vaginal masses.
- Reduce a vaginal prolapse.
- Resect or revise vaginal strictures.
- Manage dystocia resulting from vulvar or vestibular stenosis.
- Suture vaginal lacerations.
- Expose the urethral papilla for catheterization or surgery.

Surgical Procedure

Objective

- Temporarily enlarge the vulvar cleft to enhance exposure of the vestibule and vagina.

Equipment

- Standard general surgery instrument pack and suture
- Gelpi or Weitlaner retractor
- Sterile Foley catheter

Technique

1. Episiotomy can be performed under general, epidural, or local anesthesia.
2. Position the dog in ventral recumbency, preferably in a perineal stand or an end of the surgical table that is elevated to raise the hindquarters.

▼ ***Key Point*** To avoid femoral nerve palsy, make certain the edge of the table is well padded when placing animals in the perineal position.

3. Place a purse-string suture in the anus and fix the tail in an upright and forward position.
4. Prepare the perineal region for aseptic surgery.
5. Flush the vestibule and vagina with dilute antiseptic solution (e.g., chlorhexidine).
6. Place a Foley catheter in the urinary bladder using sterile technique.
7. Place surgical drapes so that the vulvar cleft and dorsal commissure are exposed. Exclude the anus from the surgical field.
8. Insert a finger in the vestibule and identify the caudodorsal aspect of the vaginal canal. This point represents the dorsal extent of the episiotomy incision (Fig. 93-1*A*).
9. Make a median skin incision, beginning at the point described above and extending ventrally to include the dorsal commissure of the vulvar cleft (Fig. 93-1*B*).
10. Using Metzenbaum scissors, complete the episiotomy by incising the muscular layer and the mucosa in the same plane as the skin incision (Fig. 93-1*C*).
11. Complete the procedure for which the episiotomy was performed (Fig. 93-1*D*).
12. Close the incision in three layers (Fig. 93-1*E*).
    a. Appose the mucosal edges with 3-0 absorbable suture material in a simple continuous pattern with knots exposed to the lumen.
    b. Appose the muscular layer and subcutaneous tissue together with 3-0 absorbable suture material in a simple continuous pattern.
    c. Appose the skin edges with 4-0 absorbable suture material, using a continuous intradermal suture pattern.
13. Remove the purse-string suture from the anus.

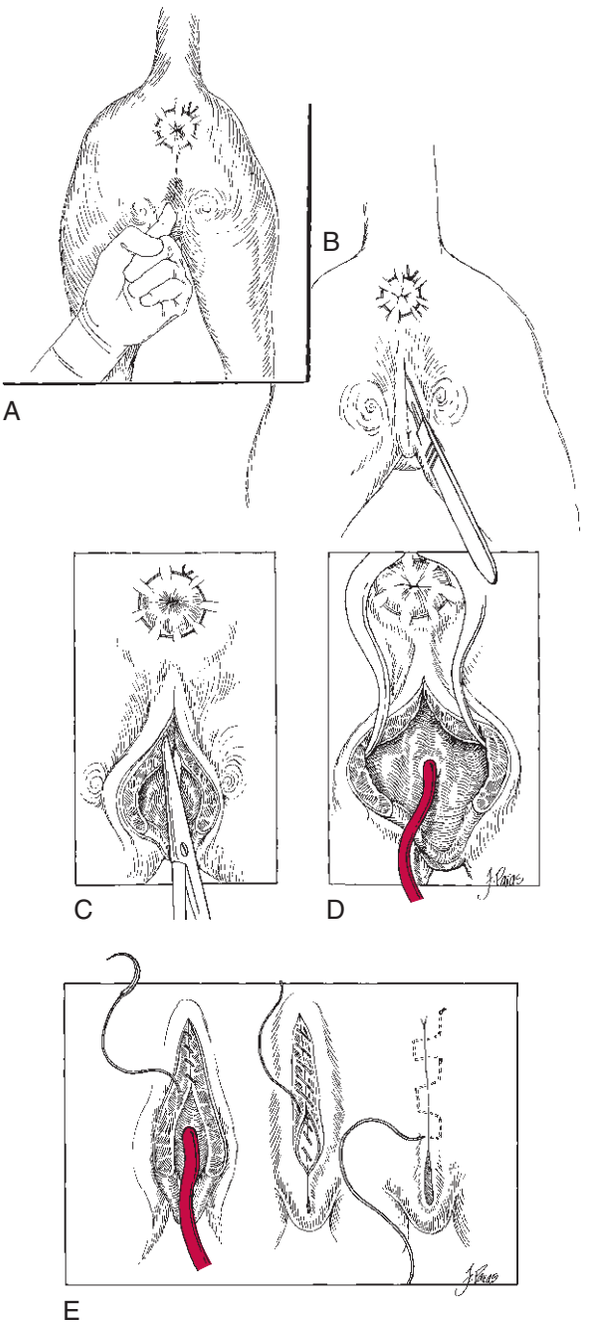

Figure 93-1. Episiotomy. *A,* After purse-string suture is placed around the anus, insert a finger in the vestibule to identify the caudodorsal aspect of the vaginal canal. *B,* Incise from the caudodorsal aspect of the vaginal canal to the dorsal commissure of the vulvar cleft. *C,* Extend the depth of the incision with Metzenbaum scissors. *D,* Complete the procedure for which episiotomy is needed (in this case, bladder catheterization). *E,* Close in three layers.

Postoperative Care and Complications

- Administer postoperative analgesics (see Chapter 6).
- An Elizabethan collar may be necessary to prevent self-trauma.
- Clean the incision if it becomes soiled.
- Postoperative complications are uncommon and usually are related to poor surgical technique (e.g., carrying the incision too far dorsally or improper suture placement).

EPISIOPLASTY

Preoperative Considerations

- Episioplasty is indicated for dogs with chronic perivulvar pyoderma resulting from redundant perivulvar skin and a recessed vulva.
- Episioplasty may also decrease the incidence chronic or recurrent urinary tract infections and urinary incontinence in dogs with a recessed vulva.

▼ ***Key Point*** Redundant perivulvar skin and recessed vulva may be associated with recurrent urinary tract infection in dogs. Episioplasty has been shown to decrease the recurrence rate of urinary infection in these dogs.

- Manage severe perivulvar pyoderma medically before performing episioplasty (see Chapter 38). Administer systemic antibiotics based on culture and susceptibility testing.

Surgical Procedure

See Chapter 54.

VAGINAL SEPTUM, SEPTAL REMNANTS, AND VESTIBULOVAGINAL STENOSIS EXCISION

Preoperative Considerations

- A number of congenital abnormalities that obstruct or constrict the vestibulovaginal opening occur in animals. Incomplete perforation of the hymen in dogs usually is observed as a vertical band of tissue of varying width or an annular fibrous narrowing at the vestibulovaginal junction.

▼ ***Key Point*** Most animals with these persistent bands of tissue are asymptomatic, requiring no treatment.

- Symptomatic animals usually present for breeding or whelping problems. Vaginal septa or septal remnants may be associated with chronic vaginitis, recurrent urinary tract infections, and urinary incontinence resulting from inadequate drainage of vaginal or uterine secretions or urine pooling. Positional incontinence occasionally is observed in animals that pool urine.
- Diagnosis of a vaginal septum, septal remnants, or vestibulovaginal stenosis can be made based on digital vaginal examination and confirmed with vaginoscopy.
- Perform endoscopic examination of the vestibule, vagina, and lower urinary system in patients with chronic vaginitis, recurrent urinary tract infections, or urinary incontinence to rule out other congenital or anatomic abnormalities.
- Vaginal septa or septal remnants are palpated as firm central bands with small stoma on either side.
- If the ostium or opening between the vestibule and the cranial vaginal vault does not allow penetration of the finger on digital examination, consider a diagnosis of annular constriction or vestibulovaginal stenosis. Evaluate patients with suspected vestibulovaginal stenosis under sedation or general anesthesia during estrus when the diameter of the ostium should be at its greatest.
- Retrograde contrast radiography of the vestibule and vagina can be helpful in diagnosing some of the congenital vestibular and vaginal abnormalities. However, it may not provide an accurate method to measure the relative size of the vestibulovaginal junction.

Surgical Procedure

Objective

- Excise the septal remnant or annular constriction.

Equipment

- Standard general surgery instrument pack and suture
- Gelpi or Weitlaner retractor
- Sterile Foley catheter

Technique

1. Perform an episiotomy, as described previously.
2. Expose the vestibulovaginal junction and place a self-retaining retractor.
3. Place a Foley catheter in the urethra to avoid inadvertent damage to the urethral papilla.
4. Identify and excise the vertical band of tissue.
   a. *Vertical band:* Place a curved instrument cranial to the band and retract the band caudally. Superficially transect the band at the dorsal and ventral attachments. Close the mucosal defects with 4-0 absorbable suture material in a simple continuous pattern.
   b. *Annular constriction:* Circumferentially excise thin membranes at the mucosal attachment. When submucosal fibrous tissue exists, make a circumferential incision in the mucosa adjacent to the membrane and submucosally dissect and excise the fibrous tissue band. Close the mucosal defect with 4-0 absorbable suture material in a simple interrupted pattern. Alternatively, suture the mucosal defect with short runs of a simple continuous pattern.

▼ ***Key Point*** Rarely, dogs have both a vertical band and annular constriction. Evaluate the diameter of the vaginal opening after a vertical band resection. Resection of an annular constriction is unlikely to be necessary.

▼ ***Key Point*** Diagnosis of vestibulovaginal stenosis is uncommon. Manual or mechanical dilation of the narrowed ostium is typically unsuccessful.

5. Close the episiotomy incision, as described previously.
6. Remove the purse-string suture from the anus.

Postoperative Care and Complications

- An Elizabethan collar may be necessary to prevent self-trauma.
- Excision of persistent hymen often is curative.
- Rarely, dogs may require intermittent digital dilation to prevent fibrous narrowing after excision of annular constrictions. Permanent stenosis is possible in animals with this complication.

VAGINAL EDEMA (VAGINAL HYPERPLASIA) EXCISION

Preoperative Considerations

- Refer to Chapter 92 for additional information on this condition.
- Application of a petroleum-based ointment or temporary labial closure with horizontal mattress sutures may provide temporary relief of the hyperplasia. Exposed vaginal mucosa is susceptible to trauma, desiccation, ulceration, and inflammation. Resection of the redundant mucosa may be necessary in severe cases if the mucosal tissues become devitalized. Warn owners of breeding bitches that recurrence may occur during subsequent heat cycles in spite of resection.
- Resection of redundant vaginal mucosa should be reserved for patients with traumatized or devitalized tissue.

▼ ***Key Point*** Ovariohysterectomy prevents recurrence and can be used as the sole means of treatment if the vaginal edema and prolapse is small and not devitalized.

Surgical Procedure

Objectives

- Excise redundant vaginal mucosa.
- Excise or biopsy vaginal tumors (e.g., fibroma, polyp, and leiomyoma).

Equipment

- See under "Episiotomy."

Technique

1. Perform an episiotomy, as described previously in this Chapter (Fig. 93-2*A* and *B*).
2. Identify the margins of the redundant mucosa on the floor of the vagina.
3. Elevate the *mucosal* mass and identify the urethral papilla on the floor of the vagina caudal to the mass (Fig. 93-2*C*).

▼ ***Key Point*** Catheterize the urethra with a Foley catheter before excising the mucosal mass.

4. Make an elliptical superficial incision around the base of the mucosal mass.
5. Excise the mucosal mass. Use electrocoagulation to control bleeding submucosal vessels. Do not extend the excision deeper than the mucosa.
6. Suture the mucosal defect with 3-0 absorbable suture material in a simple continuous pattern (Fig. 93-2*D*).
7. Close the episiotomy incision, as described previously.
8. Remove the purse-string suture from the anus.

Postoperative Care and Considerations

- Administer postoperative analgesics (see Chapter 6).
- An Elizabethan collar may be necessary to prevent self-trauma.

VAGINAL PROLAPSE EXCISION

Preoperative Considerations

- Refer to Chapter 92 for additional information on this condition.
- Vaginal prolapse may be partial or complete. Prolapse of the complete vaginal circumference through the labia results in the appearance of a doughnut-shaped mass ventral to the anus. This is in contrast to vaginal edema, in which redundant mucosa arises from the ventral aspect of the vagina. The urethral papilla may be observed on the prolapsed vaginal mucosa.
- Vaginal prolapse is significantly less common than vaginal edema. Brachycephalic breeds are more predisposed to vaginal prolapse.
- Venous congestion can result in engorgement and discoloration of the prolapsed vaginal mucosa.
- Desiccation and self-trauma lead to ulceration and infection of the mass.
- After a thorough cleaning, coat the mass with sterile lubricating jelly and gently replace the mass with a finger or appropriately sized syringe case. Place temporary non-absorbable sutures (mattress pattern) across the vulva if the vagina tends to reprolapse.
- Consider general anesthesia followed by episiotomy if the prolapse cannot be replaced digitally in the awake dog. Manual replacement still may not be possible if a large part of the vagina is prolapsed or if there is extensive mucosal edema.

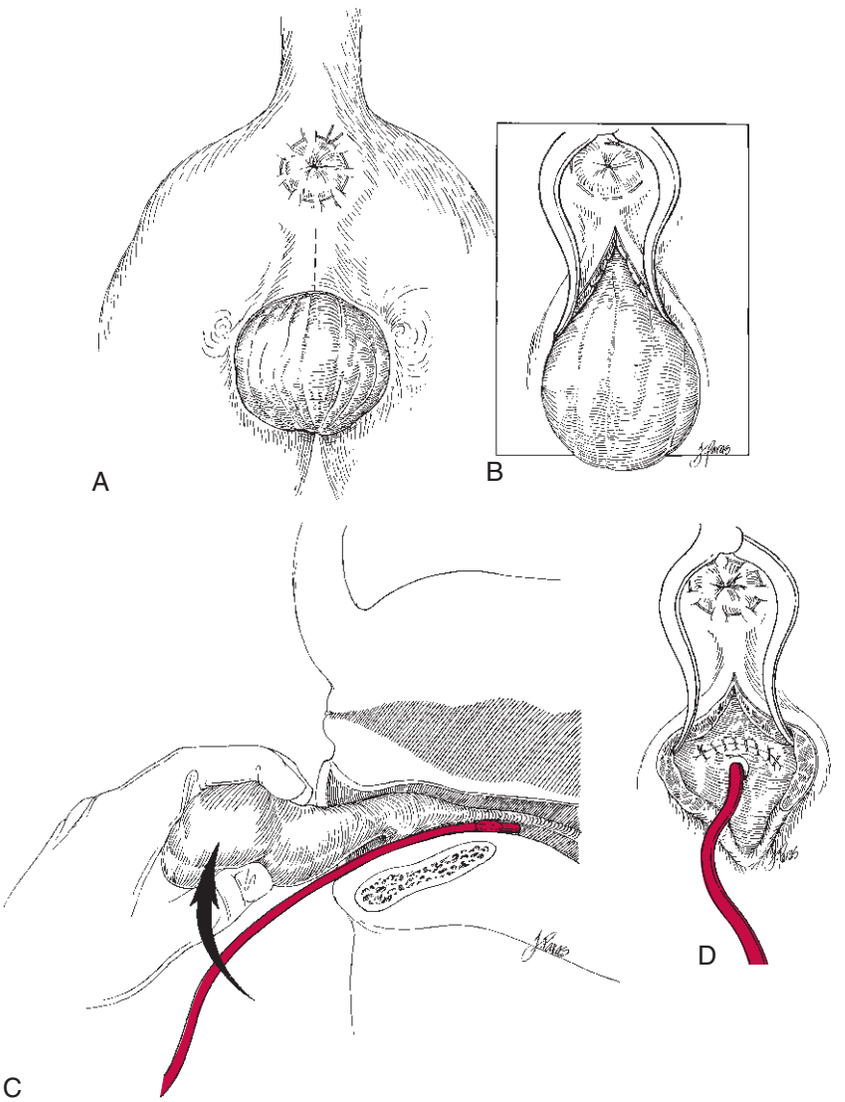

Figure 93-2. Excision of vaginal edema. *A,* Perform episiotomy as described previously. *B,* Retract the skin to expose hyperplastic tissue. *C,* Elevate the mass and identify the urethral papilla. *D,* Suture the mucosal defect in a simple continuous pattern (avoid penetrating the urethra).

- Consider repositioning by cranial traction on the uterine body through a ventral midline celiotomy when repositioning via the vulvar approach is unsuccessful and the mucosa is healthy. Perform permanent hysteropexy by suturing the uterine body or horns to the abdominal wall. Alternatively, perform ovariohysterectomy (see Chapter 91).
- Excise the prolapsed portion of the vagina when repositioning is not possible because of extensive venous engorgement or ulceration and necrosis of the vaginal mucosa.
- As in vaginal edema, ovariohysterectomy will eliminate recurrence.

Surgical Procedure

Objective

- Excise the prolapsed portion of the vagina.

Equipment

- Standard general surgery instrument pack and suture
- Sterile Foley catheter

Technique

1. Position the dog in dorsal recumbency with the rear legs tied forward (Fig. 93-3*A*).

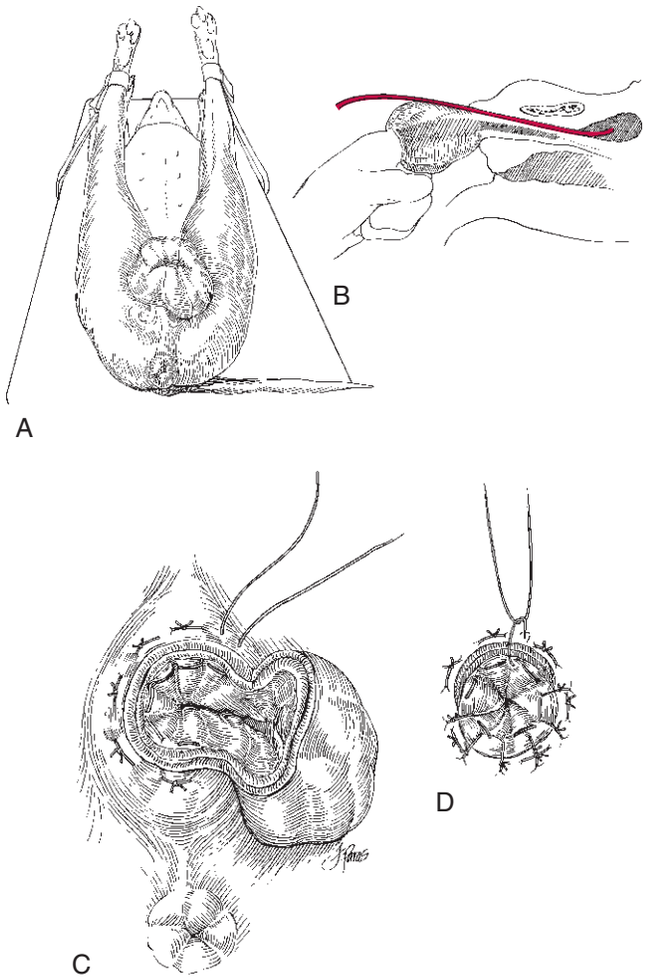

Figure 93-3. Correction of vaginal prolapse. *A,* Position the dog in dorsal recumbency. *B,* Insert an index finger or sterile syringe case into the prolapsed opening to identify the inner mucosal layer. *C,* Incise and suture the edges remaining after the prolapsed tissue is excised. *D,* Suture together the cut edges.

2. Place a purse-string suture in the anus.
3. Gently clean the prolapsed vagina. Prepare the perineal region for aseptic surgery.

▼ ***Key Point*** Perform an episiotomy only if necessary to expose the base of the prolapsed vaginal tissue.

4. Identify the urethral papilla and place a Foley catheter in the urethra.
5. Identify the proposed line of excision at the base of the prolapsed portion of the vagina. Identify the urethra by palpating the Foley catheter through the vaginal wall.
6. Incise the outer mucosal layer for approximately 4 cm along the proposed line of excision. Dissect through all layers of the vaginal wall to the inner mucosal layer. Insert an index finger or sterile syringe case into the prolapsed vaginal opening to identify the inner mucosal layer (Fig. 93-3*B*). Carefully incise the inner mucosal layer, exposing the finger or syringe case.
7. Control hemorrhage with electrocoagulation or ligation.
8. Using 2-0 absorbable suture material, place horizontal mattress sutures in the vaginal wall between the mucosal surfaces, approximately 5 mm from the cut edge.
9. Continue this incision-suture technique in approximately 4-cm increments until the prolapsed tissue is excised (Fig. 93-3*C*).
10. Appose the cut edges of the inner and outer mucosal layers with 4-0 absorbable suture material in either a simple interrupted pattern or short runs of a simple continuous pattern (Fig. 93-3*D*).
11. Remove the purse-string suture from the anus.

Postoperative Care and Complications

- An Elizabethan collar may be necessary to prevent self-trauma.
- Mild vaginal bleeding may occur for 24 to 48 hours after surgery.
- Future breeding and whelping will not be impaired by this procedure. However, breeding of females prone to vaginal prolapse is ill advised because the condition may be heritable.
- If labial sutures are placed, make certain that the animal is able to urinate spontaneously after surgery. Swelling around the urethral papilla may necessitate catheterization for several days after surgery.

SUPPLEMENTAL READING

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Chapter

94 Infertility and Breeding Disorders

Robert V. Hutchison

FEMALE DOG

Realizing the uniqueness of the reproductive system is essential when dealing with canine infertility. Unlike other domestic species, the bitch ovulates into a progesterone environment rather than estrogen. At the time of ovulation, the canine ova are a primary oocyte. Before fertilization can occur, the ova must under go a second mitotic division and shed the associated polar body. Specific knowledge of the reproductive physiology is essential to achieve successful conception and pregnancy.

Normal Estrous Cycle

The normal estrous cycle occurs approximately every 6 months but may vary between 4 and 18 months based on the individual, breed, and family history. The normal estrous cycle of the bitch consists of four distinct phases.

Anestrus

- The time period between estrous cycles.
- Anestrus is associated with a serum progesterone level of less than 2 ng/dl with no vaginal swelling or discharge.
- Follicle-stimulating hormone (FSH) levels are elevated throughout the anestrus period.
- The anestrus period ranges between 4 and 18 months in duration. Dogs require a minimum period of 4 months to permit the uterus adequate time to repair and regenerate, permitting normal implantation on subsequent breedings.

Proestrus

- The period of bloody vaginal discharge, pheromone changes, and rising estrogen levels. This phase lasts between 3 and 14 days.
- The rising estrogen levels thicken the vaginal walls, causing the changes in epithelial cells detected on vaginal smears.
- The concentration of serum progesterone during proestrus is less than 2 ng/dl.
- Cells lining the ovarian follicles begin producing progesterone levels in the 2- to 3-ng/dl range, triggering the release of LH from the pituitary and inducing ovulation within 48 hours.
- The bitch normally begins flagging and standing at the time of the LH release.
- Swelling of the vulva is observed. Although males are attracted to the bitch, they are not permitted to breed.

Estrus

- The period of ovulation, male acceptance, and conception.
- Ovulation occurs when the serum progesterone is between 4 and 10 ng/dl.
- Estrus lasts until approximately 6 days after ovulation.
- The progesterone continues to rise steadily, reaching ranges of 15 to 50 ng/dl within 72 hours post-ovulation, and continues to be elevated during the diestrus period.
- At this time, the female “flags” her tail and is willing to stand for the male to mount and breed.
- The vulva is soft, and a blood-tinged to clear or straw-colored discharge may be evident.
- It is not uncommon for the discharge to remain slightly bloody.

Diestrus

- Begins 6 days post-ovulation and is the end of the fertile period.
- Diestral progesterone levels are not affected by pregnancy.
- Diestrus lasts until the serum progesterone levels drop below 2 ng/dl. Diestrus lasts approximately 8 weeks in the pregnant bitch and can last 2 to 4 months in non-pregnant bitches.
- The first day of diestrus is characterized by a dramatic change seen on a vaginal smear. The superficial cells seen in estrus are replaced by parabasalar and intermediate cells. WBCs also begin to appear on vaginal cytology as the bitch moves from estrus to diestrus.
- A slight mucoid vaginal discharge may be apparent.

Etiology of Conception Failure

Poor Semen Quality

Few studies have been done to determine the minimum number of normal spermatozoa necessary for conception to occur. Numbers previously thought to be required were in the 100×10^6 to 150×10^6 range. There have been successful conception and whelping from bitches inseminated with less than 30×10^6 normal spermatozoa.

See later in this chapter under "Male Dog" for more information on semen evaluation.

Ovulation Failure

- The fact that a bitch shows the physiologic signs of an estrous cycle does not guarantee that the cycle will be ovulatory.
- The only laboratory method to confirm ovulation is an increase in serum progesterone level to greater than 4 ng/dl.
- Split and non-ovulatory cycles are not uncommon in the bitch. A progesterone rise to 2 to 3 ng/dl does not guarantee that ovulation will occur.

Improper Timing of Breeding

- Historically, veterinarians and breeders have timed bitches using vaginal smears, breeding guns, and physiologic signs such as color of vaginal discharge, days of the cycle, and vulvar softness. These traditional methods of breeding timing were not only flawed but also, in many cases, irrelevant to ovulation timing.
- The average length of an estrous cycle varies from 17 to 28 days. Extremes in ovulation varying from 6 to 32 days after onset of the estrous cycle with successful breeding having been confirmed.
- Fresh semen lasts an average of 4 to 6 days in the oviducts.

Methods of Timing of Ovulation

- Serum concentration of estrogen (which is not a precise method of timing)
- Luteinizing hormone assay
- Serum concentration of progesterone—more reliable in pinpointing ovulation

Luteinizing Hormone Assay

- The release of luteinizing hormone (LH) by the pituitary triggers ovulation within 48 hours. Perform LH testing and use serum progesterone to confirm that the ovary has responded to LH release and that ovulation has indeed occurred.
- Current LH testing consists of a wicking test (Status-LH, Synbiotics, San Diego, California). The test requires 4 drops of serum. A red line occurs when the LH rises above 1 ng/dl.
- Because of the short duration of LH (12–24 hours) in the bitch's circulation, perform the test daily.
- LH in the canine is species specific and assays with non-canine reagents cannot be used.

Progesterone Assay

- LH release, the initial rise in progesterone to 2 to 3 ng/dl, followed by ovulation 48 hours later has made timing the bitch an available and easily performed procedure.
- The bitch ovulates a primary oocyte, requiring 48 hours post-ovulation for ova maturation. After the ova have reached the secondary oocyte stage, it is thought that the eggs are fertilizable for up to 36 hours.
- The timing of a breeding is based on anticipated semen survival time.
- A serum progesterone level of 5 ng/dl indicates that ovulation has occurred.
- Canine progesterone is not species specific and can be tested for using a number of testing methods. Enzyme-linked immunosorbent assay (ELISA), chemiluminescence, 3-Immulite, and radioimmune assay (RIA) using conjugated and non-conjugated serum are all testing methods available to the practitioner. The preciseness needed, the type semen most frequently used, and the frequency of result reporting will dictate which method best fits a practice's needs.

▼ ***Key Point*** Frozen canine semen lasts in the bitch 12 to 24 hours. It is important that frozen semen not be inseminated until ova have reached the secondary oocyte stage due to the frozen semen's short life span.

Improper Breeding Methods

The canine breeding system is one that involves intromission into the vaginal tract of a semi-flaccid penis containing an os penis then engorgement of the penis and bulbus glandis. Ejaculation enters the vaginal tract at the external os of the cervix. The engorged bulbus glandis causes the "tie" that stimulates hormonal release, causing the semen to be "pumped" through the cervix and into the uterus. The spermatozoa then move cranially up the uterus and enter the oviducts, where conception occurs.

- The cervix in the bitch is located within the abdominal cavity, dorsal to the bladder.
- The length or distance from the vulva to the external os varies by breed size.
- It is essential that the semen be deposited at the external os of the cervix.
- Natural breeding resulting in outside ties or incomplete penetration into the bitch and poorly positioned rods for vaginal artificial insemination significantly decrease conception rates.

▼ ***Key Point*** Artificial insemination methods such as transcervical insemination (TCI) and surgical or laparoscopic intrauterine deposition of semen permit breeding that bypasses the vaginal cavity and cervix. These methods of depositing the semen into the uterus have contributed greatly to the current success of canine frozen semen.

Implantation Failure

After spending 6 to 10 days in the oviducts, the fertilized ova are released into the uterus. Implantation occurs in the bitch 17 to 18 days post-ovulation. Inflammation of the endometrium, cystic endometrial hyperplasia (CEH), and uterine fibrosis can contribute to implantation failure.

Refusal to Accept the Male

Refusal of the bitch to accept the male can be a significant problem in breeding. Use the following methods to address this problem:

- Confirm the anticipated ovulation timing. Vaginal cytology will confirm if ovulation has previously occurred.
- Change the environment (indoors versus outdoors, male's home versus female's home, etc.).
- If necessary, it is better to perform an artificial insemination than to risk injury to canine or human components.

Inability to Achieve a "Tie"

- Examine the vulva, vestibule, and vagina of the female for strictures, bands, size, etc.
- Check the male for penile abnormalities such as a persistent penile frenulum or adhesions to the prepuce (see Chapter 88).
- Check the prepuce and fornix for mass lesions, ulceration, or foreign bodies (see Chapter 88).
- Evaluate both the male and the female for nonreproductive health issues.

Resorption and Abortion

- Total resorption of fetuses can occur up to 38 days after ovulation. Numerous conditions can cause fetal death, including genetic or chromosomal anomalies, hormonal imbalance, chemicals and drugs, infectious agents, and toxins.
- Pedigree analysis, histopathology of the aborted placenta and fetuses, uterine biopsy, and microbiologic testing may help determine the cause of the problem. A thorough history of medications and chemical exposure and an evaluation of dietary supplements and ingredients are essential when confronted with resorption or abortion of fetuses.

Table 94-1. COMMON DRUGS TO AVOID DURING PREGNANCY

Antifungals
Tetracyclines
Estrogens
Testosterones
Corticosteroids
Nonsteroidal anti-inflammatory drugs

- Consult the recommendations of the manufacturer before any drug is given to a pregnant bitch (Table 94-1).

Diseases of the Breeding Bitch

Failure to Have an Estrus Cycle

- Normal females can be up to 24 months of age before having a first estrous cycle.
- Bitches over 24 months with no clinical or physiologic signs of an estrus cycle should initially be tested for thyroid and cortisol abnormalities.
- A serum progesterone level of <2 ng/dl will rule out any missed or silent season during the previous 2 months.
- If normal hormonally, a karyotypic examination should be performed. Karyotyping is performed on a heparinized blood sample by specialty labs.
  - The normal karyotype of the canine consists of 78 chromosomes (78 XX for the bitch and 78 XY for the male).
- If no hormonal or chromosomal abnormalities are detected, consider endoscopic or surgical evaluation of the ovaries (see Chapter 91).

Prolonged Anestrus after an Estrous Cycle

- Normally, anestrus can vary from 4 to 12 months. Bitches in anestrus longer than 12 months should be examined for hormonal anomalies, including thyroid, cortisol (either elevated or decreased), and progesterone levels.
- Perform an ultrasound examination of the ovaries for cystic structures.
- Endoscopic examination or exploratory surgery may be necessary to rule out fibrotic or hypoplastic ovaries, an unknown ovariohysterectomy, or ovarian cysts (see Chapter 91).
- The fluid aspirated from the ovarian cyst should be evaluated for progesterone. Many of these cystic fluids will contain progesterone levels >50 ng/dl acting to suppress the estrous cycle.

Split Estrus Cycle

- A split cycle is characterized by the bitch entering proestrus but never ovulating.
- The bitch normally will recycle in 4 to 6 weeks, the "second" cycle usually being ovulatory and breedable.

- Split cycles are diagnosed more commonly because of the routine use of progesterone testing for breeding management.

Silent Seasons

- Silent seasons are characterized by a bitch ovulating but showing no external signs of an estrous cycle.
- A silent season is usually first suspected when a bitch, having had no observable estrous cycle, has a pseudocyesis or "false pregnancy." Pseudocyesis confirms that ovulation has occurred within the last 8 to 10 weeks.
- To determine when the estral phase of a silent season occurs, perform a weekly vaginal smear, observing the cellular changes from parabasalar and intermediate vaginal epithelial cells to superficial epithelial cells.
  - The cellular changes indicate a rise in estrogen. Once the rise in estrogen is confirmed, serum progesterone levels are performed to determine the day of ovulation.

Shortened Anestrus

- Due to the inflammatory effect of progesterone on the endometrium, a minimum of 135 days (4 months) is needed for endometrial repair following an ovulatory season.
- Bitches cycling at intervals of less than 135 days may have reduced fertility due to the lack of endometrial integrity.
- This symptom is most frequently seen in German shepherds, Newfoundlands, rottweilers, and Welsh corgis.
- Mibolerone, an androgenic medication, can be given daily to delay the onset of the estrous cycle and to allow endometrial healing.

Prolonged Estrus

- Prolonged bleeding can be commonly seen in young bitches having their first estrous cycle.
- Bitches may have multiple non-ovulatory cycles. Serum progesterone concentrations from these bitches remain below 2 ng/dl.
- In young bitches, no treatment is usually necessary, and bitches will begin normal interestrous intervals after they have had an ovulatory cycle. This is not an indication of cystic ovaries.
- A prolonged estrous cycle in older bitches is of much more concern. Estrogen-secreting ovarian cysts and tumors are prime etiologies.
- Vaginal cytology showing predominately superficial cells will confirm estrogen as the cause of the vaginal bleeding.
- Examine bitches with prolonged vaginal bleeding not caused by elevated estrogen for other causes, such as bleeding disorders, vaginal disease and neoplasia, as well as hemorrhagic bladder disease.

Puppy Vaginitis

- Puppy vaginitis is the term used to describe the vaginal mucus in puppy bitches yet to have their first cycles (also see Chapter 92).
- Puppy vaginitis is a physiologic syndrome that does not require treatment. The condition is self-correcting when the estrogen surges during the bitch's first estrous cycle.

Vaginal Discharge

- Evaluate all vaginal discharges microscopically. Characterize the discharge as hormonal versus non-hormonal, inflammatory versus non-inflammatory, and infectious versus non-infectious (see Chapter 92).
- Etiologies of vaginal discharge include vaginitis, pseudocyesis, pyometritis, cystitis, estrous cycle, pre-whelping, post-whelping, mibolerone therapy, and vaginal tumors.

▼ ***Key Point*** If vaginal discharge is determined to be infectious, perform cultures for aerobes, anaerobes, and mycoplasma or ureaplasma.

▼ ***Key Point*** *Staphylococcus* spp., *Streptococcus* spp., *Escherichia coli, Pasteurella,* and *Mycoplasma* make up the normal flora found in the vestibule and vagina of the bitch. The vaginal tract is not a sterile area. The misuse of antibiotics during breeding may allow pathogens to prevail. There is no justification for the routine use of antibiotics during breeding without signs of inflammation and infection.

Premature Luteolysis

- The ovary is the primary progesterone source in the bitch throughout the pregnancy. Unlike other species, progesterone production is not transferred to the placenta.
- A serum progesterone of >2.5 ng/dl is needed to maintain the canine pregnancy.
- Consider premature luteolysis in bitches having problems with premature loss of puppies when other causes cannot be found.
- Perform serum progesterone testing periodically (the frequency of testing depends on the results obtained). A drop below 5 ng with greater than 5 days of gestation remaining may require progesterone supplementation.
- Treat with progesterone in oil, as an injection (2.2 ng/kg IM), or altrenogest (Regu-Mate, Hoechst). Regu-Mate will not show on a serum progesterone test as it is a synthetic product. Progesterone in oil will show on a progesterone test and can be monitored to determine if and when further supplementation is needed.

▼ ***Key Point*** There can be associated birth defects of the vaginal tract in female pups if progesterone supplementation is not used judiciously.

Pyometritis

Pyometritis is a disease of the uterus caused by an inflammation of the uterine lining, allowing a secondary bacterial infection. Pyometritis can also be caused by the misuse use of estrogen for mismating while the uterus is under the effects of progesterone. See Chapter 90 for a complete discussion of pyometra in dogs and cats.

Vaginal Wall Edema (Vaginal Hyperplasia)

- Vaginal wall edema occurs during the estrogen phase of estrous cycle is due to fluid uptake by the vaginal tissue.
- Brachiocephalic breeds, Labradors, and coonhounds are more frequently affected.
- Ovulation and subsequent decrease in serum estrogen causes regression of tissues.
- Vaginal edema typically does not cause whelping problems.
- It may recur during subsequent heat cycles.
- Treatment consists of preventing trauma and keeping tissue from drying until edema regresses (see Chapters 92 and 93).

Diagnosis

See Chapters 90 to 93 for discussion of diagnosis and treatment of diseases of the ovaries, uterus, vagina, and vulva.

Prebreeding Evaluation

- Perform a complete physical examination of both the brood bitch and the stud dog, including evaluation of the external genitalia. The bitch and stud should be in good health and of good weight. Overweight bitches are associated with conception, whelping, and nursing problems when compared with non-overweight bitches.
- The bitch should be free of parasites, appropriately vaccinated, and on heartworm-preventative medication. Heartworm-preventative medication should be continued during pregnancy and after whelping.
- Routine vaginal culturing without abnormal discharge or signs of inflammation is not justified.
  - Mycoplasma and ureaplasma are considered normal flora in the vagina. Obtaining routine bacteriologic cultures and treating for mycoplasma or ureaplasma without clinical signs is of no value.
- Serum thyroid levels are of minimal importance in canine reproduction, whether discussing the male or the female. However, if clinical signs of hypothyroidism are evident, perform a diagnostic evaluation (see Chapter 31).
- Be aware of genetic defects associated with any given breed. Individuals to be used for breeding should be tested for as many genetic diseases as possible.
- Assure adequate immunity for reproductive diseases.

Brucella canis

- *Brucella canis* is the bacterial organism most commonly associated with abortion in the bitch and orchitis in the male (also see Chapter 19).
- Since *Brucella canis* is passed through all body discharges, including urine, individuals should be blood tested for brucellosis even if they are being bred for the first time.
- Test the bitch for brucellosis before each mating.
- Test frequently-used males every 6 months, even if only bred to *Brucella canis*-negative bitches.
- The rapid slide agglutination test (RSAT) commonly performed as a screening test can have false-positive results in the 20% range. A negative RSAT does confirm the *Brucella*-negative status.

▼ ***Key Point*** Isolate individuals testing *Brucella* positive on the RSAT from other dogs until further testing. Agar-gel immunodiffusion, immunofluorescent antibody, and blood culturing for *Brucella canis* are confirmatory tests for brucellosis.

Pregnancy Diagnosis

There is currently no early pregnancy diagnostic test for the canine. Available midgestation techniques include the following:

- Ultrasound—After day 19 post-ovulation
- Palpation—Between day 23 and day 30 post-ovulation
- Relaxin testing (Witness Test, Synbiotics, San Diego, California)—After day 26 post-ovulation
- Radiography—After day 47 post-ovulation

Ultrasound

Ultrasound confirms pregnancy and fetal viability. It is typically the earliest method to accurately confirm a pregnancy. Ultrasound is not considered an accurate method for predicting exact litter size.

Palpation

Palpation of the caudal abdomen in a relaxed patient can accurately determine pregnancy in many breeds of dogs.

- Palpation is most commonly performed between 21 and 30 days after ovulation.
- Palpation of distinct uterine swellings dorsal and cranial to the bladder typically signifies pregnancy.
- There is a narrow window of opportunity to accurately diagnose pregnancy by palpation. As the

pregnancy progresses, the uterus enlarges and the individual fetal swellings become less distinct.
- Palpation as a method of pregnancy diagnosis can be difficult in large or nervous bitches.

Relaxin

Evaluation of serum relaxin levels, a hormone produced by the placenta, can accurately confirm pregnancy. However, false negatives can occur in litters of small numbers.

Abdominal Radiography

- Plain abdominal radiographs can accurately determine pregnancy but not until 47 days after ovulation.
- Optimal time for radiographs is 52 to 56 days post-ovulation to assure mineralization of all fetal skeletons.
- Abdominal radiography are more commonly performed to determine litter numbers and size of pups. Litter size is determined by evaluating both the lateral and the ventrodorsal views and by counting the skeletal structures of each fetus (spine or calvarium).
- Radiographic signs indicating possible fetal death or problems include collapsed calvarium, reversed "c" sign, and gas within fetuses.

Treatment

Treat any underlying diseases or problems (also see Chapters 90 to 93). Improve management strategies, such as timing of breeding, using the recommendations previously discussed under "Etiology of Nonconception." If vaginal anomalies are present, correct them if possible (see Chapter 93).

Estrus Induction

- Clinical research is currently being done using various categories of drugs to induce ovulatory cycles in the bitch.
- An interval of 4 months is the minimum anestral interval required.
- Cabergoline (5 µg/kg PO q24h), a dopaminergic agonist will shorten anestrus by lowering prolactin levels.
- Desorelin, a gonadotropin-releasing hormone (GnRH) analogue, either as an injection or an implant has shown particularly promising results.

Artificial Insemination

Due to disease concerns, cost, and restrictions of airline travel, the shipping of fresh chilled and frozen semen has dramatically increased. Knowledge of techniques for collection, handling, and shipping of semen, as well as methods of artificial insemination, has become essential for successful canine breeding.

A number of methods have been devised based on the type semen being used, the semen quality, the age of the bitch, and the expertise of the veterinarian performing the insemination. Methods of artificial insemination include vaginal, transcervical, and endoscopic or surgical intrauterine deposition of semen.

Collection of Semen

Collection of semen from male dogs is routinely performed for vaginal or intrauterine artificial insemination, cryopreservation, extension, and chilling for the purposes of shipping for a distant breeding or for evaluation as a part of the breeding soundness examination.

- Male dogs can be easily collected manually.
  - The male is stimulated using a non-intimidating female demonstrating clinical signs of estrus.
  - Semen collection should be performed in a quiet environment.
  - The ejaculate is collected into a polyvinyl chloride sheath with an attached calibrated collection container.
  - Manual stimulation of the glans bulbous of the penis permits a semen sample to be obtained. Parasympathetic stimulation produces erection of the penis, and sympathetic stimulation results in ejaculation.
- The male dog ejaculates three distinct fractions:
  - First fraction—Prostatic fluid containing no spermatozoa.
  - Second fraction—Thicker milky white volume that contains spermatozoa.
  - Third fraction—Clear fluid containing prostatic secretions and no spermatozoa. It is not necessary to collect this fraction.
- Male dogs can be collected every other day, daily for 5 to 6 days, or twice on 1 day without affecting sperm numbers.
- Evaluation of semen is essential. Abnormal sperm cannot fertilize ova.

Characteristics of Normal Semen

- *Volume*—0.5 to 30 ml or more (depends on the length of the collection, breed of dog, and size of the prostate)
- *Total count*—22 million/kg of body weight
- *Motility*—>80%
- *Morphology*—<20% abnormal sperm
- *pH*—6.2 to 6.8

Vaginal Artificial Insemination

If a natural breeding is not possible or is undesirable, vaginal artificial insemination can be performed to deposit a quantity of semen at the external cervical opening. The site of semen deposition is critical. The semen is positioned so that it can be drawn from the vagina into the uterus. Fertilization of the ova occurs

within the fallopian tubes after ovulation. Correct timing of ovulation is essential for successful breeding. (See the previous discussion in this chapter under "Methods of Timing Ovulation.")

▼ ***Key Point*** When properly performed, conception rates from vaginal artificial insemination should rival those of natural mating.

Technique

1. Determine timing of ovulation using clinical signs, vaginal cytology, and serum progesterone concentrations. An increase in the concentration of serum progesterone greater than 5 ng/dl indicates ovulation has occurred.
2. The female is positioned with her rear elevated manually or using a step or breeding ramp.
3. Avoid pressure under the abdomen, which may increase intra-abdominal pressure and affect movement of semen from the vagina to the uterus.
4. The semen sample is drawn into a sterile syringe.
5. An insemination rod of appropriate length is used to reach the external cervical opening within the vagina.
6. Sterile gloves should be worn, and aseptic technique should be applied.
7. With the assistance of a gloved hand, the insemination rod is inserted through the vulvar orifice at an upward 45-degree angle through the vestibule into the vagina. The rod is carefully manipulated over the pubis along the dorsal median fold until it is parallel with the lumbar spine at the anticipated depth of the cervical os.
8. If resistance is met when passing the insemination rod, withdraw the rod a short distance and gently redirect it.
9. With the insemination rod in the proper position, the semen is gently inseminated. It is not necessary to flush the rod with air; bubbled air may result in damage to the fragile plasma membranes of the head of the spermatozoa.
10. Digital "feathering" of the vestibule is performed for approximately 1 minute with the rear quarters of the female in an elevated position to facilitate gravitation flow of semen into the anterior vagina.
11. When the insemination is complete, the owner is instructed to restrict the dog's activity for 1 to 2 hours.

Intrauterine Insemination Techniques

Two techniques for the deposition of semen directly into the uterine body have been shown to dramatically improve conception rates in a variety of breeding situations, including the following:

- Frozen semen
- Fresh cooled, extended semen
- Females with suspected uterine disease
- Reduced semen quality
- Female anatomic abnormalities—Vulvar, vestibular or vaginal stenosis, vaginal edema, secondary to traumatic pelvic injuries
- Specific breed indications—Giant and toy breeds with known infertility

Transcervical Insemination

- A rigid operating cystoscope is used to examine the luminal surface of the vestibule, vagina, and external cervical os.
- Direct examination of the uterus is not possible during this procedure.
- A flexible catheter is passed through the biopsy channel of the cystoscope or along the side of the endoscope and manipulated through the external os of the cervix, permitting deposition of semen directly into the uterus.
- This procedure does not require general anesthesia; however, light sedation may facilitate performing this procedure in some patients.

Surgical Insemination Technique

1. The bitch is prepared for surgical insemination; the ventral abdomen is clipped and aseptically prepared.
2. A small, 4- to 6-cm ventral midline incision is made halfway between the umbilicus and the pubis.
3. The uterus is identified and exposed to the level of the incision.
4. The semen is prepared for insemination. A volume of semen between 4 and 5 ml is prepared. If the volume is greater than 4 ml, the sample should be centrifuged for 5 minutes. The supernatant is decanted and disposed. The semen pellet is gently resuspended with a semen extender. The semen is gently drawn into a sterile 6-ml syringe using an insemination rod. A 22-gauge needle is attached for insemination.
5. The surgeon inserts the needle into the lumen of the uterine body at a 45-degree angle with the bevel of the needle oriented upward. The semen should be injected easily, distending the uterine body and horns. If any resistance is met, gently redirect the needle.
6. A saline-soaked sponge is place over the injection site as the needle is removed and held in place for 1 to 2 minutes.
7. Routine abdominal closure is performed. The rear quarters of the bitch can be mildly elevated during recovery from anesthesia.

Termination of Pregnancy for Mismating

The chemical removal of unwanted pregnancies can be achieved with no pathologic changes to the endometria. Current recommendations are directed toward lysis of the corpus luteum during the second half of pregnancy. Currently two drugs are appropriate for termination of pregnancy:

- Prostaglandin $F_2\alpha$ (Lutalyse, Pfizer) is used at a dosage of 1.1 to 2.2 mg/kg SC, q8-12h. The drug is given until the fetuses have been expelled. Normally the process takes 4 to 7 days. Confirmation that all fetuses have been expelled is necessary as cases of ovaries reluteinizing have been reported.
- Cabergoline, an antiprolactin drug (5 mg/kg PO daily), will also induce luteolysis. The drop in progesterone causes premature labor and the expulsion of the fetuses. The fact that all puppies have been passed needs verification.

▼ ***Key Point*** Do not use of diethylstilbestrol (DES) to prevent conception as it promotes the development of cystic endometrial hyperplasia, pyometritis, and potential bone marrow suppression.

MALE DOG

Etiology of Infertility

Insufficient Number of Sperm

Severe reduction in the numbers of spermatozoa in an ejaculate may impact conception rate. Although 200 million sperm is considered a normal number of spermatozoa in an ejaculate, it is unknown at what point conception is reduced. Reduced sperm numbers in an ejaculate may be the result of incomplete ejaculation, reduced production by the seminiferous epithelium, or compromised outflow from at least one testicle.

Aspermia

Multiple ejaculates without any visible spermatozoa are termed aspermia or azoospermia depending on whether the second fraction of the ejaculate has been obtained.

- Males with no sperm can be divided into five categories:
  - Incomplete ejaculation
  - Retrograde ejaculation
  - Blockage
  - Testicular dysfunction
  - Immune-mediated orchitis
- To determine if the second fraction of the ejaculate has been obtained during the collection, an alkaline phosphatase level is performed on the ejaculate.
- Prostatic fluid is low in alkaline phosphatase, <2,000 IU/dl; however, epididymal fluid is high in alkaline phosphatase, >5,000 IU/dl.
- An increased concentration of alkaline phosphatase in the ejaculate confirms that a total ejaculate has been obtained.

Incomplete Ejaculation

- Failure to ejaculate the second or sperm-rich fraction upon collection.
- Incomplete ejaculation is diagnosed by a low semen concentration of alkaline phosphatase.
- Causes of incomplete ejaculation include the following:
  - Novice stud dog
  - Submissive or timid stud dog
  - Uncomfortable environment for collection
  - Intimidation by the teaser bitch
- To overcome the male's reluctance to being collected, use a change of environment, patience, complete health evaluation, or a different teaser bitch in the estrus phase of her cycle.

Retrograde Ejaculation

Retrograde ejaculation is characterized by good reproductive instincts and strong pulsation but minimal or no ejaculate is obtained. A post-collection urine sample contains an extremely high number of sperm cells.

- Retrograde ejaculation is most often associated with the retriever breeds.
- Administration of phenylpropanolamine (an alpha-adrenergic stimulant) to increase tone of the urethral sphincter mechanism prevents retrograde flow of sperm into the bladder.

Obstruction

Granulation tissue formation can obstruct the opening of the vas deferens, prohibiting the exit of sperm into the urethra. This results from a breakdown of the barrier between semen and blood that normally prevents an immune reaction.

- Granulomas can occur as a result of trauma, previous surgery, infectious disease, or genetics.
- Some granulomas may be palpable or imaged using ultrasound or urethrocystoscopy.
- The concentration of alkaline phosphatase in the ejaculate will be increased if there is a unilateral obstruction and will be low with bilateral granuloma formation.
- Microsurgical bypass would be necessary to circumvent the obstruction in patients with bilateral obstructive disease.

Testicular Dysfunction

- An increased concentration of alkaline phosphatase in the ejaculate indicates that the second fraction of the collection is present.
- Numerous etiologies can result in lack of tubular function in the testicle, resulting in aspermia, low sperm numbers, or abnormal morphology, including genetics, tumors, drug therapy, and hormones.
- Testicular palpation may reveal a "softness" that may indicate that the seminiferous tubules are failing.
- Ultrasound can be used to image and biopsy the testicle in an attempt to determine the etiology of the dysfunction and possible treatment.

Immune-Mediated Orchitis

- Lymphocytes infiltrating the testicle(s) and subsequent testicular failure are thought to be genetic.
- Breeds most commonly associated with immune-mediated orchitis are English setters, Labrador retrievers, and sighthounds.
- The testicle usually palpates normally in males with immune-mediated orchitis.
- A testicular biopsy is necessary to diagnose this condition.
- The concentration of alkaline phosphatase in the ejaculate is expected to be very high.

Sperm Motility

Abnormal motility of spermatozoa is thought to hinder the sperm's ability to reach the fallopian tubes to achieve conception. If an increased percentage of the spermatozoa demonstrate complete lack of progressive motility, there may be environmental influences that have affected the collection of the ejaculate.

- A male that has not been collected for an extended period of time may have a large number of non-motile sperm due to prolonged storage in the epididymis.
- Increased environmental temperature affecting the epididymis or inflammation may result in non-motile or dead sperm.
- Improper collection techniques can result in "cold shock" injury to spermatozoa.

If a large percentage of non-motile sperm are identified, a second or third collection on the same day or next day can be evaluated for motility. With persistent collections of non-motile or "dead" sperm, consider re-evaluating the stud dog for infections or inflammation of the urinary or reproductive tracts. Consider testicular biopsy.

Sperm Morphology

Microscopic examination of the spermatozoa morphology should be performed as part of the semen evaluation.

- *Primary defects*—Greater than 20% of morphologic abnormalities involving the head, neck, and tail can result in reduced fertility. Primary defects occur in the seminiferous tubules during development.
- *Secondary defects*—Greater than 20% of morphologic abnormalities that occur after collection, including bent or coiled tails, can also result in reduced fertility. Review collection techniques and sample handling in this situation.

Diagnosis and Treatment

See Chapters 86 to 89 for discussion of diagnosis and treatment of testicular and penile diseases in dogs and cats.

FEMALE CAT

Queens are seasonally polyestrous with ovulation being induced by LH release stimulated by multiple copulations. Unlike the bitch, non-bred females will continue to cycle throughout the year. An anestrus will normally occur due to the shortened daylight hours of winter.

Normal Estrous Cycle

Anestrus

- The normal cycle of the queen consists of anestrus, the quiescent period during which ovarian activity is minimal. This period is longest during the time of shortest natural light exposure.

Proestrus

- The follicle begins to develop secreting estrogen.
- The period of male attraction is characterized in the female by her "calling vocally," rubbing, and raising her tail. The vocalization is often mistaken as a cry of pain or discomfort by new owners.
- Proestrus is identified clinically by identifying a beginning rise in the percentage of superficial epithelial cells and increased vaginal secretion on vaginal cytology.
- It is normal for proestrus to last 1 to 2 days.

Estrus

- The breeding phase (estrus) occurs when the ovarian follicle is mature.
- Vaginal cytology taken with a moistened Q-Tip shows predominately superficial epithelial cells (>60–70%).
- The queen does not show vaginal bleeding during this time.
- The male cat mounts the queen, biting her neck for stabilization as the erect penis penetrates the vulva. Penile spines on the penis of an intact male stimulate the vaginal receptor sites, triggering LH release.
- Multiple breedings are needed for complete ovulation and for the best chance of pregnancy.
- The female cat presents herself to the male with the rear elevated and the tail moved to one side. After the breeding act, the female normally vocalizes and rolls on the floor.
- The period of male acceptance can vary considerably based on the number of breedings and the LH release. The period of male acceptance can persist for a prolonged period of time (up to 2 weeks or longer) depending on the availability and the breeding aggressiveness of the male.

Interestrous

- An unbred female will have a normal interestrous period of 5 to 14 days before returning to proestral signs.
- The estrous cycle repeats itself until the female becomes pregnant or the length of daylight shortens enough to return the female to anestrus.

Diestrus

- The period of elevated progesterone will last for 45 to 50 days in the pseudo-pregnant female and 60 to 65 days in the pregnant queen.

Diseases of the Breeding Queen

See Chapters 90 and 93 for discussion of diseases of the ovaries, uterus, vaginal, and vulva.

Diagnosis and Prebreeding Evaluation

See "Prebreeding Evaluation" under the canine section in this chapter.

- The female should be of good flesh without being overweight. A balanced commercial diet should be fed.
- Females to be bred should be free of viral diseases including feline leukemia virus (FeLV), feline immunodeficiency virus (FIV) and feline infection peritonitis (FIP) (see Chapters 8, 9, and 10, respectively).
- Vaccinations for upper respiratory diseases and panleukopenia should be current.
- A good quarantine protocol should be established in a cattery to prevent the introduction of outside pathogens when new individuals are introduced.

Treatment

Inducing Ovulation

In situations that require the female to ovulate (e.g., artificial insemination), numerous methods have been attempted.

- ***Hormonal stimulation***—Injecting 25 mg of GnRH once a day (Cystorelin, Ceva Labs) or 250 IU of luteinizing hormone or human chorionic gonadotropin (HCG). Administer when the queen shows peak receptivity to a male. The injection may be repeated 24 to 36 hours later. If successful, the queen should show signs of reduced sexual activity in 24 to 48 hours.
- ***Vaginal stimulation***—Use a moistened Q-Tip or glass rod for repeated stimulation of the vaginal tract receptors to mimic natural breeding may induce ovulation. Vaginal stimulation is most successful when an intact tom is housed nearby as this may have a psychic effect on the female to help stimulate ovulation. Restrain the female (i.e., wrapped in towel) to prevent injury to the handler when stimulating the female.
- ***Vasectomized tom cat***—This is the most reliable method of stimulation for the queen to ovulate as the vasectamized tom cat completes the natural breeding act without placing sperm cells in the female. Repeat breedings are necessary (multiple over an 8–24-hour period) to ensure ovulation. Confirm ovulation by detecting a serum progesterone rise, usually 48 to 72 hours after breeding.

Stimulation of Estrus

Numerous medical therapies have been described to induce estrus in cats.

- Administration of 2 mg of FSH intramuscularly daily until estrus is exhibited (up to 7 days), followed by mating to induce LH release or by injecting human chorionic gonadotropin (250 IU) intramuscularly on day 2 and 3 of estrus or by injecting 25 mg of GnRH intramuscularly.
- A non-medical method used to induce estrus in the queen may include the use of full spectrum light bulbs to mimic the equivalent of 14 hours of daily sunlight.

Feline Artificial Insemination

Collection of Semen

- Collection of the semen for insemination, freezing, or evaluation is normally accomplished with an electroejaculator.
- Electroejaculation is performed under general anesthesia, and the male is pretreated with an antihistamine to diminish the retrograde movement of sperm into the bladder.

Vaginal Insemination

- Insemination can be performed using a lacrimal catheter with a conical tip or a shortened plastic artificial insemination rod similar to those used in bitches.
- A maximum volume of less than 0.1 to 0.2 ml is most desirable due to the relative size of the feline vaginal cavity.

Intrauterine Insemination

- Surgical exposure of the uterus for direct deposition of semen should be considered in queens for which uterine or ovarian disease may be suspected and direct examination is desired.
- The use of frozen semen has been shown to have the greatest chance of success with direct insemination into the uterus.
- Intrauterine insemination is performed through a 3- to 4-cm caudal abdominal incision to expose the uterus or laprascopically.

- The semen is injected into the uterine lumen through a 22-gauge hypodermic needle.

Estrus Suppression

Progestogens and androgens have been used to suppress the estrous cycle in the queen. However, both methods are associated with negative behavior and deleterious side effects.

- The administration of GnRH (25 mg IM) or LH (HCG at 250 IU IM) will induce ovulation in a queen at peak estrus and delay the next cycling for 45 to 50 days.

MALE CAT

See Chapters 86 to 89 for diagnosis and treatment of diseases of the testicle, penis, and prepuce.

ABORTION

- Fetuses and placentas of the aborted fetuses should be evaluated grossly, histopathologically, and microbiologically. Microorganisms, genetic defects, toxins, drugs, progesterone deficiencies, and diet have all been described as agents leading to litter loss.
- The histopathologic evaluation of the placenta for inclusive bodies, dehydration, and signs of inflammation is critical.
- Culture vaginal discharges and perform serum titers for viral diseases and other microbial agents (i.e., toxoplasmosis). Potential surgical examination of the uterus and ovaries may be required to achieve a diagnosis.
- See Chapter 90 for more information on etiologies, diagnosis, and treatment of abortion in dogs and cats.

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Section

8 Skeletal System

Matthew Palmisano

Chapter

95 Postoperative Physical Rehabilitation

Darryl L. Millis

The appropriate postoperative management of small animals undergoing orthopedic or neurologic surgery is critical for a successful outcome. Inadequate surgical and postoperative treatment may result in fracture disease. The appropriate use of physical rehabilitation techniques in combination with pharmaceutical agents is necessary to achieve an optimal outcome.

GOALS OF POSTOPERATIVE PHYSICAL REHABILITATION

- Prevent loss of joint range of motion and stiffness
- Reduce the deleterious effects of disuse of musculoskeletal tissues
- Improve the rate of recovery
- Improve the quality and quantity of movement
- Enhance the ultimate outcome
- Enhance performance, conditioning, and endurance

PREOPERATIVE CONSIDERATIONS IN THE REHABILITATION PLAN

- Patient's age and physical condition. Obese patients and those with poor cardiovascular condition will require a less aggressive rehabilitation plan.
- Surgical condition and the repair technique. The stability of the surgical repair helps determine how aggressive the rehabilitation plan may be.
- Presence of concurrent injuries. Animals with multiple injuries generally undergo a less aggressive rehabilitation plan.
- Owner compliance. The therapist must consider the ability and willingness of the owner to participate in the rehabilitation plan.
- Expertise of the rehabilitation team.

PERIOPERATIVE PAIN MANAGEMENT

Institute preemptive pain management to allow postoperative therapy to be as comfortable and pain free as possible (see Chapter 6). Effective control of pain and postoperative inflammation allow rehabilitation to begin earlier with more rapid progress to functional activities.

Medications and Techniques

- Preoperative butorphanol or morphine.
- Epidural opioid analgesia.
- Intra-articular administration of local anesthetic agents such as bupivacaine.
- Morphine or buprenorphine are commonly used for immediate postoperative analgesia.
- Nonsteroidal anti-inflammatory drugs (NSAIDs), such as deracoxib or carprofen may be administered prior to or immediately after surgery and continued in the postoperative period in healthy patients free of renal and gastrointestinal disease or bleeding

tendencies. Knowledge of NSAID pharmacokinetics is important so that dosing strategies take advantage of peak drug effects. Medication is continued for 7 to 14 days after surgery.

- See Chapter 6 for further discussion of postoperative pain management.

REHABILITATION IN THE IMMEDIATE POSTOPERATIVE PERIOD

▼ ***Key Point*** The main objectives in the first 24 to 72 hours after surgery are to provide pain control, reduce joint effusion and tissue edema using cryotherapy, and reestablish normal joint range of motion (ROM) as soon as possible.

If normal motion is not established by 2 weeks, dogs may permanently lose some ROM. Prevention of muscle atrophy is also critical. Early use of the limb with functional weight bearing is the key to returning the patient to function as soon as possible.

Cryotherapy (Cold Packs)

- Cryotherapy is the therapeutic use of cold.
- The effects of cryotherapy include the following:
  - Vasoconstriction
  - Decreased blood flow
  - Reduced cellular metabolism and permeability
  - Attenuation of traumatic or exercise-induced edema
  - Decreased muscle spasm
  - Analgesia as a result of decreased sensory and motor nerve conduction velocity

Cryotherapy Devices

- Place crushed ice in a sealed plastic bag and wrap the bag in a thin cloth, such as a pillowcase or towel.
- Prepare a mixture consisting of two parts water and one part alcohol in a double-sealed plastic bag and place it in a freezer. The resulting pack is a frozen slush that conforms to any surface.
- Use commercially available cold packs.
- Use circulating cold water cryotherapy units.

Cryotherapy Technique

1. Apply to the affected area immediately after surgery during recovery from anesthesia.
2. Apply the cold pack for 15 to 20 minutes.
3. Use caution when applying cold packs to hypothermic or small patients.
4. Apply for 15 to 30 minutes every 6 to 8 hours for the first 3 or 4 days after surgery.
5. Monitor the patient for discomfort.
6. Do not use cryotherapy in patients with poor or absent pain sensation.
7. A compression bandage, such as a modified Robert Jones bandage, may be applied after cryotherapy to help prevent swelling and edema.

Range of Motion and Stretching Exercises

Perform ROM and stretching exercises to help maintain or improve flexion and extension of joints; improve flexibility of muscles, tendons, and ligaments; and help enhance awareness of neuromuscular structure and function. ROM exercises are important in dogs undergoing any joint surgery, especially cranial cruciate ligament rupture stabilization, elbow fractures, and fracture of the distal femoral physis in skeletally immature dogs.

Range of Motion Exercise Technique

1. Place the patient on soft padding in lateral recumbency.
2. Stabilize the limb proximal to the joint.
3. Gently grasp the limb below the affected joint. The closer the hands are placed to the joint, the lower the forces will be that are applied to the joint.
4. Slowly flex the joint over several seconds until there is the first indication of discomfort, such as tensing the limb, turning the head in recognition, or trying to gently push away. Under no circumstances should the animal vocalize in pain or attempt to bite. In general, joint flexion is more comfortable than joint extension.
5. Slowly extend the joint over several seconds until there is the first indication of discomfort.
6. Other motions may be appropriate, such as abduction and adduction or rotary motions, especially of the shoulder and hip.
7. Repeat for 10 to 30 repetitions depending on the animal's reaction to the motion, 3 to 6 times daily.
8. Do all joints in the affected limb, including the digits.

▼ ***Key Point*** Over-aggressive ROM exercises will result in pain, reflex inhibition, delayed use of the limb, and ultimately more fibrosis of the tissues around the joint.

The primary objective is to gently flex and extend individual joints through their comfortable ROM.

As the animal nears full ROM, more natural gait movement may be instituted by putting all of the joints of a limb through a ROM simultaneously, similar to the motion of riding a bicycle.

Stretching Technique

1. Stretching is often combined with ROM exercises in stiff joints with decreased ROM.
2. Stabilize the limb proximal to the joint, and grasp the limb below the affected joint and gently move it.

3. At the end range of flexion, hold the position for 15 to 30 seconds. Gradually attempt to increase flexion as long as the patient remains comfortable.
4. Extend the joint, and at the end range of extension, hold the position for 15 to 30 seconds. Gradually attempt to increase extension as long as the patient remains comfortable.
5. The main idea is to stretch and realign soft tissues and collagen, not to tear or damage tissues.
6. Repeat for two to five repetitions, 1 to 3 times daily.

THERAPEUTIC EXERCISES

Therapeutic exercises are an essential part of a physical rehabilitation program, whether a patient is being treated immediately after surgery or for chronic conditions. Therapeutic exercises may be performed by the therapist or as part of a home treatment program with owner involvement.

▼ ***Key Point*** When a home exercise program is prescribed, always demonstrate the exercise first and then have the owner demonstrate the exercises for you to ensure that they are properly performed.

Objectives

- Improve active pain-free ROM and flexibility
- Improve use of limb and reduce lameness
- Improve muscle mass and muscle strength
- Improve daily function
- Help prevent further injury

Considerations

▼ ***Key Point*** It is most important that exercises be performed correctly, rather than performing many repetitions incorrectly.

- Begin with standing exercises, assisted walking, and proprioceptive exercises in patients that have serious musculoskeletal injuries, neurologic conditions, or multiple limb involvement.
- Progress to slow, low-impact activities as the patient gains strength and stamina and is able to support its own weight.
- As the animal continues to recover, the speed, duration, and number of repetitions may be increased, and more challenging exercises may be added.
- Vary the routine so that the therapist and patient do not become bored with repetitive exercises.
- Try different activities to determine what works best in an individual patient.
- Allow the patient to guide an increase in activity, within reasonable limits. Increased activity must always be considered in response to the time frame of expected tissue healing and the strength of the healing tissues. This is especially relevant with the modern analgesic and surgical techniques used, which may result in less pain and attempts to do more activity.
- Conversely, some patients may need some encouragement if they are not progressing as expected.
- Do not hurt a patient during exercises or increase the activity level too rapidly. This may result in reflex inhibition and decreased use of the limb, which will ultimately slow progress.
- Pathologic reasons for delayed recovery should always be ruled out prior to increasing the level of activity.

Assisted Standing

These exercises bridge the gap between passive ROM and stretching exercises and more active exercises. They are useful for dogs recovering from neurologic conditions, such as intervertebral disk rupture, or severe musculoskeletal trauma, such as bilateral pelvic injuries. Assisted standing is useful for patients that have adequate strength to bear some weight but are too weak to bear complete weight.

- Position the dog with the feet squarely underneath the body.
- Support the animal with a towel or sling. Allow the dog to bear as much weight as it is able.
- As the animal weakens and begins to slowly collapse, lift it back to a standing position with the limbs squarely placed under the body.
- Start with 10 to 15 repetitions bid–tid, and gradually increase to 5 minutes per session.

Proprioceptive Exercises

These exercises help animals regain their ability to appropriately use and place their limbs, and they include weight shifting, balance board activities, and Swiss balls or PhysioRolls.

Weight Shifting and Perturbation Exercises

- Stand the dog squarely on firm footing.
- Place the hands on the side of the dog for support.
- Push the dog gently from side to side. In severely affected dogs, some support may be necessary to avoid falling. As the animal regains proprioceptive ability, the shifts may be more challenging.
- It may be necessary in some dogs to place mild pressure over the pelvis or shoulders to encourage greater stability and weight bearing.

Balance Boards

- Dogs may be placed on a traditional balance board with either the front or the hind limbs on the board, or special balance boards designed for quadruped animals may be made (Fig. 95-1).

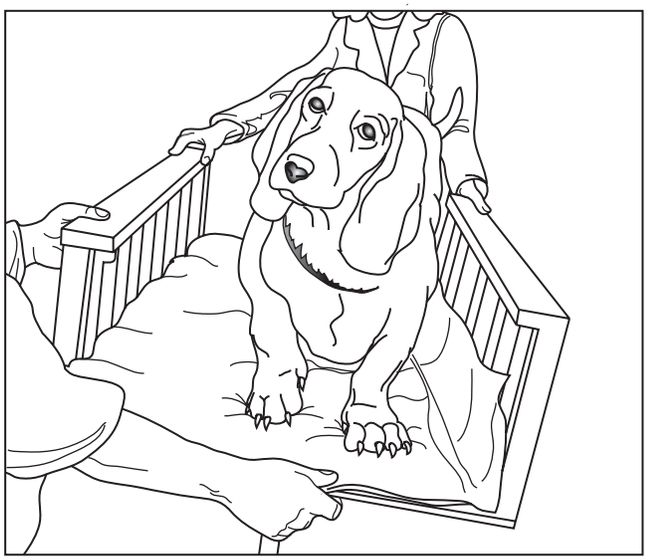

Figure 95-1. A specially made balance board may be used for proprioceptive training.

- Support the dog to avoid injury from falls.
- The balance board may be manipulated to rock the dogs from side to side, back and forth, or in all directions.

Side Bending and Cervical Flexion and Extension

With the dog standing squarely, use a treat so that the dog follows it from side to side and up and down. The ability to actively move while maintaining balance is the goal.

Swiss Balls and PhysioRolls

- Dogs with severe proprioceptive disability may be placed over a properly sized and inflated, large PhysioRoll to help provide support during weight bearing.
- As strength and ability return, the front half of the dog may be placed on the PhysioRoll, allowing some weight bearing and balancing to occur.
- To help aid limb awareness and neuromuscular activity, perform rhythmic stabilization exercises by standing the dog on a properly sized ball or PhysioRoll and gently "bouncing" the dog while maintaining support to prevent falling.
- Animals returning to good function may be challenged by standing the dog on a properly sized PhysioRoll and allowing it to bear weight while maintaining support to prevent falling.

Slow Walks

▼ ***Key Point*** Slow leash walks are the most important therapeutic exercise for patients recovering from surgery or affected with chronic musculoskeletal conditions, but they are also frequently performed incorrectly.

- Perform leash walks very slowly to allow the dog an opportunity to bear weight; perform at the speed of the dog, not the handler.
- For difficult situations, dogs may be gently "bumped" to challenge their balance and encourage touching the limb to the ground at the end of the swing phase of gait for the affected limb.
- Behavior modification is encouraged to train the dog to use the limb. Praise the dog when it touches the limb down.
- Initially perform leash walks for 2 to 5 minutes, 2 to 3 times daily. If lameness or limb use is not worse after the first couple of days, gradually increase the length and time of the walks 10% to 20% each week.
- Dogs may be walked up and down inclines, hills, or ramps to add more challenges and to encourage muscular and cardiovascular fitness.

Treadmill Walking

Treadmill walking is a useful modality to encourage use of the limb and early gait patterning. The ground moving under the dog often encourages a non–weight-bearing patient to begin using limb. Most dogs trained to leash will walk on a treadmill.

- Use a harness or sling to provide support and prevent falls. Sidewalls to prevent stepping off the treadmill, variable speed of the treadmill, a timer, and the ability to change the incline angle are all useful features for canine treadmills. Do not face the treadmill toward a wall.
- One person may be in front of the dog to encourage it.
- A person may stand beside the dog to lift and advance an affected limb during the normal gait sequence to encourage proper use of the limb for those patients with severe conditions (gait patterning training).
- Dogs may initially walk for 1 to 3 minutes, 2 to 3 times per day at a slow speed. If lameness is not worse after activity, increase the exercise increased 10% to 20% per week.

Stair Climbing

- This exercise is useful to improve power in the rear-limb muscles.
- Stair climbing may begin if the repair is stable and the dog is consistently using the limb at a walk with decreasing lameness over time.
- Walk the dog slowly up the stairs, being certain that the dog steps up with each limb rather than skipping up steps or jumping up steps by using both rear limbs ("bunny hopping").
- If possible, begin with low, gradually rising steps, and progress to increasingly steeper steps.

- Begin with 5 to 7 steps, and increase to two to four flights 1 to 3 times daily.

Sit-to-Stand Exercises

These exercises may be beneficial for dogs with hip dysplasia, a condition in which full extension of the hips is painful (see Chapter 108). Sit-to-stand exercises strengthen the gluteal muscles, but the hip joints only extend to a normal standing position, with no overextension of the hip.

- Back the dog into a corner, with the affected leg against a wall. This will encourage the dog to push up evenly with both rear limbs when rising, and not pushing up with a good leg, while pushing the affected leg out from the body.
- Concentrate on having the dog sit and stand correctly, with both rear limbs flexing equally while sitting, and pushing off evenly with both rear limbs to stand.
- Start with 5 to 10 repetitions once or twice daily, and work up to 15 repetitions 3 to 4 times daily.

Wheelbarrowing

- Wheelbarrowing exercises are designed to improve use of the forelimbs.
- Lift the rear limbs off of the ground, and move the dog forward. Dogs with normal proprioception will move the forelimbs so they do not fall.
- Some dogs with weakness of the forelimbs may require support to prevent them from collapsing.
- As dogs become stronger and endurance improves, dogs may be wheelbarrowed up and down inclines for greater effect.

Dancing Exercises

- Dancing exercises are designed to improve use and strengthening of the rear limbs.
- Because of the proximity of the handler to the dog's mouth, apply a muzzle.
- Lift the forelimbs off the ground and move the dog forward or backward. Dogs with normal proprioception will move the limbs so that they do not fall.
- In some situations, the handler should get behind the dog and place the arms under the axillary region of the dog to support it and walk forward.
- As dogs become stronger and endurance improves, dogs may dance up and down inclines for greater effect.

Jogging

- Jogging may be initiated in cases in which the fixation is stable and the dog is walking on the limb with minimal lameness and pain.
- Begin jogging slowly to improve muscle strength and cardiovascular fitness; 2 to 3 minutes, 2 to 3 times daily, and increase up to 20 minutes, 2 to 4 times daily.
- Be certain that lameness is not worse after jogging.
- The dog may jog up hills for greater effect if there are no problems jogging on flat surfaces.

Cavaletti Rails

- Cavaletti rails are raised rails or poles that are spaced apart on the ground to help increase stride length, limb use, and active ROM of joints. A ladder that is lying on the ground may act as Cavaletti rails.
- The height of the rails is raised to encourage greater active flexion and extension of the joints (Fig. 95-2).
- As the animal improves, the rails may be spaced at varying distances to provide challenges to proprioception.
- Begin with slow walking over the rails, and progress to trotting to add additional challenges to the patient.

Circling, Figure of Eight, Serpentine, and Pole Weaving

- These exercises are useful for encouraging lateral flexion of the spinal column, proprioceptive training, and weight shifting during gait in preparation for more challenging exercises, such as turning sharply while running.
- Walk the dog slowly in the desired pattern with frequent changes in direction, encouraging the dog to flex the body and spinal column and pivot on the affected limb.
- If vertical poles are used, the distance between the poles should be less than the length of the dog to encourage lateral bending of the spinal column and weight shifting.

Muscle Strengthening Activities

These exercises concentrate on strengthening muscles to improve power and speed. They include carrying weights, playing ball, and running for short distances at high speed.

- Place strap-on leg weights relatively proximal on the limb to reduce the muscle force and stress on joints during the early rehabilitation period.
- As strength and stamina improve, move the weights further distally to provide more challenges.
- In general, use 0.25-kg, 0.5-kg, 1-kg, and 2-kg weights for small, medium, large, and very large dogs, respectively.
- Use the weights 2 to 3 times per week during normal walking. Dogs may initially resist the leg weights, but most become accustomed to them and will walk with the weights.

Controlled Ball Playing

- Begin on a relatively short leash or in an enclosed kennel or room to avoid overly explosive activity in the early postoperative period.

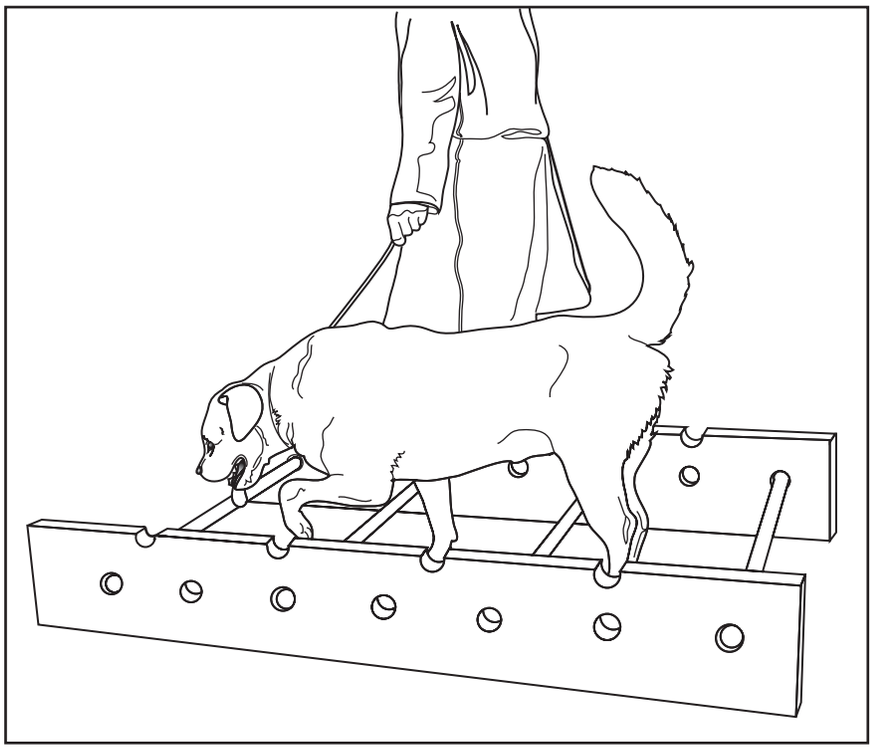

Figure 95-2. Walking over raised Cavaletti rails encourages increased active range of motion of joints and proprioceptive training of the limbs.

- Progress to ball playing in an enclosed area, such as a small dog run or room. As the animal nears full return to function, begin activity on a long leash, and if there are no problems, begin off-leash activity in a safe environment.

Aquatic Exercises

- Begin aquatic exercises when the incision is sealed. Gently test the incision to be certain that the edges do not separate. Do not perform aquatic exercises in patients with drainage from the incision, active infections, or if the incision is not sealed.
- Walking on an underwater treadmill may begin by day 5 to 7 after surgery in many patients.
- Fill the water level to the level of the elbow, and set the treadmill at a slow, comfortable walking pace for the dog.
- Initially walk dogs at a slow speed for 1 to 5 minutes, 2 to 3 times per day, gradually increasing the speed and length of activity as the patient allows.
- The goal is to exercise for 30 to 40 minutes twice daily, with some of the time spent jogging.
- Initiate swimming at a later time, generally 4 to 8 weeks after surgery. Swimming may be too stressful for some surgical procedures to begin earlier than this.

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Chapter 96

Fractures of the Skull

Mark M. Smith

Fractures of the zygomatic arch require surgery if they interfere with mastication or compress ocular structures. The most common extracranial fracture requiring surgery is a depression fracture of the frontal sinus. Intracranial fractures that require surgery are those that depress into brain parenchyma, causing significant compromise of cerebral function. Most skull fractures are amenable to conservative management.

Weigh the complications of general anesthesia in a neurologically compromised patient against the positive effects of surgical intervention. Fine motor movement is not necessarily required of small animal pets; therefore, intracranial surgery rarely is performed.

ANATOMY

Zygomatic Arch

- The cranial portion of the zygomatic arch is formed by the zygomatic bone, and the caudal portion is formed by the zygomatic process of the temporal bone.
- The zygomatic arch forms the ventral and lateral rim of the orbit.

Calvarium

- The dorsal sagittal crest courses craniocaudal over the calvarium.
- The nuchal crest courses mediolateral over the caudal edge of the skull.
- The frontal sinus of the frontal bone comprises the frontal encasement of the brain.
- The diploic calvarium has two distinct cortical bone layers between which is an interstitial layer of honeycombed bone and vessels.
- The brain is encased by the frontal, parietal, temporal, and occipital bones.
- The temporalis muscles cover almost the entire calvarium.

ZYGOMATIC ARCH FRACTURE

Preoperative Considerations

- Before anesthesia and surgery, perform a complete neurologic examination on all head trauma patients.
- General anesthesia may alter intracranial pressure (ICP), leading to exacerbation of intracranial edema and/or hemorrhage.
- To reduce ICP, consider hyperventilation (to reduce $PaCO_2$), osmotic agents, corticosteroids, and an anesthetic protocol including barbiturates (see Chapter 2).
- Obtain skull radiographs to document fracture displacement and to screen for other, less apparent fractures. If possible, perform radiography immediately before surgery, thus avoiding the necessity for, and risk of, two separate anesthetic procedures.
- If available, computed tomography (CT) provides the most accurate assessment of the presence and severity of skull and cranial fractures. CT views avoid superimposition of overlying bone that makes the interpretation of plain skull radiographs difficult.
- Confirm the presence of an intact optic nerve and vision before surgery. Surgery for a zygomatic arch fracture may be contraindicated if ocular function is irreversibly impaired.

▼ ***Key Point*** Acepromazine may lower the central nervous system (CNS) seizure threshold, and ketamine increases cerebral blood flow. Do not use these drugs in patients with a history of brain trauma.

Surgical Procedure

Objectives

- Reduce fractures that can cause compression of the eye or cosmetic deformity.
- Avoid trauma to the zygomaticotemporal and zygomaticofacial nerves.

▼ ***Key Point*** Non-displaced fractures of the zygomatic arch have a good prognosis for uncomplicated healing with conservative management.

Equipment

- Standard general surgical pack and sutures
- Gelpi or Weitlaner self-retaining retractors
- Sharp periosteal elevator
- Small Steinmann pins and orthopedic wire (multiple sizes, 18–24 gauge)
- Small malleable retractor

Technique

1. Place the patient in ventral recumbency with the head supported. Attach tape to the mandibular canines and the table to secure the head position.
2. Prepare the periocular area for aseptic surgery. Ocular lubricating ointment avoids corneal damage from antiseptic agents.
3. Incise the skin directly over the zygomatic arch.
4. Incise and elevate the periosteum using a sharp periosteal elevator. Be careful to avoid the zygomaticotemporal and zygomaticofacial nerves (medial to the zygomatic bone).
5. Use a small malleable retractor to protect the orbit.
6. Reduce and secure fracture fragments using orthopedic wire (18–24 gauge, depending on the size of the animal). Small pins may be used to make holes in the bone for wire placement. Small orthopedic plates may be required to maintain reduction in extremely comminuted fractures or when cosmesis is of paramount importance.

▼ ***Key Point*** Do not use small pins as a component of the definitive repair, because pin migration following surgery may cause ocular and intracranial trauma.

7. Appose subcutaneous tissues in a simple interrupted pattern (absorbable suture).
8. Subcuticular sutures (absorbable suture) provide skin apposition and avoid suture irritation of ocular structures.

Postoperative Care and Complications

Short Term

- Perform serial neurologic examinations to monitor changes in neurologic status.
- Monitor for clinical signs of seroma and infection.

Long Term

- Excessive bony callus may compress ocular structures and interfere with mastication.
- Periarticular fractures may lead to degenerative joint disease of the temporomandibular joint (TMJ) and bony ankylosis.
- If normal function is inhibited or pain persists, resection of the affected segment of the zygomatic arch is indicated. Reconstruction of the muscle tissue provides acceptable appearance and function.

Prognosis

- The prognosis is good with conservative management.
- With operative management, the prognosis is good to excellent.

EXTRACRANIAL FRACTURES

Extracranial fractures include fractures of the nuchal crest, sagittal crest, and frontal sinus.

Preoperative Considerations

See “Zygomatic Arch Fracture.”

Surgical Procedure

Objective

- Maintain reduction of severely displaced fractures of the nuchal crest, sagittal crest, and frontal sinus.

▼ ***Key Point*** The cranial muscle mass usually prevents severe fracture displacement and provides enough fracture stability to allow conservative management of most extracranial fractures.

Equipment

- Standard general surgical pack and sutures
- Gelpi or Weitlaner self-retaining retractors
- Sharp periosteal elevator
- Small Steinmann pins and orthopedic wire (multiple sizes, 20–24 gauge)

Technique

1. Place the patient in ventral recumbency with the head supported. Attach tape to the mandibular canines and table to secure the head position.
2. Prepare the fracture area for aseptic surgery.
3. Make a skin incision directly over the fractured bony prominence.
4. Elevate the periosteum to allow anatomic reduction.
5. Frontal sinus fractures usually are depressed, requiring elevation and fixation with orthopedic wire.
6. Reduce and fix nuchal and sagittal crest fractures with orthopedic wire.

▼ ***Key Point*** Do not use small pins as a component of the definitive repair because pin migration following surgery may cause ocular or intracranial trauma.

7. Appose muscle fascia and subcutaneous tissues in individual layers, using absorbable suture in a simple interrupted pattern.
8. Close the skin similarly, using non-absorbable suture.

Postoperative Care and Complications

Short Term

- Perform serial neurologic examination to monitor for change in neurologic status.
- Monitor for clinical signs of seroma and infection.
- Subcutaneous emphysema may occur secondary to frontal sinus fracture. Whether management of the fracture is surgical or conservative, a compressive bandage minimizes continued formation of subcutaneous emphysema until organized hematoma and fibrin deposition provide a functional barrier to air migration from the frontal sinus. Thus, bandaging is recommended for 2 to 4 days.

Long Term

- Fractures usually heal without complications, providing acceptable cosmesis.
- Most complications are related to CNS trauma, such as seizures (see Chapter 127).

INTRACRANIAL FRACTURES

Preoperative Considerations

- Preoperative anesthetic and neurologic concerns are similar to those for zygomatic arch fractures.
- Fractures may be linear cracks, depressed bony fragments, or comminuted separate bony fragments.
- Intracranial fractures are usually closed fractures.
- Comminuted calvarial fractures may lacerate meninges, venous sinuses, or the cerebral cortex.
- Calvarial fractures usually are associated with CNS compromise. Medical management of CNS trauma is indicated before diagnostic procedures requiring anesthesia.
- Progressive deterioration in CNS status despite intensive medical management is an indication for skull radiography to determine fracture severity.

Surgical Procedure

Objectives

- Elevate depressed calvarial fractures that may cause extensive functional loss of cerebral mass.
- Remove large comminuted fragments of the calvarium that may cause cerebral laceration.

▼ ***Key Point*** Linear and minor depressed intracranial fractures are best managed conservatively.

Equipment

- Standard general surgical pack and sutures
- Gelpi or Weitlaner self-retaining retractors
- Sharp periosteal elevator
- Pneumatic or electric bur drill

Technique

1. Place the patient in ventral recumbency with the head supported. Attach tape to the mandibular canines and table to secure the head position.
2. Prepare the dorsal skull area for aseptic surgery.
3. Make a dorsal incision (Fig. 96-1*A*).
4. Incise the superficial temporal fascia and elevate the temporalis muscle ventrally to expose the fracture area (Fig. 96-1*B*).

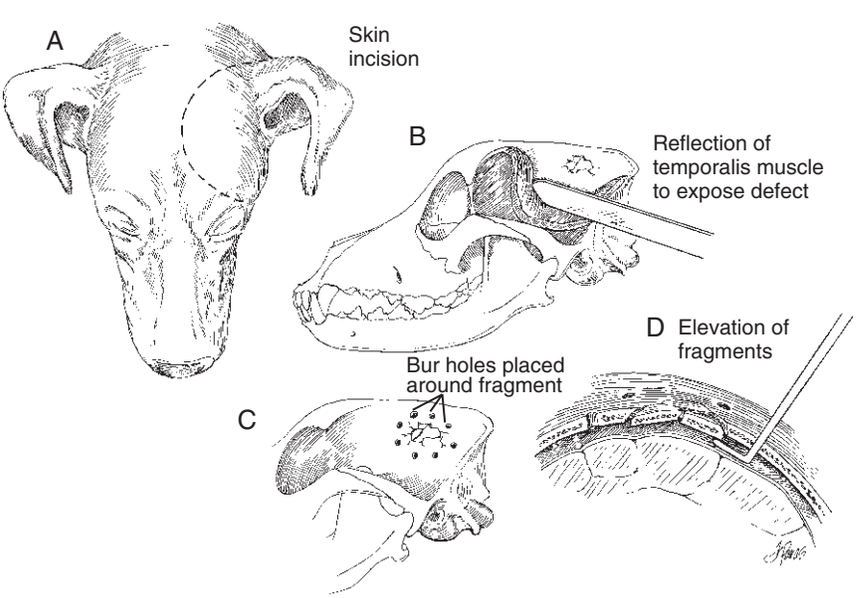

Figure 96-1. Procedure for repairing intracranial fracture. See text for explanation.

5. Drill multiple small bur holes through the calvarium around the periphery of the fracture area to allow elevation of the fracture fragments (Fig. 96-1*C*).
6. Elevate fragments with a small, blunt elevator (Fig. 96-1*D*).
7. Remove any large comminuted fragments that may cause laceration. Despite the potential for large calvarial defects, replacement of the temporalis muscle provides adequate coverage.
8. Replace the temporalis muscle and appose the superficial fascia using absorbable suture in a simple interrupted pattern.
9. Close the subcutaneous layers similarly, followed by skin closure using non-absorbable suture in a simple interrupted pattern.

▼ ***Key Point*** Meticulous, atraumatic surgical technique, prevention of cerebral edema, and removal of hematoma if calvarial fragments are removed are of the highest priority when operating on intracranial fractures.

Postoperative Care and Complications

Short Term

- Perform serial neurologic examinations to monitor for change in neurologic status.
- Monitor for clinical signs of seroma and infection.

Long Term

- Bony healing occurs without complication; however, neurologic recovery depends on the location and severity of the original traumatic incident.

Prognosis

- With cranial fracture repair, the prognosis is good.
- For neurologic recovery there is a guarded prognosis.

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Chapter 97

Fractures and Dislocations of the Mandible

Richard M. Jerram

Mandibular fractures account for approximately 2% of all fractures in dogs and 15% of all fractures in cats. Most mandibular fractures occur as a result of automobile trauma, although dog bites and gunshots are also reported causes. Pathologic fractures can occur with severe dental or metabolic disease. Young cats and dogs (<2 years of age) are more likely to have mandibular fractures. Mandibular fractures present the veterinarian with some unique clinical management considerations. Concurrent head and thoracic trauma make anesthetic management challenging, the placement of oral endotracheal tubes makes an accurate assessment of occlusion difficult, and providing postoperative oral nutrition can be critical in determining clinical success. Dislocations of the temporomandibular joints occur less frequently and can occur in conjunction with mandibular fractures or other facial trauma.

ANATOMY

The mandible consists of left and right halves that are joined by a rigid fibrous symphysis at the rostral midline. Each half is further divided into the horizontal body and the vertical ramus.

- The horizontal body contains the teeth along the alveolar border. The alveolar border is the tension surface of the mandible.
- The mandible has a mandibular canal (not a medullary cavity like axial long bones) that contains the mandibular artery and vein as well as the mandibular alveolar nerve that supply the teeth and soft tissues of the lower jaw.
- The mandibular vessels and nerve enter the canal caudally at the mandibular foramen on the medial side at the junction of the body and ramus.
- The mandibular canal opens cranially at three mental foramina located lateral to the premolar teeth.
- The condyloid process of the ramus articulates with the temporal bone in the mandibular fossa forming the temporomandibular joint. This joint contains a thin articular disc (meniscus) in the dog.
- The muscles of mastication (masseter, temporalis, pterygoideus, and digastricus) insert on the coronoid and angular processes of the vertical ramus.

CLINICAL SIGNS

Clinical signs can vary but include the following:

- Asymmetry of the jaw
- Crepitus on mandible manipulation
- Oral hemorrhage
- Oral pain
- Concurrent head and thoracic trauma

DIAGNOSIS

- Diagnosis is usually based on history and clinical examination.
- Careful oral examination is necessary as there may be more than one fracture present.
- Standard dorsoventral and lateral radiographs are performed first.
- Oblique and open-mouthed views may highlight fractures undetected on standard radiographs.
- Carefully evaluate radiographs to identify other skull fractures.
- Computed tomography (CT) scans, where available, can provide a three-dimensional impression of the fracture(s) present.

SURGICAL PROCEDURES

Preoperative Considerations

▼ ***Key Point*** Manage concurrent head, upper airway, and thoracic trauma prior to performing mandibular fracture repair.

- Establish a patent airway, control hemorrhage, and treat shock.
- Obtain thoracic radiographs and manage any pleural space disease—that is, pneumothorax, hemothorax, diaphragmatic hernia, or pulmonary contusion.
- Record an electrocardiogram to assess for the presence of cardiac arrhythmias secondary to traumatic myocarditis.

- Complete a neurologic examination of the head and treat any possible brain edema or hemorrhage.

Anesthetic Considerations

- Endotracheal intubation is essential to reduce the risk of aspiration of blood and debris.
- To assess dental occlusion intraoperatively, place the endotracheal tube through a pharyngotomy incision.

▼ ***Key Point*** Use an endotracheal tube placed through a pharyngotomy incision to help establish normal occlusion during fracture repair.

- Most mandibular fractures are open; therefore, prophylactic antibiotics are recommended prior to surgery. Cefazolin (20 mg/kg IV) is preferred.

Surgical Principles

Adherence to several basic principles of mandibular fracture management will improve clinical success and reduce complication rates.

- Restore dental occlusion. Accurate anatomic reconstruction of fracture fragments will restore normal occlusion. Use an endotracheal tube placed through a pharyngotomy incision.

▼ ***Key Point*** The goal of mandibular fracture repair is to restore normal dental occlusion.

- Rigid fixation and neutralization of the fracture forces provides a rapid return to function.
- Carefully handle soft tissues. Avoid entrapment of soft tissues, remove devitalized tissue, and avoid excessive elevation of soft tissues from bone.
- Avoid further dental trauma. Remove only teeth that are luxated or fractured. Leave teeth in the fracture site that will contribute to stabilization of the fracture.
- Intramedullary pinning of mandibular fractures is not recommended due to the shape of the mandibular canal and the presence of the tooth roots, major vessels, and nerves.

Equipment

- Standard general surgical pack
- Orthopedic wire (various sizes) and wire twisters
- External skeletal fixation devices (generally small size)
- Bone plates and screws (generally sizes 1.5 mm to 2.7 mm)

Postoperative Care

- Provide appropriate nutrition during the recovery period.
- Cats, particularly, are less willing to eat after facial trauma. Place an esophagostomy feeding tube at the time of mandibular surgery.

▼ ***Key Point*** In cats, place an esophagostomy feeding tube for postoperative nutrition (see Chapter 3).

- Gastrostomy feeding tubes may be placed endoscopically if long-term tube feeding is expected (see Chapter 3).
- If a feeding tube is not used, feed a soft gruel for 4 weeks after surgery.
- Prevent animals from chewing toys or hard objects such as bones and sticks.
- Daily oral flushing with a dilute chlorhexidine solution will reduce oral bacterial contamination and clean implants placed around the teeth.

Complications

- Malocclusion is the most important complication postoperatively. Evaluate patients every 2 weeks to ensure normal occlusion is being maintained. Further surgery may be necessary if malocclusion occurs.
- Osteomyelitis occurs rarely; long-term (6–8 weeks) treatment with appropriate antibiotics is required.
- Implant failure and non-union can occur and are generally related to poor preoperative planning and implant choice.
- Damage to remaining teeth from either the original trauma or the surgery may result in dental pain or infection after the fracture has healed. Tooth extraction or endodontic therapy may be indicated.
- Temporomandibular joint ankylosis can occur following trauma to the condyloid process of the mandible. Resection of the condyloid process (condylectomy) or osteophytes may be necessary.

MANDIBULAR SYMPHYSEAL SEPARATIONS

Separation of the mandibular symphysis accounts for the majority of the mandible fractures identified in cats. Care should be taken to ensure that there is no concurrent trauma to the caudal aspect of the mandible, particularly in the area of the condyloid processes. The fixation method should provide normal occlusion. Wire stabilization is the technique of choice.

Technique

1. Place the animal in dorsal recumbency and clip and prepare the chin for aseptic surgery.
2. Make a small stab incision in the ventral mandibular skin at the level of the caudal edge of the mandibular symphysis.
3. Insert a hypodermic needle with an internal diameter larger than the intended orthopedic wire through the incision and lateral to one hemimandible. The needle should exit orally caudal to the canine tooth (see Fig. 97-1).

4. Pass orthopedic wire (generally 18–22 gauge, depending on the size of the animal) through the needle. Remove the needle, leaving the wire in place.
5. Insert the needle through the same incision lateral to the opposite hemimandible.
6. Pass the oral end of the wire, caudal to the canine tooth, through the needle to exit ventrally. Remove the needle, leaving both wire ends ventrally.
7. Twist the wire together using wire tighteners while maintaining mandibular alignment and normal occlusion until reduction and stability is achieved. Cut off the wire, leaving three twists.
8. Leave the ends exposed and remove in 6 to 8 weeks by cutting the exposed oral wire and pulling on the twisted end.

Alternative Techniques

Interdental wire with or without dental acrylic can be performed; however, medial rotation of each hemimandible can occur with overtightened wire.

MANDIBULAR BODY FRACTURES

The fixation method of choice for mandibular body fractures depends on the age and size of the animal, fracture location, fracture stability, degree of comminution, and amount of oral or dental trauma present. Numerous surgical techniques have been described; however, only the techniques that are used most commonly and have high reported success rates will be described here. Placing an intramedullary pin in the mandibular canal is strongly discouraged due to the likely damage to the intramandibular neurovascular structures and tooth roots, as well as the high rate of malocclusion and non-union.

Tape Muzzle

Fractures in young dogs with minimal displacement of fragments can be treated using a tape muzzle. Tape muzzles can also be used to augment other methods of fracture repair if fragment stability or dental occlusion is uncertain. Tape muzzles are difficult to place and maintain in cats and brachycephalic breeds of dog due to the short length of the muzzle.

1. Make a circular muzzle from adhesive non-elastic tape (sports-strapping type) by placing both sticky surfaces together. The diameter should allow the dog to open the mouth no more than 10 mm and to maintain dental occlusion.
2. Use additional pieces of tape to complete the muzzle around the head and behind the ears (see Chapter 98, Fig. 98-1 for an illustration of a tape muzzle.)

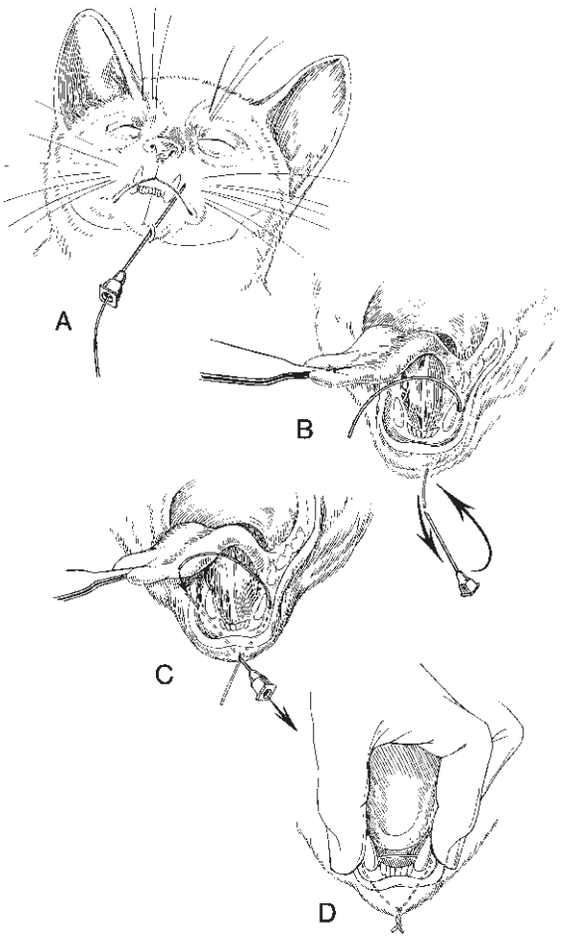

Figure 97-1. Wire stabilization for mandibular symphyseal fracture. See text for details.

3. Daily cleaning of the muzzle and underlying skin is necessary. Feed the dog a soft, gruel-type food that can be lapped through the gap remaining.
4. Alternatively, tape the mouth completely closed after an enteral feeding tube (esophagostomy, gastrostomy) has been placed.
5. The tape muzzle can be removed after 4 to 8 weeks depending on the degree of bone healing. Feed soft food for several weeks after removal of the muzzle.

Maxillary-Mandibular Fixation

Reduction of fracture fragments and dental occlusion can be achieved by securing the mandible to the maxilla, especially for animals (i.e., cats and small dogs) that have facial conformation or temperaments that make maintaining a tape muzzle difficult. Animals will be unable to reduce their body temperature by panting and should be kept out of warm environments to avoid hyperthermia during the healing phase. Animals are

also at increased risk for aspiration pneumonia if vomiting occurs. Wire loops or dental acrylic bonding have been reported.

Maxillomandibular Wiring

1. Drill a hole through the furcation of maxillary fourth premolar tooth and the mandibular first molar tooth on both hemimandibles.
2. Pass the end of a wire loop through the maxillary hole from lateral to medial. Pass the end from medial to lateral through the mandibular hole.
3. Twist the ends together laterally, ensuring dental occlusion and leaving an oral gap of up to 10 mm to enable to animal to lap gruel-type food.
4. An enteral feeding tube (esophagostomy, gastrostomy) can be used to provide nutrition during healing.
5. Alternatively, place orthopedic screws in both sides of the maxilla and mandible, avoiding tooth roots. Place an elastic band between the screw heads. This method allows simple removal of the band in an emergency.
6. The wires can be placed more rostrally at the level of the premolar teeth, but longer wires will be required due to the normal gap in dental occlusion in this region.

Acrylic Bonding of the Canine Teeth

1. Polish the canine teeth with a pumice material and etch using a phosphoric acid-etch gel.
2. Align the teeth and apply a dental self-curing, composite, temporary restorative material to cover the opposing canine teeth.
3. A gap of up to 10 mm is left to allow lapping of a gruel-type food.
4. Remove the dental acrylic using dental instruments 4 to 6 weeks after application, taking care to avoid damaging the teeth.
5. This technique requires that all four canine teeth be healthy and intact.

Interfragmentary Wiring

The wiring of mandibular fragments is acceptable for fracture fragments that are stable without loss of bone or comminution. Wires should be placed as dorsal as possible to neutralize the tensile forces acting on the oral margin of the mandible. The technique requires drilling through the mandible, so care must be taken to avoid tooth roots and neurovascular structures of the mandibular canal. Wire size is dependent on the size of the animal.

1. Make a skin incision over the ventral surface of the mandible, and elevate the soft tissues from the fragments adjacent to the fracture.
2. Drill a hole in each fragment using either an oscillating drill bit or a smooth K-wire to avoid damage to the vessels and nerve. The hole should be 5 to 10 mm from the fracture edge.
3. A loop of wire (the largest gauge that can be manipulated) is passed through the holes and tightened on the lateral aspect of the mandible.
4. The wire should be perpendicular to the fracture line to allow compression during tightening and to avoid shearing of the fracture fragments.
5. Cut the twisted wire and bend ventrally to avoid damage to the overlying skin.
6. If multiple wires are used, place all wires prior to tightening. Tightening should be performed from caudal to rostral while maintaining dental occlusion.

Intraoral Acrylic Splint

The conical shape of the teeth in cats and dogs makes application of interdental wires difficult without damage to the periodontal tissues. The use of finer orthopedic wire as support for an intraoral acrylic splint provides excellent stability for fractures without bone or tooth loss. The technique is best used for fractures rostral to the molar teeth.

1. Clean, polish, and acid-etch the teeth using a phosphoric acid gel.
2. Apply fine-gauge orthopedic wire (22–26 gauge) around the dentition in a Stout loop fashion. One end of the wire is placed along the medial surface of the teeth. The other end is passed laterally.
3. At each interdental space, pass the lateral wire medially and loop around the medial wire before returning to the medial side of the mandible. Repeat until all teeth are encircled with wire.
4. The loops of wire on the medial surface are twisted and flattened against the tooth surfaces.
5. Apply a dental self-curing, composite, temporary restorative material to cover the teeth and the preplaced wire. Acrylic should not enter the fracture site.
6. Cold-curing dental acrylic can also be applied by using dental wax to prevent acrylic from running off the teeth during the liquid phase of curing.
7. Check dental occlusion during curing and acrylic is removed from tooth surfaces where it prevents normal occlusion.
8. Perform daily intraoral flushing of the acrylic device to dislodge trapped food particles.
9. Remove the splint 6 to 8 weeks after application, following radiographic confirmation of bony healing.

External Skeletal Fixation

External skeletal fixation (ESF) is best applied to fractures that are comminuted, open, or involve bone loss. There must be sufficient bone on either side of the fracture to hold bone pins. Pin placement must be carefully

planned to avoid tooth roots. Pins should not cross the intramandibular space to avoid interfering with function of the tongue. Positive-profile threaded pins provide greater bone holding than smooth pins but may damage intramandibular neurovascular structures. Either standard metal connecting bars can be used or, more conveniently, an acrylic connecting bar can be molded to fit the pins using silicone tubing.

1. Make short stab incisions over the bone at the point of predetermined pin insertion.
2. Insert pins into the bone fragments, penetrating both the lateral and the medial cortices.
3. Connect the pins using ESF clamps and connecting bars, or place a length of silicone tubing over the bent pin ends. The connecting bars or tubing should lie approximately 10 mm from the adjacent skin.
4. Inject dental acrylic or polymethylmethacrylate bone cement into the tubing. The acrylic is allowed to cure while the mouth is held in normal occlusion.
5. An acrylic ESF device can be applied to bilateral fractures by molding the silicone tubing in a U shape around the rostral aspect of the mandible.
6. Clean the sites where the pins enter the skin daily.
7. Remove the ESF device after 6 to 8 weeks, following radiographic confirmation of bone healing, by cutting the pins against the connecting bar and removing each pin individually.

Bone Plating

Bone plating of mandibular body fractures provides rigid stability and a rapid return to normal function. The bone plate must be accurately contoured to the bone surface to avoid malocclusion, and screws should not damage tooth roots. It is often difficult to apply bone plates as close to the tension (oral) surface of the mandible as possible because screw holes are frequently over tooth roots. If the plate is secured to the ventral aspect of the mandible, then additional support with an interdental wire orally may be required. Recently, there have been reports of successful mandible fracture repair using miniplates. These small titanium plates are more easily applied to the dorsal aspect of the mandible, but special instruments are required for their application.

1. Place the animal in dorsal (for bilateral fractures) or dorsolateral recumbency (for unilateral fractures) and make a ventral incision over the mandibular body.
2. Elevate the subcutaneous tissues to expose the fracture ends.
3. Contour the bone plate to fit the mandible ventrolaterally, avoiding tooth roots. At least two screws should be placed on either side of the fracture.
4. Drill screw holes with an oscillating drill bit to avoid damage to the neurovascular structures.
5. Secure the bone plate to the mandible while normal dental occlusion is ensured.
6. The subcutaneous tissues and skin are closed routinely.
7. Place an interdental or interfragmentary wire more dorsally across the fracture line to counter tensile forces.
8. Feed soft, gruel-type food, and obtain radiographs 6 to 8 weeks later to evaluate bone healing.
9. Bone plates may need to be removed if they cause pain or erosion of the oral mucosa.

MANDIBULAR RAMUS FRACTURES

Fractures of the vertical part of the mandibular ramus are generally minimally displaced and do not require surgical treatment. The application of a tape muzzle or maxillary-mandibular fixation (previously described) may be necessary to provide adequate stability while the fractures heal. Unstable fractures may require interfragmentary wire or miniplate fixation. The surgical approach to the mandibular ramus requires elevation of the large masseter muscle.

Fractures of the condyloid process usually occur in association with other mandibular fractures. These fractures can be identified in cats with concurrent mandibular symphyseal separation that develop malocclusion following symphyseal stabilization. Treatment is generally non-surgical with a tape muzzle or maxillary-mandibular fixation. Acrylic bonding of the canine teeth is most successful in cats. In larger dogs, a lateral approach can be made to the condylar region and fracture fragments may be stabilized with interfragmentary K-wires.

Condylectomy

Intra-articular fractures may heal with ankylosis or arthrosis of the temporomandibular joint. These animals develop an inability to open the mouth and are unable to prehend solid food. Unilateral condylectomy (analogous to femoral head and neck ostectomy for severe hip fractures) is the treatment of choice for these patients.

1. Place the animal in lateral recumbency and make a skin incision along the ventral border of the zygomatic arch.
2. Approach to the temporomandibular joint by elevation of the masseter muscle from its caudal insertion on the zygomatic arch.
3. Identify the joint and resect the condyloid process. Resection can be performed using a rongeur or an osteotome.
4. Leave the temporomandibular joint meniscus in place. Closure of the muscle fascia, subcutaneous tissues, and skin is routine.
5. Postoperative physical therapy is encouraged.

TEMPOROMANDIBULAR JOINT DISLOCATIONS

Luxation of the temporomandibular joint (TMJ) is uncommon but typically occurs as a result of head trauma. TMJ luxation can be unilateral or bilateral and may occur concurrently with fractures of other areas of the mandible.

- The condyloid process generally displaces in a rostral and dorsal direction.
- The diagnosis is made on physical examination, palpation, and radiographic confirmation of luxation.
- A unilateral rostrodorsal luxation results in the mandible moving to the opposite side, whereas a bilateral luxation results in the mandible moving rostrally.
- Assess the entire mandible for other injuries.
- Most isolated luxations can be reduced using closed reduction.

Closed Reduction

1. Place the animal under general anesthesia and place in dorsal recumbency.
2. Place a rod or dowel in the mouth transversely between the mandibular and the maxillary molar teeth.
3. Using the rod as a fulcrum, close the mouth while the mandible is manipulated rostrally or caudally to reduce the condyloid process.
4. After reduction, use a tape muzzle or maxillary-mandibular fixation (as previously described) to support the reduction for 7 to 14 days.
5. If closed reduction is not possible, then open reduction or condylectomy may be necessary.

TEMPOROMANDIBULAR JOINT DYSPLASIA

TMJ dysplasia is seen in young dogs resulting from deformation of the condyloid process and mandibular fossa that causes subluxation of the TMJ and occasional open-mouthed locking of the mandible.

- Open-mouthed locking has been reported in Irish setters, basset hounds, and cocker spaniels.
- The condition presents as a locking of the mandible in an open position during yawning.
- The TMJ dysplasia results in the coronoid (vertical) process of the mandibular ramus being malpositioned lateral to the zygomatic arch.
- A subcutaneous bulge can be palpated over the zygomatic arch on the affected side.
- Some dogs will reduce the coronoid process unassisted.
- Closed reduction can be achieved by direct pressure over the palpable coronoid process while manipulating the mandible.
- Animals with chronic open-mouth locking may require surgical treatment with condylectomy or resection of the zygomatic arch.

Zygomatic Arch Resection

1. Place the animal under general anesthesia and position in lateral recumbency.
2. Make an approach directly over the zygomatic arch, and elevate the fascial attachments.
3. Manipulate the mandible to determine the portion of the zygomatic arch that is trapping the coronoid process.
4. Remove the identified section of zygomatic arch using a rongeur or a high-speed bone bur.
5. Closure is routine after ensuring that the coronoid process is no longer trapped by the remaining zygomatic arch.
6. Additional mandibular support should not be required.

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Chapter 98

Fractures of the Maxilla

Richard M. Jerram

Fractures of the maxilla generally include all fractures rostral to the orbit—that is, the maxilla, nasal, and incisive bones. Most maxillary fractures occur as a result of automobile trauma, although dog bites and gunshots are also reported causes. Young cats and dogs (<2 years of age) are more likely to have maxillary fractures. Maxillary fractures present the veterinarian with some unique clinical management considerations. Concurrent head and thoracic trauma make anesthetic management challenging, the placement of oral endotracheal tubes makes an accurate assessment of occlusion difficult, and providing postoperative oral nutrition can be critical in clinical success.

ANATOMY

The upper jaw consists of paired incisive, maxillary, and nasal bones that vary greatly in size depending on the species or breed. Brachycephalic dog breeds and cats have shorter and smaller bones than dolichocephalic dog breeds.

- The incisive bones contain the upper incisor teeth; the maxilla bones contain the canine, premolar, and molar teeth.
- The bone between the roots of the teeth and the nasal cavity is very thin and easily damaged from trauma.
- The infraorbital artery and nerve travel through the infraorbital foramen located as an elliptical opening dorsal to the upper third and fourth premolar teeth.
- The palatal aspect of the maxilla is supplied by the major palatine artery that exits the major palatine foramen at the junction of the maxilla and palatine bones on the caudal aspect of the hard palate. The vessel travels rostrally medial to the teeth along the surface of the hard palate. There are numerous anastomoses among blood vessels of the maxilla.

CLINICAL SIGNS

Clinical signs can vary but include the following:

- Asymmetry of the maxilla
- Crepitus on maxillary manipulation
- Nasal hemorrhage
- Oral hemorrhage
- Oral pain
- Concurrent head and thoracic trauma

DIAGNOSIS

- Diagnosis is usually based on history and clinical examination.
- Carefully examine the oral and nasal cavities as there may be more than one fracture present.
- Obtain standard dorsoventral and lateral radiographs.
- Oblique and open-mouthed views may highlight fractures undetected on standard radiographs.
- Carefully evaluate radiographs to identify other skull fractures.
- Computed tomography (CT) scans, where available, can provide a three-dimensional impression of the fracture(s) present.

SURGICAL PROCEDURES

Preoperative Considerations

▼ ***Key Point*** Manage concurrent head, upper airway, and thoracic trauma prior to performing maxillary fracture repair.

- Establish a patent airway, control hemorrhage, and treat shock.
- Obtain thoracic radiographs and manage any pleural space disease—that is, pneumothorax, hemothorax, diaphragmatic hernia, or pulmonary contusion (see Chapter 166).
- Record an electrocardiogram to assess for the presence of cardiac arrhythmias secondary to traumatic myocarditis.
- Complete a neurologic examination of the head and treat any possible brain edema or hemorrhage.

Anesthetic Considerations

- Endotracheal intubation is essential to reduce the risk of aspiration of blood and debris.

- To assess dental occlusion intraoperatively, place the endotracheal tube through a pharyngotomy incision.

▼ ***Key Point*** Use an endotracheal tube placed through a pharyngotomy incision to allow observation of normal occlusion during fracture repair.

- Many maxillary fractures are open; therefore, administer prophylactic antibiotics prior to surgery (Cefazolin 20 mg/kg IV).

Objectives

Adherence to several basic principles of maxillary fracture management will improve clinical success and reduce complication rates.

- Restore dental occlusion. Accurate anatomic reconstruction of fracture fragments will restore normal occlusion. Use an endotracheal tube placed through a pharyngotomy incision.

▼ ***Key Point*** The goal of maxillary fracture repair is to restore normal dental occlusion.

- Rigid fixation and neutralization of the fracture forces provides a rapid return to function.
- Restore patent nasal passages in animals with severe fracture displacement or a blocked nasal cavity.
- Carefully handle soft tissues. Avoid entrapment of soft tissues, remove devitalized tissue, and avoid excessive elevation of soft tissues from bone.
- Avoid further dental trauma. Remove only teeth that are luxated or fractured. Leave teeth in the fracture site that will contribute to stabilization of the fracture.
- The surgical approach is usually made intraorally, although more dorsal fractures require an approach through the skin of the dorsal midline.

Equipment

- Standard general surgical pack
- Orthopedic wire (various sizes) and wire twisters
- External skeletal fixation devices (generally small size)
- Bone plates and screws (generally sizes 1.5–2.7 mm)

Midline Maxillary Separations (Traumatic Cleft Palate)

Separation of the midline junction of the maxilla bones accounts for the majority of the maxillary fractures identified in cats. These fractures are seen following trauma and present as a cleft defect in the mucosa of the hard palate. Wide defects are treated by surgical closure. (Also see Chapter 64.)

Technique

1. Place the animal in dorsal recumbency and prepare the palate for aseptic surgery.
2. Debride necrotic soft tissue and gently undermine the edges of the mucosa adjacent to the defect.
3. Use digital pressure to approximate the edges of the bony defect.
4. Suture the palate mucosa across the defect using monofilament absorbable suture material (e.g., 3-0 or 4-0 polydioxanone suture).

Alternative Technique

Apply interdental wire with or without dental acrylic between the opposing third incisor and the canine teeth if the defect is considerably displaced or unstable.

Maxillary Body Fractures

The fixation method of choice for maxillary body fractures depends on the age and size of the animal, fracture location, fracture stability, degree of comminution, and amount of oral or dental trauma present. Most maxillary fractures are minimally displaced and do not require surgical treatment. Interfragmentary wiring and interdental wiring with dental acrylic are good choices for fractures that are displaced or are resulting in dental malocclusion. More recently, excellent success rates have been reported with miniplate fixation.

Tape Muzzle

Fractures in young dogs with minimal displacement of fragments can be treated using a tape muzzle. Tape muzzles can also be used to augment other methods of fracture repair if fragment stability or dental occlusion is uncertain. Tape muzzles are difficult to place and maintain in cats and brachycephalic breeds of dog due to the short length of the muzzle.

Technique

1. Make a circular muzzle from adhesive non-elastic tape (sports-strapping type) by placing both sticky surfaces together. The diameter should allow the dog to open the mouth no more than 10 mm and to maintain dental occlusion.
2. Use additional pieces of tape to complete the muzzle around the head and behind the ears (Fig. 98-1).
3. Clean the muzzle and underlying skin daily. Feed soft, gruel-type food that can be prehended through the gap remaining.
4. Alternatively, completely close the mouth after an enteral feeding tube (esophagostomy, gastrostomy) has been placed (see Chapter 3).
5. Remove the tape muzzle after 4 to 8 weeks depending on the degree of bone healing. Continue soft food for several weeks after removal of the muzzle.

Interfragmentary Wiring

The wiring of maxillary fragments is acceptable for fracture fragments that are stable without loss of bone or comminution. Place wires as ventral as possible to neu-

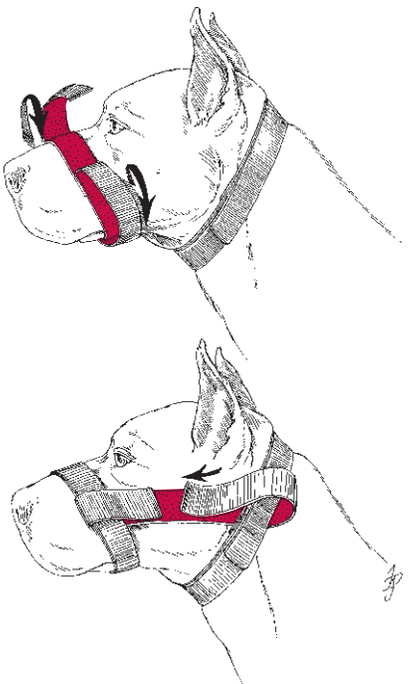

Figure 98-1. Procedure for creating a tape muzzle. See text for explanation.

tralize the tensile forces acting on the oral margin of the maxilla. The technique requires drilling through the maxilla, so take care to avoid tooth roots and neurovascular structures of the infraorbital canal. Wire size is dependent on the size of the animal.

Technique

1. Incise the skin or mucosa over the surface of the maxilla and elevate the soft tissues from the fragments adjacent to the fracture.
2. Drill a hole in each fragment using either an oscillating drill bit or a smooth K-wire to avoid damage to the vessels and nerve. The hole should be 5 to 10 mm from the fracture edge.
3. Pass a loop of wire (the largest gauge that can be manipulated) through the holes and tighten on the lateral aspect of the maxilla.
4. Place the wire perpendicular to the fracture line to allow compression during tightening and to avoid shearing of the fracture fragments.
5. Cut and bend the twisted wire ventrally to avoid damage to the overlying skin or mucosa.

Intraoral Acrylic Splint

The conical shape of the teeth in cats and dogs makes application of interdental wires difficult without damage to the periodontal tissues. Finer orthopedic wire as support for an intraoral acrylic splint provides excellent stability for fractures without bone or tooth loss.

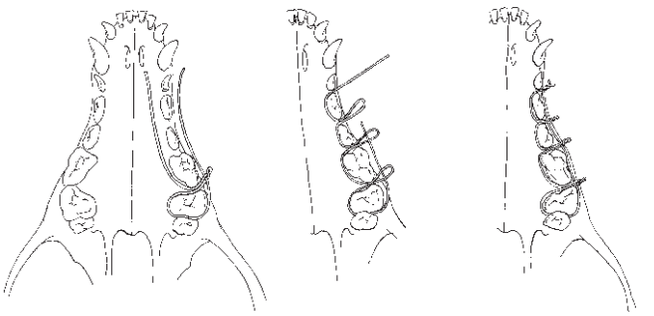

Figure 98-2. Initial *(left)* and final *(center* and *right)* appearance of Stout continuous loop wiring pattern. Note that the working wire is *not* twisted lingual to the stationary wire.

Technique

1. Clean, polish, and acid-etch the teeth using a phosphoric acid gel.
2. Place fine-gauge orthopedic wire (22–26 gauge) around the dentition in a Stout loop fashion. Place one end of the wire along the lateral surface of the teeth. Pass the other end medially.
3. At each interdental space, pass the medial wire laterally and loop it around the lateral wire before returning to the medial side of the mandible. Repeat until all teeth are encircled with wire (Fig. 98-2).
4. Twist the loops of wire on the lateral surface and flatten against the tooth surfaces.
5. Apply a dental self-curing, composite, temporary restorative material to cover the teeth and the preplaced wire. Do not allow acrylic to enter the fracture site.
6. Cold-curing dental acrylic can also be applied by using dental wax to prevent acrylic from running off the teeth during the liquid phase of curing.
7. Check dental occlusion during curing and remove acrylic from tooth surfaces where it prevents normal occlusion.
8. Perform daily intraoral flushing of the acrylic device to dislodge trapped food particles.
9. Remove the splint 6 to 8 weeks after application, following radiographic confirmation of bony healing.

External Skeletal Fixation

External skeletal fixation (ESF) is best applied to fractures that are comminuted, open, or involve extensive bone loss. There must be sufficient bone on either side of the fracture to hold bone pins. Pin placement must be carefully planned to avoid tooth roots. Positive-profile threaded pins provide greater bone holding than smooth pins but may damage maxillary neurovascular structures. Either standard metal connecting bars can be used or, more conveniently, an acrylic connect-

ing bar can be molded to fit the pins using silicone tubing.

Technique

1. Make short stab incisions over the bone at the point of predetermined pin insertion.
2. Insert pins into the bone fragments, penetrating both the lateral and the medial cortices.
3. Connect the pins using ESF clamps and connecting bars or place a length of silicone tubing over the bent pin ends. (See Chapter 111 for illustrations of the apparatus.) The connecting bars or tubing should lie approximately 10 mm from the adjacent skin.
4. Inject dental acrylic or polymethylmethacrylate bone cement into the tubing. Allow the acrylic to cure while holding the mouth in normal occlusion.
5. An acrylic ESF device can be applied to bilateral fractures by molding the silicone tubing in a U shape around the rostral aspect of the mandible.
6. Clean the sites where the pins enter the skin daily.
7. Remove the ESF device after 6 to 8 weeks, following radiographic confirmation of bone healing, by cutting the pins against the connecting bar and removing each pin individually.

Bone Plating

Bone plating of maxillary fractures provides rigid stability and a rapid return to normal function. The bone plate must be accurately contoured to the bone surface to avoid malocclusion, and screws should not damage tooth roots. It is often difficult to apply bone plates as close to the tension (oral) surface of the maxilla as possible because screw holes are frequently over tooth roots. Recently, there have been reports of successful maxillary fracture repair using miniplates. These small titanium plates are more easily applied to the dorsal aspect of the mandible, but special instruments are required for their application.

Technique

1. Place the animal in ventral (for bilateral fractures) or lateral recumbency (for unilateral fractures) and make an incision over the maxilla.
2. Elevate the subcutaneous tissues to expose the fracture ends.
3. Contour the bone plate to fit the maxilla, avoiding tooth roots. Place at least two screws on either side of the fracture.
4. Drill screw holes with an oscillating drill bit to avoid damage to the neurovascular structures.
5. Secure the bone plate to the maxilla while ensuring normal dental occlusion.
6. Close the subcutaneous tissues and skin routinely.
7. Feed soft, gruel-type food, and obtain radiographs 6 to 8 weeks later to evaluate bone healing.
8. Remove bone plates if they cause pain or erosion of the oral mucosa.

Postoperative Care

- Maintain appropriate nutrition during the recovery period.
- Cats, particularly, are less willing to eat after facial trauma.

▼ ***Key Point*** In cats, place an esophagostomy feeding tube for postoperative nutrition (see Chapter 3).

- Gastrostomy feeding tubes may be placed endoscopically if long-term tube feeding is expected.
- If a feeding tube is not used, feed a soft gruel for 4 weeks after surgery.
- Prevent animals from chewing toys or hard objects such as bones and sticks.
- Perform daily oral flushing with a dilute chlorhexidine solution to reduce oral bacterial contamination and clean implants placed around the teeth.

Complications

- Malocclusion is the most important complication postoperatively. Evaluate patients every 2 weeks to ensure normal occlusion is being maintained. Further surgery may be necessary if malocclusion occurs.
- Osteomyelitis occurs rarely; long-term (6–8 weeks) treatment with appropriate antibiotics is required.
- Implant failure and nonunion can occur and are generally related to poor preoperative planning and implant choice.
- Damage to remaining teeth from either the original trauma or the surgery may result in dental pain or infection after the fracture has healed. Tooth extraction or endodontic therapy may be indicated.
- Oronasal fistulation can occur at the site of missing teeth, resulting in passage of food from the oral cavity into the nasal cavity. Mucosal flap techniques may be required to provide complete closure of the defect.
- Altered maxillary growth resulting in facial deformity has been reported following repair of maxillary fractures in growing animals.

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Chapter 99

Neoplasia of the Maxilla and Mandible

Matthew Palmisano

ETIOLOGY

The oropharyngeal region is the fourth most common site of malignant neoplasia in the dog.

▼ ***Key Point*** The most common oral neoplasms in the dog are malignant melanoma, squamous cell carcinoma (SCC), fibrosarcoma, and epulides. In the cat, SCC in the most common oropharyngeal cancer, followed by fibrosarcoma.

Malignant melanoma and epulides occur rarely in the cat. Odontogenic tumors are the most common benign tumor in the cat. Oral tumors tend to be locally aggressive and have a low metastatic rate, except for malignant melanoma, caudal tongue tumors, and tonsillar SCC.

Certain breeds of dogs appear to be predisposed to oral tumors, including boxers, golden retrievers, and cocker spaniels. Small-breed dogs have a greater tendency to develop malignant melanoma, and large-breed dogs are more prone to develop SCC and fibrosarcoma.

Morbidity and mortality often result from local disease rather than from distant metastasis. Therefore, local tumor control is paramount to a successful outcome. Surgical resection should be considered a first line of treatment for all oral neoplasms. See Table 99-1 for a summary of oral neoplasia in dogs and cats.

DIAGNOSIS

History

- Most patients with oral neoplasms present with a chief complaint of drooling, halitosis, and dysphagia.
- Deformity of the muzzle also may be noticed by the owners.
- Oral tumors are often large, ulcerated, and painful, so patients may be anorexic.
- Oral bleeding may occasionally be seen, and some owners report seeing blood in the water dish after the pet drinks.
- Loose teeth or delayed healing after dental extraction may be observed. In the cat, teeth that are excessively loose and easily removed should lead to a suspicion of neoplasia, particularly SCC.

Physical Examination

- Physical examination may reveal palpable swelling of the muzzle or lower lip.
- Oral bleeding and halitosis are common clinical findings.
- If the tumor is associated with the temporomandibular joint (TMJ), vertical ramus of the mandible, or caudal pharyngeal region, pain may be elicited when trying to open the mouth.
- The mass may be smooth, ulcerated, or firm on oral examination and palpation.
- Many patients do not allow a complete oral examination while they are awake due to pain; consider sedation of patients.
- Since many oral neoplasms metastasize via the lymphatic system, palpate the submandibular and regional lymph nodes for enlargement.

Diagnostic Evaluation

Blood Tests

- Many of these patients are older (>8 years of age), so perform a minimum database (complete blood count, serum biochemical profile, urinalysis) to look for systemic illnesses related to the tumor or concurrent metabolic disorders.

Imaging Studies

- Obtain three-view chest radiographs to identify metastatic disease to the lungs.
- Obtain skull radiographs under anesthesia to evaluate the extent of bony involvement into the maxilla or mandible. A skull series (lateral, ventral-dorsal, right and left oblique views) is required to fully evaluate the skull (see Chapter 4). Radiographic abnormalities include changes in cortical bone density, periosteal new bone formation, involvement of adjacent soft tissues, and loose teeth.
- Computed tomography (CT) scanning and magnetic resonance imaging (MRI) of the skull is very helpful in evaluating extent of tumor invasion and presurgi-

Table 99-1. SUMMARY OF COMMON ORAL CANCERS IN THE DOG AND CAT

	Feline	
	SCC	FSA
Frequency (%)	70	20
Age (yrs)	10	10
Sex predilection	M = F	M = F
Site predilection	Mandibular or maxillary bone, tongue	Gingiva
Lymph node metastasis	Common	Rare
Distant metastasis	Rare	Occasional
Radiation response	Poor	Fair
Surgery response	Fair	Fair
Prognosis	Poor	Fair

	Canine			
	SCC	FSA	MM	Epulis
Frequency (%)	20–30	10–20	30–40	5
Age (yrs)	10	7	12	9
Sex predilection	M = F	M > F	M > F	F > M
Site predilection	Rostral Mandible	Palate	Buccal Mucosa	Rostral Mandible
Lymph node metastasis	Occasional	Rare	Common	Never
Distant metastasis	Rare	Occasional	Common	Never
Radiation response	Good	Fair	Poor	Excellent
Surgery response	Good	Fair	Poor–fair	Excellent
Prognosis	Good	Fair	Poor	Excellent

FSA; fibrosarcoma; MM, malignant melanoma; SCC, squamous cell carcinoma.

cal planning. These imaging modalities are especially helpful in evaluating caudal maxillary tumors or tumors involving the orbit, zygoma, TMJ, or vertical ramus of the mandible.

Biopsy

- Perform an incisional biopsy before surgery to obtain a definitive diagnosis.

▼ ***Key Point*** Obtain a tissue biopsy of any suspicious oral lesions. Early detection is critical to successful treatment.

- Biopsy is very important in determining the treatment, as well as the long-term prognosis, for the pet. Many oral tumors do not exfoliate easily, so fine-needle aspiration is usually not helpful. A wedge biopsy for histopathologic examination is necessary for a definitive diagnosis.
- Obtain fine-needle aspirates for cytology or histopathologic evaluation via biopsy of all enlarged, submandibular, or pharyngeal lymph nodes to look for metastatic disease. Perform fine-needle aspiration even on normal-sized regional lymph nodes. In one study, 40% of dogs with oral melanoma had normal-sized lymph nodes and had evidence of metastasis to the lymph nodes on cytologic evaluation.

TUMOR TYPES

Benign Non-odontogenic Neoplasms

Epulis

Epulides are fibrous tumors originating from the periodontal ligament. They are rarely seen in the cat but are one of the most common oral tumors seen in the dog. There is no sex predisposition, and a familial predisposition has been noted in the boxer.

Three types of epulides are characterized, based on histopathologic evaluation:

- *Fibromatous epulis* is a benign, noninvasive growth in which the periodontal ligament stroma is the predominant cell type. These epulides are pedunculated and often multiple.
- *Ossifying epulides* have a similar biologic behavior to fibromatous epulides, but histopathologically they have an osteoid component. Malignant transformation to osteosarcoma has been reported.

- *Acanthomatous epulis* is the most aggressive of the epulides. This type of epulis is characterized by extensive bony invasion into the alveolar bone and is most often seen in the rostral mandible. Acanthomatous epulides can become quite large but do not metastasize. However, approximately 30% of acanthomatous epulides undergo malignant transformation.

Treatment and Prognosis

- Since epulides are local tumors, they can be treated with aggressive curettage of the alveolar socket (with fibromatous and ossifying epulides). However, a better outcome can be achieved with en bloc resection of the tumor and surrounding bone. En bloc resection is recommended with acanthomatous epulides due to their extensive bony involvement. Recurrence rate is high if the tumor is only debulked, and a complete resection is considered curative.
- Radiation therapy of epulides without surgery can be effective and is often curative. Large or incompletely excised epulides can be treated with surgery, followed by postoperative radiation therapy. Chemotherapy is generally not effective for epulides.

Other Benign Non-odontogenic Neoplasms

Other rarely seen, benign non-odontogenic neoplasms include fibroma, hemangioma, lipoma, chondroma, osteoma, and histiocytoma. These tumors look grossly similar and require biopsy for histopathologic evaluation.

Malignant Non-odontogenic Neoplasms

Malignant Melanoma

Malignant melanoma is characterized by local invasion and early metastasis. They can be darkly pigmented (melanotic) or non-pigmented (amelanotic). Oral melanomas are often ulcerated and necrotic, so clinical signs frequently seen are halitosis and oral bleeding. Dogs with more heavily pigmented oral mucosa, such as the chow, are predisposed to malignant melanoma. Malignant melanoma is found (in order of decreasing frequency) on the gingival, buccal and labial mucosa, hard palate, and tongue.

Treatment and Prognosis

- Treatment of choice is early, complete en bloc surgical resection. Tumor size is important, as melanomas less than $50\,mm^2$ are associated with a better outcome.
- High-dose, fractionated radiation therapy has shown moderate success in treatment. One study showed an increase in survival time with surgery and radiation therapy when compared with surgery alone.
- Chemotherapy has not been effective to date in treatment of melanomas.
- Newer therapies, such as immunotherapy, have shown some promise in treatment.

▼ ***Key Point*** Overall prognosis with oral melanomas is poor, with a <10% 1-year survival even with treatment.

Squamous Cell Carcinoma

SCC is the second most common oral tumor in dogs, but it is the most common oral tumor in cats. SCC is characterized by local tissue invasion and late metastasis. SCC often looks ulcerative and friable on oral examination.

Two types of SCC are seen: non-tonsillar and tonsillar SCC. They have very different biologic behavior. *Non-tonsillar SCC* is locally invasive and slow to metastasize. SCC often invades bone, causing bony lysis and loosening of teeth. *Tonsillar SCC* is biologically very aggressive and is characterized by early metastasis to regional lymph nodes and lungs.

Treatment and Prognosis

- Wide surgical resection is the treatment of choice, with or without radiation therapy.
- Radiation therapy can be used as an adjunct for local control, especially with large tumors.
- The best long-term success can be achieved using surgical resection followed by postoperative radiation therapy.
- Chemotherapeutic agents, such as cisplatin and piroxicam, have been added to treatment protocols with some success.
- Overall prognosis is guarded. Local recurrence is high when the tumor is marginally resected, and approximately 50% of patients die within 1 year.

Fibrosarcoma

- Fibrosarcoma is the third most common tumor behind malignant melanoma and SCC, and it is the second most common tumor in cats.
- Fibrosarcomas are firm, slow-growing tumors that are characterized by locally aggressive behavior and late metastasis.
- Fibrosarcomas are seen most commonly on the gingival margin of the maxilla, between the upper canine tooth and the fourth premolar.
- Due to extensive tissue invasion, local recurrence is common, especially in tumors that cross the midline of the hard palate or are caudally located.

Treatment and Prognosis

- Wide surgical resection is the treatment of choice.
- Adjunctive radiation therapy, chemotherapy, or immunotherapy can be used to increase long-term survival.

- Overall prognosis is very guarded, since local tissue recurrence and late metastases are common.
- The 1-year survival rate has been reported to be 20%.
- Recently, a histologically benign but biologically aggressive form of oral fibrosarcoma has been described in younger golden retrievers.

Other Malignant Non-odontogenic Neoplasms

Much less common tumors include osteosarcoma, adenocarcinoma, undifferentiated carcinoma, transmissible venereal tumor, mast cell tumor, hemangiosarcoma, and tonsillar lymphosarcoma.

Malignant Odontogenic Neoplasms

Ameloblastoma arises from the dental laminar epithelium. These relatively rare tumors are seen more commonly in younger dogs and are often associated with loose teeth. Ameloblastomas are most commonly seen at the gingival margin. Radiographically, ameloblastomas are seen as expansile, bony lesions.

Odontomas are rare tumors of dental origin and can invade all of the dental tissues (enamel, cementum, dentin, and pulp).

Treatment and Prognosis

- Wide surgical resection is the treatment of choice and can be curative.
- Local recurrence is very common with inadequate excision.
- Radiation therapy has been used with some success, but recurrence locally is common.

See Table 99-1 for descriptions of common malignant oral cancers of dogs and cats and their response to therapy.

SURGICAL PROCEDURES

Preoperative Considerations

- A thorough working knowledge of anatomy is crucial to ensure a successful outcome for the patients, as well as to minimize any complications such as blood loss. In most cases, these patients should be referred to a veterinary surgeon or dentist.
- The extent of surgical excision is determined by radiographs of the skull, CT imaging, or MRI. This ensures adequate resection, especially at the deep tissue margins.
- Maxillectomies are often associated with significant blood loss, especially when the tumor is located caudally or crosses the midline. Temporary, bilateral carotid artery occlusion has been used with some success to minimize blood loss. This procedure is usually not necessary. In addition, a source of blood replacement should be available if necessary.
- Administer preoperative analgesia, using a nonsteroidal anti-inflammatory agent and fentanyl patches, to minimize postoperative pain (see Chapter 6). Since fentanyl patches need approximately 16 to 24 hours to reach therapeutic levels, place them on the skin the night before surgery. See the "Drug Appendix" for dosage guidelines.
- Place a cuffed endotracheal tube orally in the patient at induction of anesthesia. Count and place surgical sponges in the pharynx to minimize aspiration of blood and fluids.
- Nerve blocks can be useful for regional anesthesia of the surgical site and are helpful in providing local pain control while minimizing the amount of perioperative analgesia. A 2% lidocaine or 0.5% bupivacaine (with or without epinephrine) solution can be used for nerve blockage (see Chapter 6).
- Administer a prophylactic antibiotic suitable for the oral cavity (first-generation cephalosporin or synthetic penicillin) at induction of anesthesia. Due to the extensive blood supply to the oral cavity, postoperative infection is very uncommon, so antibiotics only need to be continued for 24 hours. If there is deep-seeded bone infection, continue antibiotic therapy for at least 14 days.
- Sutures recommended for oral surgery include polydioxanone (PDS, Ethicon; Somerville, NJ), polyglactin 910 (Vicryl, Ethicon), polyglycolic acid (Dexon, Davis and Geck; Manati, Puerto Rico), and polyglyconate (Maxon, Davis and Geck). 3-0 and 4-0 sutures on swaged-on cutting needles are recommended for wound closure. Simple interrupted, vertical mattress, and cruciate mattress suture patterns are recommended.

Anatomy

- The masseter muscle lies on the lateral surface of the ramus with some fibers of the superficial layer projecting around the ventral and caudal borders of the mandible to insert on the ventromedial surface.
- The temporalis muscle inserts on the coronoid process of the mandible, with some fibers inserting further down on the ventral margin of the masseteric fossa.
- The lateral pterygoid muscle inserts on the medial surface of the mandibular condyle.
- The medial pterygoid muscle inserts on the medial and caudal surfaces of the angular process of the mandible.
- The inferior alveolar artery and vein enter the mandibular foramen, which is located on the medial side of the mandible, 1 to 1.5 cm rostral to the angle of the mandible. The artery exits at the mental foramen of the mandible.
- The blood supply to the maxilla is via the major and minor palatine arteries, which lie just deep to the mucosa of the hard palate, and the infraorbital artery,

which exits through the infraorbital foramen dorsal to the upper third premolar tooth. The infraorbital vein and nerve parallel this artery.

Objectives

- Completely resection the neoplasm.
- Preserve local blood supply.
- Handle tissue atraumatically.
- Minimize the use of electrocautery. Excessive use of electrocautery has been shown to delay incisional healing and increase the dehiscence rate.
- Suture lines should be supported by bone if possible.
- Double-layer mucosal closure is preferred to single-layer closure.

▼ ***Key Point*** Avoid suturing tissues under line tension in the oral cavity. Incisions under tension are much more likely to dehisce.

- Make mucosa flaps 2 to 4 mm larger than the oronasal defect.
- Large oronasal defects, caudal defects, and oronasal defects that cross the midline have a higher dehiscence rate. Therefore, a plan for complete mucosal closure should be in place before tumor removal.

Equipment

- Standard surgical instrument pack and suture
- Oral speculum
- Electrocautery and suction
- Oscillating bone saw and osteotome and mallet
- Bone wax

Maxillectomy

Place the patient in dorsal recumbency. The mouth can be held open with an oral speculum, or the mandible can be held open with tapes attached to IV stands placed on each side of the table. Tie the endotracheal tube to the mandible.

Unilateral Premaxillectomy

Unilateral premaxillectomy is indicated for lesions that are located rostral to the second premolar and do not cross the midline.

Technique

1. Incise the labial and gingival mucosa rostral and lateral to the tumor at least 1 cm from the tumor margins. Control bleeding using either direct pressure or electrocautery. The hard palate tends to bleed profusely; use either ligation or electrocautery.
2. Cut the underlying bone with an oscillating bone saw or mallet and osteotome. Be sure to follow the mucosal incision lines.
3. Remove the incised segment of bone and tumor en bloc. Ligate or cauterize branches of the major palatine artery. After bone and tumor removal, copiously lavage the surgical site with saline.
4. Reconstruct the oronasal defect created by en bloc resection with a gingival mucosal-submucosal flap. Design the flap to allow coverage of the defect without excessive tension. Include as much mucosa, submucosa, and subcutaneous tissue as possible. Careful tissue handling is essential to preserve blood supply.
5. Suture the flap using either a one- or a two-layer closure. In the two-layer closure, suture the labial submucosa to holes predrilled into the bony hard palate. The second layer consists of simple interrupted sutures that appose the palatal mucosa to the labial mucosa. The palatal mucosa can be undermined help with mucosal apposition.
6. In most cases, a one-layer closure of palatal mucosa to labial mucosa is performed. If excessive tension is encountered, undermine the flap further, and use a vertical mattress pattern for mucosal apposition.

Bilateral Premaxillectomy

Bilateral premaxillectomy is indicated for tumors that are rostral to the second premolar and cross the midline.

Technique

1. This procedure is essentially the same as for the unilateral premaxillectomy, except that the entire rostral bony floor of the nasal cavity is removed.
2. Closure is the same as for the unilateral procedure. Undermine half of the flap from each side of the premaxillectomy defect. Suture the caudal half of each flap to the palate mucosa to the midline. Suture the rostral halves together, achieving a T-shaped closure. Use a simple interrupted or vertical mattress pattern for mucosal apposition.
3. A more secure technique for closure is the double-flap technique, in which a tissue flap is created from each side of the palatal defect. Rotate the first flap to cover the defect so that the labial mucosa is facing the nasal cavity. Rotate the second flap from the opposite side of the defect over the first flap and suture it into place (Fig. 99-1).

Hemimaxillectomy

This is the most aggressive of the maxillectomy procedures, and it leaves the largest defect to close. Hemimaxillectomy is indicated for tumors that involve the majority of the hard palate and do not cross the midline.

Any portion of the maxilla can be removed unilaterally, up to the entire hemimaxilla, and still can result in normal function and acceptable cosmesis. Caudal maxillary resections can be combined with resections of the inferior orbit, zygoma, or vertical ramus of the mandible, depending on the degree of tissue involvement.

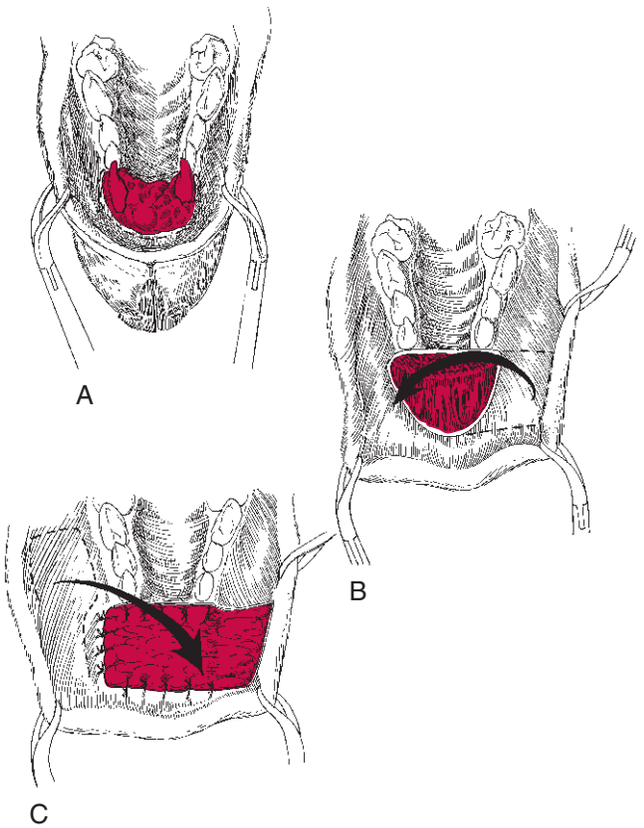

Figure 99-1. Bilateral premaxillectomy, double-flap technique. *A,* Site of incision. *B,* First flap parallel to the excised dental arch. This flap is flipped over (reversed) so that the labial mucosa is on the nasal cavity side of the defect. *C,* Second flap from the opposite side of the pre-maxilla.

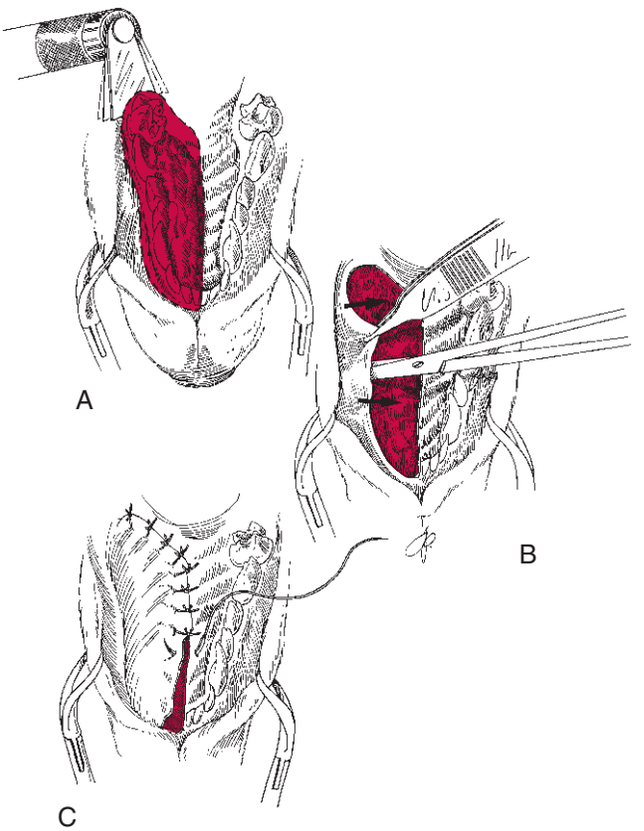

Figure 99-2. Hemimaxillectomy. Incise *(A)* around lesion, then remove the mass by ostectomy. Create *(B)* and close *(C)* the labial flap.

Technique

1. Place the patient in dorsal recumbency. Begin the mucosal incision rostrally at the labial-gingival junction and continue lateral and caudal as needed to achieve at least 1 cm of normal tissue around the tumor.
2. Use a periosteal elevator to expose the underlying bone. Osteotomize the underlying bone using either an oscillating bone saw or a mallet and osteotome (Fig. 99-2*A*).
3. Bleeding can be profuse, especially when making the caudal osteotomy. Remove the bone en bloc, and identify and ligate branches of the maxillary artery. Control bleeding from blood vessels with ligation, electrocautery, and pressure. Control bleeding from nasal turbinates with hemostatic sponges (Gelfoam).
4. Create a lip margin-based flap by undermining the labial mucosa and submucosa from the maxillectomy site toward the lip margin. Undermine the flap only enough to cover the defect without excessive tissue tension. Suture the labial mucosa-submucosal flap to the elevated edge of the hard palate mucoperiosteum with simple interrupted or vertical mattress sutures (Fig. 99-2*B,C*).

Mandibulectomy

Place the animal in lateral recumbency with the affected mandible placed dorsally. Clip the dorsal and ventral aspect of the muzzle, and flush the oral cavity with either dilute chlorhexidine or povidone-iodine solution. Tie an endotracheal tube to the maxilla, and place an oral speculum on the recumbent canine teeth.

Unilateral Rostral Mandibulectomy

Unilateral rostral mandibulectomy is indicated for tumors that are rostral to the second premolar teeth and do not cross the midline. Bilateral rostral mandibulectomy is indicated for tumors that cross the midline.

Technique

1. The labial mucosa in incised at least 1 cm outside the visible tumor margin. The dissection is continued around the body of the mandible until the symphysis and the caudal extent of the proposed ostectomy site are exposed.
2. Take care on the medial surface, making sure to identify and preserve the mandibular and sublingual salivary ducts. The ducts are located on the sublin-

gual caruncle. If the sublingual and mandibular ducts cannot be spared during the excision, ligate them.
3. After the symphysis is exposed, split the fibrous joint with a mallet and osteotome, which will separate the two hemimandibles.
4. Use an oscillating saw or Gigli wire to make the caudal osteotomy. Because the mandible is dense, do not perform the osteotomy with a mallet and osteotome.
5. Ligate or cauterize the inferior alveolar artery, and fill the marrow cavity with bone wax.
6. Extract tooth roots that have been traumatized during the osteotomy.
7. No attempt is made to fixate the two hemimandibles together.
8. Close the sublingual mucosa to labial mucosa using a one-layer, simple continuous or vertical mattress pattern using 3-0 or 4-0 absorbable suture (Fig. 99-3).

Bilateral Rostral Mandibulectomy

Bilateral rostral mandibulectomy is indicated for tumors rostral to the second premolar that cross the midline.

Technique

1. Dorsal recumbency allows the best exposure of the surgical site.
2. Perform the procedure similarly to unilateral rostral mandibulectomy.
3. Mandibular resection can be performed to the level of the first molar teeth without adversely affecting mandible function and prehension. However, warn the owner that the tongue will hang out past the lower lip after surgery.
4. Redundant skin may need to be removed before it is sutured to sublingual mucosa. A V-shaped wedge of skin can be removed from the rostral aspect of the lip. Suture the resultant skin edges in a one-layer, simple interrupted pattern. Some surgeons place tension-relieving stent sutures from holes made in the distal aspect of the mandibles to the outside surface of the lower lip. Polypropylene buttons or rubber tubing can be used to prevent these sutures from causing pressure necrosis of the skin.

Hemimandibulectomy

The most extensive of the mandibulectomy procedures, this involves total or subtotal removal of one hemimandible. This procedure is indicated for tumors that involve most of the mandible.

Technique

1. Place the patient in lateral recumbency. Incise the commissure of the lip full thickness to the rostral edge of the vertical ramus. Incise through the subcutaneous tissues to the level of the temporomandibular joint.
2. Incise the labial and buccal mucosa as needed to ensure a 1-cm tumor-free margin. The rostral aspect of the incision is to the mandibular symphysis and extends caudally to the angle of the mandible.
3. Dissect around the horizontal ramus of the mandible. Once the horizontal body is free of soft tissues, separate the mandibular symphysis using a mallet and osteotomy. Rotate the mandible laterally, allowing easier caudal dissection. Place bone-holding forceps (e.g., Kern) on the mandible to aid retraction.
4. If the tumor does not involve the caudal tissues, resect the body of the mandible at the rostral edge of the masseter muscle, leaving the vertical ramus

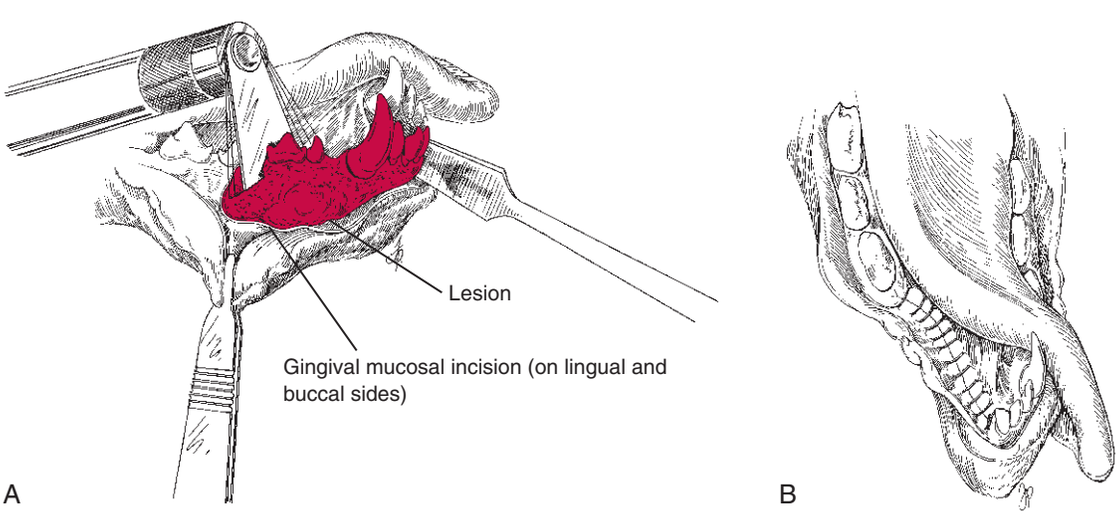

Figure 99-3. Unilateral premandibulectomy. *A,* Incise the gingival around the lesion, keeping at least 1 cm of normal tissue around it. Separate the mandibular symphysis and continue the original incision through the bone. *B,* Cover the bone and close the incision.

and the temporomandibular joint intact. Cut the bone with an oscillating saw. This procedure is technically easier than total hemimandibulectomy.

5. If total hemimandibulectomy is performed, sharply incise the masseter, digastricus, and pterygoideus muscles from the mandible. Avoid accidentally cutting the mandibular alveolar artery before identifying and ligating the vessel. This vessel passes across the lateral surface of the medial pterygoideus muscle before entering the mandibular foramen. Lateral retraction of the hemimandible helps expose this vessel for ligation.
6. Incise the capsule of the temporomandibular joint, and luxate the joint. Incise the temporalis muscle as it inserts on the coronoid process of the mandible. Incise any loose fascial attachments to complete resection.
7. Perform three-layer closure to minimize dead space. The first layer apposes remaining muscle tissue, followed by a submucosal closure. The mucosa is closed in a simple interrupted or vertical mattress pattern using 3-0 or 4-0 suture.
8. Hemimandibulectomy results in loss of lateral tongue support. Advance the commissure of the lip to provide a pouch for the tongue and to provide lateral support. Incise upper and lower lip full thickness to the level of the first premolar tooth. Perform three-layer suture closure of mucosa, subcutaneous tissues, and skin.

Postoperative Care

- Continue postoperative analgesia for pain control.
- Continue antibiotics IV for 24 hours postoperatively.
- Place an Elizabethan collar to prevent self-mutilation of the incisions by the patient.
- Feed soft food or gruel for the first month. Gently flush the oral cavity with water or saline after eating. Most dogs eat readily within 48 hours, but cats are often reluctant to eat after maxillectomy or mandibulectomy. If postoperative feeding is a concern, consider placing an esophagostomy tube for enteral nutrition.
- Chemotherapy or radiation therapy can be started if indicated 3 weeks after the surgery.
- Reevaluate the patient every 3 months for the first year. Perform an oral examination to evaluate for tumor recurrence. Palpate cervical lymph nodes for lymph node enlargement, and evaluate thoracic radiographs for metastasis.

Complications

- Transient facial edema and ranula formation after mandibulectomy usually resolve in 2 to 3 weeks. Drooling may occur for several days and improves in a few weeks.
- Nasal discharge, facial swelling, noisy respirations, and inappetence often occur after maxillectomy but usually improve in 5 to 7 days.
- Due to the vascular supply of the oral cavity, infections are relatively rare.
- Dehiscence of the suture line and oronasal fistula is the most common complication seen. Nasal discharge is often seen when this occurs. Minor dehiscences can be managed conservatively and often heal by second intension. For complete dehiscence or minor dehiscence that will not heal, resuture the mucosal edges. Most dehiscences are related to excessive flap tension. Minimize recurrence of dehiscence by elevating the labial and palatal mucosal-submucosal flaps and using a tension-relieving suture pattern such as a vertical mattress pattern.
- Postoperative cosmesis generally is good, even with major resections of the maxilla and mandible. Protrusion of the tongue often is seen with bilateral rostral mandibulectomy.
- Removal of the one hemimandible causes some medial drift of the other hemimandible due to loss of bony support and normal muscular contraction. Occasionally, it is necessary to the lower the crown height of the lower canine tooth to prevent chronic erosion and ulceration of the hard palate mucosa due to malocclusion (see Chapter 64).

▼ ***Key Point*** Owner satisfaction is high after mandibulectomy or maxillectomy. One study found that the percentage of satisfied owners is directly proportional to the increase in pet life span. Although difficulty in eating was noted in 44% of dogs, pain was perceived to be reduced by the surgery for most animals. All owners found the cosmetic appearance of their dogs acceptable after facial hair regrew.

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Chapter

100 Fractures and Dislocations of the Spine

Matthew Palmisano

Congenital and acquired diseases of the spine are seen frequently in small animal practice. Early diagnosis and effective treatment are crucial for success in preservation or return of normal neurologic function in these patients.

ATLANTOAXIAL INSTABILITY

Anatomy

- The atlantoaxial joint is a pivot joint that allows the head and atlas to rotate around a longitudinal axis.
- The dens is a peg-like eminence along the ventral surface of C2 (axis) that projects rostrally to lie on the floor of C1 (atlas) in the spinal canal.
- The dens is secured to the ventral arch of the atlas by the transverse atlantal ligament, to the occipital condyles by the paired alar ligaments, and to the ventral aspect of the foramen magnum by the apical ligament. The dorsal arches of the atlas and axis are stabilized by the dorsal atlantoaxial ligament.

Etiology

Atlantoaxial instability can arise from either congenital or acquired etiologies.

Congenital Causes

Congenital causes are by far the most common presentation and are most often seen in the young, small, and toy-breed patient. Congenital instability arises from malformation (hypoplasia or aplasia) of the dens, nonunion of the dens with the body of the axis, or lack of ligamentous support, such as congenital absence of the transverse or atlantoaxial ligaments.

Acquired Causes

Acquired causes of atlantoaxial instability are usually the result of traumatic injury. Fracture of the dens and cranial body of the second cervical vertebra (C2) or rupture of the supporting ligaments is usually seen with traumatic injury. These injuries are the result of falls or automobile accidents that cause hyperflexion of the cranial cervical spine. In contrast to congenital atlantoaxial instabilities, acquired instabilities can occur in any age and any size dog and cat.

Clinical Signs

- Clinical signs vary from cervical pain alone to tetra-ataxia or tetraparesis and tetraplegia. The severity of clinical signs is usually dependent on the degree of atlantoaxial subluxation.
- The severity of clinical signs is also dependent on whether the patient has an intact dens. Luxation with an intact dens and luxation resulting from congenital dens malformation allows the dens to dorsally deviate into the spinal cord (Fig. 100-1). This will cause more spinal cord compression than in the patient with congenital atlantoaxial instability secondary to aplasia of the dens.
- In the most severe cases of spinal cord compression, respiratory arrest and death can occur.

▼ ***Key Point*** Use extreme care when performing a neurologic evaluation in these patients. Avoid flexion of the neck.

- Consider atlantoaxial instability as a diagnosis in any young patient with cervical pain and varying degrees of tetra-ataxia and paresis.

Diagnosis

- The diagnosis of atlantoaxial instability is usually made with radiography. Carefully flexed lateral radiographs of the atlantoaxial space will revealed a widened space between the dorsal arch of C1 and the dorsal spine of C2. Ventrodorsal and open-mouthed views may best outline the dens.
- Computed tomography (CT) imaging and magnetic resonance imaging (MRI) are usually not required for diagnosis. Myelography is contraindicated due to the degree of flexion required for cisternal needle placement and dorsal deviation of the spinal cord in the canal.

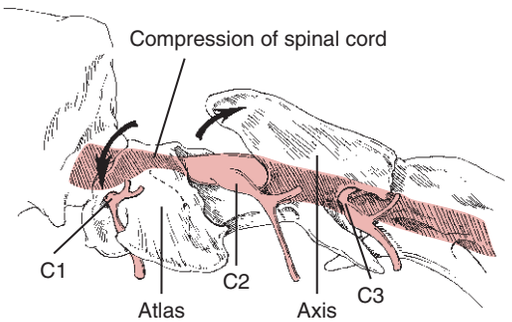

Figure 100-1. Dorsal displacement of the axis.

Surgical Procedures

Preoperative Considerations

- Be careful when manipulating the neck while under anesthesia. Do not flex the spine, which would exacerbate cord compression and cause respiratory arrest and death.
- Ventilator therapy is helpful in these patients, especially when there is concern about respiratory impairment.
- The surgical techniques are technically demanding, and intense perioperative care is crucial to a successful outcome. Therefore, refer these cases to a surgical specialist.

Objectives

- Remove the fractured or ununited dens
- Stabilize the C1 to C2 articulation
- Prevent spinal cord injury

Equipment

- Standard orthopedic and neurologic surgical pack
- Self-retaining retractors
- Reduction forceps
- High-speed air drill
- Kirschner wires and small Steinman pins
- Polymethyl methacrylate (PMMA)

Technique

Dorsal Approach (Overview)

- Dorsal approaches involve fixation of the dorsal spine of the axis to the dorsal arch of the axis using heavy-gauge suture material, orthopedic wire, or nuchal ligament grafts.
- Complications with the dorsal approach include breakage of the implant material and fracture of the dorsal arch of the atlas or dorsal spine of the axis. This can lead to acute reluxation of the atlantoaxial joint, which often causes acute neurologic decline.
- Although technically more demanding, most surgeons prefer ventral fixation of the atlantoaxial joint due to a higher success rate.

Ventral Approach

1. Place the patient in dorsal recumbency with a rolled towel positioned under the neck and the chin and chest gently taped to the table.
2. Make a skin incision on the ventral cervical midline extending from the laryngeal cartilages to the manubrium.
3. Separate the paired sternohyoideus muscles on the midline.
4. Bluntly dissect and lateralize the trachea, esophagus, and carotid sheath. Access to the ventral aspect of the atlantoaxial joint is made easier with myotomy of one of the sternothyroid muscles. Tag the cut muscle ends with suture to allow easier identification upon closure.
5. Separate and retract the paired hypaxial muscles ventral to the atlantoaxial joint using self-retaining retractors.
6. Identify and open the joint capsule of the atlantoaxial joint using a #11 scalpel blade.
7. The joint may be reduced into normal position using two-point reduction forceps placed on the body of the axis.
8. When the dens is either fractured or ununited, remove it through the atlantoaxial articulation. If necessary, remove a small window of bone from the ventral arch of the atlas to assist in dens removal.
9. To perform arthrodesis of C1 to C2, remove the articular cartilage using a high-speed air drill or bone curettes, then place bone graft obtained from the greater trochanter of the humerus.
10. Several modifications of ventral fixation using K-wires, screws, and PMMA bone cement have been described. The original description of ventral stabilization involved divergent Steinmann pins, K-wires, or cortical screws placed across the atlantoaxial joint. Recent studies suggest that strongest fixation involves placement of three pairs of pins, with one set going across the atlantoaxial joint and the other two pairs fixed to C1 and C2, respectively.
11. If only two pins are going to be used for fixation, drive them from the center of the axis across the atlantoaxial joint and seat them in the atlas just medial to the alar notch. This ensures that the pins do not enter the spinal canal (Fig. 100-2).
12. For additional stability, place the second set of pins into the atlas. Direct the pins perpendicular to the long axis of the spine from ventral to dorsal into each of the pedicles of the atlas. Leave the pins long and notch them using a pin cutter. This allows better bonding with the PMMA.
13. Place the third pair of pins into the caudal body of C2. Drive the pins from the center of the body obliquely to the origin of the transverse process, taking care not to enter the spinal canal. Leave these pins long and notch them.

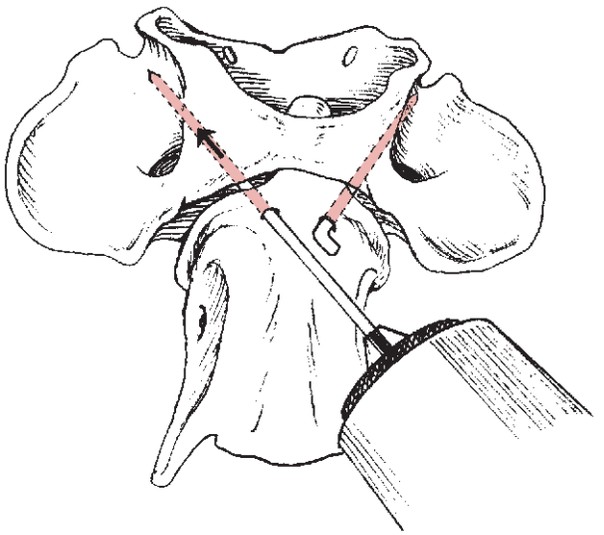

Figure 100-2. Divergent atlantoaxial pinning. The pins are kept out of the spinal canal by aiming for the medial aspect of the alar notch.

14. Place a small mass of PMMA ventrally to incorporate each pin, and apply cool saline flush during polymerization of the cement to dissipate heat and minimize tissue damage.
15. Close the sternothyroideus muscle if a myotomy was performed. The hypaxial muscles often cannot be reapposed due to the mass of cement.
16. Close muscle, subcutaneous, and skin closure routinely.

Postoperative Care and Complications

- Administer postoperative analgesics.
  - Place a Fentanyl patch at least 12 hours preoperatively, and give nonsteroidal anti-inflammatory drugs (NSAIDs) unless they are contraindicated (see Chapter 6).
- Give first-generation cephalosporin or potentiated penicillin PO for the first 5 days.
- Place an Elizabethan collar for the first 2 weeks postoperatively.
- Restrict exercise for 4 to 6 weeks. Avoid any high-impact activity. If necessary, confine the animal to a cage.
- Obtain radiographs monthly until a complete bony fusion of the atlantoaxial joint is seen. Radiographic fusion is usually seen by 8 to 12 weeks.
- Complications include infection of the PMMA, dysphagia, and laryngeal paralysis, which are usually related to technical issues with soft tissue handling. The most serious complication is implant failure, with recurrence or worsening of neurologic signs.

CAUDAL CERVICAL SPONDYLOMYELOPATHY

Caudal cervical spondylomyelopathy (Wobbler's syndrome) is a disease that encompasses several syndromes based on the location and nature of the compressive lesion. Understanding the pathogenesis of this complex disease is important when choosing the type of surgical treatment.

▼ ***Key Point*** It is crucial that the correct surgical procedure be picked based on the specific type of spinal cord compression affecting that individual dog.

For example, distraction and fusion techniques are most appropriate for dynamic disc lesions and dorsal laminectomy for articular process disease. In addition, early diagnosis and treatment of the disease is important to ensure the best outcome.

Anatomy

- Relevant anatomic structures in the dorsal compartment of the cervical spine that play a role in caudal cervical spondylomyelopathy include the dorsal vertebral lamina, the articular facets and joint capsule, and the ligamentum flavum.
- In the ventral compartment of the cervical spine, the vertebral bodies, the dorsal fibers of the annulus fibrosus of the intervertebral disc, and the dorsal longitudinal ligament are significant.

Etiology

- Two distinct populations of patients are seen, and their etiologies are somewhat different. Of dogs with Wobbler's disease, 10% to 15% are young, adolescent Great Danes with osseous malformations of the cervical spine.
- The remainder are middle-aged to older patients with acquired disease that is usually secondary to cervical vertebral instability. Doberman pinschers are the largest percentage of this group of dogs (approximately 80%), although dalmatians and Labrador retrievers are also predisposed.
- No sex predilection is seen.

Pathologic Changes Associated with Wobbler's Syndrome

Congenital Osseous Malformation

- This is seen in young Great Danes, with clinical signs occurring in the first or second year of life.
- The disease is characterized by malformation or malarticulation of the articular facets and vertebral bodies, causing dorsal and lateral stenosis of the canal.

- Congenital osseous malformation most commonly affects the C3 to C7 vertebral bodies.
- Vertebral canal stenosis is seen and usually worsens as the puppy grows.
- Proposed etiologies for this disorder include heredity, nutritional imbalances, and trauma. Osteochondrosis may also have a role in the pathology.

Vertebral Tipping

- This is usually seen in the middle-aged to older patient.
- There is a malposition of the vertebral body caudal to the affected intervertebral disc. The cranial aspect of the affected vertebra dorsally displaces into the spinal canal, causing ventral compression.
- This change is seen with chronic cervical vertebral instability and degenerative disc disease.
- The C5 to C6 and C6 to C7 intervertebral disc spaces are most commonly affected. The lesion can be either dynamic or static.

Chronic Degenerative Disc Disease and Cervical Vertebral Instability

- Most of these patients are middle-aged to older Doberman pinschers.
- The compression is caused by concurrent dorsal annulus and dorsal longitudinal ligament hypertrophy.
- The caudal cervical intervertebral disc spaces are most commonly involved.
- The compressive lesion is usually dynamic (i.e., the degree of compression changes).

Ligamentum Flavum Hypertrophy

- This disease causes dynamic, dorsal spinal canal compression. This lesion is often associated with vertebral arch abnormalities.
- The caudal cervical vertebra (C4–C7) is most commonly affected.
- The compressive lesion is often dynamic but can be static.

Hourglass Compression

- This combination of pathologies is associated with dorsal, ventral, and lateral compression. The young Great Dane is most commonly affected.
- Compression is caused by hypertrophy of the dorsal annulus fibrosis and dorsal longitudinal ligament ventrally, hypertrophy of the ligamentum flavum dorsally, and malformation or degenerative joint disease laterally.
- The lesion may occur at any level of the cervical spine and is often dynamic.

Clinical Signs

- Most patients have a chronic, progressive history of neck pain, hypermetria, tetra-ataxia, and tetraparesis.
- These dogs have a low-neck carriage due to the dynamic nature of the disease, and the compression worsens upon neck extension.
- Often, the clinical course is waxing and waning. Occasionally, chronically affected dogs will have an acute deterioration.
- Wide hind-limb stance with forelimb hypermetria and varying degrees of ataxia is often seen. Ataxia is often worse in the rear limbs. This is due to the greater degree of compression by the disc on the long motor tracts to the pelvic limbs, which are peripherally located within the spinal canal.
  - Proprioceptive deficits are seen, with paraparesis progressing to tetraparesis.
  - Evidence of lower motor neuron disease in the thoracic limbs is usually restricted to muscle atrophy of the spinatus muscles of the shoulder.

Diagnosis

Differential diagnoses include degenerative spinal cord disease, ischemic myelopathy, discospondylitis, congenital spinal cord disease, inflammatory central nervous system disease, spinal neoplasia, brachial plexus tumor, subarachnoid cysts, and trauma (see Chapter 128). Ischemic myelopathy (also called fibrocartilaginous embolization) can usually be ruled out because this process is not associated with cervical pain (see Chapter 128).

Blood Tests

Since many of these patients are older, perform a complete blood count, serum biochemical profile, and urinalysis to rule out other systemic illness. Submit a thyroid panel to rule out hypothyroidism. Studies have shown that neuronal regeneration is dependent on adequate levels of thyroid hormone, so postoperative recovery may be slowed in the undiagnosed hypothyroid patient.

Diagnostic Imaging

- Obtain thoracic radiographs to rule out metastatic disease and evaluate cardiac changes.
- Radiographs of the cervical spine in the non-sedated or anesthetized patient are usually not helpful, unless overt bony pathology (i.e., bony neoplasia or vertebral tipping) is present.

Myelography

- Cisternal myelography is helpful in identifying the site of compression (see Chapter 4). Perform a cisternal spinal tap, and obtain cerebrospinal fluid for analysis (see Chapter 125). Inject 0.33 ml/kg of iodinated contrast material into the subarachnoid space. After injection, obtain lateral and ventrodorsal projections of the cervical spine. Traction views of the

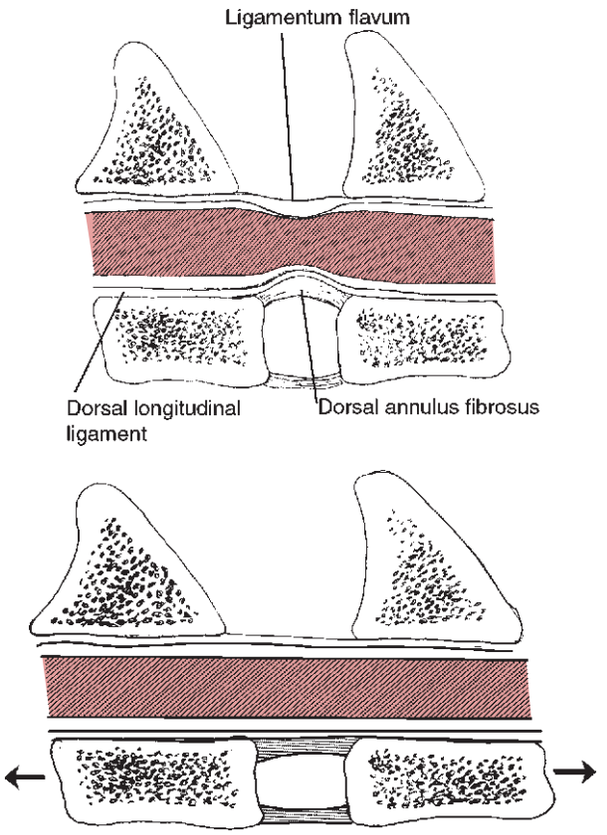

Figure 100-3. Dynamic compressive lesion. Spinal cord compression caused by hypertrophied ligamentum flavum, dorsal longitudinal ligament, and dorsal annulus fibrosus *(top);* alleviation of the compression by spinal traction *(bottom).*

spine are helpful in differentiating dynamic from static spinal cord lesions (see Chapter 4).

- If there is a reduction of spinal cord compression caused by redundant annulus fibrosis or ligamentous tissue during traction of the spine, the lesion is termed *dynamic* (Fig. 100-3). In contrast, herniation of the nucleus pulposus is not significantly improved by traction and is termed *static.* Differentiating between dynamic and static compression is important when deciding which surgical procedure to use.
- Avoid extended stress views of the spine because of increased compression of the spinal cord and the possibility of worsening clinical signs.

Computed Tomography and Magnetic Resonance Imaging

- A CT scan of the cervical spine is generally not rewarding in evaluating soft tissue changes to the cervical spine, but it may be helpful in identifying dorsal arch abnormalities and osseous malformations in the young Great Dane. A CT scan after a myelogram (CT myelography) may increase the diagnostic accuracy of CT.
- MRI is the diagnostic gold standard for imaging of the spine (see Chapter 4). MRI gives the greatest detail of soft tissue structures, including nerve roots and the intervertebral disc. In addition, signal changes within the spinal cord parenchyma may suggest chronic demyelination of the spinal cord (spinal cord atrophy), which will warrant a more guarded prognosis.

Preoperative Considerations

- Choose the most appropriate surgical procedure indicated by the nature and location of the compression. Table 100-1 provides guidelines for surgical decision making.
- The three primary decompressive surgeries used are the ventral decompression using a ventral slot technique, ventral distraction and fusion using a PMMA plug, and dorsal decompression using a dorsal laminectomy.
- These surgical procedures require clinical experience and appropriate instrumentation. Consider referral of these cases to a surgical specialist.

Surgical Procedures

Objectives

- See Table 100-1
- Ventral slot
  - Remove extruded disc material
  - Minimize surgical trauma to the spinal cord

Table 100-1. SURGICAL DECISION MAKING FOR CAUDAL CERVICAL SPONDYLOMYELOPATHY

Compression	Number of Spaces	Dynamic/Static	Surgical Procedure
Dorsal	One	Static	Dorsal laminectomy
Dorsal	Multiple	Static	Dorsal laminectomy
Dorsal	One	Dynamic	Distraction and fusion
Ventral	One	Static	Ventral slot
Ventral	One	Dynamic	Distraction and fusion
Ventral	Two	Dynamic	Distraction and fusion
Ventral	Multiple	Dynamic or static	Dorsal laminectomy

- Ventral distraction and fusion
  - Treat spinal cord compression by distracting and fusing the affected vertebral bodies
  - Minimize surgical trauma to the spinal cord
- Dorsal laminectomy
  - Decompress the spinal cord by removing the dorsal lamina of the appropriate vertebrae
  - Minimize surgical trauma to the spinal cord

Equipment

- Same as for atlantoaxial instability

Techniques

Ventral Slot

1. Place the patient in dorsal recumbency, with the front limbs tied caudally and the neck slightly hyperextended using a rolled towel.
2. Incise the skin from the laryngeal cartilages to the manubrium.
3. Separate the paired sternohyoideus muscles on the midline, and bluntly and laterally retract the trachea, esophagus, and neurovascular structures using Gelpi self-retaining retractors.
4. Elevate the longus colli muscles from the ventral aspect of the involved intervertebral disc space.
5. Landmarks on the cervical spine include a sharp ventral tubercle at C1 that marks the C1 to C2 intervertebral space cranially and the large, ventrally directed transverse processes at C6 caudally. The correct intervertebral disc space can be easily located using these two landmarks.
6. Make a small fenestration at the ventral annulus of the involved disc space. Perform the ventral slot in the bone using a high-speed surgical drill. Make an oval or rectangular slot, with the width of the slot being no greater than 50% of the diameter of the vertebral body. This minimizes the risk of postoperative subluxation of the slot site.
7. Visually determine the depth of the slot by looking for color change in the bone, going from the white ventral cortex of the vertebra to the purple color of the cancellous bone and finally white again as the dorsal cortex of the vertebra is approached. Take care at this point to avoid inadvertent entry into the spinal canal.
8. Control bleeding from the cancellous bone with bone wax.
9. Remove the dorsal part of the annulus fibrosus with a blunt tartar scraper or #11 blade. Avoid the venous sinuses to prevent excessive bleeding.
10. Any extruded or compressive disc material can now be removed from the spinal canal. A complete decompression is achieved when the dura (which is a light blue-gray) is clearly visible along the spinal canal floor. With caudal cervical spondylomyelopathy, it is uncommon to identify an obvious mass of herniated disc material as seen with the typical type I disc extrusions in the dachshund. Rather, the compression often appears to be caused by fibers of the annulus fibrosus infiltrated by degenerate nuclear material.
11. Close the longus colli and sternohyoideus muscles using an absorbable suture material in a simple interrupted or continuous pattern. Subcutaneous and dermal closure is routine.

Ventral Distraction and Fusion

Numerous techniques have been described for ventral distraction and fusion for dynamic disc lesions. A ventral distraction and fusion technique using an interbody PMMA plug is technically easier to perform that some of the other procedures, while providing consistently good to excellent results. In addition, there are fewer complications with this procedure when two concurrent spaces need to be distracted and fused at the same time.

1. Patient positioning and approach to the cervical spine are described above for the ventral slot technique. The only difference here is that the surgical prep and draping should be wider to include one or both greater tubercles of the humerus for procurement of bone graft.
2. After identification of the involved disc space, fenestrate the ventral annulus fibrosus and remove all of the nucleus pulposus using hemostats or a small rongeur.
3. Temporarily distract the vertebrae using Gelpi retractors that have been modified by blunting of the tips. Make two small slots in the ventral aspect of the vertebral bodies cranial and caudal to the involved disc that are just big enough to fit the tips of the retractors. Place the retractors in the slots, and perform the distraction.
4. Make two small holes in the cranial and caudal vertebral endplates using the surgical drill. This allows inflow of the bone cement for a more stable fixation.
5. Place mixed PMMA into the intervertebral disc space while still in the liquid phase. The PMMA creates an exothermic reaction when it cures; copiously lavage the surgical site with saline to prevent thermal damage to the surrounding tissues.
6. Once the cement has hardened, pack cancellous bone graft taken from the greater tubercle ventrally into the site (Fig. 100-4).
7. Closure is as described above for the ventral slot technique.

Dorsal Laminectomy

Dorsal laminectomy is indicated for dorsal bony or static soft tissue lesions of the spinal canal. In addition, dorsal laminectomy may be indicated for dogs with greater than two ventral compressive lesions. In these dogs, ventral techniques are less effective and have a higher complication rate when more than two spaces are involved.

1. Place the patient in ventral recumbency with the front limbs tied forward. In some cases of caudal cer-

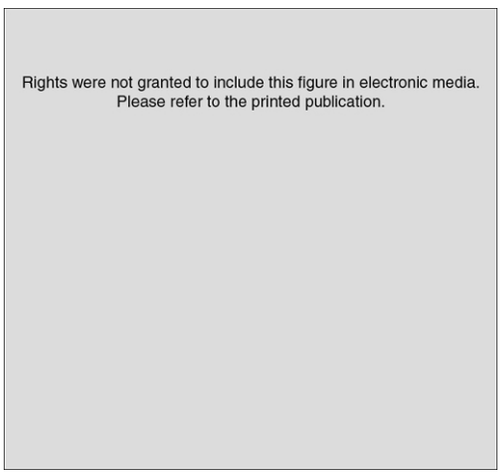

Figure 100-4. Insertion of polymethylmethacrylate plug (PMP) to maintain distraction. CG, cancellous bone graft; DAF, dorsal annulus fibrosus. (From Dixon BC, tomlinson JL, Kraus KH: Modified distraction-stabilization technique using an interbody polymethylmethacrylate plug in dogs with caudal cervical spondylomyelopathy. J Am Vet Med Assoc 208:61, 1996.)

vical vertebral involvement, the legs are crossed under the body, which will separate the spinal blades and allow easier dissection.

2. Incise the skin from the caudal aspect of the dorsal spine of C2 to T3.
3. Incise the muscles and aponeuroses along the midline until the nuchal ligament is identified. The nuchal ligament originates at the large dorsal process of C2 and inserts to the prominent dorsal spinous process of T1, continuing caudally with the supraspinous ligament. The ligament can be retracted laterally, divided on midline, or sectioned to gain exposure. If sectioned, the ligament will need to be repaired upon closure.
4. Separate the muscles from the spinous processes and lamina of the vertebra. Place two pairs of Gelpi self-retaining retractors to expose the laminae.
5. Remove the involved spinous processes using rongeur. Remove the fascia associated with the ligamentum flavum using a #11 blade. Take care to avoid trauma to the spinal cord, since it is unprotected under the larger interarcuate spaces.
6. Perform the laminectomy over the involved spaces using a bur, with close attention paid to the layers of bone as they are encountered.
7. The lateral limits of the laminectomy include the articular facets, but the laminectomy may be continued laterally to remove proliferative articular processes or to gain access to the nerve roots. Take care when dissecting lateral and ventral to the articular facets; inadvertent injury to the vertebral artery can result in severe hemorrhage.
8. Close the muscle in layers using an absorbable suture material. Repair the nuchal ligament if necessary. Close subcutaneous tissues and skin routinely.

Postoperative Care and Complications

- Pain management includes a transdermal Fentanyl patch (placed 12 hours preoperatively) plus NSAID therapy (see Chapter 6).
- Administer first-generation cephalosporin or potentiated penicillin PO for the first 5 days postoperatively.
- Use nursing care as needed for recumbent animals. Maintain clean, padded bedding to prevent decubital ulcers.
- Restrict activity and avoid all high-impact activity for 3 to 6 months postoperatively. Use a harness for the dog instead of a collar.
- With vertebral distraction and fusion, obtain radiographs monthly until a complete bony fusion of the atlantoaxial joint is seen radiographically. A radiographic fusion is usually seen by 8 to 12 weeks.
- Overall success with surgical management of caudal cervical spondylomyelopathy is an approximately 80% return to normal or near-normal neurologic function. However, approximately 30% of these patients will suffer a recurrence of neurologic dysfunction within approximately 2 years. This is due to increased stress at the disc space cranial or caudal to the original surgical site, leading to another compressive lesion (called a domino lesion).
- Positive prognostic factors for outcome include minimal neurologic signs at the time of diagnosis, a brief period of neurologic dysfunction, and one compressive lesion without evidence of spinal cord atrophy.
- Negative factors include moderate to severe clinical signs, a protracted time course of clinical signs, multiple levels of involvement, and spinal cord atrophy.

SPINAL FRACTURES AND DISLOCATIONS

Most cases of fracture and dislocation of the spinal cord are the result of high-impact trauma, such as automobile accidents. Repair of spinal fractures and dislocations depends on the area of spinal cord involvement, degree of neurologic dysfunction, patient size, amount of vertebral displacement ventral instability, concurrent injuries, and continued neurologic deterioration despite medical management.

- Consider surgical stabilization for animals with spinal fractures or dislocations that are unstable and are not responsive to medical therapy.
- The thoracolumbar and lumbosacral junctions are prone to fracture and luxation because they are the sites of marked transition between the stiff and the mobile sections of the spine.
- Due to the complex surgical anatomy and expertise required, promptly refer these cases to a surgical specialist or neurosurgeon.

Anatomy

- The overall stability of the spine is dependent on both the bony and the soft tissue structures that make up the dorsal and ventral compartments.
- The dorsal compartment of the spine consists of the vertebral arch (comprising the dorsal lamina and lateral pedicles), paired articular facets with joint capsule, the dorsal spinous process, interspinous and supraspinous ligaments, and the ligamentum flavum.
- The ventral compartment comprises the vertebral body, intervertebral disc (nucleus pulposus and annulus fibrosus), dorsal longitudinal ligament, and ventral longitudinal ligament.
- The paraspinal musculature is a strong auxiliary support, providing stability to both the dorsal and the ventral compartments.
- Other than the atlanto-occipital joint, atlantoaxial joint, and sacrum, all vertebrae articulate similarly.
- The basic motion unit of the spine consists of two adjacent vertebrae with an interposed intervertebral disc, paired dorsolateral articular facets, and supporting ligaments.
- The intervertebral disc forms an elastic cushion between adjacent vertebrae and functions to absorb shock and allow spinal movement.
- The dorsal and ventral longitudinal ligaments reinforce the annulus fibrosus of the intervertebral discs. These ligaments together limit the degree of vertebral flexion, extension, and transverse sliding motion.
- The articular facets are located at the junction of the pedicle and lamina and vary in shape and position within each segment of the vertebral column. Articular facets play an important role in spinal stability and provide landmarks for alignment during fracture or luxation reduction.
- The supraspinous and interspinous ligaments connect the dorsal spinous processes of adjacent vertebrae and resist flexion during hyperflexion.
- The cervical dorsal spinous processes are short and thin, whereas the dorsal spinous processes of the thoracic and lumbar spine are large and can support orthopedic implants if necessary.
- The cervical vertebral bodies are flat ventrally and are suitable for application of fixation devices. The ventral approach to the cervical spine is generally easier than the dorsal approach.
- The lumbar vertebral bodies are long, allowing orthopedic implant fixation on the dorsolateral surface if the major nerve roots from L4 to L5 through L7 to S1 can be avoided. The origin of the transverse processes provide an important landmark for screw or pin fixation as this site minimizes the risk of entrance of the implant into the spinal canal.
- Lateral surgical exposure to the thoracic vertebrae is hindered by the rib head and potential entrance into the thoracic cavity.

Etiology

Spinal fractures and dislocations are usually due to trauma, such as being hit by a car. Spinal fractures and luxations can be quite varied. An understanding of the forces causing the injury, and of the resultant pathology, is important in formulating a treatment plan and prognosis.

Biomechanics of Spinal Fracture and Luxation

Traumatic fractures and luxations are created by forces resulting in severe hyperextension, hyperflexion, compression, and rotation. Several forces may act together, and they often occur at or near the transition between a movable and an immovable vertebral segment.

▼ ***Key Point*** Fractures and luxations most commonly occur at the craniocervical, thoracolumbar, and lumbosacral junction.

Spinal fractures have a characteristic failure pattern that depends on the forces placed on them during failure. Understanding these forces is crucial in determining the resultant stability of the segment, which will help with the decision to institute conservative (nonsurgical) therapy or surgical fixation.

Hyperextension

- Hyperextension results from a direct blow to the dorsal aspect of the spine.
- Failure is usually due to collapse of the dorsal compartment, especially at the articular facets.
- Damage to the ventral compartment includes tearing of the ventral bands of the annulus fibrosus.
- Predicting inherent stability of these fractures can be difficult.

Hyperflexion

- This usually results in a wedge compression fracture of the vertebra, sparing the dorsal compartment.
- These fractures are generally stable.

Compression

- A compression fracture of the vertebral body occurs with axial load forces.
- Fragments and extruded nucleus pulposus can be driven into the spinal canal, contributing to spinal cord injury.
- The dorsal compartment may be involved, which will result in an unstable fracture.

Rotation

- This force seldom occurs alone and is usually associated with hyperflexion.

- Disruption of both ventral and dorsal compartments usually occurs, resulting in an unstable fracture or luxation with significant displacement.

Clinical Signs

- Depending on the severity of the fracture and associated compression of the spinal cord, animals with these injuries may present with signs ranging from pain or loss of proprioception to loss of motor function.
- See Chapter 128 for more information on clinical signs of spinal cord trauma.

Diagnosis

- Since most of these patients have suffered severe trauma, perform a complete general, neurologic, and orthopedic evaluation. Special care should be taken in evaluating the thoracic and abdominal cavities by thoracic auscultation and abdominal palpation.
- Perform a complete blood count to rule out anemia secondary to blood loss and a biochemical analysis to evaluate for other organ damage.
- Obtain thoracic and abdominal radiographs to rule out evidence of blunt trauma, such as rib fractures and pneumothorax with chest trauma (see Chapter 166). On abdominal radiography, loss of serosal detail may suggest peritoneal effusion, such as blood secondary to organ laceration or urine due to bladder rupture (see Chapter 76).

Neurologic Evaluation

- Once the patient is systemically stable, perform a complete neurologic evaluation to determine location and severity of neurologic injury (see Chapter 125). Overall prognosis is most dependent on the degree of neurologic impairment at the time of presentation.
- Patients with varying degrees of voluntary motor function have a good to excellent prognosis for return to normal neurologic function.

▼ ***Key Point*** The most important prognostic factor is the presence of deep pain sensation. Patients with intact deep pain sensation have an 85% to 90% chance to recover normal neurologic function. Patients with absent deep pain sensation have a 15% chance to recover neurologic function.

- In comparison to intervertebral disc extrusions, the prognosis with spinal fracture or luxation cases presenting with absent deep pain sensation may be even worse due to the amount of injury to the spinal cord.
- If the patient is to be managed medically, perform serial neurologic evaluations (i.e., every 6 hours) to evaluate changes in neurologic status.
- Immobilize the animal during the initial stabilization period to prevent additional spinal cord damage prior to imaging or surgery. Use a small cage, place a body cast, or strap the animal to a rigid body board.

Diagnostic Imaging

- Be very careful when manipulating the patient, since many spinal fractures and dislocations are associated with instability. Further shifting of fracture segments or dislocations from too much manipulation of the spine will result in more spinal cord injury and worsening neurologic function.
- In most cases, plain spinal radiography will identify spinal fracture or luxation (see Chapter 4). Myelography is generally not indicated and is usually an unrewarding method of identifying spinal cord compression due to the degree of spinal cord swelling, hematoma formation, and contrast leakage secondary to meningeal tearing at the trauma site.
- CT imaging of the spine is most helpful at identifying bony pathology, such as fractures of the articular facets. When there is concern for spinal cord compression from traumatic disc rupture, hematoma, or fracture fragment, then MRI is the diagnostic test of choice.

Preoperative Considerations

Patients can be managed conservatively (non-surgically) if they have good motor function with a stable and minimally displaced spinal fracture or luxation.

Indications for Spinal Fracture and Luxation Repair

- An unstable or significantly displaced spinal or fracture luxation
- Severe or persistent spinal pain despite medical therapy
- Diminished or absent motor function, or absent deep pain sensation on initial presentation
- Evidence of declining neurologic function on serial neurologic evaluations

Surgical Procedures

A thorough knowledge of the spinal anatomy and familiarity with surgical approaches is a must for consistent success. Surgical repair of spinal fractures and luxations requires experience and proper instrumentation.

Objectives

- Stabilize the spine
- Decompress the spinal cord, if indicated
- Minimize surgical trauma to the spinal cord

Equipment

- Same as for atlantoaxial instability, plus
  - Plastic spinal plates and associated nuts and bolts

Techniques

Cervical Fractures and Luxations

▼ ***Key Point*** Approximately 80% of fractures of the cervical spine occur at either the dorsal spine or the body of C2. Fractures and luxations rarely occur from C3 to C7.

- A propensity for traumatic luxation at C5 to C6 may occur.
- The choice of surgical fixation technique is dependent on location of the injury, skill level of the surgeon, and whether decompression alone or decompression with stabilization is indicated.
- The choice to perform a decompressive laminectomy will be dependent upon seeing significant compression from extruded disc material, hematoma, or fracture fragments within the spinal canal on myelography, CT, or MRI. Be cautious when performing decompressive procedures, as aggressive removal of the dorsal arch may lead to further instability at the fracture or luxation site. If a ventral slot is required to remove material from the canal at the traumatized space, also perform a stabilization procedure.
- Dorsal stabilization of cervical fractures or luxations is difficult because the thinner bone dorsally provides weak fixation of orthopedic implants. In addition, neurovascular structures make dorsolateral bone plating very difficult.
- Dorsal approaches to the cervical spine are most useful with alignment and fixation of dorsal facets and laminectomy for dorsal decompression.
- Fractures of the dorsal spine of C2 can be repaired dorsally using orthopedic wire or heavy-gauge suture material (toy- and small-breed dogs only), with the goal of anatomic reconstruction and re-establishment if ligamentous structures.
- Ventral approaches to the cervical spine provide the best bone structure for fixation. Ventral fixation using either plastic or metal bone plates can provide stable fixation. Place a minimum of two screws cranial and caudal to the fracture or luxation site for optimum stability. Start the screws on midline and angle as far laterally as possible to avoid penetration of the spinal canal. The difficulty with angling screws within the holes of a bone plate necessitates the use of shorter screws that only engage one cortex, which results in weaker fixation.
- One surgical technique that is adaptable to most fracture and luxation repairs is the use of pins and PMMA placed ventrally in the cervical vertebrae.

Ventral Fixation Using Pins and Polymethyl Methacrylate

1. The approach to the cervical vertebrae is the same as the previously described ventral slot technique (under "Caudal Cervical Spondylomyelopathy").

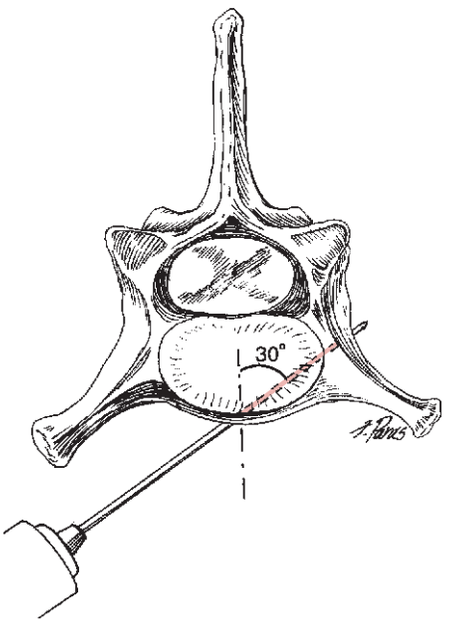

Figure 100-5. Proper pin placement for ventral fixation of cervical fractures. The pins enter the ventral cortex on midline and are angled approximately 30–35 degrees laterally to enter the lateral cortex and miss the spinal canal.

2. Reduce the fracture or luxation site. If decompression of the spinal canal is needed, perform a ventral slot. Reduction of the fracture fragments can be maintained using a Gelpi retractor with the tips blunted.
3. Place a minimum of two Steinmann pins in each cranial and caudal segment, respectively. Start the pins on midline, and angle 30 to 35 degrees laterally to prevent entrance into the spinal canal. Engage the lateral cortex of the lumbar vertebrae for best pin fixation (Fig. 100-5).
4. Cut the pins with 1.5 to 2 cm of pin exposed. Notch the exposed pin using pin cutters for increased bonding between the pin and the PMMA.
5. Place the PMMA ventrally, covering the exposed pins. Lavage the surgical site with cool sterile saline to dissipate the heat of polymerization and prevent thermal injury to the spinal cord.
6. Close the muscles, subcutaneous tissue, and skin routinely.

Thoracic and Lumbar Spinal Fractures and Luxations

▼ ***Key Point*** The most common locations of fracture or luxation of the thoracic and lumbar spine occur at the transition zones (thoracolumbar junction and lower lumbar-lumbosacral space).

Numerous stabilization techniques have been described for fixation of thoracic and lumbar spinal fractures and luxations. The two most common and

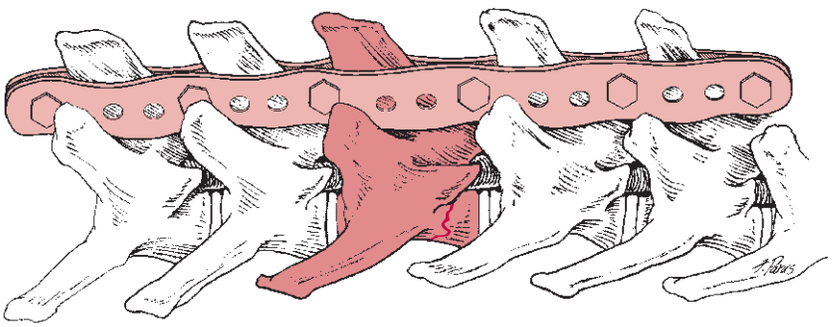

Figure 100-6. Dorsal spinal fixation of the thoracolumbar spine using plastic spinal plates.

technically easiest procedures for repair will be described here: dorsal spinous process plating using plastic spinal plates and pin and PMMA fixation. Dorsolateral vertebral body plating can be performed, but it is technically more demanding and requires removal of rib heads in the thoracic spinal segments.

Dorsal Spinous Process Plating Using Plastic Spinal Plates

1. Perform a dorsal approach to the thoracic and lumbar spine. Expose a minimum of three dorsal spines on each side of the fracture or luxation, and preserve the supraspinous and interspinous ligaments if possible.
2. Reduce the fracture or luxation site, which is dictated by the normal anatomic relation between the cranial and the caudal articular facets. For auxiliary fixation, place a pin or small bone screw across the involved articular facets if they are intact.
3. Place an appropriately sized plastic spinal plate on each side of the dorsal spinous process, with the rough side of the plate against the bone. Several sizes are available.
4. Attach the plates to each other using appropriately sized nuts and bolts between the dorsal spinous processes (Fig. 100-6). For optimal fixation, place the plates as close to the base of the dorsal spinous process as possible.
5. Close dorsal lumbar fascia, subcutaneous tissue, and skin routinely.

Pin and Polymethyl Methacrylate Fixation of Thoracic and Lumbar Fractures

1. Perform a dorsal approach to the involved segments. Expose the dorsal spinous processes, articular facets, and transverse processes bilaterally for pin placement.
2. Place two appropriately sized Steinmann pins into the vertebral bodies on each side of the fracture or luxation. In the thoracic vertebrae, landmarks for pin placement into the vertebral bodies include the tubercle of the rib heads and the base of the accessory process. For lumbar vertebrae, the landmarks for pin placement include the base of the transverse process.
3. Direct the Steinmann pins obliquely through the vertebral body, exiting approximately 2 to 3 mm from the ventral aspect of the vertebral body. Approximately 1.5 to 2 cm of pin is left exposed and is notched using a pin cutter to allow fixation of PMMA.
4. Apply PMMA in a mass, incorporating the Steinmann pins, as well as the articular facets and the dorsal spinous processes. Lavage the PMMA with saline during curing to dissipate the heat of polymerization.
5. Routinely close the lumbodorsal fascia, subcutaneous tissue, and skin.

The primary disadvantage of this procedure is the exposure needed for placement of the implants. Recently, reports describing fluoroscopic placement of the pins through the vertebral bodies using minimally invasive approaches and external spinal fixation have given encouraging results.

Fractures of L6, L7, and the Sacrum

- Fractures of this region are common because of the transition of the relatively mobile lumbar spine with the more rigid pelvis and sacrum.
- The spinal cord ends at the caudal aspect of L6. Fractures in this area usually involve the nerves of the caudal equina. Therefore, clinical signs relate to sciatic, femoral, and sacral nerve deficits.
- The peripheral nerves are more resistant to compression and tension that the spinal cord. Animals with as much as 60% to 70% compromise of the spinal canal may still have a favorable prognosis.

Transileal Pinning

1. Perform a dorsal approach to the lumbosacral region.
2. Since the caudal segment is often displaced cranially and ventrally, use bone forceps to bring the caudal segment into alignment.
3. Place an appropriately sized Steinmann pin through the wing of the ilium, across the dorsal lamina of L7,

and into the opposite wing of the ilium. The ends of the pins can be bent to prevent pin migration.

4. A modification of this technique that may provide more stable fixation involves the use of plastic dorsal spinous process plates and transileal pins. Place the plastic dorsal spinous process plate as described previously in this chapter, incorporating at least three dorsal spinous processes cranial to the fracture or luxation. The plastic plate extends cranial to S2 and S3.
5. Drive a Steinmann pin through one ileal wing, through the plastic plate at the level of L7 to S1, and through the opposite ileal wing. Bend both ends of the pins upward to prevent migration. A second pin may be placed in similar fashion for increased rigidity.
6. Routinely close the lumbodorsal fascia, subcutaneous tissues, and skin.

Postoperative Care and Complications

- Administer postoperative analgesics (see Chapter 6).
- Begin antibiotic therapy (first-generation cephalosporins, potentiated penicillins) intraoperatively and continue for 7 days after surgery.
- Turn recumbent animals every 4 to 6 hours. Maintain clean, dry, padded bedding to prevent decubital ulcers.
- A cervical collar or body cast may be placed for additional stabilization but is usually not necessary.
- Begin physical therapy soon after surgery (see Chapter 95). Passive range of motion exercises, massage therapy, and hydrotherapy are helpful in maintaining muscle mass and preventing joint contracture.
- If voluntary urinary control is absent, express the bladder every 6 hours. Intermittent catheterization can be performed, but avoid indwelling catheters due to the potential for ascending infection.
- The primary complications include loosening of orthopedic implants and infection due to the extensive soft tissue dissection required for exposure and use of large implants and bone cement.

Prognosis

Overall prognosis depends on the presenting neurologic evaluation. In patients with intact deep pain sensation, approximately 85% will regain normal or near-normal neurologic function. With absent deep pain sensation, the overall prognosis is very poor.

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Chapter

101 Neoplasia of the Axial Skeleton

Mark M. Smith

ETIOLOGY

Osteosarcoma and chondrosarcoma are the two most common primary neoplasms affecting the axial skeleton. These neoplasms have a similar radiographic appearance, with osteolytic, osteoblastic, or mixed osteoblastic/osteolytic characteristics. Hemangiosarcoma and fibrosarcoma are other primary bone tumors that must be considered. Overall, these tumors more commonly affect the ribs and pelvis than the vertebrae. Multilobular osteoma (chondroma rodens) is the most common tumor of the skull.

Early recognition and accurate diagnosis are of paramount importance for client education and rationale for surgical intervention. Surgery may be diagnostic (vertebrae), palliative (pelvis), or curative (rib), depending on tumor invasiveness and location of axial skeletal involvement. Tumors of the mandible, maxilla, and nasal cavity are discussed in other chapters in this section. The types of neoplasms and principles of treatment discussed in this chapter are similar to those for tumors of the cranium. Removal of cranial tumors requires specialized equipment and skills and therefore is best handled by a surgical specialist. Tumors of the appendicular skeleton are discussed in Chapter 116.

CLINICAL SIGNS

- Patients usually are presented for swelling over a bony prominence.
- Intrathoracic extension of neoplasia of the rib may cause respiratory compromise.
- Pain or an unusual gait secondary to neurologic dysfunction (transverse myelopathy) may be related to neoplasms of the vertebrae.
- Animals with skull tumors usually are presented because of a palpable mass. Neurologic signs may develop if brain impingement occurs.
- Constipation may result from pelvic tumors.

DIAGNOSIS

Pelvis and Ribs

- Include two radiographic projections of the lesion.
- Radiographic signs of primary bone neoplasms (e.g., osteosarcoma, chondrosarcoma) may range from primarily lytic to proliferative lesions.
- Polyostotic lytic lesions are seen with malignant lymphoma and multiple myeloma (see Chapter 27).

▼ ***Key Point*** Do not use radiography as the sole basis for determining tumor type.

- Determine if metastatic disease is present.
- Perform palpation and fine-needle aspiration of enlarged regional lymph nodes.
- Perform abdominal palpation for mass lesions, vertebral palpation for metastasis-related pain, and a rectal examination for intrapelvic masses.
- Evaluate three-projection thoracic radiographs (ventrodorsal, left, and right lateral) to detect pulmonary metastasis.

Skull and Vertebrae

- Survey radiographs of the spine often show osteolysis secondary to primary bone neoplasia or to invasion of soft tissue neoplasia.
- Osteosarcoma or multilobular osteoma of the cranium appears radiographically as a proliferative bony lesion of the flat bones.
- Perform cerebrospinal fluid (CSF) analysis to rule out infection and inflammation (see Chapter 125). CSF of patients with vertebral neoplasia may have increased levels of protein and elevated pressure.

▼ ***Key Point*** Because most tumors affecting the spinal cord are extradural, cytologic examination of the CSF may be normal.

- Myelography and computed tomography (CT) are important to detect the exact site of the vertebral tumor and the extent of spinal cord compression (see Chapter 128).

▼ ***Key Point*** Metastatic lesions from remote malignant tumors may mimic primary neoplasms of the axial skeleton. Histopathologic examination of biopsy tissue is required for differentiation.

- CT or magnetic resonance imaging (MRI) is useful to evaluate intracranial effects of skull tumors (see Chapter 126).

Bone Biopsy

Objectives

- Obtain multiple tissue samples of the tumor for histopathologic diagnosis.
- Avoid causing iatrogenic trauma to the vertebrae or skull, if they are involved.

Equipment

- Small suture pack and suture material
- Jamshidi-type biopsy needle or bone trephine
- Sterile ruler

Technique

1. Prepare the cutaneous area over the tumor site for aseptic surgery.
2. Make a skin incision large enough to introduce the biopsy instrument over the center of the lesion.
3. Measure the center of the tumor from the nearest prominent anatomic landmark.
4. Take a minimum of two biopsies: one from the center of the tumor and one from the center directed to the periphery. Use extreme caution when performing biopsy of tumors of the cranium.
5. Using a horizontal mattress pattern, place sutures of absorbable material in the subcutaneous or fascial layers to minimize hemorrhage from the biopsy site.
6. Close the skin with non-absorbable suture material in a simple interrupted pattern.

▼ ***Key Point*** Biopsy of vertebral lesions is best performed during decompressive laminectomy or with the aid of fluoroscopy to guide biopsy needle placement.

TREATMENT

Surgical Procedures for Rib Neoplasia: Resection and Thoracic Wall Reconstruction

Objectives

- Completely remove the thoracic wall mass.
- Attempt to obtain wide tumor-free margins.
- Minimize hemorrhage.
- Provide rigid reconstruction to prevent abnormal chest wall movement.
- Perform airtight closure to prevent pneumothorax.

Equipment

- Standard general surgical pack and suture material
- Two large Gelpi or Beckman self-retaining retractors
- Gigli wire or Liston bone cutters
- Chest tube, three-way stopcock, and large syringe
- Polypropylene mesh

Technique

1. Place the animal in lateral recumbency with the hindlimbs extended caudally and the forelimbs extended cranially.
2. Prepare the lateral chest wall for aseptic surgery.
3. Incise the skin over the mass. If the tumor is adhered to the dermis, make a large, elliptical skin incision around the tumor.
4. Incise or, preferably, reflect the latissimus dorsi muscle if it is not adhered to the tumor.
5. Incise all remaining muscle layers one intercostal space cranial and caudal to the mass.
6. Cut all involved ribs and intercostal muscles 2 cm dorsal and ventral to the tumor, using Liston bone cutters and Metzenbaum scissors.
7. Clamp and ligate the intercostal arteries and veins.
8. Place a chest tube a minimum of two intercostal spaces cranial or caudal to the resection site.

▼ ***Key Point*** Consider giving an intraoperative lidocaine intercostal nerve block to decrease pain during the acute postoperative period (see Chapter 167).

9. Use polypropylene mesh (e.g., Marlex) to reconstruct large thoracic wall defects.
10. Place polydioxanone or polypropylene sutures, using an interrupted horizontal mattress pattern, in a paracostal location to secure the mesh.
    a. A slight fold may be created along all borders of the mesh to provide a double-thickness layer for holding sutures.
11. Secure the mesh to the cut ribs with sutures of similar material, using a circumferential simple interrupted pattern. Create slight tension on the mesh to provide rigidity.
12. Suture the latissimus dorsi and external abdominal oblique muscles over the defect with absorbable suture material in an interrupted pattern to provide a tissue seal.
13. Close subcutaneous tissues with absorbable suture material in an interrupted pattern to minimize dead space.
14. Appose the skin routinely, using non-absorbable suture material.

15. Use the chest tube system to reestablish negative intrathoracic pressure.

▼ ***Key Point*** Small thoracic wall defects may be closed using adjacent latissimus dorsi and external abdominal oblique muscles without the need for a mesh implant.

Postoperative Care and Complications

Short Term

- Closely monitor for hemorrhage, seroma formation, and pneumothorax.
- Apply a light chest bandage to minimize seroma formation and air migration along the chest tube.

▼ ***Key Point*** Place the bandage loose enough to allow normal chest excursion and optimal pulmonary function.

- Analgesics (hydromorphone, 0.05 mg/kg q4h IV) will be required in the acute postoperative period (see Chapter 6).

Long Term

- Repeat physical and radiographic examinations every 4 to 6 months to monitor for recurrence or metastasis.
- Consider adjuvant chemotherapy if the tumor is malignant or if tumor cells are present in resected tissue margins (see discussion of chemotherapy in Chapter 26).

Prognosis

- Chest wall neoplasms usually are malignant and carry a poor prognosis if incompletely excised. This is especially true for osteosarcoma.
- The prognosis is guarded even if the tumor is completely resected because subclinical distant metastasis may have occurred before surgery.
- Dogs with rib chondrosarcoma have longer survival than those with osteosarcoma.

Surgical Procedure for Pelvic Neoplasia: Resection of the Ilial Wing

Preoperative Considerations

Perform ilial wing resection for localized tumors. Invasive, malignant tumors may require hemipelvectomy, which involves resection of part of the lateral pelvis and hind limb. Refer the patient to a surgical specialist for hemipelvectomy.

Objectives

- Completely remove the pelvic mass.
- Obtain wide, tumor-free margins.
- Minimize hemorrhage.
- Avoid damage to major pelvic limb nerve tracts in order to maintain limb function.

Equipment

- Standard general surgical pack and suture
- Two large Gelpi or Beckman self-retaining retractors
- Gigli wire or osteotome and mallet

Technique

1. Place the animal in lateral recumbency.
2. Prepare the lateral pelvic area and proximal hindlimb for aseptic surgery.
3. Incise the skin over the mass. If the tumor is adhered to the dermis, make a large elliptical incision around the tumor.
4. Incise through the superficial, middle, and deep gluteal muscles cranial to the acetabulum.
5. Incise the sartorius and tensor fascia lata muscles before their insertion on the ilium.
6. Incise the iliocostalis and longissimus muscles cranial to the pelvic mass.
7. Incise the quadratus lumborum and iliacus muscles before their insertion on the medial aspect of the ilium.
8. Cut the sacroiliac joint and ilial body using a Gigli wire or osteotome and mallet.
9. Elevate the other fascial attachments to free the proximal ilial segment.
10. Control hemorrhage with electrocoagulation or individual vessel ligation.

▼ ***Key Point*** Maintain wide margins of excision with no gross evidence of tumor.

11. Closure
    a. Appose the resected muscle ends by simple interrupted sutures of absorbable material placed in the fascia.
    b. Extensive resection may require Penrose drain placement to minimize potential dead space.

▼ ***Key Point*** Make separate small incisions in the surgical area for entrance and exit of drains, avoiding the primary wound incision.

    c. Close subcutaneous tissues with absorbable sutures in a simple interrupted pattern.
    d. Appose the skin similarly, using non-absorbable sutures.

Postoperative Care and Complications

Short Term

- Use a modified Robert Jones bandage to decrease the incidence of seroma. Bandage application and maintenance is more cumbersome in male dogs.

- Monitor the wound for signs of seroma and infection.
- Administer analgesic therapy (hydromorphone 0.05 mg/kg q4h IV) during the acute postoperative period.

Long Term

- Repeat physical and radiographic examinations every 4 to 6 months to monitor for recurrence and metastasis.
- Consider adjuvant chemotherapy if the tumor was malignant or if tumor cells are present in resected tissue margins (see discussion of chemotherapy, Chapter 26).

Prognosis

- Prognosis is the same as for rib neoplasia.

Surgical Procedure for Vertebral Neoplasia: Dorsal Laminectomy

Because laminectomy is a difficult surgical procedure that should be performed only by surgical specialists, only an overview of the procedure is given here. (See Chapter 128 for more information on principles of surgery of the spinal cord.)

Objectives

- Debulk the tumor.
- Decompress the spinal cord.
- Obtain tissue for histopathologic diagnosis.

Equipment

- Standard general surgical pack and suture material
- Two large Gelpi or Beckman self-retaining retractors
- Pneumatic or electric power equipment for laminectomy
- Kerrison or Lempert bone rongeurs
- Iris scissors

Procedure Overview

- Preoperatively administer dexamethasone (0.5 mg/kg IV) to decrease edema of the spinal cord related to surgical manipulation.
- Save adequate amounts of tumor tissue in 10% buffered formalin for histopathologic evaluation.
- The laminectomy procedure ends when the spinal cord is relieved of the compression effect of the tumor.
- Dorsal laminectomy can be combined with hemilaminectomy if additional lateral exposure is required.

▼ ***Key Point*** Iatrogenic vertebral fracture/luxation is unlikely, because reactive bone and scar tissue secondary to the neoplasm compensates for the destabilizing sequelae of laminectomy and tumor debulking.

Postoperative Care and Complications

Short Term

- Monitor for seroma formation and infection at the wound site.
- Perform serial neurologic examinations to monitor neurologic status.
- Administer prednisolone (0.5 mg/kg q12h PO) for anti-inflammatory therapy (if necessary) until neurologic status is improved.
- Urine retention requires frequent manual decompression of the bladder or maintenance of a closed indwelling catheter system. Monitor for development of urinary tract infection.
- Turn the patient every 4 hours to prevent decubital ulcers secondary to prolonged recumbency.
- Administer analgesics as needed (see Chapter 6).

Long Term

- Supportive therapy and good nursing care are mandatory during the neurologic recovery period.
- Limit exercise but perform physical therapy as needed to regain limb function (see Chapter 95).
- Consider adjuvant chemotherapy and/or radiation therapy (see Chapter 26), based on the histopathologic diagnosis, because complete resection of the tumor is not possible.

PROGNOSIS

- The prognosis for malignant tumors of the vertebral axial skeleton is poor.
- Neoplasms secondarily affecting vertebrae (e.g., lymphoma) may warrant a guarded prognosis, based on responsiveness to chemotherapy.

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Chapter

102 Fractures of the Shoulder

James K. Roush

Recognition of shoulder fractures is important to allow acute lameness diagnosis and treatment and to protect normal shoulder joint mobility and function. Fractures of the shoulder are often associated with concurrent thoracic trauma and may be associated with ipsilateral brachial plexus injuries or trauma to the overlying soft tissues.

ANATOMY

The shoulder is a diarthrodial joint with a shallow ball-and-socket configuration. Major support structures of the shoulder are the loosely defined medial and lateral glenohumeral ligaments and the joint capsule. Stability is also provided by a number of muscles and tendons that cross the joint to insert on the humerus, including the supraspinatus tendon, acromial and spinous heads of the deltoideus muscle, infraspinatus tendon, coracobrachialis tendon, and teres minor tendon. The biceps brachii tendon provides minimal cranial support to the normal shoulder but is commonly transposed to provide medial or lateral support after traumatic joint luxation.

The scapula is a broad, flat bone with a prominent spine and numerous muscle origins and insertions. It is loosely attached to the chest wall through the insertions of a number of muscles, including the rhomboideus, subscapularis, and trapezius. Scapular areas can be anatomically divided into the body, spine, neck, and glenoid cavity, with differing surgical approaches and treatments recommended for fractures in each area (Fig. 102-1). In immature animals, the dorsal border of the scapula serves as a physis for long bone growth. The distal scapula has no physis for long bone growth, but the supraglenoid tubercle is a secondary center of ossification in the immature dog and this apophysis is often misdiagnosed as a fracture in dogs until radiographic closure from 6 to 7 months of age.

The proximal humerus has a number of defined tubercles with important muscle insertions. The greater tubercle provides insertions for the supraspinatus tendon cranially and the infraspinatus and teres minor tendons laterally. The deltoid tuberosity is a linear protuberence on the lateral aspect of the humerus serving as the insertion for the acromial and spinous heads of the deltoid muscle. The coracobrachialis tendon inserts on the medially located coracoid process of the proximal humerus. There is a proximal humeral physis that closes functionally at approximately 8 months and radiographically at 10 months of age in the dog, and a secondary ossification center composing the greater tubercle is visible in dogs under 5 months of age.

Important soft tissue structures that may be affected by trauma or that are important during surgical approaches include the suprascapular nerve, which crosses the scapular neck from cranial to caudal beneath the acromion; the circumflex humeral vessels, which lie just distal to the teres minor muscle beneath the spinous head of the deltoideus muscle; and the cephalic vein, which lies superficially on the craniolateral aspect of the greater tubercle.

DIAGNOSIS

Clinical Signs

Clinical signs associated with canine scapular and proximal humeral fractures include partial or non–weight-bearing lameness of a forelimb, pain or crepitus during palpation of the scapula or proximal humerus, and pain during manipulation of the scapulohumeral joint. Malposition and soft tissue of the limb at the scapulohumeral joint may be visible and palpable during physical examination. It is important to apply direct pressure along all borders of the scapula and along the scapular spine while observing the animal for signs of pain to detect greenstick or minimally displaced scapular fractures.

Radiography

Definitive diagnosis of scapular fractures is by radiography. Reported radiographic views of the scapula include caudocranial, mediolateral, dorsally displaced mediolateral, and distoproximal. Any or all of these views may be useful for the surgeon's understanding of the fracture's configuration. Frequently, computed tomography (CT scan) of the scapula is useful to determine the degree of comminution and provide operative plan-

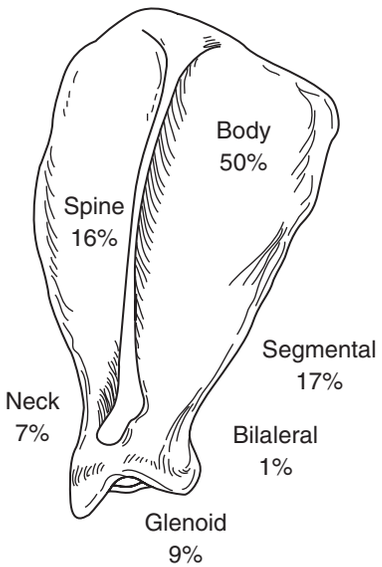

Figure 102-1. Percentage of canine scapular fractures occurring in various regions of the scapula from a study of 107 scapular fractures. (Rohn D, Roush JK: Unpublished data.)

ning, particularly with the addition of three-dimensional reconstructions of the fracture available in some software. In a study of 107 dogs with scapular fractures, 28% were comminuted fractures, but only one fracture was an open fracture. Nuclear scintigraphy of the scapula may be useful to identify non-displaced scapular fractures. In young animals, diagnosis of supraglenoid tubercle fracture should not be made until comparison with radiographs of the opposite scapula indicates an obvious displacement of the affected supraglenoid tubercle.

FRACTURES OF THE SCAPULA

Preoperative Considerations

- Treatment of scapular fractures varies by the location and configuration of the fracture, the degree of displacement of the fragments and their effect on distal limb position, and the location and degree of involvement of the articular surfaces by the fracture.
- In a study of 107 dogs with scapular fracture, the scapular body had the most fractures (50%). Fractures of the articular surface of the glenoid were found for only 9% of dogs, with 6 of 9 dogs involving only the supraglenoid tubercle (Fig. 102-1).
- Non-displaced or minimally displaced fractures of the scapula body and spine are best treated by strict cage confinement.
- Application of a Velpeau sling has been advocated, but it generally provides no advantages over adequate cage confinement and has the disadvantage of resulting in decreased humeral joint function and increased joint stiffness from the immobility period.
- Perform surgery for fractures of the scapula or proximal humerus in lateral recumbency with the limb prepared for aseptic surgery. Surgical approach is dependent on the area of exposure needed for the particular fracture, but a number of described surgical approaches are useful, including the lateral, craniolateral, and caudolateral approaches and variations of these approaches combined with acromion osteotomy, greater tubercle osteotomy, and infraspinatus tenotomy.
- Because of the extensive number of muscles and tendons crossing the joint, adequate exposure of the glenoid surface during surgery may require osteotomy of any or all supraglenoid or greater tubercles or of the acromion. These are reattached at the conclusion of the primary fracture repair by lag screw or tension band fixation.

Equipment

- Standard orthopedic pack and bone reduction forceps
- Orthopedic wire (20 and 22 gauge, or 0.8 and 1.0 mm) and wire twisters
- Selection of Kirschner wires and small Steinmann pins
- Bone plating sets, including 2.0-, 2.7-, and 3.5-mm screws to accommodate all animal sizes, and a variety of bone plates, including miniplates, dynamic compression plates, T plates, L plates, and reconstruction plates

Scapular Body Fractures

Fractures of the scapular body comprise 50% of all scapular fractures and are often transverse or oblique. The thinness of the scapular body results in difficulty in finding purchase for surgical implants; thus, minimally displaced or non-displaced fractures are treated by cage confinement. Fractures of the proximal half of the scapular body are often comminuted but are also adequately treated by cage confinement for an extended period.

Technique Overview

- If internal fixation is necessary to prevent limb shortening and malalignment, treat fractures of the scapular body by placement of appropriately sized plates across the fracture fragments.
- Surgical approach is by removal of the insertion of the trapezius, omotransversarius, and supraspinatus muscles from the scapular spine and by separation of the infraspinatus muscle from the spine for caudal fractures.
- Plates used in previous reports include standard DCP of all sizes, reconstruction plates, stackable miniplates, T and L plates, and semitubular plates.
- Fractures that transverse the scapular body may benefit from the addition of plates both cranially and

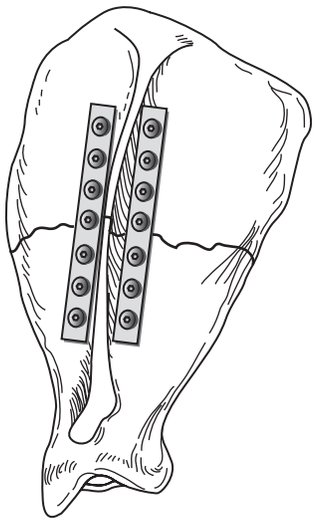

Figure 102-2. Transverse fracture of the scapular body stabilized with 2.7-mm hole dynamic compression plates along the scapular spine.

caudally to the scapular spine (Fig. 102-2). Comminuted fractures may be reduced individually by hemicerclage wire and may be stabilized individually by small bone plates or bridged with a plate in buttress fashion.

▼ ***Key Point*** When fracture configuration allows, screws near the scapular spine should be directed to the center of the scapula beneath the spine to take advantage of the thicker bone and better subsequent screw purchase in those areas.

Scapular Spine and Acromion Fractures

Fractures of the scapular spine comprise about 16% of scapular fractures and often do not require internal fixation because the origin of multiple muscles along the spine minimizes displacement and provides some stability.

Technique Overview

- Fractures of the spine not involving the acromion may be managed by cage confinement.
- Avulsions of the acromion require treatment to restore function of the deltoideus muscle group.
- Treat avulsions of the acromial process with tension band or lag screw fixation (Fig. 102-3). When the acromion is removed to facilitate surgical approach for glenoid or neck fractures, replace with tension band fixation.

Scapular Neck Fractures

Scapular neck fractures override due to conflicting muscle pulls on the proximal and distal fragments. Treat by internal fixation. Adequate surgical exposure requires acromion osteotomy and infraspinatus tenotomy to adequately visualize and expose fractures.

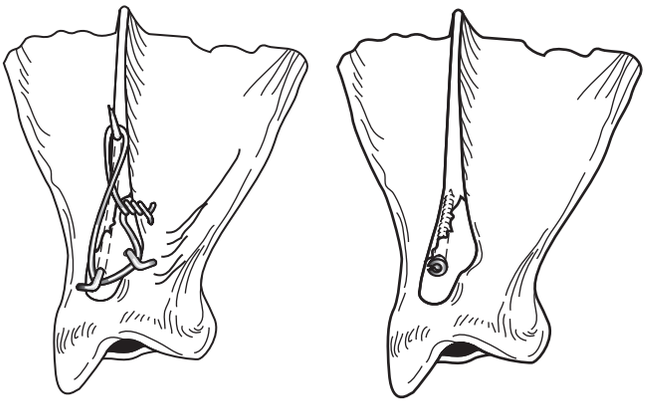

Figure 102-3. Fracture of the acromion stabilized with two Kirschner wires and a figure-eight cerclage wire applied in tension band *(left)* or lag screw *(right)* fashion.

▼ ***Key Point*** During surgery for scapular neck fractures, identify and protect the suprascapular nerve.

Technique Overview

- Adequate internal fixation is achieved by the use of 2.7- or 2.0-mm dynamic compression plates, miniplates, or reconstruction plates in a straight, T-shaped, or L-shaped fashion.
- Place the proximal aspect of these plates as close as possible to the scapular spine, and place the distal aspect with care taken not to impinge on the joint surface with the plate or screws (Fig. 102-4).

Supraglenoid Tubercle Fractures

Separations of the supraglenoid tubercle are avulsions of the tubercle with the biceps brachii origin attached and are often distally displaced. While it occurs frequently in immature animals, the secondary center of ossification of the supraglenoid tubercle should be differentiated from true fractures.

▼ ***Key Point*** In immature animals, base diagnosis of supraglenoid tubercle fractures on obvious distal displacement of the tubercle on comparison with radiographs from the opposite (unaffected) shoulder to avoid confusion with the normal apophyseal appearance.

Technique Overview

- Osteotomy of the greater tubercle of the humerus provides adequate exposure for this fracture.
- Stabilize the fracture with a lag screw and an antirotational Kirschner wire (Fig. 102-5).
- If there is difficulty in reduction, the biceps tendon may be transected from the origin to remove its opposing pull on the fragment. In this case, the

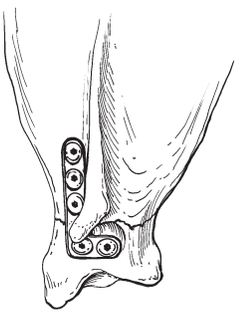

Figure 102-4. Fracture of the scapular neck stabilized with an L oblique bone plate of sufficient size.

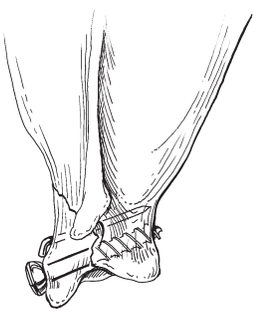

Figure 102-5. Fracture of the supraglenoid tubercle stabilized with a lag screw and antirotation Kirschner wire.

biceps brachii tendon should be transposed to the humerus and attached with a lag screw and spiked washer.

Glenoid Fractures

▼ ***Key Point*** Glenoid fractures are intraarticular and require open reduction and internal fixation for acceptable alignment and restoration of normal joint function.

Technique Overview

- Approach fractures of the glenoid by acromion osteotomy, greater tubercle osteotomy, transection of the insertion of the acromial and spinous heads of the deltoideus muscle, or a combination of these. The suprascapular nerve should be identified and protected.
- Fracture fragments are anatomically positioned and stabilized with a lag screw parallel to the joint surface or between the fragments and the scapular neck.
- Rotational stability of fragments is improved by addition of a second lag screw or Kirschner wire in each fragment.
- In the case of T-shaped combinations of glenoid and neck fractures, first reduce the articular surface with a lag screw parallel to the joint, and then repair the neck fracture with a T or L plate (Fig. 102-6).

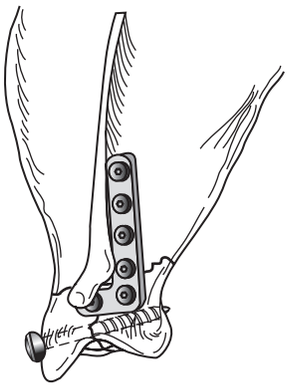

Figure 102-6. T fracture of the scapula stabilized with a lag screw and L bone plate.

Postoperative Considerations

- The prognosis is good for both fracture healing and normal shoulder function provided good orthopedic technique during implant fixation is followed.
- Restrict activity until healing is adequate as demonstrated on radiographs (8–12 weeks average).
- For animals treated only by cage confinement, periodic reexamination or radiographs may be required to evaluate fracture healing and guard against changes in limb alignment during healing.

Complications

- Injury of the suprascapular nerve can result in atrophy of the supraspinatus muscle.
- Malalignment at the articular surface leads to osteoarthritis and decreased limb function. Salvage procedures that provide good limb function include glenoid excision and total scapulectomy.
- Screw loosening and migration are common problems due to poor purchase in thin scapular bone. If implants move or migrate, fracture fixation is considered failing and further surgical intervention is indicated.
- Nonunion of scapular fractures is rare.

PROXIMAL HUMERAL FRACTURES

Preoperative Considerations

- Fractures of the proximal humerus occur rarely, but such occurrences are most common in skeletally immature animals in the form of a Salter-Harris type I, II, or III fracture.
- The proximal humeral physis functionally closes at approximately 8 months of age and is radiographically closed beginning at 10 months of age.
- If the proximal humerus is fractured in a mature, aged dog, radiographs of the fracture should be carefully evaluated for periosteal proliferation, bone lysis, bony sclerosis, or cortical thinning around the

fracture margins. Such findings indicate pathologic fractures likely due to osteosarcoma.

Surgical Procedures

- Perform a craniolateral approach to the scapulohumeral joint for Salter-Harris type I or II fractures.
- Salter-Harris type III or comminuted proximal fractures in mature animals require osteotomy of the acromion and scapulohumeral capsulotomy.
- Articular fractures of the humeral head require anatomic reduction of the articular surface to prevent later osteoarthritis.

Equipment

- Standard orthopedic pack and pointed bone reduction forceps
- Selection of Kirschner wires and small Steinmann pins
- Bone plating sets, including 2.0-, 2.7-, 3.5-, and 4.5-mm screws to accommodate all animal sizes

Fractures or Osteotomy of the Greater Tubercle or Lesser Tubercle

Technique Overview

- Fractures occur primarily in immature animals as avulsion fractures due to ligamentous attachments.
- Stabilize the tubercle with a tension band device or with a lag screw and an antirotational Kirschner wire through the tubercle into the metaphysis or caudal humeral cortex.

Salter-Harris I or II Fractures of the Proximal Physis

Technique

1. Place the animal in lateral recumbency and the limb is prepared for surgery.
2. Perform a craniolateral approach to the proximal humerus.
3. In very young (<7 months of age) animals, stabilize the fracture using two or more smooth Kirschner wires or Steinmann pins placed in parallel fashion from the greater tubercle into the proximal metaphysis or caudal cortex of the metaphyseal region (Fig. 102-7).
4. In older animals for which skeletal growth is complete, stabilize the fracture using one lag screw and a Kirschner wire or two lag screws placed from the greater tubercle into the proximal metaphysis (see Fig. 102-7).

Fractures of the Humeral Head (Salter-Harris III Fractures)

Technique

1. Place the animal in lateral recumbency and aseptically prepare the limb for surgery.

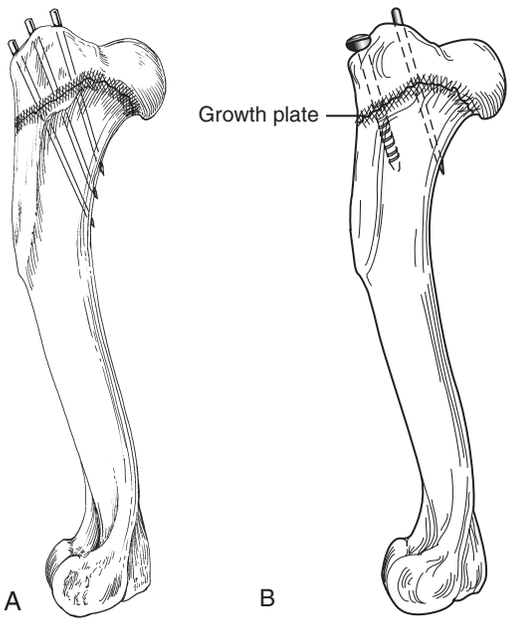

Figure 102-7. Salter-Harris type I fracture of the proximal humerus stabilized with multiple parallel Kirschner wires *(A)* or stabilized with a lag screw and Kirschner wire *(B)*.

2. Perform a craniolateral approach to the proximal humerus. Combine with an osteotomy of the acromion.
3. In young (<7 months of age) animals, reduce and stabilize the epiphyseal fragments with two lag screws or a lag screw and an antirotational Kirschner wire driven parallel to the joint surface from the greater tubercle into the caudal humeral head. The epiphysis is then reattached to the metaphysis using two or more Kirschner wires or Steinmann pins placed in parallel fashion from the greater tubercle into the proximal metaphysis.
4. Older animals may be repaired in a similar fashion or repaired using a T plate that spans the proximal humeral fragments cranially and caudally and reattaches them to the metaphysis.

Fractures of the Humeral Neck

Technique

These types of fractures occur in older animals.

1. Anatomically align the fracture fragment and then stabilize it with a T plate or other plate engaging six cortices on each side of the fracture.
2. Alternatively, stabilize the fracture using Rush pins or Kirschner wires placed in Rush pin fashion (Fig. 102-8).

Postoperative Care

- Restrict the animal to a cage until radiographic healing is demonstrated.

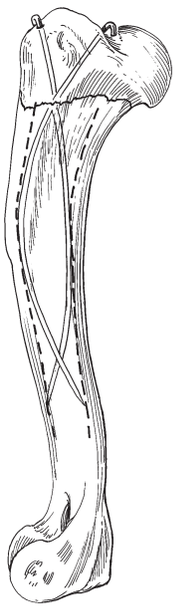

Figure 102-8. Fracture of the proximal humeral neck stabilized with pins in Rush fashion.

- Obtain appropriate radiographs immediately postoperatively and at 4-week intervals until the fracture is healed.
- Malalignment at the articular surface leads to osteoarthritis and decreased limb function. Salvage procedures that provide good limb function include glenoid excision and total scapulectomy.

Complications

- Nonunion or malunion occurs rarely.
- Premature closure of the proximal humeral physis may occur and may affect limb function in animals < 7 months of age at the time of fracture.

Prognosis

- If adequately reduced and stabilized, these fractures heal rapidly and consistently.
- Range of shoulder motion generally remains normal, provided that anatomic reduction of the articular surface was achieved.

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Chapter

103 Scapulohumeral Luxation

Robert A. Taylor

Scapulohumeral luxation is an uncommon clinical condition. Both congenital and traumatic luxations occur; the latter is more common.

Medial luxation of the humeral head is most common, especially in smaller-breed dogs. Lateral luxation of the humeral head, while less common, usually occurs in larger dogs (Fig. 103-1). Cranial and caudal luxations are rare.

ANATOMY

- The shoulder joint is a ball-and-socket joint. The articular surface of the scapula forms the concave glenoid, and the convex humeral head articulates within it. Although the joint is capable of movement in any direction, its major actions are flexion and extension.
- The joint capsule is continuous and blends with the medial and lateral glenohumeral ligaments (Fig. 103-2). These ligaments help to support the joint and may be 2.0 mm or greater in thickness.
- The subscapularis, supraspinatus, infraspinatus, and teres minor muscles provide periarticular support.
- The tendon of origin of the biceps brachii and its sheath join with the joint capsule on its cranial medial aspect and provide additional stability. The bicipital tendon is held in the bicipital groove by the small but sturdy transverse humeral ligament.
- Luxation is not possible unless the glenohumeral ligaments and joint capsule have been ruptured.

CLINICAL SIGNS

- The principal signs are varying degrees of lameness, depending on the severity of the luxation.

DIAGNOSIS

- Diagnosis is made by physical examination and confirmed by radiography.
- Careful palpation of the area between the acromion of the scapula and greater tubercle can be helpful.
- In medial luxations, hold the elbow in a flexed position and abduct the lower limb.
- In lateral luxations, hold the elbow in a flexed position and adduct the lower limb.
- Examine both shoulders simultaneously and use the normal limb for comparison.

PREOPERATIVE CONSIDERATIONS

- Radiograph the shoulder to rule out intra-articular fractures.
- Use general anesthesia for all shoulder reduction procedures, whether open or closed.
- Closed reduction is a non-surgical treatment.

PROCEDURES FOR CLOSED REDUCTION

Procedure for Medial Luxation

1. Flex the elbow and pull the limb laterally while exerting digital pressure on the scapular spine.
2. Gently rotate the limb downward to reduce the luxation.
3. Place the limb in a Velpeau sling for 10 to 14 days.
4. If the joint is stable on removal of the sling, begin passive range-of-motion exercises. When possible, encourage swimming as an adjunct to physical therapy, but restrict exercise for 1 month.

Procedure for Lateral Luxation

1. Flex the elbow and extend the shoulder to reduce the luxation.
2. Gently rotate the humeral head upward to facilitate reduction.
3. Use a spica splint to support the joint for 10 to 14 days.

▼ ***Key Point*** Surgical stabilization of complete or partial luxations (chronic instability) can be challenging. When possible use tissue anchors and non-absorbable sutures to enhance the stability. In some cases of medial glenohumeral instability

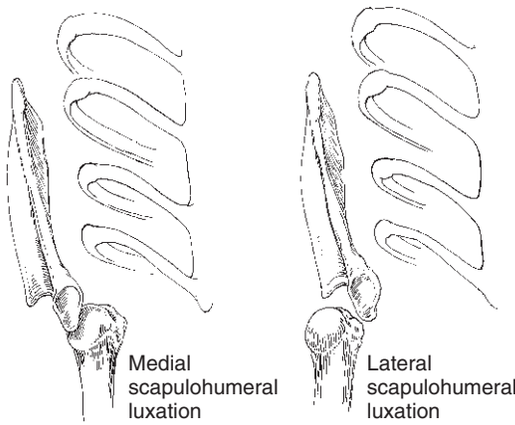

Figure 103-1. Medial *(left)* and lateral *(right)* luxations of the scapulohumeral joint.

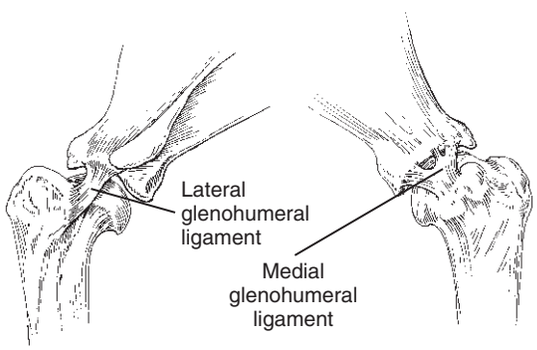

Figure 103-2. The glenohumeral ligaments.

I have successfully used radio-frequency tissue shrinkage to increase the stability of the joint. In cases with severe secondary changes consider scapulohumeral arthrodesis as a salvage procedure.

SURGICAL PROCEDURE FOR OPEN REDUCTION

Objectives

- Surgically repair the ruptured glenohumeral ligament and joint capsule.
- Stabilize the shoulder joint and prevent recurrent luxations.

Equipment

- Standard general surgical pack and suture material
- Standard orthopedic set
- Oscillating bone saw
- Osteotomes and mallet
- Kirschner wires and pin chuck
- Appropriate retractors

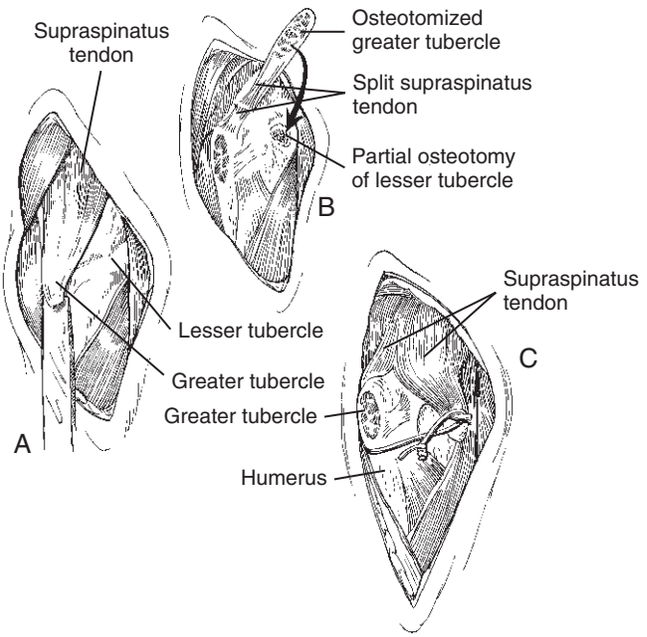

Figure 103-3. *A,* Use an oscillating bone saw or osteotome to partially osteotomize the greater tubercle. *B,* Split the supraspinatus tendon with a scalpel blade. *C,* Attach the split portion of the supraspinatus tendon to the region of the lesser tubercle.

Surgical Repair of Medial Luxation

Technique

1. Place the dog in lateral recumbency with the affected leg up. After preparing the limb for aseptic surgery, place the distal extremity in a sterile stockinette so that it is accessible to intraoperative manipulation. Make an incision on the craniomedial aspect of the joint.
2. Reflect the skin and subcutaneous tissue and incise the brachiocephalicus muscle along its medial edge and retract it.
3. Incise the superficial and deep pectoral muscles near their point of insertion on the humerus. Be sure to separate the supraspinatus muscle from the deep pectoral muscle.
4. Using an osteotome or oscillating saw (Fig. 103-3*A*), partially osteotomize the greater tubercle of the humerus. Hold the osteotome on the crest of the greater tubercle and make the medial line of the cut parallel to the humeral border of the transverse humeral ligament. Avoid cutting the infraspinatus tendon.
5. Using sharp dissection, carefully split the supraspinatus tendon (Fig. 103-3*B*).
6. Partially osteotomize the lesser tubercle and prepare it to accept the bony fragment of the greater tubercle. Secure the greater tubercle fragment (with the attached portion of the supraspinatous tendon) in place with two Kirschner wires (Fig. 103-3*C*). A tension band wire may be used.

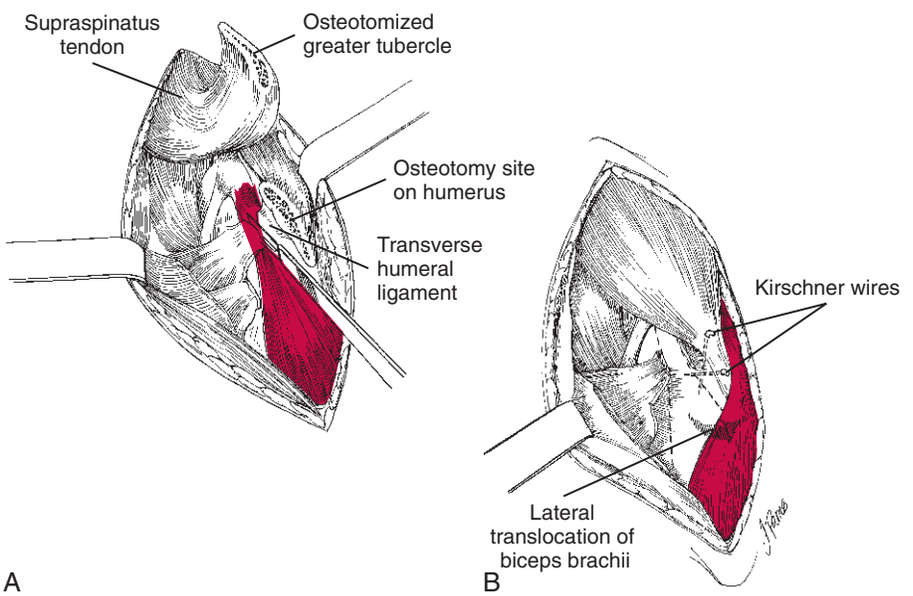

Figure 103-4. *A,* Transection of the transverse humeral ligament. *B,* Lateral translocation of the bicipital tendon. Use Kirschner wires to stabilize the greater trochanter back to its origin.

7. Suture the deep pectoral muscle over the lesser tubercle. Advance the superficial pectoral muscle over the proximal cranial border of the humerus and suture it to the deltoideus muscle. Suture the brachiocephalicus muscle to the brachial fascia.
8. Close the subcutaneous tissue and skin routinely.

Monitor for signs of seroma formation, hemorrhage, and infection.

Repair of Lateral Luxation

Technique

1. Positioning and draping is similar to that for surgical repair of medial luxation.
2. Skin incision and tissue retraction are the same as for medial luxation repair.
3. Incise the superficial and deep pectoral muscles. Incise the deltoideus muscle near the point of insertion on the cranial lateral aspect of the proximal humerus.
4. Transect the transverse humeral ligament and free the bicipital tendon from the surrounding tissue (Fig. 103-4*A*).
5. Completely osteotomize the greater tubercle to allow reflection of the intact tendon.
6. Translocate the bicipital tendon laterally on the opposite side of the osteotomized greater tubercle (Fig. 103-4*B*). Secure the greater tubercle with several Kirschner wires.
7. Reattach the muscles and close the skin and subcutaneous tissue routinely.

POSTOPERATIVE CARE

- Following open repair of a scapulohumeral luxation treat postoperative pain, minimize post-surgical inflammation, and encourage movement of the distal extremity. Use ice packs, gentle massage, and passive range of motion of the elbow and carpus to minimize these problems.
- If the limb is not bandaged, supervised weight bearing can occur. During the first 3 weeks after surgery strict crate confinement and careful leash walks must occur. Following skin staple removal, begin water therapy in an underwater treadmill with the water level at the top of the scapula. This type of rehabilitation allows early weight bearing, and the buoyancy of the water reduces the weight-bearing forces on the operated leg.
- As the surgical wound and repair heals, more directed and vigorous rehabilitation can occur.
- The goal is to match the rate of tissue repair and healing with the postoperative rehabilitation.

PROGNOSIS

The prognosis is good with adequate stabilization.

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Chapter

104 Fractures of the Humerus

Robert B. Parker

ANATOMY

- The proximal portion of the humerus has strong, thick cortices cranially and extends to the large deltoid tuberosity. The musculospiral groove starts caudally and twists cranially over the lateral aspect of the bone. The brachialis muscle and neurovascular structures, including the clinically significant radial nerve, lie within the musculospiral groove.
- The lateral portion of the distal humeral condyle is termed the *capitulum* and the medial portion is termed the *trochlea*.
- When viewed cranially, the bone is essentially straight; however, the medullary canal runs slightly lateral to medial from proximal to distal. Distally, the trochlea is larger than the capitulum, and is in a more direct line with the medullary canal. The capitulum has a thinner epicondylar attachment to the bone and is the main weight-bearing surface for the radial head.
- Important muscles to identify laterally are the lateral head of the triceps, the brachialis, the brachiocephalicus, and the acromial head of the deltoid. The radial nerve is important to identify laterally.
- Important medial soft tissue structures include the medial head of the triceps, the biceps brachii, and the median and ulnar nerves.

ETIOLOGY

- Most humeral fractures occur secondary to motor vehicle trauma or are caused by a fall from excessive height.

DIAGNOSIS

- Rule out injuries associated with thoracic trauma. Perform a complete clinical and radiographic examination to rule out pneumothorax, hemothorax, diaphragmatic hernia, rib fractures, chylothorax, and traumatic myocarditis.

▼ ***Key Point*** Obtain thoracic radiographs in all animals with humeral fractures.

- The neurovascular integrity of the limb is of paramount importance. Fully assess the injured forelimb.
- Obtain radiographs of the involved humerus to characterize the fracture(s). If necessary (e.g., for prebending bone plates), obtain radiographs of the normal humerus.

PROXIMAL HUMERAL PHYSEAL FRACTURES

Preoperative Considerations

- This type of fracture is seen infrequently in young dogs prior to physeal closure. Closure of the proximal physis occurs between 9 and 15 months of age.
- The fracture typically is complete, but incomplete and impaction fractures can also occur.
- Except for incomplete fractures, closed reduction is very difficult. Open reduction of complete fractures is recommended.
- In selected cases (e.g., non-displaced fractures) use a Velpeau sling or spica cast to immobilize the shoulder joint.

Surgical Procedure

Objectives

- Provide stable fixation while allowing continued physeal growth.
- Provide early range of motion.

Equipment

- General surgical instrument pack
- Jacob's pin chuck and a complete assortment of Steinmann pins and Kirschner wires
- Bone-holding forceps
- Small and large reduction forceps with points
- Cerclage wire equipment
- Periosteal elevator
- Kirschner apparatus (external pin fixators)
- Additional (AO) equipment (Synthes, Wayne, PA) for plate and screw fixation (for selected fractures)

Technique

Open Reduction

1. After preparing the limb for aseptic surgery, use a cranial approach with cranial retraction of the brachiocephalicus muscle to elevate and expose the fragments.
2. Use small pointed forceps to carefully grasp the epiphysis and use the elevator to lever the fragments into reduction.
3. Achieve fixation with double Kirschner wires or Steinmann pins, beginning at the greater tubercle. To prevent compression of the physis, do not use a figure-eight tension band.
4. Cancellous lag screws have been used by some surgeons, but they can cause interfragmentary compression and premature physeal closure.
5. Close the incision routinely.

Postoperative Care

- Encourage early range-of-motion exercise by allowing restricted activity.
- Remove fixation devices when healing is complete.

▼ ***Key Point*** Premature closure of the physis may occur as a result of the initial or surgical trauma; however, this rarely causes a clinical problem.

PROXIMAL DIAPHYSEAL FRACTURES

Preoperative Considerations

- Proximal fractures are the least common diaphyseal fractures owing to the comparative strength of the humerus in this area.
- Most proximal diaphyseal fractures occur just proximal to the deltoid tuberosity. The distal fragment is displaced cranially due to the pull of the deltoid muscle, and medially due to the pull of the pectoral muscle.
- Evaluate the brachial plexus and the radial nerve. Accurate reduction is important because excessive callus production can produce postoperative pressure on these neural structures.
- Many of these fractures occur secondary to metabolic bone disease. Carefully evaluate radiographs of the fracture for evidence of bone disease. Perform appropriate tests if metabolic or neoplastic disease is suspected.

Surgical Procedure

Objective

- Because closed reduction with external coaptation probably is not an option, perform open reduction with internal fixation.

Equipment

- Same as for proximal physeal fractures

Technique

Open Reduction

1. For open reduction, use a cranial approach. Incise the skin along the craniolateral aspect of the humerus, beginning at the scapular tuberosity. Incise the fascial attachment of the brachiocephalicus muscle on the cranial aspect of the humerus to allow cranial retraction of the muscle. Elevate the deltoid muscle from the deltoid tuberosity and retract it caudally to gain access to the fracture site.
2. Place single or double Steinmann pins retrograde from the fracture site into the proximal fragment (Fig. 104-1), or place the pins normograde starting at the greater tubercle of the humerus.
3. Because the fractures often are transverse, a single intramedullary pin may not provide rotational stability. Use a type I external fixator (see Chapter 111) or hemicerclage wires to provide rotational stability in a transverse or short oblique fracture.
4. Alternatively, two Rush pins provide excellent rotational stability in fractures of this type.
5. In very large dogs, a bone plate applied to the cranial surface of the humerus is an excellent method of fixation. The basic principle of three screws (six cortices) above and three screws below the fracture site applies.
6. Close the incision routinely.

Postoperative Care

- External fixation is not desirable following internal fixation.

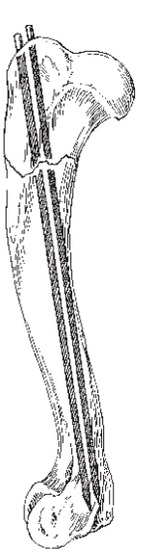

Figure 104-1. Steinmann pin placement for repair of a proximal diaphyseal fracture.

- Encourage early range of motion by allowing restricted exercise.

DIAPHYSEAL FRACTURES

Preoperative Considerations

- Muscle contracture causes overriding of the fragments.
- The fractures often are spiral or oblique and may entrap the radial nerve.
- Consider early closed reduction and closed normograde pinning. Attempt this only within the first few days following the injury.

Surgical Procedure

Objective

- Provide stable fixation without jeopardizing important neurovascular structures.

Equipment

- Same as for proximal physeal fractures

Technique

1. For open reduction, make a lateral approach to expose midshaft to distal fractures. Incise the fascia cranial to the lateral head of the triceps muscle to allow cranial retraction of the brachiocephalicus and superficial pectoral muscles, and caudal retraction of the triceps. At the distal one-third of the incision, use extreme care to identify the radial nerve as it crosses from caudal to cranial between the brachialis and lateral head of the triceps. Use the brachialis muscle as a cushion to protect the radial nerve. Retract the brachialis either proximally or distally to expose the fracture site. Reduction may be facilitated by careful myotomy of the brachialis.
2. Many humeral fractures in small to medium-sized dogs can be successfully repaired with a combination of pins, stacked pins, full or hemicerclage wires, or external skeletal fixation. This is especially true with oblique or spiral fractures.
   a. When using pin fixation, retrograde the pins into the proximal fragment from the fracture site. When the fracture is reduced, the pin should enter the trochlea when driven into the distal fragment. Correct pin placement is slightly lateral to medial to engage the trochlea (Fig. 104-2, *left*).

▼ ***Key Point*** Try to direct the pin slightly laterally when retrograding it into the proximal humeral fragment.

   b. Rotational stability may not be achieved without additional pins, orthopedic wire, or external skeletal fixation.

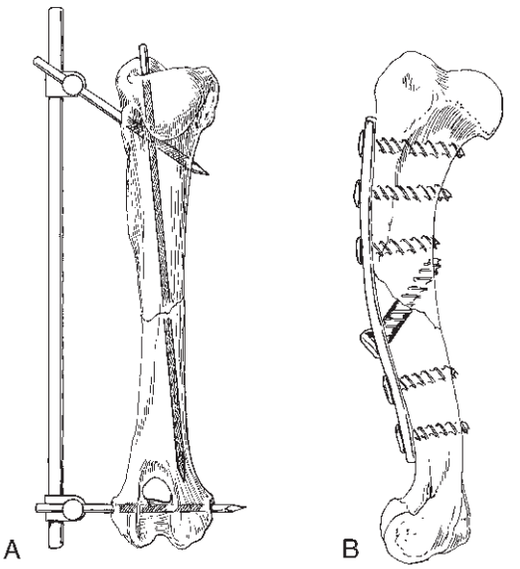

Figure 104-2. Fixation of diaphyseal fracture. *A,* External skeletal fixation. *B,* Internal cranial plate placement.

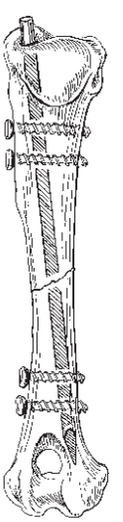

Figure 104-3. Caudo-cranial view of humerus with an interlocking nail and four locking screws.

3. Interlocking nails (Innovative Animal Products, Rochester, MN) have been successful in stabilizing diaphyseal fractures in larger breeds. By statically locking the nail both proximally and distally, rotational forces can be effectively neutralized (Fig. 104-3).
4. Because the humerus is difficult to expose and is an anatomically complex bone, the exposure for plate fixation can be difficult. However, cranial, lateral, or medial plate fixation can produce excellent results.
   a. Cranial plate placement is preferred for midshaft fractures. After exposure and reduction, contour an appropriately sized plate to fit the cranial

aspect of the bone (see Fig. 104-2, *right*). Protect the radial nerve distally. Freeing the origin of the extensor carpi radialis muscle may enhance distal exposure; however, the supratrochlear foramen may limit the distal extent of the plate.

b. Lateral plate placement is difficult because of the contours of the musculospiral groove and lateral epicondylar ridge.

c. Medial plate placement affords a fairly flat bony surface, and the plate can be contoured onto the trochlea. Medial placement is especially useful for distal diaphyseal fractures. The medial approach involves a medial skin incision and careful division between neurovascular structures. Retract the biceps brachii muscle, the median and musculocutaneous nerves, and brachial artery and vein cranially, and retract the medial head of the triceps and ulnar nerve caudally. The pectoral muscles limit exposure proximally.

5. Close the incision routinely.

Postoperative Care

- Restrict activity, but encourage early range of motion.
- If external skeletal fixation is used to supplement rotational or axial stability, remove it in 4 to 6 weeks.
- Remove intramedullary pins following fracture healing; supplemental cerclage or Kirschner wires are usually left in place.
- Do not remove bone plates unless they are causing a problem.

SUPRACONDYLAR FRACTURES

Preoperative Considerations

- The supratrochlear foramen creates a weak point in the distal humeral metaphysis.
- The trochlea is in a straight line with the diaphysis of the humerus. Additionally, the majority of the forces are transmitted through the capitulum, which articulates with the radial head. The capitular junction with the shaft in the area of the supratrochlear foramen is smaller and weaker than the medial side.
- Rigid internal fixation generally is indicated. Excessive callus formation from inadequate immobilization can result in impairment of normal elbow function.

Surgical Procedure

Objective

- Provide stable internal fixation to allow early weight bearing and range of motion.

Equipment

- Same as for proximal physeal fractures

Technique

1. The surgical approach is similar to the previously described lateral and medial approaches.
   a. The caudal approach to the elbow joint by olecranon osteotomy also provides excellent exposure to the supracondylar area. This approach is particularly useful for comminuted fractures in this area in large-breed dogs, when plating is anticipated.
2. Steinmann pin(s) placed well into the trochlea, with an additional cross-pin from the capitulum to produce rotational stability, may provide adequate stability. A type I external fixator, using a transcondylar distal fixation pin, can provide additional fixation and rotational stability.
   a. To seat the Steinmann pin adequately in the trochlea, initially retrograde the pin distally into the trochlea from the fracture site. The pin exits the condyle medial to the ulna and can be withdrawn until the tip is flush with the fracture site. After reduction, advance the pin proximally to exit the humerus at the greater tubercle. Withdraw the pin proximally until the distal tip is flush with the trochlea.
3. Alternatively, double Rush pins can provide excellent stability.
4. Because of the propensity for nonunion in medium- and large-sized dogs and in dogs with severely comminuted fractures, small bone plates can be applied to the caudal medial or lateral ridges of the epicondyles. This is usually done through a caudal approach (osteotomy of the olecranon). See Chapter 105 for repair of olecranon fractures.
5. Close the incision routinely.

Postoperative Care

▼ ***Key Point*** Physical therapy (e.g., active or passive elbow flexion and extension) is critical to prevent postoperative limitation of elbow function.

- See the previous discussion of postoperative care under Diaphyseal Fractures.

CONDYLAR FRACTURES

Preoperative Considerations

- About 90% of condylar fractures involve the lateral portion of the condyle.
  - The lateral portion of the condyle (capitulum humeri) carries most of the force through the elbow joint by way of its articulation with the radial head. The capitulum sits lateral to the humeral diaphysis when compared with the medial portion (trochlea humeri). Also, the lateral epicondylar crest is smaller than the medial epicondylar crest.

- Anatomic reduction is necessary to prevent secondary degenerative joint disease.
- Spaniel-type and Rottweiler dogs have been shown to have a heritable defect producing incomplete ossification of the humeral condyle, predisposing them to this injury.

Surgical Procedure

Objectives

- Achieve anatomic reduction and interfragmentary compression because the joint surface is involved.
- Restore range of motion of the elbow joint.

Equipment

- Same as for proximal physeal fractures

Technique

1. Open reduction and internal fixation usually are necessary. However, closed reduction maintained with a condyle clamp and fixation with a percutaneously applied transarticular lag screw has been described.
2. For open reduction, use a lateral or craniolateral approach.
3. Align intercondylar and supracondylar fracture lines perfectly and hold with a Vulsellum or AO pointed reduction forceps.
4. Use a transcondylar lag screw with an antirotation Kirschner wire to achieve interfragmentary compression (Fig. 104-4, *left*).
   a. The starting point for the drill bit is slightly distal and cranial to the most prominent point of the lateral epicondyle. Aim the drill at the corresponding point on the medial side. After measuring and tapping, place an appropriate screw.
   b. When using a fully threaded screw, overdrill the lateral fragment to achieve interfragmentary compression ("lag" effect).

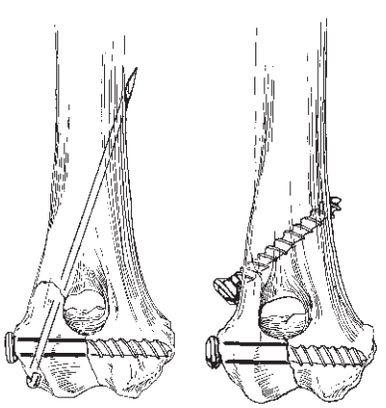

Figure 104-4. Fixation of condylar fractures. *Left,* Transcondylar lag screw and antirotation K-wire. *Right,* With oblique fractures, use two lag screws for increased stability.

   c. As an alternative method of achieving precise screw location with a fully threaded screw, use the overdrill bit to make the gliding hole in the capitulum. To do this, rotate the condyle laterally to expose the intercondylar fracture surface of the capitulum. Center the drill at the fracture surface and direct it laterally to exit the bone just distal and cranial to the lateral prominence. Then reduce the fracture and use a drill sleeve insert (in the drill hole in the capitulum) to direct the smaller drill (thread hole) into the trochlea. Place the screw routinely.
   d. Place an antirotational Kirschner wire across the condyles or across the distal diaphysis of the humerus (Fig. 104-4, *left*).
   e. If the supracondylar portion of the fracture is oblique enough, place additional screws along this aspect for additional stability (Fig. 104-4, *right*).
   f. Fixation of the condyle has also been achieved with self-compressing Orthofix pins.
   g. Using crossed Kirschner wires to achieve intercondylar stability is not recommended.
   h. Close the incision routinely.

Postoperative Care and Complications

- Encourage early range of motion but restrict activity.
- The lag screws usually are not removed.
- Reduced range of motion and arthritis of the elbow joint are the most common complications. Accurate alignment and apposition of fracture fragments reduces the incidence of these problems.

T OR Y (INTERCONDYLAR) FRACTURES OF THE HUMERAL CONDYLES

Preoperative Considerations

- In this type of fracture, both the lateral and medial portions of the condyle are fractured from the humeral metaphysis; in addition, an intra-articular fracture occurs, splitting the condyle.
- The basic principles of repair are the same as for supracondylar and single condylar fractures.
- These usually are very difficult to repair adequately. Consider referring these cases to an orthopedic specialist.

Surgical Procedure

Objective

- Achieve accurate anatomic reduction and stability in an unstable area.

Equipment

- Same as for proximal physeal fractures

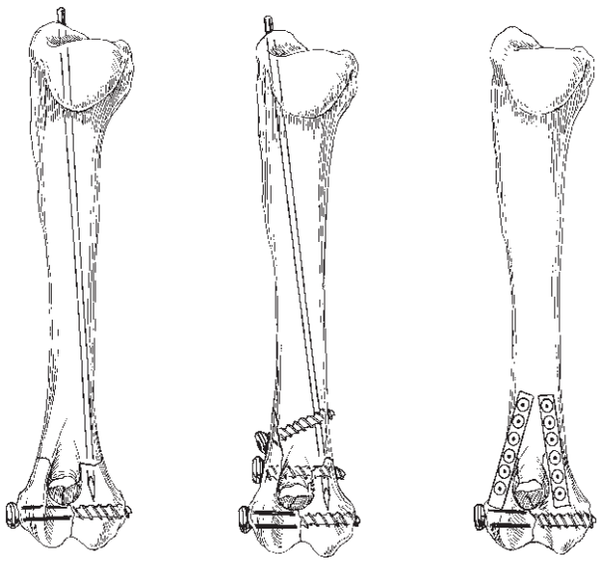

Figure 104-5. Fixation methods for intercondylar fractures. *Left,* Repair condyle with lag screw, then secure to humeral diaphysis with Steinmann pins. *Center,* Attach medial portion of the condyle to humerus with lag screw, then attach lateral portion of the condyle with lag screws and pin. *Right,* Caudal bone plates provide further stability.

Technique

1. Expose the fracture through a caudal approach via olecranon osteotomy (see Chapter 105 for olecronon repair).
2. Lag the condyles together initially to create a "two-piece fracture" (now similar to a supracondylar fracture), which is attached to the humeral diaphysis; or attach the trochlea to the humerus; follow with lag-screw fixation of the capitulum to the trochlea (Fig. 104-5, *left and center*).
   a. For more rigid stability, stabilize the supracondylar portion of the fracture with two small caudally placed bone plates (Fig. 104-5, *right*).
3. Close the incision routinely.

Postoperative Care and Complications

- Encourage early function or passive range-of-motion exercises.
- In one series, 46% of dogs regained moderate to normal limb function; 18% had severe lameness as a result of deformity and osteoarthritis.

SUPPLEMENTAL READING

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Nunamaker DM: Fractures of the humerus. In Newton CD, Nunamaker DM (eds): Textbook of Small Animal Orthopedics. Philadelphia: JB Lippincott, 1985, p 357.

Chapter

105 Fractures and Growth Deformities of the Radius and Ulna, Luxation of the Elbow

James Tomlinson

FRACTURES OF THE RADIUS AND ULNA

Fractures of the radius and ulna are commonly seen in small animal practice. Although most of these fractures occur as a result of automobile accidents, they also result from falling or jumping. Fractures of one or both bones and a wide variety of fracture types are seen. Open fractures of the distal one-half of the radius and ulna are common, owing to minimal soft tissue coverage. Complications include delayed union, nonunion, joint stiffness, and arthritis.

Anatomy

Radius

- The radius and ulna make up the antebrachium.
- The radius is the main weight-bearing bone of the antebrachium and is shorter than the ulna. The radius is composed of the head, neck, body, and distal extremity. The medullary canal is elliptical in shape owing to flattening of the radius.
- The radius is attached to the ulna by an interosseous ligament that helps to maintain their spatial relationship following fracture. The short radial collateral ligament runs from the styloid process of the radius to the radial carpal bone and provides medial support to the antebrachiocarpal joint.
- The cranial surface of the distal radius contains three grooves that contain (from medial to lateral) the tendons of abductor pollicis longus, extensor carpi radialis, and common digital extensor muscles.

Ulna

- The ulna is the longest bone in the body and is composed of the olecranon, trochlear notch, anconeus, body, and the distal extremity called the styloid process.
- The olecranon has a strong muscular attachment, the triceps muscle.
- The ulnar body tapers as it crosses caudal to the radius to articulate with the palmarolateral aspect of the carpus. The medullary canal of the ulna functionally ends about one-third from the distal end.
- The strong, short ulnar collateral ligament runs from the tip of the styloid process of the ulna to the ulnar carpal bone, giving lateral support to the antebrachiocarpal joint.

Vascular Supply

- The radial and interosseous arteries provide the main arterial supply to the antebrachium and are subject to injury from trauma or surgery.
- The radial artery travels along the palmaromedial aspect of the radius just under the flexor carpi radialis muscle.
- The interosseous artery branches into other interosseous arteries that run in the space between the radius and ulna.

Nerve Supply

- The radial, median, and ulnar nerves supply the antebrachium and manus.

General Preoperative Considerations

- Evaluate the thorax for pulmonary contusions, pneumothorax, and diaphragmatic hernia with thoracic radiography. Evaluate for traumatic myocarditis with electrocardiography.
- Examine the animal for concurrent injuries; inspect other limbs for fractures or other significant injury.
- Inspect the antebrachium for evidence of wounds indicating an open fracture.
- Evaluate nerve function of the affected limb by testing reaction to a painful stimulus to the skin of the various dermatomes and by withdrawal of the limb.
- Initially place the limb in a Robert Jones bandage or splint to prevent further soft tissue damage and

to prevent the fracture from becoming an open fracture.
- Obtain two radiographic views of the fractured limb to include the elbow and carpus.

General Objectives of Surgical Procedures

- Align and stabilize the fracture(s) to permit uncomplicated healing with normal joint and limb function.

▼ ***Key Point*** Exact anatomic alignment and rigid fixation (compression) of articular fractures is imperative.

- Allow early return to weight bearing.
- Preserve neurovascular structures during repair.

General Postoperative Care and Complications for Radial and Ulnar Fractures

- Place the limb in a soft padded bandage for 3 to 10 days to reduce postoperative swelling. Provide more rigid external support if needed.
- Reevaluate the fracture radiographically every 3 to 4 weeks until the fracture has healed.
- Restrict activity until the fracture has healed.

Complications

- Delayed and nonunion healing (see Chapter 122), osteomyelitis (see Chapter 121), and implant failure may occur.
- Joint fractures are prone to subsequent degenerative joint disease and callus that interferes with joint mobility if anatomic alignment and rigid stability have not been achieved.
- Joint stiffness can develop with articular fractures. Rigid stability of the fracture allows early, controlled use of the joint.

▼ ***Key Point*** Radius and ulna fractures in immature animals may cause premature closure of the growth plates and synostosis of the radius and ulna. Both conditions cause growth deformities of the limb. Early recognition and intervention is necessary to minimize growth deformities.

Olecranon Fractures

Objective

- Counteract the distractive force of the triceps and convert it into a compressive force using the tension band principle.

Equipment

- General surgery pack and standard suture material
- Monofilament stainless steel surgical wire (20 and 18 gauge)
- Intramedullary pins and Kirschner wires (K-wires)
- Jacobs chuck or power drill
- Wire-tightening device (vise grips or wire twister)
- Pin and wire cutter
- Bone reduction forceps

Technique

1. Place the patient in lateral recumbency, with the affected leg up, and prepare the limb for aseptic surgery.
2. Make a caudolateral skin incision centered over the olecranon.
3. Reflect the skin and subcutaneous tissue to expose the olecranon and proximal shaft of the ulna. Subperiosteally elevate the extensor and flexor carpi ulnaris muscles from the proximal shaft of the ulna.
4. Reduce the fracture and hold it in reduction with bone reduction forceps.
5. Drive two K-wires or small intramedullary pins parallel from the tip of the olecranon across the fracture line and into the distal segment of the ulna (in very small animals, drive only one K-wire).
6. Drill a hole (perpendicular to the ulnar long axis) in the distal ulnar segment 1.5 to 2 times the distance from the olecranon to the fracture line.
7. Insert surgical wire in the hole and place the wire around the pins in a figure-eight fashion.
8. Twist the wire to achieve equal tension on the wire.
9. Bend the pins over and cut them off short. Cut the wires leaving two to four twists and bend the wire tips over (Fig. 105-1).
10. Close the subcutaneous tissue and skin routinely.

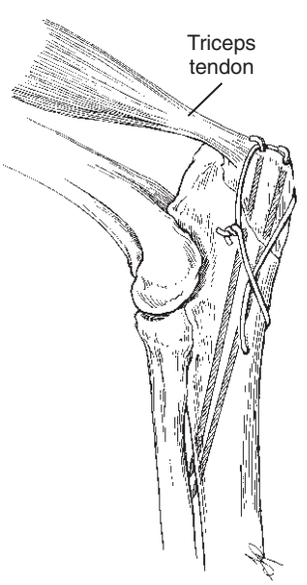

Figure 105-1. Pin and wire placement for olecranon fracture repair.

Trochlear Notch Fractures

Objectives

- Maintain precise anatomic alignment of the fracture (because it is an articular fracture).
- Perform rigid fixation of the fracture to minimize periosteal callus.
- Counteract the distractive forces of the triceps muscle using the tension band principle.

Equipment

- Same as for olecranon fractures with the addition of bone plating equipment.

Technique

Small and Medium-Sized Dogs; Cats; No Fracture Comminution Present

1. Repair the fracture with a tension band wiring technique, as described previously under Olecranon Fractures.
2. Maintain anatomic alignment of the fracture while driving the pins and tightening the wire in a figure-eight configuration.

Large Dogs; Fractures with Comminution

1. Expose the trochlear notch, as described for olecranon fractures.
2. Reattach butterfly segments of bone with lag screws and Kirschner wires.
3. Contour a bone plate to the caudal or caudolateral side of the ulna and secure it to the ulna with bone screws (Fig. 105-2).
4. If comminution is not present, apply the plate with a compression technique. If comminution is present, apply the plate in a neutralization manner (e.g., no compression).

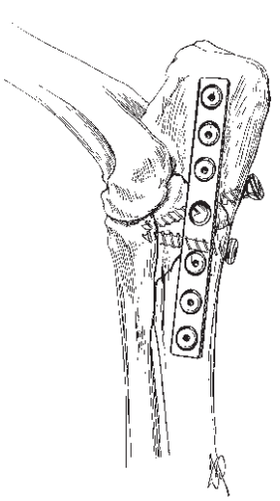

Figure 105-2. Bone plate and screw replacement for trochlear notch fracture repair.

Radial Head Fractures

Objective

- Perform precise anatomic reduction of the fracture with rigid fixation of the fragments.

Equipment

- General surgery pack and standard suture material
- Hohmann retractor
- Bone screws and bone screw insertion equipment
- Power drill and Jacobs pin chuck
- K-wires

Technique

1. Place the patient in lateral recumbency, with the affected limb up, and prepare the limb for aseptic surgery.
2. Incise the skin, beginning at the proximal end of the lateral epicondyle of the humerus and continuing distally over the radial head to the proximal one-fourth of the radius.
3. Incise the subcutaneous tissue and the antebrachial fascia along the same line to expose the extensor muscles of the antebrachium.
4. Dissect between the ulnaris lateralis muscle and the lateral digital extensor. Cut the ulnaris lateralis tendon, leaving sufficient tendon for suturing. If necessary, incise the anconeus muscle from the lateral epicondyle of the humerus.
5. Reflect the lateral digital extensor muscle cranially with a Hohmann retractor to expose the fracture.
6. Drive a K-wire across the fracture line to hold the fracture in reduction.
7. Insert a screw in "lag screw" fashion to compress the fracture line.
8. For small fragments, place two or three K-wires in a divergent pattern.
9. Reattach the ulnaris lateralis tendon with nonabsorbable monofilament suture material in a horizontal mattress pattern. Suture the muscle fascia and subcutaneous tissue in a simple continuous pattern, using absorbable suture material. Close the skin routinely.

Radial Neck and Proximal Physeal Fractures

Objectives

- Stabilize the fracture in immature animals without fracture compression to help prevent premature closure of the growth plate.
- Stabilize and align the radial head so that it articulates properly with the humeral condyle.

Equipment

- General surgery pack and standard suture material
- Jacobs pin chuck
- K-wires

Technique

1. Approach the fracture as described for radial head fractures, and reduce the fracture.
2. Stabilize the fracture with two K-wires placed in cross-pin fashion from the lateral side. Start one pin just below the articular surface of the radius and drive it distomedially. Start the second pin distal to the fracture and drive it proximomedially.
3. Bend the pins over and cut them off short.
4. Take care not to penetrate the articular surface of the radius.
5. Close the incision as described under Radial Head Fractures.

Postoperative Care

- Remove the K-wires in 3 to 4 weeks and monitor for premature closure of the growth plate.

Monteggia Fractures

This is a fracture of the ulna that can occur at various levels, combined with a radial head luxation.

Objectives

- Reduce and stabilize the radial head luxation.
- Align and stabilize the ulnar fracture.

Equipment

- General surgery pack and standard suture material
- Bone plating equipment
- Power drill
- Bone reduction forceps

Technique

1. Expose the ulnar fracture, as described under Olecranon Fractures and Trochlear Notch Fractures. Expose the ulna as far distally as needed.
2. Expose the radial head, as described under Radial Head Fractures, if the luxation cannot be reduced closed.
3. Reduce the ulnar fracture and hold it in reduction with bone reduction forceps.
4. If the annular ligament is ruptured, contour and apply a bone plate to the caudal aspect of the ulna. Insert a screw in "lag screw" fashion into the radius from the ulna through the plate to secure the radial head in position (Fig. 105-3).
5. If the annular ligament is intact, contour and apply a bone plate to the caudolateral aspect of the ulna.

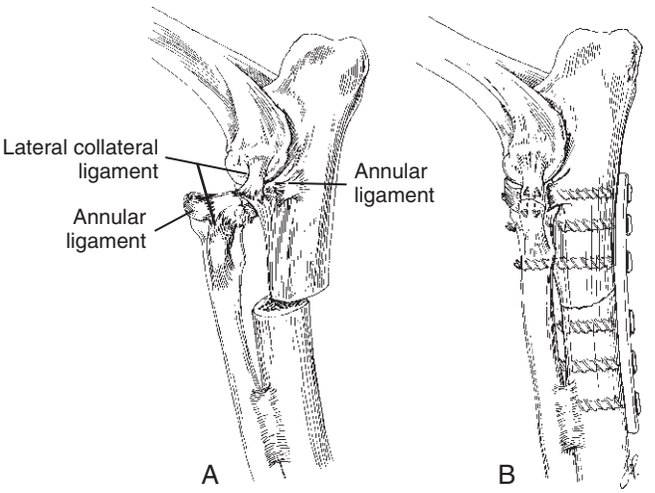

Figure 105-3. Monteggia fracture repair. *A,* Anatomy of fracture and ligament damage; *B,* plate placement and ligament repair. See text for details.

Mid-Shaft Radial and Ulnar Fractures

Objectives

- Achieve healing of the fracture with proper angulation, rotation, and length of the limb.
- Prevent synostosis of the radius and ulna in immature animals.

Equipment

- Fiberglass casting tape, stockinette, 1-inch–wide medical tape
- General surgery pack and standard suture material
- Bone reduction forceps
- Jacobs pin chuck and power drill
- Kirschner-Ehmer apparatus (external skeletal fixators)
- Bone plating equipment

Closed Reduction and Cast Fixation for Minimally Displaced Transverse Fractures

Technique

1. Place 1-inch–wide medical tape stirrups on the dorsal and plantar surface of the foot.
2. Apply a snug-fitting double layer of stockinette over the limb. Make the stockinette long enough to extend 1 inch past the tip of the toes and as far proximal above the elbow as possible.
3. Reduce the fracture and position the limb for correct angular and rotational alignment.
4. Place the carpus in a slight varus position, flexed 5 to 10 degrees.
5. Flex the elbow to a functional angle (approximately 140 degrees).
6. After wetting, apply the fiberglass casting tape, starting at the tip of the second and fifth nails.
7. Overlap the casting tape 50% with each wrap, working from distal to as far proximal as possible above the elbow.
8. Apply four or five layers of fiberglass casting tape.

9. Reflect the stockinette and stirrups over the end of the cast and incorporate them into the final layer of cast material.
10. Hold the limb in the proper position until the cast has set.

External Skeletal Fixation for Comminuted Fractures and Simple Fractures

Technique

1. Reduce comminuted fractures closed.
2. Use a limited open approach if the fracture cannot be reduced closed.
3. Make small stab incisions in the skin before driving the transfixation pins.
4. Drive the most distal transfixation pin across the radius perpendicular to the long axis of the radius from medial to lateral and parallel to the radial carpal joint (Fig. 105-4, pin a). Drive the transfixation pins through the skin on both sides of the limb.
5. Drive the most proximal transfixation pin (Fig. 105-4, pin b) in a similar manner, parallel to the articular surface of the radial head.
6. Apply connecting bars (Fig. 105-4, pin c) to the transfixation pins on both the lateral and medial sides.
7. Place the appropriate number of single connecting clamps on the connecting bar.

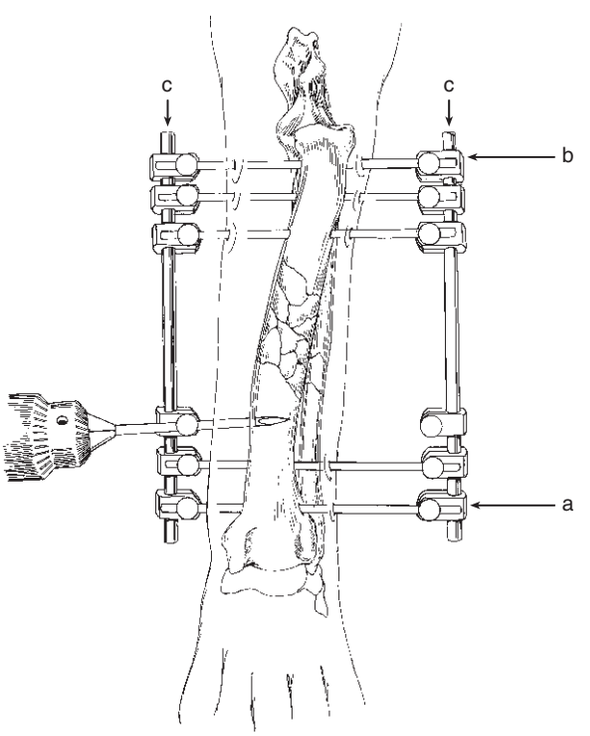

Figure 105-4. External skeletal fixation for radius and ulna fractures. See text for explanation.

8. Align the fracture and tighten the end connecting clamps to maintain reduction of the fracture.
9. Drive the remaining transfixation pins through the connecting clamps and tighten them (see Chapter 111).
10. If possible, place three or four transfixation pins on each side of the fracture line.
11. Cover the external skeletal fixation device with gauze and tape to protect the fixator and furniture surfaces. Clean pin tracts daily (see Chapter 111).

Plate Fixation for Distal Metaphyseal Fractures

These fractures occur primarily in small dogs. There is a high incidence of nonunion if these fractures are not treated correctly.

Objectives

- Achieve anatomic alignment with compression of the fracture.
- Insert a cancellous bone graft.

Equipment

- General surgery pack and standard suture material
- Mini-bone plating equipment (1.5- and 2.0-mm screws and plates)
- Power drill
- Curette (Brun 3-0)
- Small bone reduction forceps

Technique

1. Place the patient in lateral recumbency, with the affected leg up, and prepare the limb for aseptic surgery.
2. Make a skin incision on the dorsal aspect of the leg, starting at the cephalic vein and extending distally to the mid-metacarpus. Make the incision lateral to the cephalic vein.
3. Incise the subcutaneous tissue and fascia along the same line.
4. Identify the extensor carpi radialis and the common digital extensor tendons and subperiosteally elevate them from their grooves in the radius.
5. Incise the abductor pollicis muscle for additional proximal exposure.
6. Reduce the fracture and hold it in reduction with bone reduction forceps.
7. Contour a bone plate to the cranial surface of the radius and apply the plate. In small dogs, use a 1.5- or 2.0-mm bone plate.
8. Make a 2-cm–long incision over the craniolateral aspect of the greater tubercle of the humerus.
9. Incise the subcutaneous tissue along the same line. Drill a small hole in the greater tubercle.
10. Use a #3-0 Brun curette to collect a cancellous bone graft from the greater tubercle. During the collec-

tion process, place the graft on a blood-soaked sponge.
11. Pack the bone graft around the fracture site.
12. Close the subcutaneous tissue and the skin incisions routinely.
13. After surgery, apply a soft padded bandage to the leg.

Fractured Styloid Process of Ulna

Objective

- Reduce and stabilize the fracture to reestablish lateral support to the carpus.

Equipment

- General surgery pack and standard suture material
- Surgical stainless steel wire (20 and 18 gauge)
- K-wires
- Jacobs pin chuck
- Wire tightening device (vise grips, wire twister)
- Pin and wire cutter
- Bone reduction forceps

Technique

1. Place the patient in lateral recumbency with the affected leg up and aseptically prepare the limb.
2. Make a skin incision over the lateral aspect of the styloid process. Incise the subcutaneous tissue along the same line.
3. Dissect between and elevate the tendons of the lateral digital extensor and the extensor carpi ulnaris.
4. Reduce the fracture and drive a K-wire from the distal tip of the ulna just above the ulnar collateral ligament into the proximal segment.
5. Drill a hole in the proximal segment of the ulna and pass a wire through the hole.
6. Place the wire around the tip of the pin in a figure-eight configuration, and tighten the wire on both arms of the figure-eight.
7. Close the deep fascia and subcutaneous tissue with absorbable suture in a simple continuous pattern. Close the skin routinely.
8. Splint the fracture for 3 to 4 weeks postoperatively.

GROWTH DEFORMITIES OF THE RADIUS AND ULNA

Growth deformities of the radius and ulna result from trauma and disruption of the blood supply to the physis; retained cartilaginous cores (see Chapters 117 and 119); and synostosis (bony bridging) of the radius and ulna. Specific treatment depends on the physis injured, the extent of deformity, and the age of the animal.

Anatomy

- The radius and ulna form the largest paired bones of the body. Abnormal growth of one bone may affect the other bone, elbow, or carpus.
- In dogs, the growth plates (physes) of the radius and ulna close at about 7 to 9 months of age (see Chapter 119 for more information about physeal structure).
- The distal ulnar physis is conical in shape, making it vulnerable to crushing during trauma. The two radial physes are relatively flat.
- The distal ulnar physis contributes 85% to the longitudinal growth of the ulna; the proximal physis (olecranon) contributes 15%.
- The proximal and distal radial physes contribute 40% and 60%, respectively, to the longitudinal growth of the radius.
- The radius and ulna must grow in a synchronous manner to retain a normal shape and joint congruity. As the radius and ulna grow, they normally slide past each other.

Preoperative Considerations

- Early recognition and treatment of physeal injury of the radius and ulna is the key to prevention or minimization of deformities.
- Base treatment of a growth deformity on whether the dog is mature or immature (whether physes are still growing) and on the specific deformity.

▼ ***Key Point*** The general principles of treatment of growth deformities are prevention or correction of angular deformities and joint abnormalities and maintenance of acceptable leg length.

- Obtain lateral and craniocaudal radiographs of the affected and normal forelimbs. Include both the elbow and carpus.
- Preplan corrective procedures on paper or cleared radiographic film by making tracings and cutouts copied from the radiographs.

General Postoperative Care and Complications for Growth Deformities

- In immature dogs, splint the limb when ostectomy has been performed. The other intact bone will hypertrophy to withstand the added stress.
- Reevaluate the leg radiographically at least every 3 weeks until the dog has stopped growing.
- If bone bridges the ostectomized gap before growth has ceased, repeat the original surgery.
- If the procedure for immature dogs does not correct the deformity, perform the procedure recommended for mature dogs after bone growth stops.

General Prognosis

- The prognosis is guarded, especially for mature dogs with severe deformities.

Surgical Procedure to Correct Premature Closure of the Distal Ulnar Physis

Immature Dogs

Objectives

- Remove a section of the ulna to allow unrestrained growth of the radius.
- Prevent regrowth of the ulna by placement of a free fat graft.

Equipment

- General surgery pack and standard suture material
- Gigli wire saw or oscillating bone saw
- Gelpi retractor

Technique

1. Place the patient in lateral recumbency, with the affected leg up, and prepare the limb for aseptic surgery.
2. Make a 6-cm incision over the lateral aspect of the distal third of the ulna. Incise the subcutaneous tissue and antebrachial fascia along the same line.
3. Dissect between the extensor carpi ulnaris and the lateral digital extensor muscles to expose the ulna. Elevate the muscles and tendons from the ulna on top of the periosteum all the way around the bone.
4. Using the Gigli wire saw or the oscillating saw, osteotomize at least 2 cm of the ulna at the junction of the distal one-third and middle one-third of the bone.
5. Remove all the periosteum to prevent rapid bone regrowth.
6. Make a 3-cm incision over the flank just in front of the wing of the ilium.
7. Dissect down to the subcutaneous fat and collect a piece of fat large enough to completely fill the defect in the ulna.
8. Place the fat graft in the ulnar defect and close the antebrachial fascia in a simple continuous fashion with absorbable suture material.
9. Close the subcutaneous tissue and skin routinely.
10. Place the limb in a splint for the first month following surgery.

Mature Dogs

Deformities

- Cranial and/or medial bowing with lateral torsion of the radius
- Carpal valgus with external rotation
- Limb shortening
- Malalignment of radius and/or ulna in the elbow joint

Objectives

- Correct angular and rotational deformity.
- Correct joint incongruity.
- Maintain as much leg length as possible.

Equipment

- General surgery pack and standard suture material
- Gigli wire saw or oscillating bone saw
- Kirschner-Ehmer fixation device (alternatively: circular external skeletal fixator)
- Jacobs pin chuck or power drill

Technique

1. Place the patient in lateral recumbency, with the affected leg up, and prepare the limb for aseptic surgery.
2. Drive a transfixation pin across the most distal aspect of the radius, aligned parallel with the craniocaudal plane and mediolateral plane of the articular surface of the radius (Fig. 105-5).
3. Drive a second transfixation pin in the same manner as the first pin, except as far proximal as

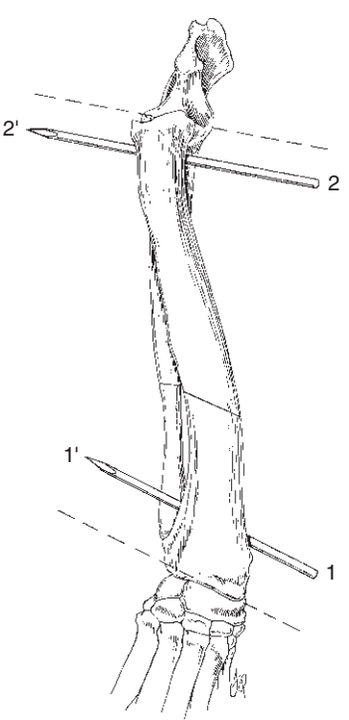

Figure 105-5. Pin placement for repair of premature closure of the distal ulnar physis. Place the first pin (1–1') parallel to the cranial-caudal and medial-lateral plane of the articular surface of the radius. The second pin (2–2') is parallel to the articular surface of the proximal radius.

possible and parallel to the articular surface of the proximal radius.
4. Approach the radius as described previously under Plate Fixation for Distal Metaphyseal Fractures.
5. Perform an osteotomy of the radius at the point of maximal curvature of the radius.
6. Fracture the ulna at the same level, either manually or with a saw.
7. Connect the transfixation pins on the lateral and medial sides with single connecting clamps and connecting bars. Place the appropriate number of single connecting clamps on the connecting bars.
8. Manually align the proximal and distal transfixation pins so that they are parallel to each other in both planes. Tighten the connecting clamps to hold the proper alignment (Fig. 105-6).
9. If there is any concern over the alignment, obtain radiographs of the leg at this point.
10. Drive the remaining transfixation pins through the open single connecting clamps.
11. Close the incisions routinely.
12. Cover the K-device with gauze and tape.
13. If elbow incongruity is not severe, it will resolve with weight bearing after the ulna is cut.

Surgical Procedure to Correct Premature Closure of the Proximal Radial Physis

Generally this deformity is recognized after the bone growth of the radius is finished. If it occurs in an immature dog, use the technique described for complete premature closure of the distal radial physis in immature dogs.

Deformities

- There is distal luxation of the radial head from the humerus.
- Leg is straight.

Objective (Mature Dogs)

- Reposition the radial head into the elbow joint so that it articulates properly with the humerus and ulna.

Equipment

- General surgery pack and standard suture material
- Bone plating equipment
- Power drill
- Oscillating saw

Technique

1. Place the animal in lateral recumbency, with the affected leg up, and prepare the limb for aseptic surgery.
2. Approach the radial head as described previously under Radial Head Fractures.
3. Approach the mid-shaft of the radius as described previously for mid-shaft radial fractures.
4. Perform a stepped radial osteotomy. Make the longitudinal arm of the osteotomy long enough to accept two bone screws (Fig. 105-7).

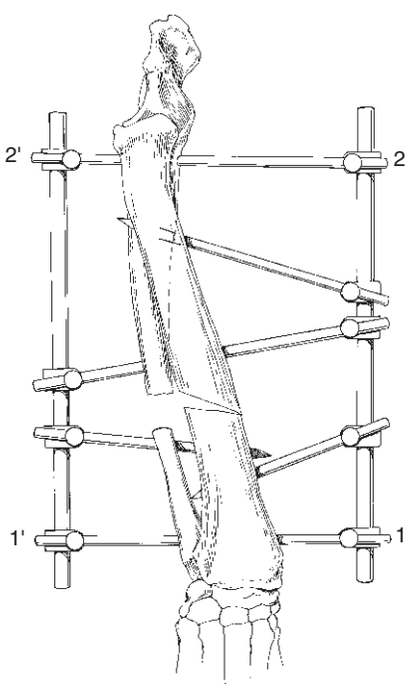

Figure 105-6. Final pin placement (see Fig. 105-5), osteotomy, and ulnar fracture for repair of premature closure of the distal ulnar physis.

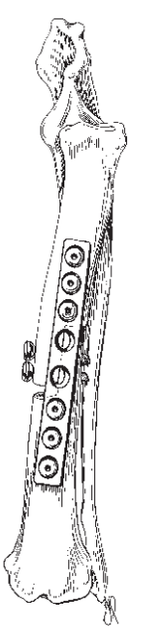

Figure 105-7. Plate and screw placement for stepped radial osteotomy performed for repair of premature closure of the proximal radial physis.

5. Slide the radial head proximally so that it articulates correctly with the humeral condyle and the ulna.
6. Place two screws, from medial to lateral, in "lag screw" fashion across the osteotomy site.
7. Apply a bone plate on the cranial aspect of the radius to further stabilize the osteotomy.
8. Collect a cancellous bone graft from the proximal humerus.
9. Place the bone graft in the defect in the radius.
10. Close the incisions routinely.
11. Place the leg in a soft padded bandage for 10 to 14 days postoperatively.

Surgical Procedure to Correct Premature Closure of the Distal Radial Physis

Premature closure of the distal radial physis can be complete or partial. If partial closure occurs, the lateral aspect of the physis usually is affected.

Complete Closure (Immature Dog)

Deformities

- Distal luxation of the radial head and elbow joint incongruity occur.
- The limb is shortened.
- Usually the leg remains straight.
- Bowing of the radius and ulna occurs rarely.

Objectives

- Remove a section of the radius to allow unrestricted growth of the ulna.
- Prevent regrowth of the radius until the other growth plates have stopped growing.

Equipment

- General surgery pack and standard suture material
- Gigli wire saw or oscillating saw

Technique

1. Place the animal in lateral recumbency, with the affected leg down, and prepare the limb for aseptic surgery.
2. Approach the mid-shaft radius as described previously for mid-shaft radial fractures.
3. Ostectomize a 2-cm section of radius, including the periosteum. Protect the interosseous artery.
4. Collect a free fat graft from the flank, as described previously for premature closure of the distal ulnar physis in immature dogs.
5. Place the fat graft in the radial defect and close the antebrachial fascia with absorbable suture material in a continuous pattern.
6. Close the incision routinely from the toes to the distal humerus.
7. Place the leg in a splint postoperatively.
8. When the dog has stopped growing, reconstruct the defect in the radius with a cancellous bone graft.

Partial Lateral Closure (Immature Dog)

Deformities

- Carpal valgus with external rotation
- Cranial and medial bowing of the forelimb
- Shortening of the limb
- Elbow joint incongruity

Objectives

- Remove the closed portion of the distal radial physis.
- Prevent bony bridging of the removed physis with a fat graft.

Equipment

- General surgery pack and standard suture material
- Curets

Technique

1. Place the patient in lateral recumbency, with the affected leg up, and prepare the limb for aseptic surgery.
2. Approach the distal radius as described previously for distal radial fractures.
3. Carefully expose the physis to minimize damage.
4. Probe the physis with a 25-gauge needle to determine the extent of the closure.
5. Use a curet to remove the closed section of the physis.
6. Place a free fat graft collected from the flank in the defect.
7. Close the incision routinely.
8. Splint the leg until bone growth is complete.
9. When bone growth is complete, remove the fat graft, if necessary, and graft the defect with cancellous bone.

Mature Dogs

Deformities

The deformities are the same as described for complete and incomplete closure in immature dogs.

Objectives

- Reestablish congruity to the elbow joint.
- Correct angular deformity of the limb.

Equipment

- Equipment is same as listed for premature closure of the proximal radius and distal ulna in mature dogs.

Technique

- If the radial head is luxated distally and the limb is straight, use the technique described previously for

correction of premature closure of the proximal radius in mature dogs.
- If angular and rotation deformity is present, use the techniques described previously for correction of premature closure of the distal ulna in mature dogs.

TRAUMATIC LUXATION OF THE ELBOW

- Lateral luxation of the elbow is common because the medial condyle of the humerus is larger and is slightly beveled downward, preventing medial luxation of the radius and ulna.

Clinical Signs

- The animals present with acute non–weight-bearing lameness.
- The foot and antebrachium are usually abducted, and flexion and extension of the elbow are not possible.

Diagnosis

- Obtain radiographs of the elbow (lateral and anteroposterior) to demonstrate the luxation.

Preoperative Considerations

- Most elbow luxations can be treated by closed reduction if the procedure is performed within the first 3 days after injury.
- If closed reduction is not possible, or if elbow fractures are present, open reduction is indicated. Open reduction of an elbow luxation can be a difficult procedure and is best handled by a surgical specialist.

Procedure for Closed Reduction

Objectives

- Reduce the luxation to reestablish normal function.
- Prevent recurrence of luxation with external coaptation.

Equipment

- Bandage material for constructing a spica, or lateral splint

Technique (Fig. 105-8)

1. Place the animal in lateral recumbency with the luxated leg up.
2. Place the elbow joint in full flexion.
3. With one hand on the radius and ulna, and the other hand on the distal humerus, pull the radius and ulna distally along the lateral aspect of the humerus.
4. While continuing distal traction on the radius and ulna, rotate the radius and ulna inward to place the anconeal process over the lateral humeral epicondyloid crest.

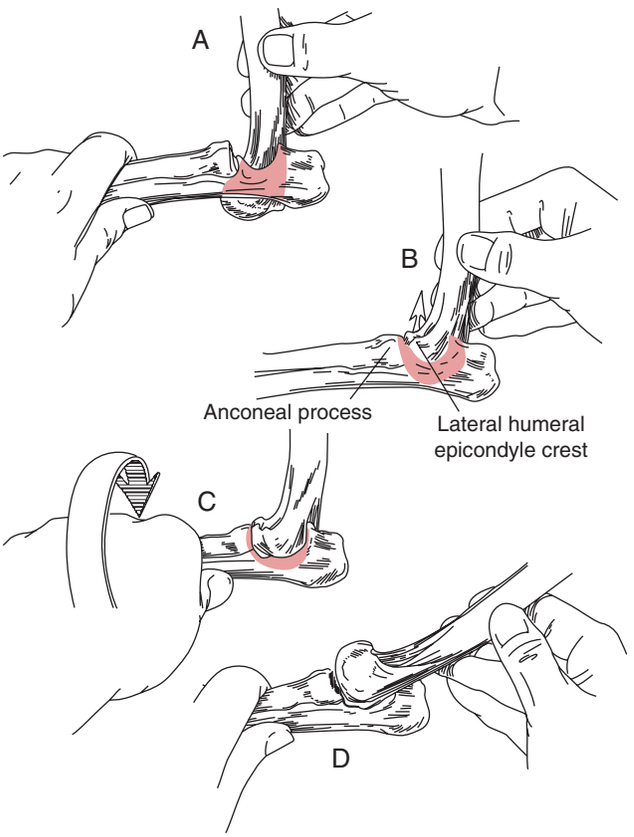

Figure 105-8. Reduction of the elbow. *A*, Hold the limb in traction. *B*, Pull radius and ulna distally. *C*, Internally rotate the ulna and radius. *D*, Extend the elbow.

5. Use the thumb of one hand to maintain lateral to medial pressure on the olecranon while slowly extending the elbow with the other hand.
6. Keep the elbow extended to maintain reduction.
7. Evaluate the joint for instability of the collateral ligaments.

Postoperative Care

- Obtain lateral and craniocaudal radiographs of the elbow to confirm reduction and evaluate for other injuries.
- Place the affected leg in a spica or lateral splint to keep the elbow in extension.
- Maintain the splint for 2 weeks, then allow leash walking only for another 2 weeks.
- Reevaluate at 2, 4, and 6 weeks postoperatively.
- If open reduction or ligament repair of the elbow is necessary, refer the patient to a surgical specialist.

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Chapter

106 Fractures and Dislocations of the Carpus

Michael P. Kowaleski

Injuries to the carpus occur most commonly as a result of trauma, and consist primarily of ligamentous injury resulting in hyperextension, subluxation, luxation, or fracture. Isolated fractures of the carpus are rare, and occur most commonly in racing greyhounds and working dogs.

▼ ***Key Point*** Fractures of the carpus typically involve the articular surface, and therefore, anatomic reduction, rigid internal fixation, inter-fragmentary compression, and early return to function are essential for a successful outcome.

ANATOMY

The carpal joint is a complex three-level hinge joint. The seven bones of the carpus are arranged in a proximal and distal row, and articulate with the radius and ulna proximally and the metacarpal bones distally creating the antebrachiocarpal joint proximally, the middle carpal joint centrally, and the carpometacarpal joint distally.

Osseous Structures (Fig. 106-1)

- The seven bones of the carpus are arranged in two rows; a small sesamoid bone in the tendon of insertion of the abductor pollicis longus is regionally associated with the carpal joint.
- The proximal row consists of the radial, ulnar, and accessory carpal bones.
- The radial carpal bone is the largest of the carpal bones. It is located medially, and articulates with the radius proximally, and with the first, second, third, and fourth carpal bones distally.
- The ulnar carpal bone is the lateral bone of the proximal row. It articulates with the radius and ulna proximally, with the accessory carpal bone on its palmar aspect, and with the fourth carpal bone and fifth metacarpal bone distally.
- The accessory carpal bone is located on the palmar aspect of the lateral side of the proximal row. It articulates with the styloid process of the ulna proximally, and with the ulnar carpal bone.
- The distal row consists of the numbered carpal bones, the first (C1), second (C2), third (C3), and fourth (C4) carpal bones.
- C4 is the largest bone of the distal row, and articulates with the fourth and fifth metacarpal bones; the size of carpal bones C3 to C1 progressively decreases with the number of the bone.

Articulations

- The antebrachiocarpal joint is located between the distal radius and ulna, and the proximal row of carpal bones. It normally provides 70% of carpal range of motion.
- The middle carpal joint, between the proximal and distal rows of carpal bones, allows a small amount of flexion and extension, about 25% of carpal range of motion.
- The carpometacarpal joint, located between the distal row of carpal bones and the metacarpal bones, provides about 5% of carpal range of motion.
- The joints formed between the individual carpal bones are termed *intercarpal* joints; these articulations provide very limited movement.

Ligamentous Structures

- No continuous collateral ligament spans all three joints of the carpus.
- Support to the carpus is provided by two superimposed sleeves of collagenous tissue, with tendons in between.
- The superficial sleeve is a thickening of the deep carpal fascia.
- The deep sleeve is the thickened fibrous layer of the joint capsule.
- The two sleeves fuse laterally and medially to form short collateral ligaments.
- The short radial collateral ligament has two parts, both of which originate from the styloid process of the radius; the straight part inserts on the medial part of the radial carpal bone and the oblique part inserts on the palmeromedial surface of the radial carpal bone.
- The short ulnar collateral ligament extends from the styloid process of the ulna to the ulnar carpal bone.

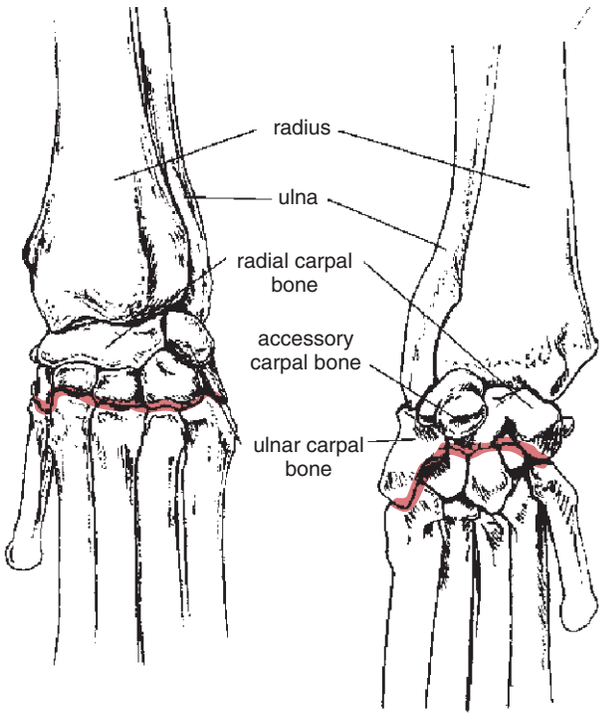

Figure 106-1. Osseous anatomy of the carpus. Left: red line denotes carpometacarpal joint. Right: red line denotes middle carpal joint.

- The flexor retinaculum (transverse carpal ligament) provides support to the palmaro-proximal aspect of the carpus; it attaches laterally to the medial part of the accessory carpal bone and medially to the styloid process of the radius, the radial carpal bone and the first carpal bone.
- The palmar carpal fibrocartilage is quite thick and well defined; it crosses the palmar surface of the carpus and attaches to all of the bones except the accessory carpal bone. It also has strong attachments to the proximal aspect of the third, fourth, and fifth metacarpal bones.
- The accessory carpal bone is stabilized distally by two ligaments, which originate from its free end; one attaches to the fourth metacarpal bone (accessoro-metacarpal IV ligament) and the other to the fifth metacarpal bone (accessoro-metacarpal V ligament).
- Many other small ligaments attach the carpal bones to each other and to the metacarpal bones.

FRACTURES OF THE RADIAL CARPAL BONE

Preoperative Considerations

- Fractures of the radial carpal bone are rare and most commonly occur in working dogs during strenuous activity, resulting from jumps or falls.
- Chip fractures of the proximal dorsal border result from hyperextension of the radio-carpal joint.
- Slab fractures occur from the dorsal surface.
- Body fractures and avulsion fractures may occur rarely.
- Moderate to severe lameness occurs immediately following the injury; however, in chronic cases only mild lameness, which resolves with rest, may be evident.
- Diagnosis requires a high index of suspicion since the majority of fractures are only minimally displaced.
- High-detail radiographs are frequently required.
- Oblique radiographic views are often necessary.
- Bone fragments rarely reattach, resulting in joint incongruency, synovitis, osteoarthritis, and periarticular fibrosis.

Surgical Procedure

Objectives

- Treat non-displaced or incomplete fractures with coaptation (Mason meta-splint) for 6 to 8 weeks.
- Remove small fracture fragments, which are too small to reattach.
- Stabilize larger fragments with internal fixation utilizing screws placed in lag fashion or multiple, divergent Kirschner wires.

Equipment

- General surgical pack and standard suture material
- Sterile elastic bandage material (Vetwrap) for Esmarch bandage, and tourniquet
- Small pointed bone-holding and/or pointed reduction forceps
- Orthopedic drill bits, taps, and bone screws or Kirschner wires (K-wires)

Technique

1. Place a tourniquet at the elbow and an Esmarch bandage from the nail bed to the proximal antebrachium.
2. Perform a dorsal approach to the carpus (see the description under Pancarpal Arthrodesis).
3. Reduction and anatomic alignment can be achieved with small, pointed bone-holding or reduction forceps.
4. Place bone screws in lag fashion across the fracture line, ensuring the screw head is adequately countersunk below the joint surface or positioned such that it does not interfere with joint motion.
5. If K-wires are used, ensure adequate interfragmentary compression is provided and maintained by the bone-holding forceps during wire insertion, and counter-sink the wires below the cartilage surface.

Postoperative Care and Complications

- A splint may be used 1 to 3 weeks postoperatively for support.
- Strict exercise restriction is necessary for 6 to 8 weeks, or until there is radiographic evidence of bony union.

- Osteoarthritis is common following these injuries, and may result in chronic intermittent lameness.

FRACTURES OF THE ACCESSORY CARPAL BONE

Preoperative Considerations

- Accessory carpal bone fractures are uncommon except in racing greyhounds.
- These fractures are typically avulsion fractures (Fig. 106-2). Treat with internal fixation if the fragments are large enough.

Surgical Procedure

Objectives and Equipment

- The same as for fractures of the radial carpal bone.

Technique

1. Perform a palmaro-lateral approach to the accessory carpal bone.
2. Excise fragments that are too small to reattach.
3. If the fragment is large enough, reduction and anatomic alignment can be achieved with small, pointed bone-holding or reduction forceps.

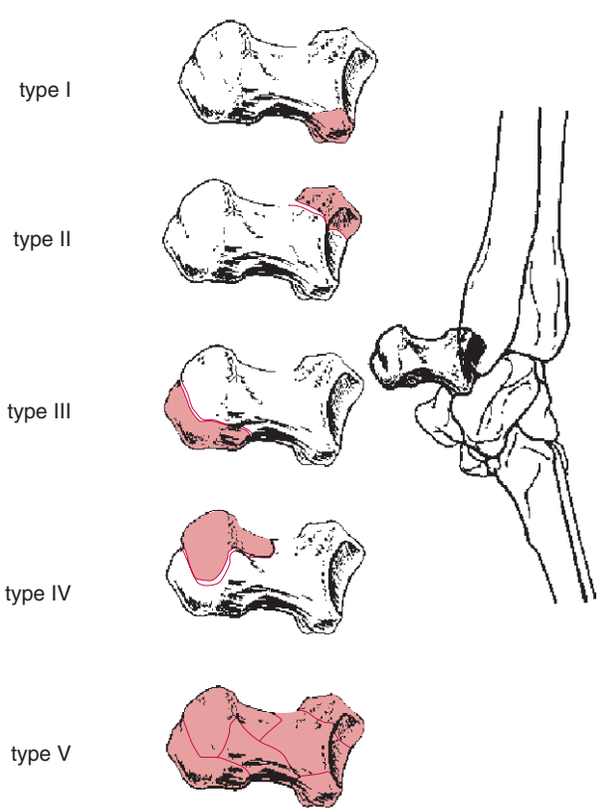

Figure 106-2. Classification of fractures of the accessory carpal bone.

4. Place bone screws in lag fashion across the fracture line, ensuring the screw head is adequately countersunk below the joint surface or positioned such that it does not interfere with joint motion.
5. If K-wires are used, ensure that adequate interfragmentary compression is provided and maintained by the bone-holding forceps during wire insertion.

Postoperative Care and Complications

- Place and maintain a splint for 4 to 6 weeks post-operatively.
- Working dogs may resume training 12 to 16 weeks post-operatively.

FRACTURES OF THE ULNAR CARPAL BONE AND THE NUMBERED CARPAL BONES

- Fractures of these bones are very rare even in the racing greyhound.
- Most often these are small chip fractures from the dorsal margin resulting from hyperextension injuries.
- Since these fragments are generally very small, fragment excision followed by splintage for 2 weeks and exercise restriction for 8 weeks is the usual treatment.
- Large fragments can be reattached as described for radial carpal bone fractures.
- Comminuted fractures of the ulnar carpal bone may necessitate pancarpal arthrodesis.

LUXATIONS, SUBLUXATIONS, AND HYPEREXTENSION INJURIES OF THE CARPUS

Luxations, subluxations, and hyperextension injuries are the most common injury of the carpus in non-working dogs. These injuries typically result from a fall or jumping from a height. The traumatic force causes tearing and rupture of the palmar joint capsule, ligaments, and fibrocartilage, resulting in a loss of support in any or all of the three carpal joint levels.

Clinical Signs and Diagnosis

- The injury typically results in an acute-onset, non–weight-bearing lameness; however, most animals begin partial or full weight bearing shortly after the injury.
- Regional or localized soft tissue swelling and discomfort are evident in the carpus, and manual extension demonstrates the area of instability.
- Carpal hyperextension results in a plantigrade stance, and in most animals, the carpal pad contacts the ground.
- This injury may occur bilaterally, and if so, bilateral surgery is indicated.

- Standard radiographic views generally do not demonstrate the injury, since the carpus is not loaded during the radiographic procedure. Obtain a stressed lateromedial projection to create carpal hyperextension to demonstrate the level(s) of the lesion.
- The distribution of joint involvement has been reported as antebrachiocarpal, 10% and 31%; middle carpal, 50% and 22%; and carpometacarpal, 40% and 47%.

▼ ***Key Point*** Splinting of the carpus is rarely if ever successful, since the randomly organized fibrous scar tissue does not have sufficient strength to support the carpus. In general, many injuries appear improved initially following splinting; however, recurrence of hyperextension occurs within 1 to 2 weeks of splint removal.

Preoperative Considerations

- Appropriate treatment depends on the joint level involved.
  - Pancarpal arthrodesis has been used to treat injuries to all levels of the carpus; however, partial carpal arthrodesis may be better for injuries involving only the middle carpal or carpometacarpal joint.
  - Although it is technically possible to fuse only the antebrachiocarpal joint, pancarpal arthrodesis is recommended in cases of isolated antebrachiocarpal injury. Partial carpal arthrodesis of the antebrachiocarpal joint results in increased stresses on the middle carpal and carpometacarpal joints, predisposing them to injury postoperatively.
  - Since 70% of carpal range of motion occurs in the antebrachiocarpal joint, preservation of this joint, if uninjured, results in very little gait alteration postoperatively.
- Bone plate fixation is the preferred method of pancarpal and partial carpal arthrodesis of most surgeons.

Surgical Procedure

Objectives

- Successful arthrodesis requires strict adherence to basic principles.
  - Debride the articular cartilage from the joint surfaces.
  - Apply an autogenous cancellous bone graft.
  - Provide rigid fixation (internal or external) until complete bony fusion has occurred.
  - Perform the arthrodesis at an appropriate angle.

Equipment

- General surgical pack and standard suture material
- Sterile elastic bandage material (Vetwrap) for Esmarch bandage, and tourniquet
- Sterile orthopedic drill and high-speed bur
- Bone curettes
- Kirschner wires (K-wires)
- Fixation devices
  - Orthopedic drill bits, taps, bone screws, and bone plates, or external skeletal fixation (circular or planar)

Technique

Pancarpal Arthrodesis

1. Place the patient in lateral recumbency with the affected limb up, and prepare the patient for aseptic surgery, including the site for bone graft collection.
2. Place a tourniquet at the elbow and an Esmarch bandage from the nail bed to the proximal antebrachium.
3. Make a skin incision centered on the dorsal midline and extending from the distal third of the radius to the distal extent of the third metacarpal bone, lateral to the accessory cephalic vein (Fig. 106-3).
4. Incise the deep fascia midway between the tendon of the extensor carpi radialis and the tendon of the common digital extensor; deepen the incision into the periosteum of the distal radius, and elevate the periosteum medially and laterally to retract the tendons to expose the joint capsule.
5. Perform arthrotomy incisions around each bone to expose the articular surfaces; exposure is enhanced by flexion of the carpus.
6. Débride the articular cartilage with a high-speed bur or curettes.
7. Collect an autogenous cancellous bone graft from the proximal humerus (or ilial wing) and place it in all joint spaces.
8. K-wires placed obliquely across multiple joint levels can be used to temporarily stabilize the joint intraoperatively.
9. Apply a dynamic compression plate dorsally to the radius, radiocarpal bone, and third metacarpal bone.
   a. A seven-hole bone plate is usually sufficient, with three screws in the radius, one in the radiocarpal bone, and three in the third metacarpal bone (Fig. 106-4, *left*). The bone plate should extend at least 50% of the length of the third metacarpal bone. Bone plates specifically designed for pancarpal arthrodesis are commercially available.
   b. Contour the plate to provide 10° to 15° of extension of the carpus primarily at the antebrachiocarpal joint, and ensure that the foot is aligned properly prior to and during plate application.
10. Alternatively, stabilize the joint with a Type II external skeletal fixator (Fig. 106-4, *right*), or a circular external skeletal fixator (Fig. 106-5), placing at least

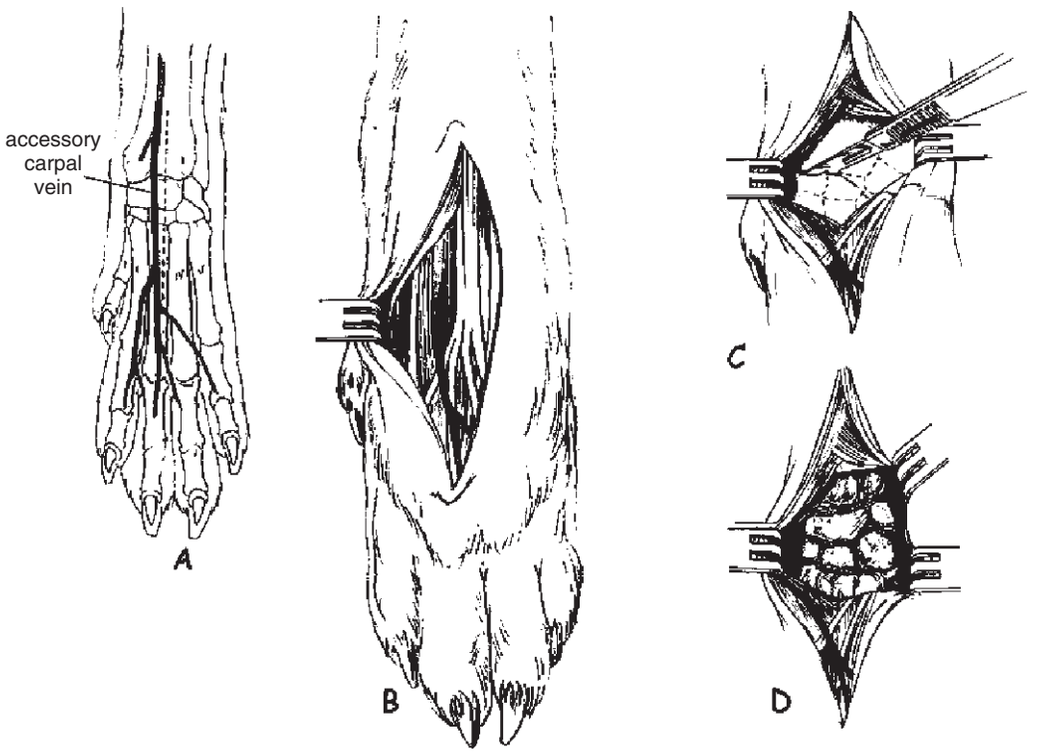

Figure 106-3. Dorsal approach to the carpus for pancarpal arthrodesis. The skin incision is centered on the dorsal midline and extends from the distal third of the radius to the distal extent of the third metacarpal bone, lateral to the accessory cephalic vein *(A)*. The deep antebrachial facial incision is located midway between the tendon of the extensor carpi radialis and the tendon of the common digital extensor *(B)*. Make arthrotomy incisions to expose each joint space *(C)*. Following débridement of articular cartilage, place autogenous cancellous bone graft in all joint spaces *(D)*.

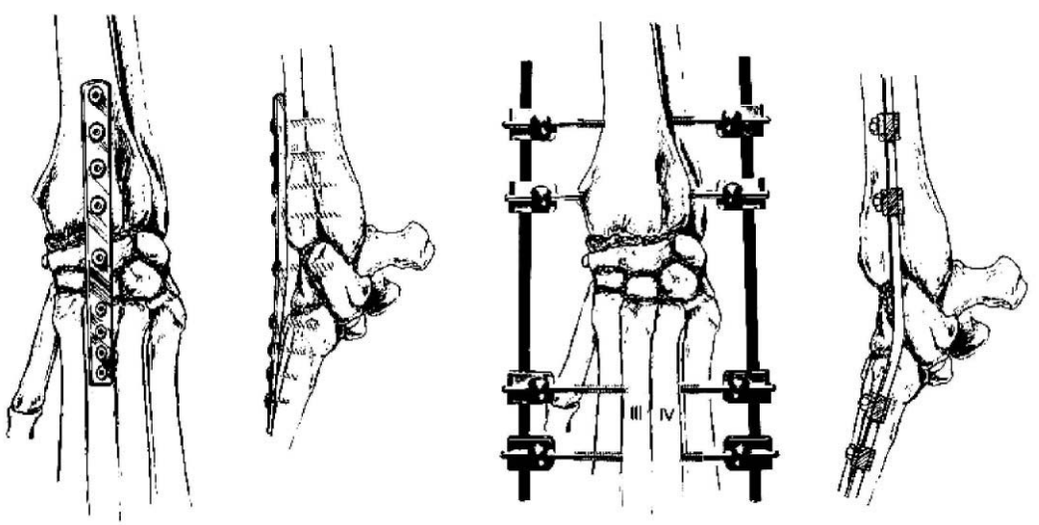

Figure 106-4. Pancarpal arthrodesis performed with a bone plate and screws *(left)* or a planar external skeletal fixator *(right)*.

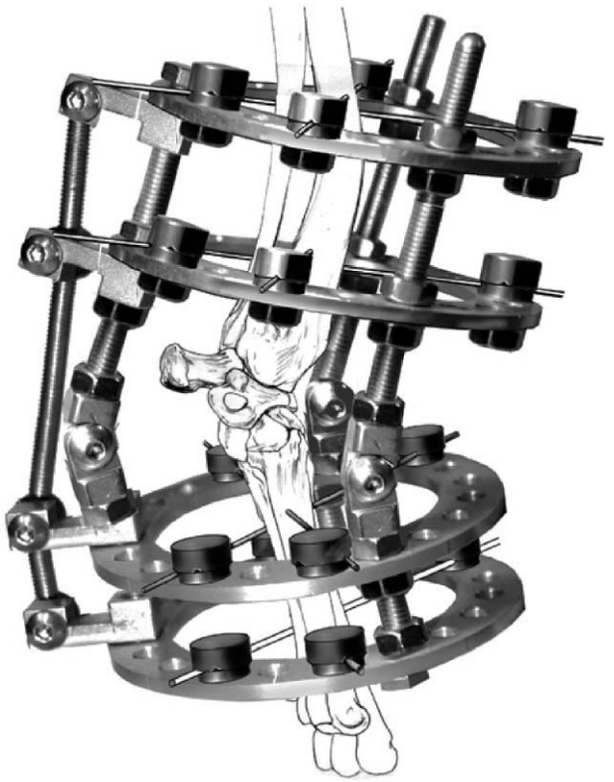

Figure 106-5. Pancarpal arthrodesis performed with a circular external skeletal fixator.

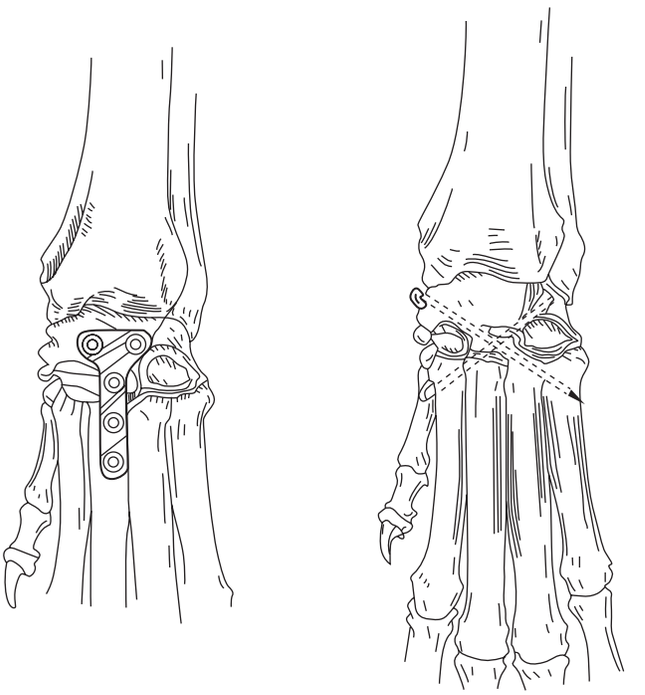

Figure 106-6. Partial carpal arthrodesis may be performed with a t-plate and screws *(left),* or cross pins *(right).*

two pins or wires in the distal radius and third and fourth metatarsal bone.

Postoperative Care

- In the case of bone plate fixation, place the limb in a palmar splint for 6 to 8 weeks after surgery, or until radiographic union is evident.
- The splint can be changed to a cast 3 to 5 days postoperatively once soft tissue swelling has subsided, if greater support of the limb and repair is desired.

Partial Carpal Arthrodesis

- Partial carpal arthrodesis is only indicated when the joint capsule, fibrocartilaginous, and ligamentous support of the antebrachiocarpal joint and accessory carpal bone are intact.

1. Place the patient in lateral recumbency with the affected limb up, and prepare the patient for aseptic surgery, including the site for bone graft collection.
2. Place a tourniquet at the elbow and an Esmarch bandage from the nail bed to the proximal antebrachium.
3. Perform a dorsal approach to the carpus and third metacarpal bone as described under Pancarpal Arthrodesis; however, limit the approach to the distal radius.
4. Perform arthrotomy incisions in the middle carpal and carpometacarpal joints only; exposure is enhanced by flexion of the carpus.
5. Débride the articular cartilage of the middle carpal and carpometacarpal joints with a high-speed bur or curettes.
6. Collect an autogenous cancellous bone graft from the proximal humerus (or ilial wing) and place it in the joint spaces.
8. Apply a T- or L-shaped dynamic compression plate dorsally to the radiocarpal bone and third metacarpal bone with the T- or L-shaped portion attached to the radiocarpal bone (Fig. 106-6, *left*).
   a. Ensure that the bone plate does not interfere with the distal radius during full extension of the antebrachiocarpal joint, and that the foot is aligned properly.
9. Alternatively, partial carpal arthrodesis can be performed with pin fixation.
   a. Place two cross pins to stabilize the middle carpal and carpometacarpal joints. Place the first obliquely from the proximal third of metacarpal II across the numbered carpal bones, into the ulnar carpal bone to a level even with the lateral styloid process of the ulna. Place the second

obliquely from the medial aspect of the radiocarpal bone immediately distal to the radius, across the numbered carpal bones, to exit from the proximal third of metacarpal V (Fig. 106-6, *right*).

Postoperative Care

- Place the limb in a palmar splint for 6 to 8 weeks after surgery, or until radiographic union is evident.
- The splint can be changed to a cast 3 to 5 days postoperatively once soft tissue swelling has subsided, if greater support of the limb and repair is desired.

Postoperative Complications

- Soft tissue swelling caused by surgical trauma and impaired lymphatic and venous drainage is common, and usually subsides within a few days.
  - Monitor the limb carefully during this period, and change the bandage if it becomes restrictively tight due to swelling.
- Complications are rare once bony fusion has occurred.
- Metacarpal bone fracture following pancarpal arthrodesis has been associated with bone plates, which extend less than 50% of the length of metacarpal III.
- The most frequent causes of arthrodesis failure are associated with failure to adhere to the principles of arthrodesis.
  - Incomplete removal of the articular cartilage.
  - Failure to apply sufficient bone graft.
  - Inadequately rigid internal or external support for a sufficient period of time to allow bony fusion to occur.

Chapter

107 Fractures of the Pelvis

Mark C. Rochat

Pelvic fractures in dogs and cats are extremely common. Severe trauma, such as motor vehicular accidents, is usually the cause of pelvic fractures. Concurrent injuries to other body systems, including life-threatening injuries, are also common and must be identified and treated in a timely fashion. Several specific types of injury occur in the pelvis, including sacroiliac luxation, fractures of the non-articular portions of the pelvis, and articular fractures. Specific management protocols for each are described below.

ANATOMY

- Each half of the pelvis is composed of the ilium, ischium, pubis, and acetabulum, which are fused as the os coxae, or hip bone (Fig. 107-1).
- The sacroiliac joint has a limited range of motion and is composed of a synchondrosis craniodorsally and a synovial articulation ventrally.
- The sacrotuberous ligament extends from the caudolateral part of the apex of the sacrum and the transverse processes of the first caudal vertebra to the lateral part of the ischiatic tuberosity. The sacrotuberous ligament is absent in the cat.
- The sacrum and pelvic bones form a complete bony canal. Therefore, pelvic fractures usually are multiple, or pelvic fracture may be accompanied by sacral fracture or sacroiliac luxation. If a pelvic fracture appears to be single, examine radiographs carefully for evidence of additional undisplaced fractures. There are two exceptions to this general rule: fractures in very young dogs and impaction fractures of the acetabulum in adult dogs and cats. In the former case, the bones of young dogs can allow a fracture in one location and an incomplete fracture or plastic deformation (bending) without actual fracture of the bones of the pelvis in other areas. In the second instance, the femoral head is driven through the acetabulum by a lateral blow to the greater trochanter.
- The major weight-bearing regions of the pelvis are the sacroiliac joint, body of the ilium, and acetabulum.

DIAGNOSIS

Concurrent Thoracic and Abdominal Injuries

- Thorough physical examination may be difficult in injured animals that are in pain or shock.
- Treat aggressively for shock and pain (see Chapters 6 and 156). After emergency treatment, complete the general physical examination as soon as possible.
- Concurrent thoracic, abdominal, intrapelvic, and spinal cord or peripheral nerve injuries are common with pelvic fractures. Management of cardiopulmonary, neural, and urinary system injuries and management of uncontrollable hemorrhage have priority over orthopedic injury.
- Radiograph the thorax routinely in animals with suspected pelvic fractures to identify pulmonary contusions, pneumo- or hemothorax, diaphragmatic herniation, and preexisting cardiac disease.
- Perform a 10-lead electrocardiogram and lead 2 rhythm strip every 12 hours for the first 48 to 72 hours following the trauma to identify cardiac dysrhythmias.
- Obtain abdominal radiographs, ultrasound examination, or diagnostic peritoneal lavage if free blood, urine, or bile is suspected in the abdomen.
- Perform excretory urography, cystography, or urethrography to identify the specific location of injury if rupture of the urinary tract is suspected.
- Urethral injuries are more common in male dogs where the urethra crosses through the ventral pelvic canal. The ability to urinate, presence of bruising or pubic fractures, and hematuria are not accurate predicators for or against urethral or bladder injury.
- Caudal abdominal hernias can also occur in conjunction with pelvic fractures, especially pubic fractures. Radiograph and carefully palpate the caudal abdomen to identify this injury.

Pelvic Injuries

- When the patient is in stable condition, perform an orthopedic examination.

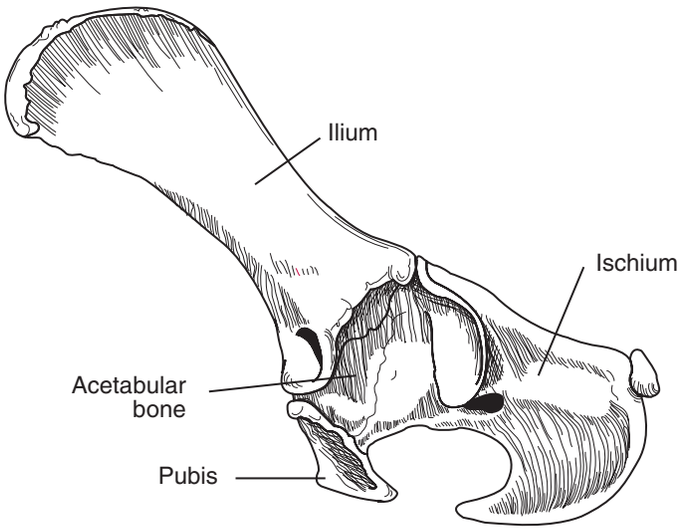

Figure 107-1. Bony anatomy of the pelvis. (From Evans S: Miller's Anatomy of the Dog, 2nd ed. Philadelphia: WB Saunders, 1993.)

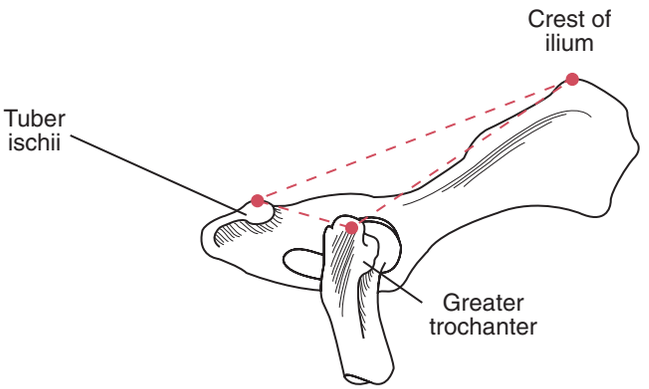

Figure 107-2. Diagram illustrating the normal position of the greater trochanter, iliac crest, and ischiatic tuberosity. (From Fossum TW: Small Animal Surgery, 2nd ed. St Louis: Mosby, 2002.)

- Carefully palpate the pelvic bones, manipulate the hip joints, and perform a rectal examination to detect pelvic fractures and to check for a palpable defect in the rectal wall.
- Palpate the craniodorsal iliac crest, greater trochanter, and ischiatic tuberosity for symmetry, motion, and pain (Fig. 107-2).
- Radiograph the pelvis in at least two projections to fully evaluate bone injury. Sedate or anesthetize the patient to obtain high-quality diagnostic radiographs. Closely examine the coccygeal vertebrae and sacral foramina for fractures that may result in neurologic injury to the tail, perineum, and bladder.
- Although rectal tears are not commonly associated with pelvic fracture, failure to make an early diagnosis usually results in severe pelvic infection, sepsis, and patient death.
- If an animal is not in shock but is unwilling to stand, do not attempt to make the animal stand unless you have palpated the dorsal spinous processes for malalignment and pain (point tenderness). Check the animal's spinal reflexes, including the sciatic and femoral nerve tracts; perception of noxious sensation over the pelvic limbs; withdrawal response; anal tone; and perineal sensation.

▼ ***Key Point*** If *any* question exists as to the integrity of the spinal column, do *not* allow the animal to stand or twist the spine until you have reviewed lateral and ventrodorsal radiographs of the spine. The ventrodorsal view can be made by either using a cross table lateral beam projection technique or carefully rolling the animal on its back without twisting the spine (known as a log roll maneuver).

- Pelvic fractures readily heal, but malunions are very common. Repair pelvic fractures as soon as the animal's general condition and anesthetic level of risk allow. Fractures that are over 5 days old are often difficult to repair anatomically.

TREATMENT

Non-surgical Treatment

In many animals with pelvic fractures, conservative treatment is all that is needed for successful fracture healing and normal pelvic limb function. However, careful nursing is required for several weeks because multiple fractures are often present. Patient size is an important consideration in making the decision to manage pelvic fractures without surgery. Small dogs and cats are much easier to manage for extended periods of time.

Indications

Medical management is a viable method of treatment for:

- Unilateral fractures
- Fractures that are minimally displaced
- Fractures of the non–weight-bearing portion of the pelvis (iliac wing, pubis, ischium)
- Animals with pelvic fractures that fit the above criteria and have intact neurologic function
- Animals with pelvic fractures that fit the above criteria and have no soft tissue injuries (urethral injury, prepubic tendon rupture, etc.) that require surgical repair

Nursing Care

- Dogs and cats with pelvic fractures often are reluctant to stand and may be unable to turn over. Turn these

animals regularly, use a padded bed, and keep these animals clean and dry to help prevent decubital ulcers.
- Give analgesics as needed. Typically, at least 1 to 2 weeks of analgesic therapy is indicated (see Chapter 6).
- Pain, bone instability, and neurologic injury may make it difficult for animals with pelvic fractures to urinate and defecate normally. If necessary, give a mild laxative or stool softener to prevent constipation.
- Empty the urinary bladder regularly by manual expression or catheter drainage, to prevent excessive distention, overflow incontinence, and urine soiling. If a urinary catheter is placed, follow strict aseptic technique to slow the onset of bacterial urocystitis.
- Some patients are able to stand and walk within a few days; however, restrict activity to a cage for 3 to 4 weeks followed by activity limited to only leash walking for 3 to 4 weeks. Avoid slick floors and any uncontrolled activity.
- Make certain the animal has access to food and water and assistance as needed to eat and drink.
- Physical therapy, in the form of passive range of motion, will lessen the degree of disuse atrophy and loss of joint range of motion.
- If limb adduction is weak as a consequence of ventral pelvic fractures or muscle trauma, use a body sling or towel support around the abdomen as necessary to assist recovery.
- Radiograph the pelvis every 4 to 6 weeks during recovery to monitor fracture healing.

Surgical Treatment

Indications

▼ ***Key Point*** The main advantages of surgical treatment of pelvic fractures are reduced pain, early return to normal function, avoidance of fracture-associated disease, and minimal hospitalization time.

Pelvic fractures may result in marked narrowing of the pelvic canal if left untreated, with the risk of subsequent obstipation, dystocia, dysuria, or sciatic nerve entrapment. If operative treatment of pelvic fractures is delayed beyond 5 days, muscle spasm and fibrosis may make reduction of the fracture fragments difficult, because of the large muscle mass surrounding the pelvis.

Surgical treatment is indicated for the following injuries:

- Fracture of the ilium with associated fracture of the pubis and ischium creating an unstable acetabulum.
- Intra-articular fractures (acetabulum).
- Markedly displaced, unstable, or excessively painful sacroiliac fracture or luxation.
- Severe bilateral fractures of the pelvis or displaced pelvic fractures associated with an additional major orthopedic injury of a pelvic limb, such as hip luxation or fracture of the femur.
- Fractures of the ischium that have an intra-articular component in the acetabulum, or that are suspected of entrapping the sciatic nerve.
- Fracture of the pubis or separation of the pubic symphysis associated with abdominal wall rupture and herniation of abdominal or pelvic organs.
- Gross displacement of the iliac crest or ischiatic tuberosity. These portions of the pelvis serve as the point of origin for the sartorius and semitendinosus and semimembranosus muscles, respectively. Significant distraction of these fragments may result in loss of mechanical advantage and proper function of these muscles.

FRACTURES OF THE ILIUM

Preoperative Considerations

- Fractures of the ilium are usually oblique and are often accompanied by fractures of other regions of the pelvis.

▼ ***Key Point*** If fracture displacement is present, the caudal fragment usually is displaced medially, and the pelvic canal is narrowed.

- Perform a thorough neurologic examination (see Chapter 125), particularly with markedly displaced fractures. Damage to the sciatic nerve may be present.
- Surgical repair of fractures of the ilium is generally recommended because most fractures of the ilium are displaced or unstable and the ilial shaft is a component of the weight-bearing portion of the pelvis.
- Precontouring the bone plate to the ilium of an intact pelvis from a cadaver of similar size reduces operating time for the inexperienced surgeon.
- Administer prophylactic antibiotics at the time of anesthetic induction. A first-generation cephalosporin such as cefazolin is generally appropriate.
- Have the radiographs (ventrodorsal and lateral projections) on a radiographic view box in the operating room for review.

Surgical Procedure

Objectives

- Anatomically reduce and stabilize the ilium.
- Relieve pain.
- Provide early restoration of pelvic limb function.
- Avoid damage to the sciatic nerve as it passes medial to the ilial shaft.

Equipment

- Standard general surgical pack and suture material.
- Hand-held retractors such as Myerding retractors and an assistant. Alternatively, Gelpi or Weitlaner self-retaining retractors can be used but generally are not as efficient at making adjustments as an assistant using a hand-held retractor.
- Orthopedic surgical pack with AO-ASIF "clamshell" and Kern bone-holding forceps and Hohmann retractors.
- Bone-plating equipment. Use dynamic compression plates (DCP) or the newer limited contact (LC-) DCP. For complex fractures, reconstruction plates can be used. The latest advance in plating, locking compression plates (LCP) allow the screws to be locked to the plate and are helpful for areas where the bone is weak or subject to failure. Avoid semitubular plates, finger plates, and other thin plates.
- Freer or Adson periosteal elevator.
- Suction with Frazier or Yankauer tips and electrocautery.

Technique

1. Perform a hanging limb prep by preparing the skin for aseptic surgery on the lateral and medial sides of the pelvic limb from the tarsocrural joint to the dorsal and ventral midline and from the midlumbar area to the base of the tail.
2. Place the animal in lateral recumbency on a circulating warm water blanket and stabilize the pelvis by placing sandbags under the animal and securing the animal to the table. Rotate the animal table toward the surgeon with towels, inflatable positioners, or a tilting table to improve exposure and reduce back strain of the surgeon.
3. Perform a ventrolateral (gluteal roll-up) approach to the ilium.
   a. Make a skin incision from the iliac crest to the greater trochanter.
   b. Incise the subcutaneous fat to expose the pelvic musculature.
   c. Achieve hemostasis by careful electrocoagulation.
4. Identify and separate the tensor fasciae latae and middle gluteal muscles. Retract the tensor fasciae latae muscle ventrally, and retract the middle gluteal muscle dorsally to expose the ilium (Fig. 107-3). Subperiosteal elevation of the middle and deep gluteal muscles ventrally from the surface of the ilium exposes the lateral surface of the body of the ilium. Retract the sartorius muscle cranially as needed. Remember that there is little to no plane of dissection at the confluence of sartorius, middle gluteal muscles, and tensor fasciae latae. Sharply incise these muscles where they join and continue the dissection dorsally along the cranial edge of the iliac crest as needed to "roll up" the gluteal to provide adequate exposure of the ilium. The iliolumbar artery is present along the ventral edge of the cranial ilium in these muscles and is usually severed during the muscular dissection. Electrocoagulate or ligate this artery when it is encountered.
   a. During exposure of the body of the ilium, it may be necessary to retract or transect branches of the cranial gluteal vein, artery, and nerve that supply the tensor fasciae latae muscle.
   b. Preserve the lateral circumflex femoral vessels immediately cranial to the acetabulum.

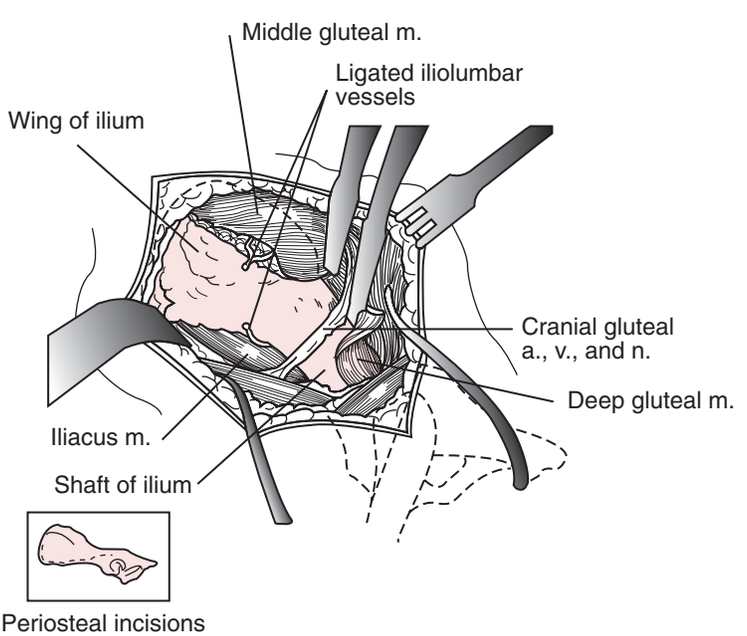

Figure 107-3. Diagram illustrating the final stages of the gluteal "roll-up" approach to the ilial wing and body.

▼ ***Key Point*** Avoid damage to the sciatic nerve, which lies dorsomedial to the ilium during reduction and stabilization of the fracture.

5. After exposing the fracture, carefully clean the ends of the fractured bone of hematoma and fibrin tags that interfere with accurate reduction. Do *not* overclean the fragments. Doing so may remove soft, cancellous bone from the edges of the fracture and damage the anatomic alignment between fragments. If reduction of the caudal ilial fragment is difficult, reduce the caudal fragment by grabbing the ischium with bone-holding forceps through a separate smaller incision over the ischiatic tuberosity.
6. After reducing the fracture, contour a bone plate to the body of the ilium. The tendency is to undercontour the plate, leading to under-reduction of the fracture. When in doubt, it is usually better to create more curve in the plate. If possible, position the plate so that one to two screws in the cranial fragment can be placed in the body of the sacrum to engage more bone. The cranial part (the wing) of the ilium is thin and screws strip easily if the body of the sacrum is not engaged.
7. Initially, attach the plate to the caudal fragment. Lateral traction on the caudal fragment or ischium assists final reduction of the fracture.
8. If the fracture is a transverse, linear fracture, compress the fracture by using the drill guide in the load position before screw placement. Place at least three screws on each side of the fracture. Select implant sizes according to the guidelines in Table 107-1.
9. If fracture comminution is present, smaller fracture fragments may be stabilized with Kirschner wires (K-wires) or lag screws to further assist fracture reduction. Do not compress the fracture in this situation.
10. It may be possible in some instances to stabilize oblique fractures of the body of the ilium with ventrodorsally oriented bone screws alone, particularly in large dogs. Use the screws for lag effect by overdrilling the cortex closest to the head of the screw, or use partially threaded screws. The fracture will be compressed as the screws are tightened (Fig. 107-4).
11. Closure. Irrigate the surgical site with saline and close the muscle and fascia (simple continuous or cruciate pattern, absorbable suture), subcutaneous tissue (simple continuous pattern, absorbable suture), and skin (interrupted or cruciate pattern, non-absorbable suture) or skin staples.

Table 107-1. GUIDELINES FOR IMPLANT SIZES FOR FRACTURES OF THE ILIUM OF DOGS AND CATS

Body Weight (kg)	Plate Size (mm)/Type
<10	2.0 DCP or 2.0 LRP or 2.4 LRP
10–20	2.7 DCP or 2.7 RCP or 2.4 LRP
>20	3.5 DCP or 3.5 RCP or 3.5 LCP or 2.4 LRP

DCP, dynamic compression plate; LCP, locking compression plate; LRP, locking reconstruction plate; RCP, reconstruction plate.

Postoperative Care and Complications

Short Term

- Evaluate immediate postoperative radiographs for plate contouring and screw placement, particularly any screws inserted into the body of the sacrum.
- Continue analgesic therapy for 10 to 14 days.
- Monitor for seroma formation. If a seroma occurs, warm compresses and time will resolve the seroma. Do *not* aspirate or place drains in seromas unless the seroma is extremely large and fails to resolve with conservative care. Any aspiration attempt should be done only with strict aseptic technique. If necessary, use a closed, suction-type drain that is emptied and maintained with strict aseptic technique.
- Good patient care is essential to encourage early mobility and return to normal function (see "Nonsurgical Treatment").
- Reassess the neurologic status of the patient.
- It is not necessary to continue antibiotic usage after surgery unless there was a break in aseptic technique during surgery or other risk factors for infection, immunosuppression, significant tissue injury, prolonged surgery time, etc.

Long Term

- Restrict activity to leash walking only on non-slick surfaces for 6 to 8 weeks to minimize the risk of fixation failure.
- If neurologic deficits are present, reevaluate these regularly.

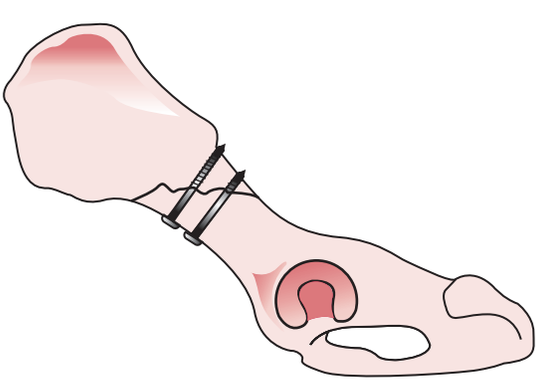

Figure 107-4. Diagram of an oblique ilial body fracture repaired with ventrodorsally oriented lag screws. (From Fossum TW: Small Animal Surgery, 2nd ed. St Louis: Mosby, 2002.)

- Obtain radiographs every 4 to 6 weeks to monitor fracture healing.
- Do not remove plate and bone screws unless there are clinical signs of implant-associated problems. Stress protection by the plate is not a recognized complication.

Prognosis

- The prognosis is very good with anatomic reduction, stable fixation, and no neurologic damage. Pelvic fractures usually heal in 6 to 10 weeks. Delayed union or nonunion is uncommon because the pelvic bones have a large proportion of cancellous bone, and the extensive muscle coverage maintains a good blood supply to the fractured bone and also provides some degree of fracture stabilization.
- If neurologic deficits are present after surgery, the prognosis is fair to poor, and recovery of normal function may be delayed by weeks to months, or may not occur at all.
- If the plate is too small or thin or if insufficient screws are placed on each side of the fracture, plate breakage or screw loosening may occur.

FRACTURES OF THE ACETABULUM

Preoperative Considerations

▼ ***Key Point*** Acetabular fractures are among the most difficult of all fractures to properly repair. The surgical approach is difficult, and anatomic reduction and rigid fixation are mandatory. Refer these cases to a surgical specialist.

- Fractures of the acetabulum are usually accompanied by fractures of other regions of the pelvis unless an impaction fracture has occurred. If other major weight-bearing regions of the pelvis are fractured, multiple surgical procedures may be necessary.
- Fractures of the acetabulum are classified by the anatomic region (cranial, central, or caudal acetabulum), the degree of comminution, and the degree of displacement.
- Historically, conservative management has been advocated for undisplaced and caudal fractures of the acetabulum. However, the treatment of choice for all intra-articular fractures of the acetabulum is surgical stabilization, because this minimizes the severity of subsequent osteoarthritis.

▼ ***Key Point*** When it is not possible to anatomically reconstruct comminuted acetabular fractures, conservative management or stabilization of the major fragments is indicated. Excision arthroplasty (femoral head and neck ostectomy) can be performed concurrently or after the fractures have healed (see Chapter 108). Total hip arthroplasty may be performed to relieve residual hip pain and improve hip function but must be done after the fractures have healed (see Chapter 108).

- Damage to the joint capsule may be associated with fractures of the acetabulum, especially if the hip is luxated.
- Evaluate withdrawal and femoral and sciatic nerve reflexes, particularly with displaced fractures of the caudal acetabulum. Damage to the sciatic nerve may be present.
- Administer prophylactic antibiotics (e.g., catrazolin) at the time of anesthetic induction.

Surgical Procedure

Objectives

- Anatomically reduce and stabilize the acetabulum to restore joint congruity and limb function.
- Relieve pain.
- Provide early restoration of pelvic limb function.
- Avoid iatrogenic sciatic nerve damage.

Equipment

- Standard general surgical pack and suture material.
- Hand-held retractors such as Myerding retractors and an assistant. Alternatively, Gelpi or Weitlaner self-retaining retractors can be used but generally are not as efficient at making adjustments as an assistant using a hand-held retractor.
- Orthopedic surgical pack with AO-ASIF "clamshell" and Kern bone-holding forceps and Hohmann retractors.
- Bone-plating equipment. Acetabular or reconstruction plates can be used. Acetabular plates are only useful for linear central or cranial fractures. Reconstruction plates can be contoured in multiple planes and lend themselves to the complex geometry of the acetabulum. The latest advance in plating, locking compression plates (LCP) allow the screws to be locked to the plate and are helpful for areas where the bone is weak or subject to failure or when precise anatomic reconstruction of the fracture is impossible. Avoid semitubular plates, finger plates, and other thin plates.
- Another method of fixation uses a combination of K-wires, screws, positional wire, and polymethylmethacrylate bone cement.
- Freer or Adson periosteal elevator.
- Suction with Frazier or Yankauer tips and electrocautery.

Technique

1. Prepare the patient as described under Fractures of the Ilium.
2. If the ischium will be approached as part of the reduction, place a tampon or lubricated gauze

sponge in the rectum, and place a pursestring suture in the anus. Place a piece of white 1-inch tape with a warning about the pursestring across the animal's forehead, or make a note on the anesthetic chart so the pursestring will not be forgotten at the conclusion of the surgery.

3. For fractures of the cranial, central, and caudal regions of the acetabulum, use a dorsal approach to the hip. For some central and all caudal fractures, use a combined dorsal and caudolateral approach to the hip joint. Make a separate surgical approach to the ischium and elevate the internal obturator and gemelli muscles to expose the table of the ischium. Place a Kern bone-holding forceps on the table of the ischium to manipulate the caudal bone fragment, while minimizing risk of iatrogenic damage to the sciatic nerve. If possible, precontour a bone plate to an intact pelvis of an equivalent-size cadaver to minimize operating time.
4. Make a curved skin incision, centered over the caudal surface of the greater trochanter, beginning close to the dorsal midline, and ending at the junction of the proximal and middle thirds of the femur. Achieve hemostasis by careful electrocoagulation.
5. Incise and retract the subcutaneous tissues to expose the underlying musculature.
6. Incise the fascia of the biceps femoris muscle along its cranial border.
7. Free the cranial part of the origin of the biceps femoris muscle from the sacrotuberous ligament. Transect the insertion of the superficial gluteal muscle on the third trochanter, and retract this muscle dorsally. Retract the biceps femoris muscle caudally. Identify and avoid the sciatic nerve.
8. Perform a dorsal approach to the hip by osteotomy of the greater trochanter of the femur. Alternatively, perform a tenotomy of the middle and deep gluteal muscles in young dogs. For a caudal approach to the hip, transect the combined tendons of the internal obturator and gemelli muscles close to their insertion in the trochanteric fossa or remove a small block of bone in the trochanteric fossa of the femur where these muscles insert. A small osteotome works well for this procedure. Retract these muscles and/or the block of bone with a stay suture in the tendons. Retraction of these muscles indirectly retracts the sciatic nerve caudally.
9. Retract the gluteal muscles dorsally. Part of the origin of the deep gluteal muscle may need to be elevated to expose the more cranial region of the acetabulum.
10. Preserve as much of the joint capsule as possible. Do not elevate it from the acetabular bone. To observe the joint surface, perform a small radial arthrotomy.
11. After exposing the fracture, use AO-ASIF small reduction forceps in combination with the Kern bone-holding forceps placed on the ischium to manipulate and reduce the fracture fragments. Bone-holding forceps placed on the greater trochanter also provide lateral traction and aid in manipulation of the femoral head for better identification of the fracture.
12. Fractures of the acetabulum are rarely stable immediately after reduction. If the fracture configuration allows, maintain reduction of the fracture by placing pointed bone-holding forceps craniocaudally across the acetabulum. If necessary, place shallow drill holes (1.1 or 1.5 mm) in each fragment to prevent the point-to-point forceps from slipping. This is usually only applicable to linear fractures. Other fracture configurations, including comminuted fractures, often require diverging K-wires or other methods of maintaining reduction while definitive fixation is applied.
13. After the fracture has been reduced, apply a precontoured bone plate. Stabilize the fracture with an acetabular plate, a reconstruction plate, or an LCP. Engage at least six cortices on each side of the fracture. Because of the thin cortical bone that is present in the pelvis, carefully drill and tap the screw holes. Select implants according to the guidelines in Table 107-2.
    a. Alternatively, if a combination of K-wires, screws, and bone cement is to be used, maintain fracture reduction crosspinning the fracture with K-wires. Place a screw on either side of the fracture line and a figure-of-eight wire around the screws. Encase the pins, screws, and wire in a moderate amount of bone cement.
14. Closure:
    a. If the joint capsule has been torn or incised, appose it with sutures in a simple interrupted pattern using monofilament absorbable suture. Reattach the tendons of the internal obturator and gemelli muscles using monofilament absorbable or non-absorbable suture and a tension-relieving suture pattern such as the horizontal mattress or locking loop pattern. Drill two small holes parallel to each other and perpendicular to the long axis of the femoral neck through the neck of the femur to pass the suture through. Tie the suture on the cranial aspect of

Table 107-2. GUIDELINES FOR IMPLANT SIZES FOR FRACTURES OF THE ACETABULUM OF DOGS AND CATS

Body Weight (kg)	Plate Size (mm)/Type
<10	2.0 AP, RCP, or LRP
10–30	2.0 or 2.7 AP; 2.7 RCP; or 2.4 LRP
>30	2.7 AP, 3.5 RCP, 3.5 LCP

AP, acetabular plate; LCP, locking compression plate; LRP, locking reconstruction plate; RCP, reconstruction plate.

the femoral neck. Stabilize the osteotomy of the greater trochanter of the femur with a tension band wire technique (Fig. 107-5), or reattach the gluteal muscles with a tension-relieving pattern such as a horizontal mattress or locking loop pattern. Reattach the tendon of insertion of the superficial gluteal muscle to the distal aspect of the greater trochanter (third trochanter).

b. Reattach the biceps femoris to the sacrotuberous ligament (cruciate or simple interrupted pattern, absorbable suture). Close the biceps femoris fascia (simple continuous pattern, absorbable suture), subcutaneous tissue (simple continuous pattern, absorbable suture), and skin (interrupted pattern, absorbable suture; or skin staples).

c. Remove the pursestring suture and tampon from the anus.

Postoperative Care and Complications

- See "Fractures of the Ilium."

Prognosis

- The prognosis is good if anatomic reduction of the acetabulum and rigid fixation are achieved and neurologic function is normal.

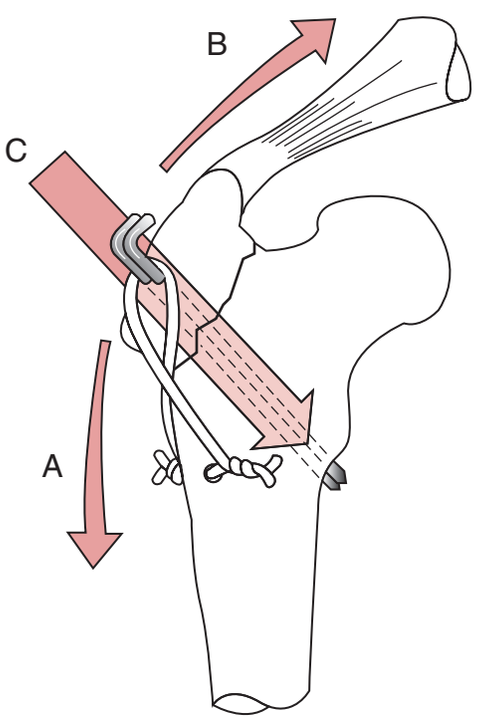

Figure 107-5. Diagram of the tension band principle. The distractive forces placed on the greater trochanter by the gluteal muscles is converted by the figure-of-eight tension wire to forces that compress the osteotomized greater trochanter against the femur. (From Slatter D: Textbook of Small Animal Surgery, 2nd ed. Philadelphia: WB Saunders, 2003.)

- If anatomic reduction and rigid fixation are not achieved, the prognosis is fair to poor. Osteoarthritis is likely to develop, and further surgical or medical treatment may be necessary.
- The prognosis is guarded to fair if femoral head excision is performed to repair a comminuted acetabular fracture.

SACROILIAC FRACTURE OR LUXATION

Preoperative Considerations

- If luxation of the sacroiliac (SI) joint has occurred, craniodorsal displacement of the ilium is usually present, together with fractures in other regions of the pelvis. Bilateral SI joint separation without concurrent fractures of the remainder of the pelvis may also occur.
- Perform a thorough neurologic examination (including bladder function, anal tone, and perineal sensation), particularly when displacement of the fracture is marked or SI joint luxation is severe, because damage to the cauda equina nerve roots may be present.
- Review dorsoventral radiographs carefully for sacral fractures. Fracture lines that traverse the spinal canal or sacral foramina are especially prone to suggest the likelihood of concurrent neurologic deficits and a poorer prognosis.
- Because surgical treatment of SI fracture or luxation is technically difficult, undertake surgical treatment only after careful consideration of other options, including conservative management or referral.

▼ ***Key Point*** In many animals with SI luxation the displacement is not severe and the injury responds well to conservative management. However, successful reduction and stabilization of the SI joint relieves pain more quickly and allows more rapid return to normal function. Anatomic reduction and rigid stabilization has a higher priority as a treatment option if neurologic deficits are present or if pelvic injuries are bilateral.

- Administer prophylactic antibiotics at the time of anesthetic induction.

Surgical Procedure

Objectives

- Anatomically reduce and stabilize the sacrum and SI joint.
- Relieve pain.
- Provide early restoration of pelvic limb function.
- Avoid iatrogenic damage to the cauda equina nerve roots and sciatic nerve.

Equipment

- Standard general surgical pack and suture material.
- Hand-held retractors such as Myerding retractors and an assistant. Alternatively, Gelpi or Weitlaner self-retaining retractors can be used but generally are not as efficient at making adjustments as an assistant using a hand-held retractor.
- Orthopedic surgical pack with AO-ASIF "clamshell" and Kern bone-holding forceps and Hohmann retractors.
- Bone screws and application equipment.
- Freer or Adson periosteal elevator.
- Suction with Frazier or Yankauer tips and electrocautery.
- Aiming device for bilateral luxations.

Technique

1. For unilateral SI luxation, perform a hanging limb prep by preparing the skin for aseptic surgery on the lateral and medial sides of the pelvic limb from the tarsocrural joint to the dorsal and ventral midline and from the mid-lumbar area to the base of the tail. For bilateral luxation, clip and prep the dorsal half of the pelvis from tail base to cranial to the ilial wings. For unilateral SI luxation, place the patient in lateral recumbency, and stabilize the pelvis by using a vacuum-assisted positioner bag. Secure the patient to the table. Rotating the operating table toward the surgeon with towels, inflatable positioners, or a tilting table greatly improves exposure and reduces back strain.
2. Make a dorsal approach to the sacroiliac joint.
   a. Make a skin incision over the crest of the ilium extending caudally along the shaft of the ilium.
   b. Incise and retract the cutaneous trunci muscle and the subcutaneous fat to expose the pelvic musculature.
   c. Obtain hemostasis by careful electrocoagulation.
3. Incise the middle gluteal muscle along its origin at the dorsal border of the wing of the ilium, and subperiosteally elevate it, beginning cranially. Medially, the sacrocaudalis and intertransversarius muscles and dorsal sacroiliac ligament are usually disrupted and therefore require little additional dissection.
4. Maneuver the ilium using Kern bone-holding forceps. Initially, displace the ilium ventrally and laterally to expose the articular surface of the sacrum.
5. Place a drill hole in the body of the sacrum. There is a C-shaped ridge that outlines the sacral body from caudodorsal, caudally to cranioventral (Fig. 107-6). Center the drill bit in the C for optimal alignment. Align the drill hole perpendicular to the midsagittal plane both dorsoventrally and craniocaudally. Make the depth of the drill hole at least two-thirds of the width of the sacral body, and measure the hole with a depth gauge and tap the hole. Be careful not to extend the tap to the end of the drill hole if the hole does not go all the way through the sacral body. Doing so will result in stripping of the threads in the drill hole and failure of the screw to properly engage the bone.
6. The site on the medial surface of the ilium that corresponds to the drill hole in the sacrum determines the exact location of the drill hole on the lateral surface of the ilium. The site can usually be felt but is often hard to see. Overdrill the hole in the ilium to allow compression of the SI joint with a fully threaded screw.
7. Determine the length of the screw by adding the thickness of the ilium to the depth of the sacral drill hole. Select the size of the bone screw using the guidelines in Table 107-3. Again, if the drill hole in the sacral body does not exit the opposite side of the body, do *not* place a screw that is longer than the hole and ilium. Doing so will result in stripping of the threads in the bone and failure of the screw to properly engage the bone. Use a screw that is 2 to 3 mm shorter than the measured depth to take into account slight errors in measurement.
8. Place the screw into the ilium until the tip of the screw just protrudes from the medial surface. Reduce the SI joint and insert and tighten the screw to stabilize and compress the joint.
9. Generally, a single large screw is sufficient. If indicated (usually only giant breed dogs or, occasionally, dogs with sacral fractures), place a second

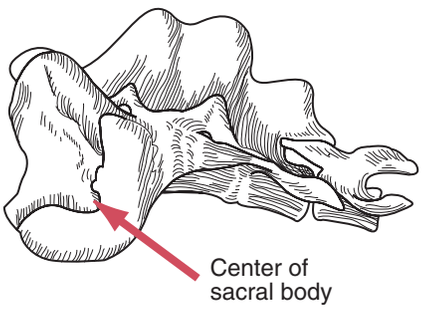

Figure 107-6. Anatomy of the sacrum. The sacroiliac joint surface appears as C, the center of which is the center of the sacral body. (From Evans S: Miller's Anatomy of the Dog, 2nd ed. Philadelphia: WB Saunders, 1993.)

Table 107-3. GUIDELINES FOR SCREW SIZES FOR REPAIR OF SACROILIAC LUXATION OF DOGS AND CATS

Body Weight (kg)	Screw Diameter (mm)/Type
<10	2.0–2.7
10–20	2.7–3.5
20–30	3.5–4.5
>30	4.5–5.5

screw to give two-point fixation. If two screws are to be placed, consider using the next size smaller screw than you would choose if only one screw is to be placed.

10. With bilateral fractures or luxations, screws may be placed bilaterally, or a single screw may be placed through both ilial wings and the sacral body. In the latter instance, use an aiming device to ensure that the drill hole is placed in the correct plane. The tip of the aiming device is placed in the center of the C of the contralateral surface of the sacrum and the drill guide placed on the C of the ipsilateral sacrum while the ilial bodies are depressed ventrally. If a single large screw is placed across both SI joints, the ipsilateral joint can be compressed but the contralateral joint is held in neutral fashion. If compression of both joints is desired and the size of the sacral body allows a 4.5-mm screw to be used, thread a nut onto the screw on the contralateral side for compression.
11. Close the middle and deep gluteal muscle fascia to the dorsal fascial insertion on the ilium or to the fascia of the sacrocaudalis and intertransversarius muscles with monofilament absorbable suture in a simple interrupted or cruciate pattern. Close the subcutis and skin as for other incisions.

Postoperative Care and Complications

Short Term

- See "Fractures of the Ilium."

Prognosis

- The prognosis is good to excellent with correct positioning of the bone screw and no neurologic damage.
- If the bone screw does not correctly engage the sacral body, fixation failure is more likely.
- If neurologic deficits are present after surgery, the prognosis is guarded.

FRACTURES OF THE ISCHIUM

- Fractures of the ischium are usually associated with fractures of other major weight-bearing regions of the pelvis. If appropriate surgery is performed to anatomically reduce and stabilize other, functionally more important fractures, additional fixation of ischial fractures is usually unnecessary.
- Fractures of the ischium are usually displaced ventrally as a consequence of tension created by the caudal thigh muscles (the biceps femoris, semitendinosus, and semimembranosus muscles).
- Occasionally, isolated fractures of the ischium may be encountered. If severe pain is associated with the fracture(s) or if displacement of the fracture fragments is such that the function of the hip joint is impaired, internal fixation may be indicated. Fixation of these fractures can be accomplished with small plates, lag screws, or diverging K-wires.

▼ ***Key Point*** Surgical repair of fractures of the ischium is usually unnecessary.

FRACTURES OF THE PUBIS

- Fractures of the pelvic symphysis, which is composed of the pubic and ischial symphyses, may be associated with fractures of other regions of the pelvis. This problem is more common in young animals in which bony union of the pelvic symphysis has not yet occurred.
- Anatomic reduction and stabilization of the other, functionally more important pelvic fractures usually makes surgical treatment of pubic fractures unnecessary. However, internal fixation of pubic fractures may occasionally be indicated.
- If pubic fractures are associated with a caudal abdominal wall rupture and herniation of abdominal or pelvic organs, surgical repair of the hernia may be assisted by internal fixation of the fractures. Interfragmentary wire is usually the preferred method for fixation.

NARROWED PELVIC CANAL ASSOCIATED WITH HEALED PELVIC FRACTURES

- Obstipation and dystocia are occasionally associated with healed pelvic fractures and a narrowed pelvic canal. This problem is most commonly encountered in cats and small dogs whose pelvic fractures are more likely to be managed conservatively.
- Manage dystocia by cesarean section or ovariohysterectomy (see Chapter 91).
- Operations designed to widen the pelvic canal have been described. Osteotomy of the ilium, the ischium, and the pubis, and lateralization of the caudal fragment with a plate, is the preferred method.
- In dogs and cats with obstipation as a consequence of a narrowed pelvic canal, subtotal colectomy may be necessary (see Chapter 70), because colonic dysfunction is not always relieved by corrective osteotomy or use of a motility modifier such as cisapride.

▼ ***Key Point*** If megacolon secondary to obstipation has been present for longer than 6 months, normal colonic motility does not always return after the bony pelvic canal has been widened, and obstipation can continue to be a problem. Subtotal colectomy is usually the preferred solution in cats. Resection of portions of the pelvic girdle is also an option and is probably preferred in dogs.

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Chapter

108 Disorders of the Coxofemoral Joint

Marvin L. Olmstead

The coxofemoral joint is the most proximal of the free-moving joints of the pelvic limb. Surgery is frequently performed on or near this joint to treat conditions such as coxofemoral luxations and hip dysplasia. Avascular necrosis of the femoral head, which occurs infrequently, also can be treated surgically.

Anatomic considerations, diagnosis, and treatment of these conditions of the coxofemoral joint are discussed in this chapter.

ANATOMY

- The coxofemoral joint is a ball-and-socket joint made up of the femoral head and the acetabulum.
- In a normal animal, the joint capsule attaches to the rim of the acetabulum and around the circumference of the femoral neck just distal to the junction of the head and neck. When the limb is taken through range-of-motion exercises, the joint capsule helps maintain joint congruency.
- The ligament of the head of the femur runs between the acetabular fossa and the fovea capitis of the femoral head.
- The fovea and the fossa are sometimes mistakenly identified as radiographic abnormalities.

▼ ***Key Point*** The fovea causes a natural flattened area on the femoral head that can be mistaken for the flattening associated with hip dysplasia. The fossa creates a shadow that can be mistaken for a fracture line.

- The blood supply to the femoral head is extensive.
  - Small arterial loops arise from the iliolumbar artery cranially; the lateral circumflex femoral artery dorsally, cranially, and ventrally; and the medial circumflex femoral artery dorsally, caudally, and ventrally. They all penetrate the femoral head at the joint capsule attachment.
  - No significant blood vessels penetrate the femoral head from the ligament of the head of the femur.
- Several surgically important muscles have their insertions or origins close to the coxofemoral joint, either on the proximal femur or the pelvis (see Chapter 107).
  - The middle and deep gluteal muscles originate on the wing of the ilium and insert on the dorsal and cranial border of the greater trochanter.
  - The superficial gluteal muscle originates on the sacrum and the first coccygeal vertebra and inserts on the third trochanter.
  - The internal and external obturator and gemelli muscles insert in the caudal trochanteric fossa.
  - The vastus lateralis and intermedius muscles originate on the cranial aspect of the femur, whereas the rectus femoris originates on the pelvis cranial to the acetabulum.
  - The tensor fascia lata muscle originates along the caudolateral edge of the femur, covering the vastus lateralis muscle, and along the cranial edge of the biceps femoris muscle via three or more tissue slips.
  - The origin of the pectineus muscle is just ventral to the acetabulum.
- Two angles of surgical significance have been described in the proximal femur:
  - *Angle of inclination:* When the femur is viewed from a cranial position, the *angle of inclination* is the angle formed between a line that bisects the long axis of the femur and a line that bisects the femoral neck. In the normal dog, this angle is 135 to 145 degrees.
  - *Angle of anteversion:* When the femur is viewed from a straight lateral position, part of the femoral head is displaced forward of the femoral shaft due to the anteversion angle of the femoral neck. One method of measuring this angle involves taking radiographs of the femur with the dog on its back with the long axis of the femur positioned 90° to the radiographic plate and the stifle joint flexed 90°. The radiographic beam must pass directly down the center of the femur, parallel to its long axis. One line is drawn parallel to the caudal edge of the femoral condyles, and a second line is drawn that bisects the femoral head and neck. The angle created by the intersection of these two lines is the *anteversion angle,* which in normal dogs is 20 to 27 degrees.
- Abnormal alterations can occur in these angles during hip development, resulting in pathology in the hip or further distally in the limb.

COXOFEMORAL LUXATIONS

Most coxofemoral luxations are craniodorsal displacements of the femoral head; almost all others are caudoventrally displaced. Usually these are associated with motor vehicle accidents; thus, fully evaluate other organ systems for trauma (see Chapters 3 and 166), as well as coxofemoral joint evaluation.

Diagnosis

▼ ***Key Point*** Evaluate the coxofemoral joint for luxation by analyzing the gait, manipulating the hip, comparing hindlimb lengths, and obtaining two radiographic views of the pelvis.

- Animals with a luxated hip usually will not bear weight on the affected limb. If a craniodorsal luxation is present, the limb may be externally rotated and adducted.
- Range-of-motion evaluation of the hip may reveal grating and/or pain in the area of the coxofemoral joint.
- Evaluate the relationship between the caudal edge of the greater trochanter and the cranial edge of the ischiatic tuberosity to determine the position of the proximal femur.
  - If a craniodorsal luxation is present, there will be a wide space that does not close (as in the normal animal) when the limb is externally rotated.
  - If a caudoventral luxation is present, there will be no space between these two structures.
- When both hindlimbs are pulled directly caudally, they will be of equal length in a normal animal. If they are uneven in length, this is a strong indication that the coxofemoral joint is dislocated.
- The primary method of diagnosis is radiography of the coxofemoral joint to rule out fractures of the proximal femur, which can mimic a luxation on physical examination.
  - Evaluate the acetabulum for an avulsion fracture from the femoral head or acetabular fracture.

▼ ***Key Point*** Avulsion fracture of the femoral head is an absolute indication for surgery.

Treatment: Closed Reduction

If there is no avulsion fracture, perform closed reduction of the joint under general anesthesia.

- To perform reduction for a craniodorsal luxation:
  - Grasp the foot just distal to the talocrural joint and externally rotate the limb.
  - Then externally rotate the femoral head.
  - Apply distal traction to the limb until the femoral head is even with the acetabulum; then rotate the femoral head internally, causing it to drop into the acetabulum (Fig. 108-1).

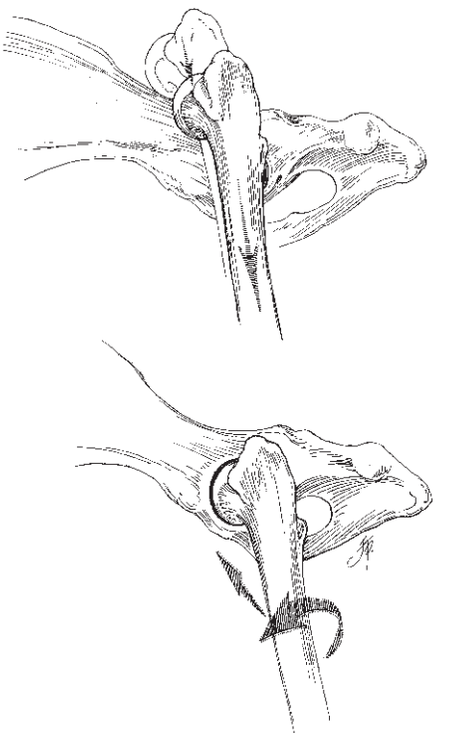

Figure 108-1. Closed reduction of the coxofemoral joint. External rotation and distal traction of the limb *(top)* is followed by internal rotation of the femoral head *(bottom)*.

- Reduce a caudoventral luxation by abducting and externally rotating the limb.
- The longer the femoral head is luxated craniodorsally, the more damage that is done to the dorsal joint capsule. An intact joint capsule is helpful in maintaining reduction.
- If the reduced hip easily luxates again, perform open reduction.
- If the reduced hip snaps solidly into position, place the hip in a flexion sling for a craniodorsal luxation; place the legs in hobbles for a caudoventral luxation (Fig. 108-2). Apply these restriction bandages for 10 to 14 days in the adult and 7 to 10 days in the immature animal. Limit exercise during this period, and for an additional 2 to 4 weeks.
- Examine the reduced hip physically on a daily basis or instruct the owner to do this, until the restriction bandage is removed.
- If there is any question about the hip's position, reevaluate with lateral pelvic radiographs. If the hip is reluxated, perform an open reduction.

Treatment: Open Reduction

Surgical Procedures

Objectives

- Reduce the luxated coxofemoral joint.
- Reconstruct as much soft tissue as possible.

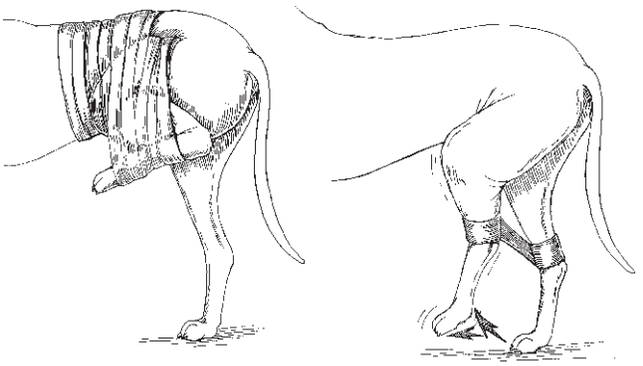

Figure 108-2. After reduction, use a flexion (Ehmer) sling for a craniodorsal luxation *(left)* and hobbles for a caudoventral luxation *(right)*.

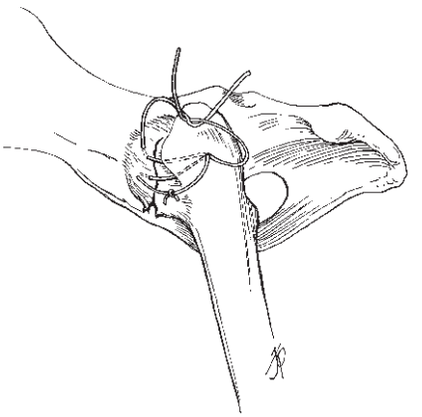

Figure 108-3. Surgical repair of luxation if adequate capsule remains attached to the acetabular rim. An anchor hole has been drilled in the proximal femur.

- Remove fibrous tissue from the acetabulum, remnants of the ligament of the head of the femur, and avulsed bone fragments that cannot be stabilized.

Equipment

- Standard surgery pack and suture material
- Special equipment as needed for specific procedures (noted in following text)

Techniques

1. The standard approaches used for surgical repair of luxations are the cranial lateral approach to the hip and the trochanteric osteotomy approach (see Chapter 107). Occasionally a caudal approach (caudal to the greater trochanter of the femur) to the coxofemoral joint may be used.
2. Initially, assess the overall damage and the status of supporting tissues, remove abnormal tissue and debris from the acetabular cup, and reduce the femoral head into the acetabulum.
3. Once reduced, use one or more stabilization techniques to secure the femoral head into the acetabulum.
4. If the joint capsule is minimally damaged and adequate capsular tissue is present on either side of the tear, suture the capsule (this may be the only support necessary).
   a. Use an absorbable monofilament suture of significant size (2-0, 0, or 1, depending on the animal's size), placed in a cruciate pattern.
   b. If adequate capsule is attached to the acetabular rim but not enough solid capsule is attached to the femoral neck, drill an anchor hole with lateral to cranial orientation in the proximal femur. Pass one-half of the suture strands through the hole and tie them tightly to the other half of the strands (Fig. 108-3).
5. The capsule may be so severely damaged that it cannot hold a conventionally placed suture. (This may occur if there is a long delay between the time of injury and repair.)
   a. In these cases suture support can be provided by making anchor points for the sutures. Drill a hole (as described in Step 4b above) for an anchor site in the femur. Place one to three bone screws (usually a 3.5-mm cortical screw) in the dorsal rim over the acetabulum as anchor points on the pelvis. Place the suture support between these to form a dorsal reinforcement (Fig. 108-4).
   b. Alternatively, place a temporary intramedullary pin in the proximal femur, parallel with the neck axis, and through the acetabular fossa. Be sure that the pin does not extend too far into the pelvic canal (Fig. 108-5). Keep the limb immobile with a flexion sling until the pin is removed, 7 to 10 days after surgery.

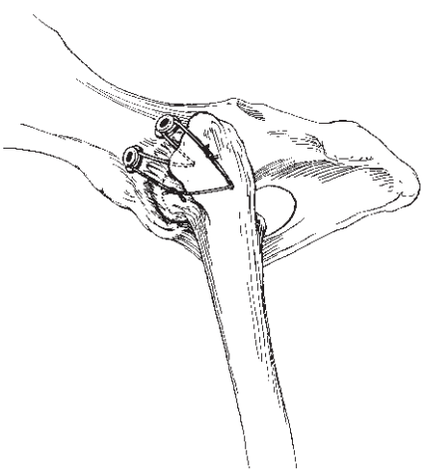

Figure 108-4. Suture support for coxofemoral luxation with a damaged joint capsule.

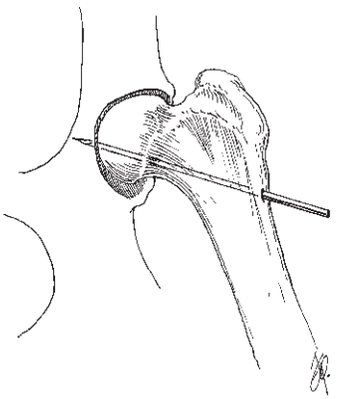

Figure 108-5. Temporary intramedullary pin for open reduction of coxofemoral joint.

   c. Another alternative is to place a toggle pin through a hole in the acetabular fossa with suture attached to it. This creates an artificial ligament between the head of the femur and the acetabulum. Pass the suture through a hole drilled, from lateral to medial, in the proximal femur. The hole enters the femur just dorsal to the third trochanter and exits at the insertion point of the ligament of the head of the femur on the femoral head. Pull all the suture strands through this hole, and then pass half the suture strands through a second hole in the femur drilled in a cranial to caudal direction. Tie the two sets of suture strands together.
6. Rotate the femoral head inwardly, and tighten the gluteal muscle pull on the femur by moving the greater trochanter to a position caudal and distal to its original location. This technique can be used with a trochanteric osteotomy approach.
   a. Do not depend on this technique as the sole means of stabilization.
   b. Any positional changes in gait caused by this relocation are temporary, because the gluteal muscles eventually will stretch.
7. If the femoral head does not remain in the acetabulum even with the application of support techniques, consider a primary salvage procedure such as excision arthroplasty or total hip replacement.

Postoperative Care and Complications

- If there is any doubt about the strength or security of the stabilization, place the limb in an immobilization sling or bandage for 7 to 14 days.
- Examine the sling or bandage and the visible parts of the limb daily for odor, chewing, swelling, pressure sore development, and slippage.
- Check the spatial relationship between the greater trochanter and the ischiatic tuberosity daily. If this changes, evaluate the position of the femur with lateral radiography of the pelvis. This can be accomplished without removing the sling.
- Restrict the animal's activity (leash walking only) for 1 month after the surgery.
- The most common complication following surgery or closed reduction is reluxation. If reluxation occurs after open reduction, consider excision arthroplasty or total hip replacement.

AVASCULAR NECROSIS OF THE FEMORAL HEAD

- This condition (also known as Legg-Perthes or Legg-Calvé-Perthes disease, osteochondritis juvenilis, and coxa plana) is most commonly found in adolescent, small-breed dogs of either sex; occasionally it occurs in large breeds.
- Trauma is not usually associated with the onset of lameness, and the lameness can progress to non–weight-bearing.
- The condition occurs bilaterally in about 15% of the animals.
- Changes in the proximal femur seen radiographically and grossly are the result of collapse and remodeling of the trabecular bone of the femoral head following the avascular episode.
- It is not clear what causes the femoral head to become avascular; following this, the bone revascularizes and remodels as the dead bone undergoes resorption.
- Weight bearing causes the weakened subchondral bone to collapse, which, in turn, leads to fracture of the cartilage.

Diagnosis

- Base the diagnosis on physical examination and radiographic findings. Abduction of the limb often elicits a pain response, even before radiographic signs are evident. Crepitus is sometimes observed with flexion and extension of the joint.
- The limb may be shortened and the muscles atrophied.
- Radiographs are needed for a definitive diagnosis. The ventrodorsal straight-leg view of the pelvis is the most helpful in assessing the femoral heads.
  - The joint space may be widened, and numerous foci of decreased bone density may be seen in the femoral head and neck.
  - In advanced stages, there may be irregular indentations, flattening, and possibly fragmentation of the femoral head. Osteophytes on the acetabular rim and secondary osteoarthritis in the joint may also be seen.

Treatment

Some dogs respond to non-surgical treatment including limited activity and analgesics. However, in most cases surgery is ultimately necessary.

▼ ***Key Point*** Surgical treatment of avascular necrosis of the femoral head has a much higher success rate than non-surgical treatment.

Preoperative Considerations

- Because most of the dogs with this condition are small breeds, excision arthroplasty (discussed below) is the most common procedure performed for this disease.
- In large dogs, consider total hip replacement (see next section) as an option.

Surgical Procedures

Objectives

- Eliminate painful bone-to-bone contact.
- Preserve hip motion as close to normal as possible.

Equipment

- Standard surgical pack and suture material
- Specialized equipment, depending on the specific procedure

Technique

- Perform either excision arthroplasty or total hip replacement (see subsequent sections in this chapter).

HIP DYSPLASIA

Hip dysplasia is a faulty development of the hip joint characterized by varying degrees of joint laxity that permit subluxation early in life. As the condition progresses, deformation of the architecture of the acetabulum and femoral head is accompanied by the development of degenerative joint disease.

▼ ***Key Point*** Hip dysplasia is the most prevalent disorder of the canine hip and the most important cause of osteoarthritis in that joint.

- Although almost all breeds are at risk, hip dysplasia most commonly affects large- and giant-breed dogs, and its mode of inheritance is polygenic.
- Joint instability occurs as muscle development and maturation lag behind the rate of skeletal growth.
- The first 60 days of life are the most critical period for the developing soft tissue structures.
- When the stress and weight exerted at the hip joint exceed the strength limits of the supporting soft tissues, joint instability results.

Diagnosis

Base the diagnosis of hip dysplasia on the history, physical examination, and radiographic evaluation of the coxofemoral joints.

Physical Examination

- Lameness of the hindlimb and gait abnormalities frequently are seen, especially after exercise periods; motion of the coxofemoral joint often is limited because of joint pain.
- Joint laxity and pain may be elicited by examination of the range of motion of the coxofemoral joint. Joint laxity is present in mild to moderately dysplastic animals.
- *Ortolani sign:* With a hand placed on the knee of the affected limb, apply dorsal pressure to the femur while moving the bone from an adducted to an abducted position.
  - The click or pop that is heard or felt as the femoral head reenters the acetabulum is a positive Ortolani sign and an indication of joint laxity.
  - If the hip is normal or if arthritic changes in the acetabulum preclude movement of the femoral head in and out of the acetabulum, the Ortolani sign is negative.

Radiography

Radiographs are needed for a positive diagnosis of hip dysplasia.

- In early cases, proper positioning of the ventrodorsal view is extremely critical; in advanced stages, the changes are pronounced and positioning is less important.
- Radiographic changes associated with hip dysplasia range from subluxation of the femoral head to severe secondary degenerative joint disease, with marked alterations in the architecture of the femoral head and the acetabulum.

Treatment

Medical

Non-surgical therapy is recommended for animals mildly affected by hip dysplasia and those with an initial episode of lameness.

- Restrict activity to allow the inflammatory response within the joint capsule to subside.
- Give medication to relieve pain and reduce the inflammation associated with the degenerative joint disease. Carprofen (2.2 mg/kg q12h PO) or deracoxib (1–2 mg/kg q24h PO) is sometimes adequate.

▼ ***Key Point*** When non-surgical therapy is no longer effective or if the patient is constantly disabled over an extended period, consider one of the following surgical therapies.

Surgical Procedures

Various surgical procedures that have been effective in the treatment of hip dysplasia are discussed. An improved quality of life for the patient is the ultimate goal. The procedures are not listed in any order of preference.

Triple Pelvic Osteotomy

Preoperative Considerations

- In the ideal candidate for the procedure, there is some coverage of the femoral head by the acetabulum, the Ortolani sign is positive, and there are no signs of degenerative joint disease in the hip.
- Most dogs that meet the above criteria are 5 to 11 months of age.
- The animal should show clinical signs associated with hip dysplasia.

Objectives

- Increase the amount of acetabular coverage over the femoral head by rotating the acetabular portion of the pelvis.
- Maintain the normal architecture and congruency of the femoral head and acetabulum.
- Prevent or minimize the development of degenerative joint disease.

Equipment

- Standard surgical pack and suture material
- Equipment necessary to insert bone screws
- Bone plates designed for pelvic osteotomy (e.g., pelvic osteotomy plate; Synthes USA, Paoli, PA; Slocum Enterprises, Inc., Eugene, OR)
- Orthopedic wire
- Oscillating bone saw
- Osteotomes

Technique

1. Expose the ilium, pubis, and ischium.
   a. Make a lateral approach to the wing of the ilium with dorsal elevation of the middle and deep gluteal muscles (see Chapter 107).
   b. Approach the pubis through a second incision over the pectineus muscle or through the lateral approach to the ilium by retracting the vastus muscles caudally and the rectus femoris muscle cranially.
   c. The approach to the ischium depends on the site of the osteotomy. If the osteotomy is performed from the ischial tuberosity cranial to the obturator foramen, make an approach directly over the tuberosity. If the osteotomy is performed just caudal to the acetabulum, extend the lateral incision and reflect the biceps femoris muscle caudally.
2. Perform osteotomies at the ilium, pubis, and ischium so that the acetabulum can be rotated in a manner that provides more dorsal coverage of the femoral head.
3. Hold the tilt on the acetabulum in place with bone plates if a transverse osteotomy has been performed, or with screws and orthopedic wire if a stair-step osteotomy is done.
4. The osteotomy of the ischium may be stabilized with orthopedic wire.
5. Close the incisions routinely.

Postoperative Care and Complications

- Restrict activity for 8 weeks.
- Immediate postoperative radiographs may indicate no apparent change in the acetabular coverage of the femoral head. In some cases, subsequent radiographic evaluations reveal improved acetabular coverage and a femoral head well seated in the acetabulum.
- Occasionally, the desired amount of femoral head coverage is never achieved. This most often occurs when a patient has a totally luxated hip or when many degenerative changes are present at the time of surgery.
- If the acetabulum is rotated too far at the time of surgery, extension of the coxofemoral joint will be limited and result in a gait alteration.

Femoral Head and Neck Excision Arthroplasty

Preoperative Considerations

This palliative, salvage procedure can be performed in dogs of all ages; it is most successful in dogs weighing less than 18 kg. This procedure does not preserve the bony articulation of the head of the femur to the pelvis. Therefore, full locomotive potential of the leg will not be achieved.

Objectives

- Remove the femoral head and neck.
- Eliminate painful contact points in the joint.
- Allow a fibrous tissue joint ("false joint") to replace the ball-and-socket joint.

Equipment

- Standard surgical pack and suture material
- Mallet and osteotome, oscillating bone saw, or bone cutter
- Rongeur or rasp

Technique

1. Use a cranial lateral approach or a ventral approach (pectineal myotomy near its origin on the prepubic tendon).

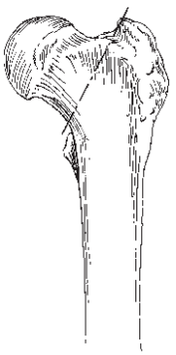

Figure 108-6. Site of osteotomy for femoral head and neck excision arthroplasty.

2. Perform osteotomy of the femoral neck by cutting the bone from the lateralmost edge of the trochanteric fossa to a point just dorsal to the lesser trochanter (Fig. 108-6).
3. Remove the femoral head and neck. It may be necessary to incise the ligament of the head of the femur. If using a ventral approach, this is done following osteotomy of the femoral neck. If using a cranial lateral approach, this is done before osteotomy so that the head and neck can be better exposed by rotating the femur externally 90° and luxating the femoral head from the acetabulum.
4. Examine the remaining portion of the proximal femur for rough areas or bone spurs and remove any, if present.
5. If necessary to eliminate bony contact, remove a portion of the dorsal acetabular rim.
6. Close the incision routinely.

Postoperative Care and Complications

- Encourage use of the operated limb 3 to 7 days postoperatively. Use passive range-of-motion exercise on patients that do not willingly use the limb. (See Chapter 95 for more information on physical therapy.)
- Obtain radiographs to document the amount and configuration of the remaining bone.
- On the average it will take 2 to 3 months for the limb to reach its satisfactory functional level. In some animals the gait is indistinguishable from normal; in others an obvious gait abnormality is present.
- Because a false joint is formed after surgery, all animals have a limited range of motion. The clinical significance of this limitation depends on the activity of the animal, the animal's size, and the amount of restrictive scar tissue that is present.
- Because normal muscle mass is not regained, there may be marked atrophy of the limb.
- The femur may displace dorsally relative to the pelvis. If the displacement is large, a post-legged gait with the stifle at nearly full extension can result.

Pectineal Myectomy

Preoperative Considerations

- This procedure can be done on dogs of all ages.
- Performance of this procedure does not exclude attempting other procedures, should this be unsuccessful.
- This procedure does not alter the progression or intensity of changes in the joint caused by hip dysplasia, but may palliate joint pain.

Objectives

- Remove all of the belly of the pectineus muscle bilaterally.
- Decrease tension on the medial aspect of the coxofemoral joint capsule.

Equipment

- Standard surgical pack and suture material

Technique

1. Place the patient in a dorsal recumbent frog-leg position.
2. Make an incision 10 to 16 cm long over the pectineus muscle on the medial aspect of the thigh.
3. Isolate and incise the muscle at its origin proximally and its muscle-tendon junction distally. Take care to avoid the femoral artery and vein that pass just lateral to the middle of the muscle belly.
4. Close the dead space by meticulous suture of the fascia and subcutaneous layers.

Postoperative Care and Complications

- Restrict activity for 2 weeks.
- The most common postoperative complication is seroma formation. This requires aspiration or drainage only if the seromas become very large. Usually the fluid is absorbed and no treatment is needed.
- In some dogs, the gait is noticeably improved and there seems to be marked pain relief. The length of time for which this relief persists varies.

Total Hip Replacement

This procedure, which provides an artificial femoral head and artificial acetabular cup, demands a high degree of technical proficiency and strict adherence to good aseptic and surgical techniques. Refer the patient to an experienced specialist.

Preoperative Considerations

- The growth plates must be closed before this procedure can be performed; thus, the animal must be at least 9 months of age. There is no upper age limit,

but older animals should be fully evaluated for systemic disease.
- Depending on the size of the femur and the depth of the acetabular cup, the minimum weight of the animal is 13 to 18 kg.
- Consider total hip replacement when a disabling condition of the hip exists with no other systemic or hindlimb pathology. The dog must be totally free of infection anywhere in the body.

▼ ***Key Point*** Both cemented and cementless hip prostheses are available for use in dogs, but clinical studies have not indicated superiority of one system versus the other.

Objectives

- Replace the degenerative coxofemoral joint with one of the following:
  - Cemented implant: high-density polyethylene cup and a cobalt chrome femoral prosthesis.
  - Cementless implant: metal-backed high-density polyethylene cup and a cobalt chrome stem.
  - Hybrid implant: cemented prosthesis on one side of the joint, cementless prosthesis on the other side of the joint.
- Provide a mechanically sound, pain-free joint that will last the dog's life.

Equipment

- Standard surgical pack and suture material
- Reaming and implantation instruments designed specifically for canine total hip replacements (BioMedtrix, Allendale, NJ)
- High-density polyethylene cup or a metal-backed polyethylene cup that promotes bone in-growth into the metal surface, a cobalt chrome femoral head, and a cobalt chrome femoral stem, or a special chrome stem that promotes bone in-growth into a portion of the stem (BioMedtrix)
- Oscillating bone saw
- Power drill

Technique

1. Approach the coxofemoral joint through a craniolateral approach.
2. Remove the femoral head and a portion of the neck along an osteotomy line that parallels the collar of the prosthesis, and ream the acetabular cup to the medial pelvic wall. Ream and broach the medullary cavity of the femur to accept a trial femoral stem.
3. Cement the prosthetic acetabular cup and the femoral stem into position with polymethylmethacrylate (Howmedica) or impacted into place so that a press fit secures the prosthesis until bone grows into the metal surface.
4. After the femoral head is secured onto the stem, reduce it into the cup.
5. Close the joint capsule tightly; close the remaining tissues in layers.

Postoperative Care and Complications

- Restrict activity to leash walking for 2 months, after which the dog can return to full activity, even if it includes vigorous work.
- Over 95% of dogs treated with this procedure have satisfactory function if established techniques are followed. Increased muscle mass, extended exercise tolerance, and improved hip motion commonly are observed.
- Although degenerative joint disease usually is present in both hips, 80% of dogs receive sufficient relief that the other hip does not need to be replaced. The limb with the hip replacement becomes dominant, thus reducing the unoperated limb's weight-bearing load.
- Complications include infection, implant loosening, luxations, fractures, and neurapraxia. The majority of these can be successfully treated.

SUPPLEMENTAL READING

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Johnson AL, Hulse DA: Coxofemoral joint. In Fossum T (ed): Small Animal Surgery, 2nd ed. St Louis: Mosby, 2002.

Shultz KS, Dejardin LM: Surgical treatment of hip dysplasia. In Slatter D (ed): Textbook of Small Animal Surgery, 3rd ed. Philadelphia: WB Saunders, 2003.

Wallace LJ, Olmstead ML: Disabling conditions of canine coxofemoral joint. In Olmstead M (ed): Small Animal Orthopedics. St Louis: Mosby, 1995.

Chapter

109 Fractures of the Femur

Peter Shires

Surgery of the femur usually is performed to repair fractures. Biopsy of tumors or cysts and obtaining samples for bone cultures are less common reasons for femoral surgery. The femur is the bone most commonly associated with traumatic fractures in the dog. Surgical repair of femoral injuries may be divided into surgery of the proximal, diaphyseal, and distal femur.

PROXIMAL FEMUR

Anatomy

- The proximal femur includes the femoral head, the femoral neck, the trochanters, and their attachments to the femoral shaft.
- The ligament of the head of the femur runs from the fovea capitis of the femoral head to the acetabular fossa.
- The articular surface and epiphysis of the femoral head are separated from the femoral neck by the capital physis.
- The joint capsule of the hip joint inserts at about the midpoint of the femoral neck.
- The primary blood supply to the epiphysis of the femoral head is through vessels running longitudinally in folds of the joint capsule (Fig. 109-1).
- The greater trochanter is the point of attachment for the deep and middle gluteal muscles and the piriformis muscle (see Fig. 109-1).
- The trochanteric fossa is the site of insertion of the internal obturator, external obturator, and the gemelli muscles.
- The articularis coxae inserts on the cranial aspect of the femoral neck.
- The lesser trochanter on the medial aspect of the proximal femur is the site of insertion of the iliopsoas muscle.
- The third trochanter (lateral and distal to the greater trochanter) is the site of insertion of the superficial gluteal muscle and the origin of the quadratus femoris muscle and part of the vastus lateralis muscle.
- The proximal femur is the site of origin of the vastus lateralis, vastus medialis, vastus intermedius, quadratus femoris, and adductor longus muscles and of the proximal part of the adductor magnus and adductor brevis muscles.
- The deep muscles of the femur are covered by the tensor fasciae latae and biceps femoris muscle confluence.
- The sciatic nerve runs caudal to the hip on top of the gemelli, internal obturator, and quadratus femoris muscles. It is covered by the biceps femoris and the superficial gluteal muscles.
- The femoral artery, nerve, and vein are very superficial in the femoral triangle on the medial aspect of the proximal to midfemur.
- The nutrient artery for the femur enters caudally just distal to the greater trochanter as a branch of the medial circumflex femoral artery.

PROXIMAL FEMORAL FRACTURES

Preoperative Considerations

▼ ***Key Point*** Evaluate the entire patient for trauma-related problems; neurologic, urologic, and intrathoracic injuries are common with blunt trauma.

- Stabilize the patient before considering surgery.
- Obtain a minimum of two radiographic views to evaluate the proximal femur.
- Give intraoperative broad-spectrum antibiotics intravenously (at induction of anesthesia; repeat if necessary) if the surgery will take longer than 2 hours.
- Continue treatment with systemic antibiotics if the fracture is open (see Chapter 120).

Surgical Procedure

Objectives (for All Proximal Femoral Injuries)

- Expose the femoral neck.
- Osteotomize the femoral neck.
- Repair fractures of the capital physis and femoral neck.

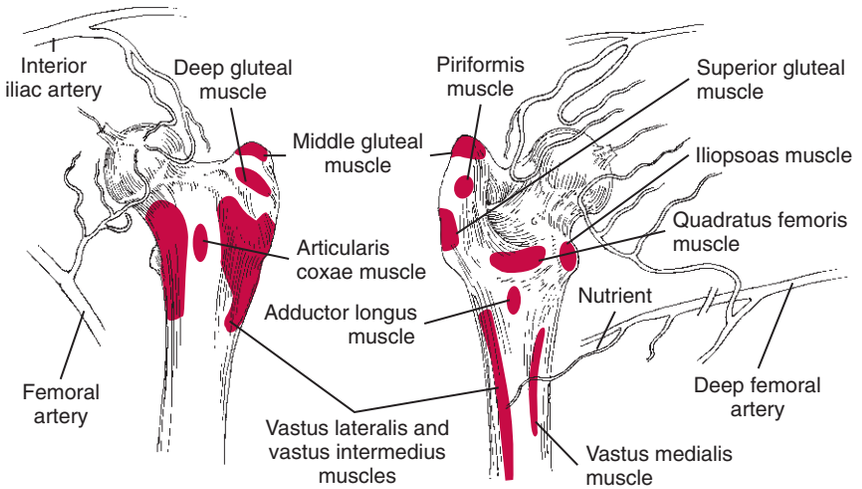

Figure 109-1. *Left,* Cranial view; *right,* caudal view. Proximal femur showing the muscle attachments and main blood supply.

- Expose the greater trochanter for osteotomy and fixation.
- Expose the proximal femur for fracture repair.

Equipment

- Standard general instrument pack and suture material
- Orthopedic instruments, as required (e.g., for fracture fixation, ostectomy, subtrochanteric derotational osteotomy), including:
  - Intramedullary pins
  - Orthopedic and Kirschner wires (K-wires)
  - Osteotomes and mallet or oscillating bone saw
  - Plates and screws
  - Bone reduction forceps
- Self-retaining retractors (e.g., Gelpi, Weitlaner)
- Hohmann retractors (for femoral head ostectomy)

Operative Techniques

Techniques are similar for all objectives listed. Increased exposure is necessary to accomplish more complicated procedures. Techniques are described in order of procedure completion.

Common (Craniolateral) Approach

Technique

1. Prepare the affected leg for aseptic surgery.
2. Make a linear or slightly curved skin incision centered over the cranial aspect of the greater trochanter, starting near the dorsal midline and ending on the cranial aspect of the proximal one-third of the femur.
3. Incise the subcutaneous tissue to expose the tensor fasciae latae muscle. Incise two layers of the fasciae latae along the cranial border of the biceps femoris muscle to expose the underlying vastus lateralis muscle.
4. Extend the fascial incision proximally through the gluteal fascia along the cranial border of the superficial gluteal muscle.
5. Bluntly dissect the loose connective tissue between the vastus lateralis muscle and the gluteal muscles to allow insertion of self-retaining retractors to expose the joint capsule.

▼ ***Key Point*** Several vessels, including the cranial femoral artery and vein and the branches of the femoral nerve, crisscross the connective tissue and will be significantly damaged if dissection is rough.

6. Using a scalpel, incise through the joint capsule from the acetabulum, longitudinally along the femoral neck, to the proximal femur at the insertion of the vastus lateralis muscle.
7. If necessary, partially incise the tendon of insertion of the deep gluteal muscle and the origin of the vastus lateralis muscle to increase exposure of the femoral neck.

Femoral Head and Neck Ostectomy

- See Chapter 108.

Femoral Neck/Capital Physeal Fracture Repair

Technique

1. Rotate the femur outward to expose the fractured surface.
2. Retrograde a K-wire of appropriate size through the femoral neck fracture surface to exit the lateral surface of the proximal femur.
3. If a compression (lag) screw is used, drill a gliding hole through the center of the femoral neck to exit the lateral surface of the proximal femur.
4. If multiple K-wires are used, preplace them all through the femoral neck, using the same technique as described in Step 2 above.

5. Withdraw the wires from the lateral surface until the pinpoints are flush with the fracture surface.
6. Rotate the femur inward to reduce the fracture.
7. Rotate the femoral head until the fracture is anatomically aligned.
8. Advance one K-wire into the femoral head without penetrating the articular surface (Fig. 109-2, *left*).
9. If a compression screw is used, insert a drill sleeve into the gliding hole and drill into the femoral head. The articular cartilage should not be penetrated. Measure and tap the hole and place a screw of suitable length. Compress the fracture without penetrating the articular surface with the screw (Fig. 109-2, *right*).
10. If K-wires are used, drive these individually into the head without penetrating the articular cartilage.

▼ ***Key Point*** Lifting and rotating the proximal femur allows limited examination of the femoral head surface to check for penetration by the implants. Movement of the femur should be unrestricted and smooth and should not produce crepitation.

11. Bend the K-wires over close to the lateral aspect of the trochanter and cut them off as short as possible.

Trochanteric Osteotomy

This technique is used for exposure of the hip joint as part of open reduction of coxofemoral luxation or as an approach to acetabular fractures (see Chapters 107, 108).

Technique

1. Incise the tendon of the superficial gluteal muscle near the third trochanter.
2. Retract the belly of the superficial gluteal muscle proximally.
3. Incise the proximal origin of the vastus lateralis muscle and elevate the muscle to expose the trochanteric osteotomy (or fracture) site, or the femoral neck fracture site.
4. If necessary for exposure, incise and elevate the adductor muscle origin caudally.
5. If a trochanteric osteotomy is planned, pass a curved Kelly forceps under the deep gluteal insertion.
6. Using the curved Kelly forceps as a guide, direct the osteotome (or pull the Gigli wire through), and osteotomize the trochanter off the proximal femur, leaving the medial and deep gluteal muscles attached to the osteotomized bone.

▼ ***Key Point*** Identify and protect the sciatic nerve, which is caudal to the femur and can be traumatized by excessive manipulation.

Trochanter Fracture Osteotomy Repair

Technique

1. Drill a hole transversely through the femur at least 1 cm distal to the osteotomy (fracture) site.
2. Thread a strand of 18-gauge orthopedic wire through the hole.
3. Clamp the proximal fragment in its anatomic position with a small-fragment bone reduction forceps.
4. Drive two appropriate-size K-wires from the proximal end of the trochanter, across the osteotomy (fracture) line, and into the femur until they are seated in compact bone.
5. Pass one free end of the orthopedic wire proximal to the pins and under the gluteal tendons (Fig. 109-3).

▼ ***Key Point*** Form a figure-eight configuration (tension band wire) around the pin ends and through the hole.

6. Twist the free ends of wire together and twist a loop of wire on the other crossover strand.
7. Tighten both twists evenly until the osteotomy (fracture) is securely closed.
8. Bend the pin ends over laterally and cut off the excess.
9. Cut the twisted wire, leaving two twists in place.

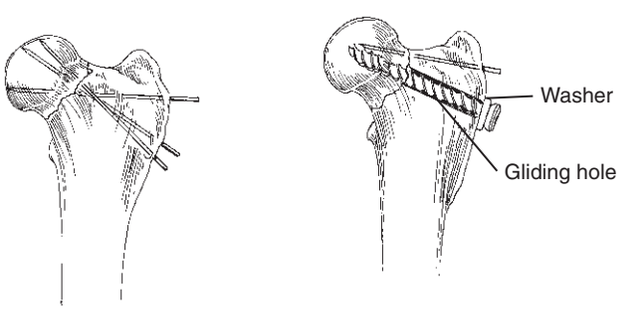

Figure 109-2. Fixation of femoral neck fractures. *Left,* Multiple Kirschner wires; *right,* compression screw and Kirschner wire.

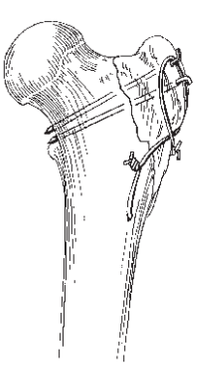

Figure 109-3. Tension band fixation of trochanter fracture or osteotomy.

Proximal Femoral Shaft Fracture Repair

Technique

1. Extend the subperiosteal/sub–vastus lateralis dissection distally and elevate the adductor caudally until the fracture is adequately exposed.

▼ ***Key Point*** Both muscles (vastus lateralis and adductor) can be entirely released if necessary, but they must be reattached.

2. Repair the fracture(s) with appropriate orthopedic techniques and implants.
3. Use cerclage wires, hemicerclage wires, pins, K-wires, skewers, and lag screws to rebuild the fragments into a two-piece fracture.
4. Stabilize the fracture with a plate and screws or an interlocking nail.

▼ ***Key Point*** The femoral neck and trochanters provide excellent anchors for screw fixation.

5. Place an autogenous cancellous bone graft harvested from another site (e.g., proximal tibia or wing of ilium) around the fracture to aid in healing.
6. Reattach the vastus lateralis and adductor muscles to their origins with absorbable sutures.
   a. If necessary, elevate the periosteum to obtain enough tissue for suturing.
   b. Alternatively, use surrounding musculature or drill holes in the femur to anchor the proximal ends of these muscles.

Closure

1. Close the incised tendon of the superficial gluteal muscle with several mattress sutures using absorbable suture material.
2. Close the fascia of the gluteal muscles to the cranial edge of the superficial gluteal muscle with a simple continuous absorbable suture.
3. Close the fascia of the tensor fasciae latae muscle to the cranial edge of the biceps femoris muscle with a simple continuous absorbable suture.
4. Close the subcutaneous tissue with a simple continuous absorbable suture.
5. Close the skin with simple interrupted, monofilament, non-absorbable sutures.

Postoperative Care

Femoral Neck/Capital Physeal Fracture Repair

- Take two radiographic views of the repair.
- Restrict activity (cage rest) for 3 days, and then allow leash walking only for 2 to 3 weeks.
- Perform non–weight-bearing physical therapy (swimming, passive flexion-extension exercises).
- Repeat radiographs of the fracture at 4 weeks to evaluate healing.
- If healed, start a gradual return to full function.
- Remove pins (K-wires) if palpable, any time after 6 weeks if the bone has healed radiographically.
- Remove screws and plate only if causing a problem and only after 6 months.

Trochanteric Osteotomy/Fracture

- Recommendations are the same as for femoral neck/physeal fracture repair, except:
  - Restrict activity (cage rest) for at least 24 hours.
  - Repeat radiographs at 6 weeks to evaluate healing.

Proximal Femur Fracture

- General recommendations are the same as for femoral neck/physeal fracture repair, except:
  - Remove implants, if indicated, after 3 to 6 months.
  - The proximal femur is subject to considerable and variable stresses that jeopardize all fixations. If any doubt exists as to the stability of a fracture fixation, a conservative postoperative approach is recommended.
  - Apply an Ehmer sling (see Chapter 108) to prevent weight bearing during the initial 1 to 2 weeks of healing.
  - Start physical therapy (non–weight-bearing) and gradually increase controlled activity from week 2 to week 4.
  - After week 4 obtain repeat radiographs before starting significant activity levels.

Postoperative Complications

- Femoral neck/physeal fracture healing includes a period during which increased vascularity causes bone demineralization of the femoral neck. This "apple coring" effect is transient and of no significance unless the fracture is unstable or infected. Monitor with serial radiographs if necessary.
- Implant failure and improper selection or application of orthopedic techniques can lead to failure of healing.

FEMUR DIAPHYSIS

Anatomy

- The shaft of the femur has muscle attachments on its caudal and medial aspects. Proximally and laterally, the adductor muscles are attached to most of the length of the femur. The origin of the vastus medialis muscle is found medial and proximal, whereas the insertion of the pectineus muscle is medial and distal. The insertion of the semimembranosus muscle is distal and medial.
- The femoral shaft is encased in a sheath of muscles including the vastus medialis, lateralis, and inter-

medius; rectus femoris; semimembranosus; semitendinosus; and pectineus muscles.
- On the lateral aspect, this muscle mass is surrounded by a fascial compartment made up of the tensor fasciae latae and biceps femoris muscle sheaths. Medially the sartorius muscle continues this fascial sheath.
- The femoral artery and nerve pass medially down the length of the shaft within this compartment.
- The sciatic nerve is lateral to the semimembranosus muscle and caudal to the vastus lateralis muscle.

FEMORAL SHAFT FRACTURES

Preoperative Considerations

- See under "Proximal Femur."

Surgical Procedure

Objectives

- Expose the femoral shaft.
- Repair fractures of the femoral shaft.

Equipment

- Standard general instrument pack and suture material
- Orthopedic instruments as required for pinning, wiring, interlocking nail, and plating
- Self-retaining retractors (e.g., Gelpi, Weitlaner) or an assistant with hand-held retractors (e.g., Army-Navy)
- Several bone-holding forceps (e.g., Self-Retaining Speed Lock, Synthes; Lane, Kirschner)

Technique

1. Prepare the patient's leg for aseptic surgery.
2. Incise the skin from the trochanter to the patella on the cranial lateral aspect of the femoral shaft.
3. Expose the tensor fasciae latae muscle where it joins the biceps femoris muscle aponeurosis.
4. Incise both fascial layers, from the trochanter to the patella.
5. Retract the biceps femoris muscle caudally and the vastus lateralis muscle cranially.
6. Incise the intermuscular septum between the vastus lateralis and the biceps femoris muscles to expose the femoral shaft.
7. Bluntly separate the vastus intermedius muscle from the cranial aspect of the femur (Fig. 109-4).
8. Elevate (only as much as necessary) the adductor muscles subperiosteally on the caudal aspect of the femur; minimal elevation helps to preserve the blood supply to the bone.
9. Isolate the bone fragments and clean the fracture surfaces carefully.

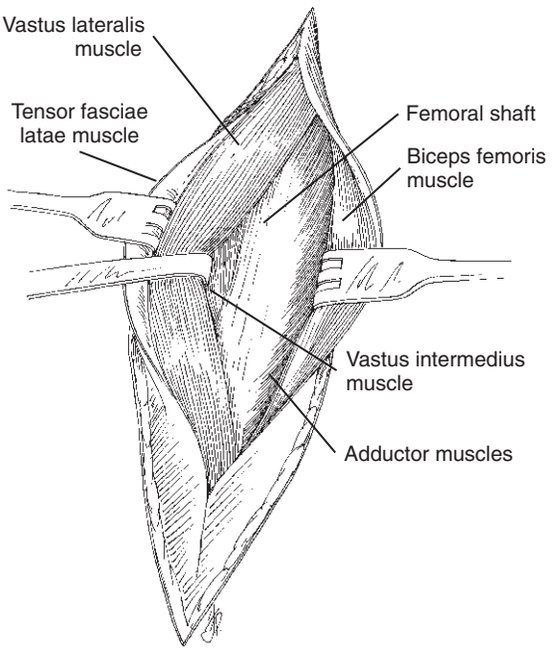

Figure 109-4. Lateral approach to the midshaft of the femur.

▼ ***Key Point*** Remove fragments that are without muscle attachments and wrap them in blood-soaked sponges; maintain all soft tissue attachments to the remaining fragments.

10. Rebuild the proximal and distal fragments with the appropriate orthopedic devices until a two-piece fracture remains. A combination of cerclage, hemicerclage, and K-wires and interfragmentary screws, skewer pins, and figure-eight wire can be used to achieve a stable, two-piece fracture.
11. Use avascular bone fragments only if they are necessary to obtain stability in the fracture. These fragments must be securely fixed in order to be incorporated into the healing callus.
12. Reduce and align the two major fragments and apply the appropriate orthopedic fixation device to maintain these in alignment under stable conditions.
13. In general, a two- or three-piece fracture with long oblique fracture lines can be rebuilt with cerclage wire and supported with one or more normograde (driven proximal to distal) intramedullary pins (Fig. 109-5, *left*). Intramedullary pins also can be driven retrograde from the fracture site to the proximal femur.

▼ ***Key Point*** Extend and adduct the hip joint while driving the intramedullary pin through the proximal femur to avoid trauma to the sciatic nerve.

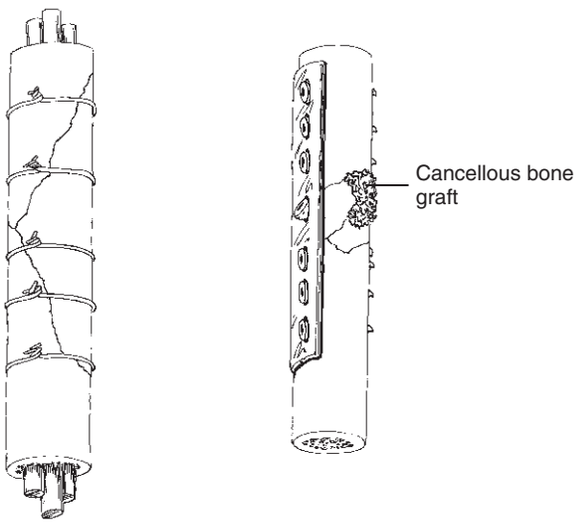

Figure 109-5. Diaphyseal femoral fracture fixation. *Left,* Simple long oblique fracture repaired with cerclage wires and intramedullary pins; *right,* comminuted transverse fracture repaired with a plate, screws, and cancellous bone graft.

a. Reduce the fracture and drive the pin into the distal fragment.
b. Highly comminuted fractures are relatively unstable after being rebuilt and require added fixation devices to maintain alignment and stability. In these less stable situations, plating techniques or a combination of intramedullary and external skeletal fixation may be necessary to achieve stability (Fig. 109-5, *right*).

▼ ***Key Point*** All implants should lie directly against the bone; hence limited local muscle elevation is necessary to attach wires and plates.

14. Where accurate reconstruction and stabilization of the bone fragments is considered inappropriate because of small size and a high degree of comminution, one of several minimally invasive techniques should be considered. Closed or limited exposure of the bone through keyhole incisions can be used to apply interlocking nails, plates, and pin-plate combinations.
15. Harvest autogenous cancellous bone graft from another site and pack around the fracture before closure. This is especially prudent if defects are present after reconstruction.
16. Flush the area copiously with warm normal saline solution *before* placing the cancellous bone graft in defects.

Closure

1. Close the fascia of the tensor fasciae latae to the biceps femoris with absorbable sutures in a simple interrupted pattern.
2. Close the subcutaneous tissue and skin routinely.

Postoperative Care

- General measures are the same as for femoral neck/physeal fracture except
  - Use a non–weight-bearing sling if the fixation is unstable in any respect.
  - Start leash walking at 3 to 5 days if the fixation is stable. Increase exercise slowly over a 4-week period.
  - Repeat radiographs at 6 weeks to evaluate fracture healing.
  - Remove implants, if indicated (e.g., intramedullary pins usually are removed), when there is radiographic evidence of healing; with intramedullary pins this is generally 6 to 8 weeks postoperatively.

Postoperative Complications

- Orthopedic implant failure, improper implant selection, and improper use of implants are the most common causes of fracture collapse, malunion, and nonunion (see Chapter 122). Osteomyelitis may result from contamination.
- Large devitalized bone fragments that are not stabilized can lead to chronic draining tracts and osteomyelitis.
- Extensive subperiosteal dissection and rough handling of bone can produce an excessive periosteal reaction and large callus formation.

DISTAL FEMUR

Anatomy

- The distal femur includes the metaphysis, condyles, trochlea, and patella.
- The quadriceps muscle group inserts on the proximal tibia through the patellar tendon, which includes the patella within it.
- The two heads of the gastrocnemius muscle originate on the distal, caudal aspects of the medial and lateral metaphyses, and include the fabellae in their tendons of origin.
- The superficial digital flexor muscle originates just medial to the lateral head of the gastrocnemius muscle next to the fabella.
- The long digital extensor muscle originates in a fossa on the distal lateral condyle.
- The popliteus muscle originates on the caudal lateral condyle.
- The joint capsule on the stifle extends from above the trochlea, around both condyles, and underneath the fabellae bilaterally.
- The aponeuroses of the biceps femoris muscle laterally and the sartorius muscle medially blend with the fibrous joint capsule over the distal femur.
- The femoral artery divides into the popliteus and saphenous arteries, which run laterally and medially, respectively, on the caudal aspect of the distal femur.

- Several small branches of these two arteries supply the femur, the patella, and the vastus lateralis muscle.
- The muscular branch of the caudal femoral artery bridges the fascial separation between the biceps femoris muscle and the vastus lateralis muscle just above the lateral fabella.
- The peroneal and saphenous nerves supply the lateral and medial aspects of the distal femur, respectively, and run caudal to the femur.

FRACTURES OF THE DISTAL FEMUR AND PATELLA

Preoperative Considerations

- Obtain a minimum of two radiographic views for evaluation of the distal femur.
- Palpate joint stability with the animal under sedation or anesthesia to investigate the possibility of simultaneous ligamentous injuries in the stifle.
- The age of the patient influences choice of implant for repair of distal femoral fractures. In young animals, bone is softer, and healing is more rapid than in older animals (see Chapter 119).
- The majority of distal femoral fractures are physeal fractures; warn owners of the consequences of physeal closure in younger animals.

Surgical Procedure

Objectives

- Expose the distal femur and repair fractures of the metaphysis and epiphyses of the distal femur.
- Expose the articular surface of both distal femoral condyles for accurate intra-articular fracture reconstruction.
- Expose the patella and repair fractures of the patella.

Equipment

- Standard general instrument pack and suture material
- Orthopedic instruments as required for specific procedures, including pinning, wiring, and screw fixation

Technique

1. Prepare the patient's leg for sterile surgery.
2. Expose the distal femur and patella using a lateral, medial, or cranial approach. For patient positioning convenience, the lateral approach is most frequently used.
3. Extensive reconstruction of the articular surface may require an osteotomy of the tibial crest for added exposure of the distal femur.

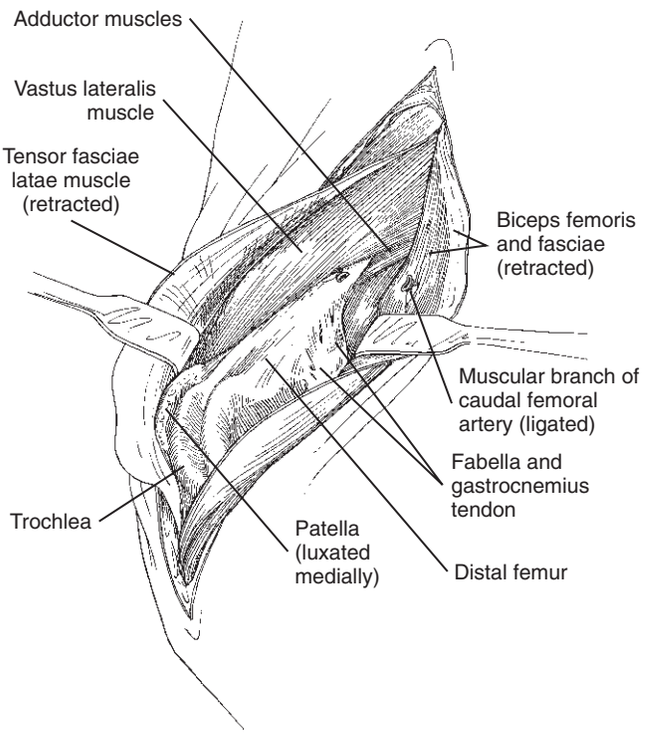

Figure 109-6. Lateral approach to the distal femur.

Lateral Approach

1. Make a slightly curved skin incision from the distal one-third of the femur to the tibial crest just lateral to the patella.
2. Incise the subcutaneous tissue to expose the fascial layer.
3. Incise the fibrous joint capsule and fascia starting at the tibial plateau just lateral to the patella tendon and extending proximally, parallel to the patellar tendon and the patella.
4. Follow the border of the vastus lateralis muscle caudally to the septum between the biceps femoris and the vastus lateralis muscles. Separate these two muscles, double-ligating the muscular branch of the caudal femoral artery that bridges them distally.
5. Bluntly elevate the quadriceps muscles from the distal femur and luxate the patella medially to expose the distal femur (Fig. 109-6).
6. Expose and gently clean the fracture ends.

▼ ***Key Point*** Handle the metaphyseal bone gently, especially in young animals.

7. Apply the appropriate orthopedic implants as indicated by the fracture type. For simple physeal fractures, cross-pinning, multiple pinning, and modified Rush pinning techniques are appropriate.

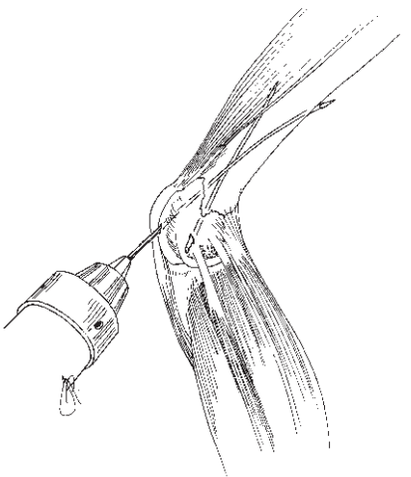

Figure 109-7. Cross-pinning of a distal femoral physeal fracture using a lateral approach.

a. Start the pins from the fracture line and retrograde distally out through the epiphysis, avoiding the articular surface; or start from the caudolateral and caudomedial aspect of the epiphysis and drive (normograde) pins to the fracture line.
b. With retrograde pinning, adjust the pins until the pinpoint is flush with the fracture line, realign the fracture anatomically, and drive the pins proximally up the shaft of the femur in one of the previously mentioned configurations (Fig. 109-7).
c. Cut off the pins flush with the condyles and lavage the joint copiously with saline solution before closure.

Bendable plates can be configured to the bowing and flare of the distal femur and condyles but the plate strength is relatively low so consider double, or bilateral, plate application if this method is chosen.

Medial Approach

1. The technique is basically identical to that for the lateral approach except that it is made on the medial aspect of the distal femur.
2. In addition, one may substitute medial for lateral (vastus medialis muscle for vastus lateralis muscle, and cranial sartorius muscle for biceps femoris muscle) to achieve medial exposure of the distal femur.

Cranial Approach

1. Incise the skin from the lateral distal one-third of the femur to the medial aspect of the proximal tibia.
2. Separate the fascia as described for the medial and the lateral approaches, which are combined to give wider bilateral exposure of both condyles.

Tibial Crest Osteotomy

1. A tibial osteotomy can be combined with any of the previously described approaches to achieve additional exposure for complicated fractures.
2. Isolate the patellar tendon through the original skin incision.
3. Place an osteotome under the patellar tendon, aimed distally, and osteotomize the tibial crest free from the proximal tibia.

▼ ***Key Point*** Be sure to remove enough bone to facilitate fixation when reattaching the tibial crest.

4. Retract the quadriceps muscle proximally to fully expose the joint.
5. Repair intra-articular fractures with good visibility of the critical articular surface.
6. Compression (lag) screw fixation of intra-articular fracture fragments is recommended to allow accurate reconstruction and avoid movement, thus reducing the potential for arthritis.
7. Repair the osteotomy by pinning the tibial crest into position with two large K-wires transversely placed through the osteotomized bone fragment and into the proximal tibia. Place a figure-eight tension band wire around the base of the pins and through a hole in the cranial tibia, distal to the osteotomy site.

Patella Fracture Repair

1. Expose the patella via the lateral approach, as previously described. Identify the patella by rotating the distal quadriceps muscle.
2. Pass two K-wires lengthwise through the patella across the fracture line.
3. Rotate the quadriceps muscle back to its normal position and loop a figure-eight orthopedic wire around the pin ends on the cranial surface of the patella.
4. Twist both long strands of the figure-eight wire to tighten the tension band apparatus and close the fracture line of the patella.
5. Cut the pin ends as short as possible. Cut the twisted wire, leaving two twists.

Closure

1. Close the joint capsule with monofilament absorbable suture in a simple continuous pattern.
2. Close the fascial layer with absorbable sutures in a simple interrupted pattern.
3. Close the subcutaneous tissue and skin routinely.

Postoperative Care

- General recommendations are the same as for femoral neck/physeal fracture except:

- Restrict activity (cage rest) for at least 24 hours.
- If fixation is judged to be stable, start leash walking 1 to 2 days postoperatively.
- If fixation is unstable, support the leg in a flexion sling.

Postoperative Complications

- Quadriceps tie-down (contracture) occurs when adhesions form between the healing fracture callus and the overlying quadriceps muscle and the patella tendon. This is most likely to happen if the leg is fixed in an extended position (e.g., with a Thomas splint). Tie-down can be prevented by early mobilization and/or a flexion sling for support.

▼ ***Key Point*** To help avoid quadriceps tie-down, do not apply splints that place the stifle in extension.

- If intra-articular fractures are not reduced anatomically, degenerative joint disease and postoperative joint pain can result. Accurate reduction and stable fixation is essential.
- If the animal is very young at the time of the physeal fracture, femoral shortening is to be expected if premature physeal closure occurs. If shortening is less than 20% compared with the normal leg, clinical signs are unlikely.

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Chapter

110 Orthopedic Disorders of the Stifle

R. Tass Dueland / Matthew Palmisano

Common traumatic and congenital or developmental conditions of the stifle include patella luxation, cruciate disruptions, meniscal problems, collateral ligament injuries, and stifle luxation. The first three listed (excluding fractures) comprise 95% of stifle disorders in dogs and cats.

ANATOMY

Cranial Stifle

- The quadricep muscles, patella, trochlear groove and notch, patellar tendon, and tibial tuberosity are linearly aligned with the coxofemoral joint, talocrural joint, and paw. Normally there is no medial or lateral deviation of these structures.
- Craniomedial and caudolateral ligamentous bundles constitute the cranial cruciate ligament, which originates on the caudomedial aspect of the lateral femoral condyle and inserts centrally on the tibial plateau caudal to the cranial intermeniscal ligament (Fig. 110-1).
- The caudal cruciate ligament originates on the craniolateral aspect of the medial femoral condyle and inserts on the caudocentral tibial plateau and medial popliteal notch.
- The fat pad lies caudal to the patella tendon.
- The long digital extensor tendon originates on the lateral femoral condyle cranial to the lateral collateral ligament and popliteus muscle.
- Retinacular fibrous tissue overlies the craniolateral and craniomedial aspects of the stifle joint.
- The trochlear notch is the more distal non–weight-bearing portion of the trochlear groove.

Caudal Stifle

- Medial and lateral fabellae articulate intracapsularly with the femoral condyles and have strong fabellofemoral ligaments (Fig. 110-2).
- The medial meniscus is attached to the tibia and to the medial collateral ligament, whereas there are tibial and femoral attachments of the lateral meniscus.
- The popliteus muscle courses under the lateral collateral ligament.
- Neurovascular structures run longitudinally and centrally close to the caudal joint capsule.

GENERAL PREOPERATIVE CONSIDERATIONS

- Client communication and cooperation and a successful return to function by the patient are enhanced by meticulous evaluation of the stifle joint preoperatively and intraoperatively. This facilitates an accurate diagnosis and selection of the appropriate procedure(s).
- Radiography is useful for the following:
  - To confirm the diagnosis
  - For comparison with the opposite joint
  - For medical and legal documentation
- Perform a thorough orthopedic examination, including the joints, bones, and muscles of the affected extremity.

Orthopedic Evaluation

Include the following maneuvers in palpation of the stifle:

- Palpation of the patellar tendon and parapatellar tissue should reveal a distinct “sharp” feel to the tendon edges. If they feel indistinct or “doughy,” this indicates stifle effusion, which is often associated with cranial cruciate rupture or degenerative joint disease secondary to rupture.
- Perform gentle, full range of stifle motion in normal flexion and extension, then repeat with internal and external rotation.
- Often, clicks caused by meniscal pathology and crepitation from osteoarthritis can be detected.
- With the femur held motionless with one hand and the proximal tibia held securely by the other hand, attempt cranial movement of the tibia after placing the stifle in slight to moderate flexion (drawer sign or Lachman test).
- With a finger held over the tibial tuberosity and the femur held securely, flex the hock to detect cranial movement of the tibia (tibial compression test). This

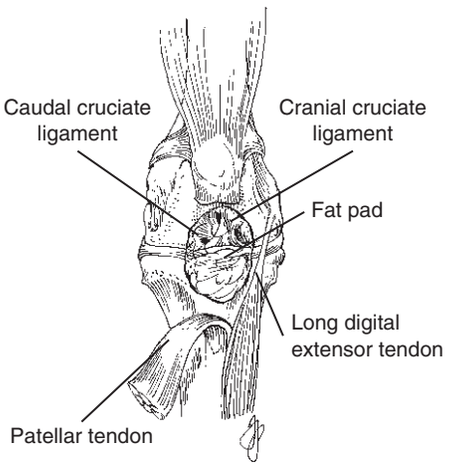

Figure 110-1. Anatomy of the cranial stifle.

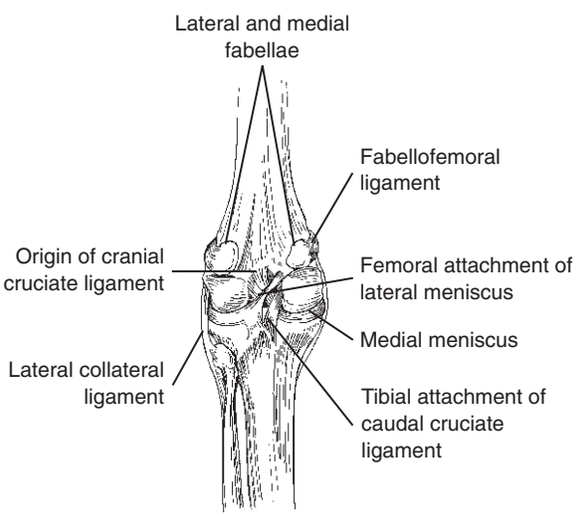

Figure 110-2. Anatomy of the caudal stifle.

test (and the Lachman test) indicates laxity of the cranial cruciate ligament.

- With the femur held motionless, determine internal and external movement of the tibia on the femur by grasping the hock and rotating the tibia. Normal range of motion is 20 to 30 degrees of internal rotation and 5 to 10 degrees of external rotation with the stifle in flexion.
- Exert medial and lateral digital pressure on the patella while putting the stifle through its range of motion to detect any patellar luxation.
- Exert pressure with the thumbs on the lateral side of the femoral condyle and proximal tibia, and then repeat on the medial side. Laxity of the collateral ligaments is detected by increased laxity of the joint space.
- Exert deep pressure of the stifle area with a fingertip to ascertain focal points of pain from soft tissue tears and bone bruises.

▼ ***Key Point*** Perform the tests sequentially while the animal is conscious, and repeat when the animal is sedated or anesthetized. Plan appropriate surgical procedures based on this diagnostic information.

PRINCIPLES OF STIFLE SURGERY

- For the majority of the surgical procedures, place the dog in dorsal recumbency with the forelegs and unaffected rear limb secured. This gives good access to both sides of the stifle in a comfortable operating position. Place the instrument table over the dog's trunk.
- Perform an arthrotomy of sufficient length to facilitate luxation of the patella. Using flexion and retraction, identify, inspect, and assess the articular surfaces of the patella, trochlear groove, tibial plateau, pericondylar, and supracondylar areas of the femur, patellar tendon, fat pad, and long digital extensor tendon.
  - When operating alone, place the sterile, covered paw on your (gowned) abdomen.
  - By moving your body forward and backward you can adjust the amount of flexion of the stifle.
- Place a small, sharp rake retractor (Senn) deeply behind the fat pad; retract cranially and inspect both cruciates.
- Place a second retractor on either side of the first to examine the menisci.
  - To see the caudal horns well, place the tip of a narrow Hohmann retractor (Synthes 399.18) or curved hemostat just behind the tibial plateau. Positioning the instrument against the trochlear notch acts as a lever to move the tibia forward and increase exposure.

PATELLAR LUXATION

Medial and parapatellar luxations affect miniature breeds most commonly and large and giant breeds less often. Medial patellar luxations are most common in both small- and large-breed dogs. However, when lateral patellar luxations occur, they most commonly occur in large and giant breeds. Patellar luxations generally are congenital or developmental. Contributing factors include structural abnormalities such as coxa vara and coxa valga (decrease and increase, respectively, in the angle formed by the head and neck of the femur and the axis of its shaft), bowing or torsion of the distal portion of the femur, shallow trochlear groove, increased internal or external tibial rotation, and malpositioned tibial tuberosity.

Patellar luxations are classified as follows:

- Grade I—The patella lies in the trochlear groove but can be manually subluxated or luxated.

- Grade II—Spontaneous luxation occurs clinically. The patella can be luxated manually but reduces spontaneously or with gentle manipulation.
- Grade III—The patella is luxated most of the time but can be reduced manually.
- Grade IV—The patellar luxation cannot be reduced manually. Often, flexure contracture has occurred and limb use is minimal.

Diagnosis

- History usually reveals intermittent rear-leg lameness. The lameness classically is characterized by rapidly alternating use and disuse of the limb, particularly during exercise.
- Definitive diagnosis is based on physical examination. Palpate the patella while placing the stifle through its full range of motion. In a grade I or II patellar luxation, the patella can often be luxated when the stifle is in extension.

Preoperative Considerations

- Evaluate the maximum internal and external rotation of the tibia on the femur. An increase in internal rotation of >30 degrees (often occurring in miniature breeds) indicates lateral retinacular laxity and the need for lateral imbrication.
- Patellar luxation procedures vary; some animals require only one step, whereas others need combined procedures.
- In some cases, combined parapatellar arthrotomy and release is necessary (to release means to diminish the pull or tension on tissue, often accomplished by incising perpendicularly to the line of tension).
- In other cases, combined arthrotomy and imbrication is needed (to imbricate means to tighten, either by suturing alone or by excision and subsequent closure of tissue).

Surgical Procedures

Objective

- Stabilize the patella anatomically in the trochlea while maintaining the full range of pain-free motion.

Equipment

- Standard orthopedic surgical pack and suture material
- Preferably power bur, oscillating saw, and drill *or*
- Double-action rongeur, bone curettes, and fine handsaw (hacksaw or Exacto saw #236), file, or rasp
- Sharp osteotomes and mallet

Surgical Principles

- Reduce the patellar luxation and determine whether the tissues are tight on the side toward which the patella luxates and whether the tissues opposite the luxated side are very lax.
- If the former is present, perform combined parapatella arthrotomy and release to diminish the pull of the tissues.
- If the latter is present, combined arthrotomy and imbrication is indicated to tighten the lax side.
- With an adequately deep trochlear groove and no excessive tibial rotation, a release may be the only step needed to maintain the patella in its anatomic position.
- With a shallow trochlea, deepening can be accomplished by trochleoplasty, chondroplasty, or wedge resection. Techniques in which the articular cartilage is preserved (e.g., wedge resection) are preferred over those in which articular cartilage is not preserved.
- Correct excessive medial rotation of the tibia with a lateral antirotational nylon suture (fabella to tibial tuberosity drill hole; see Fig. 110-4) or by translocation of the tibial tuberosity laterally.

Techniques

Trochleoplasty

1. Following arthrotomy and inspection of the stifle, mark the medial and lateral boundaries of the planned trochlear groove by longitudinal cuts in the trochlear cartilage using a scalpel blade. To prevent fracture, try to obtain as much width and height as possible without weakening the remaining condylar bone.
2. Remove the articular cartilage within the marked lines by power burring or with a rongeur.
3. Reduce the luxated patella for a trial fit and, if necessary, smooth the new surface with a fine, half-round file, or rasp. The depth of the new trochlea should accommodate the patella so that one-half to two-thirds of the patella's height is in the groove.
4. Verify depth, smoothness, and stability by palpating the patella while putting the joint through its range of motion (flexion and extension with internal and external rotation of the tibia).
5. Close the synovia and joint capsule with appropriately sized monofilament nylon sutures in an interrupted cruciate pattern. If possible, perform partial-thickness closure whereby the suture is not within the joint. Close skin and subcutis routinely.

Postoperative Care

- Begin physical therapy, consisting of ice packs and gentle, passive flexion and extension to half the normal range of motion on the day of surgery. Twenty repetitions 4 to 6 times daily are recommended. Swimming after suture removal is permitted.
- Restricted activity (leash walking only, no stairs, no ball playing, etc.) for 1 month.

- Give analgesics as needed (Bufferin, 10 mg/kg PO bid; Carprofen, Rimadyl, 2.2 mg/kg PO bid; Deracoxib, Deramaxx, 2–4 mg/kg PO sid, with food). (See Chapter 6.)

Chondroplasty

1. Make a trochlear outline, as described for trochleoplasty, down to subchondral bone (Fig. 110-3).
2. Using a thin, sharp, curved osteotome (Zimmer #2881-00-01, #2881-00-02) perform an osteotomy and create a rectangular cartilage flap with the hinge either proximally or distally. Include 1 to 2 mm of bone in the thickness of the flap.
3. Remove underlying bone with power burring, a bone curette, or a rongeur.
4. After adequate depth is obtained, press the flap manually into the new groove. Pressure from the patella helps keep the flap in position.
5. Close the skin and subcutis routinely.

▼ ***Key Point*** This technique is best used in dogs less than 6 months of age in which the mineralized tissue is relatively soft and pliable for creating a flap.

Postoperative Care

- Perform physical therapy and administer analgesics, as described previously for trochleoplasty.

Wedge Resection

1. Make a trochlear outline as described for trochleoplasty.
2. With a power saw or fine handsaw, make two pie-shaped cuts at the peripheral borders previously outlined. Medial and lateral condylar osteotomies should meet centrally. Remove this central piece of bone and articular cartilage and place it in a blood-soaked sponge.
3. The shallowness of the trochlea determines the width of the next two saw cuts, which are parallel and peripheral to the first cuts. Remove these two pieces of bone. Place the trochlear segment with its intact cartilage into the recess; this results in a deeper trochlea with preservation of most of the articular surface.
4. Pressure of the articulating patella ensures good contact of the osteotomized segment.
5. Close the skin and subcutis routinely.

Postoperative Care

- Perform physical therapy and administer analgesics, as described for trochleoplasty.

▼ ***Key Point*** Use caution with this technique in immature animals with open physes. Premature closure may occur; therefore, it is better suited for animals older than 8 months.

Imbrication

After the depth of the trochlear groove is reestablished, reevaluate the status of tibial rotation. If there is medial or lateral rotary instability, perform imbrication of the lax side using one of several techniques.

1. DeAngelis technique (fabella to patellar tendon; Fig. 110-4, *left*): Using non-absorbable monofilament suture, place mattress pattern sutures around the medial and lateral fabellae and running extracapsularly, engaging the distal patellar tendon.
2. Flo technique (see Fig. 110-4, *right*): Place the proximal aspect of the sutures similarly, but distally engage the proximal tibia through a transverse drill hole in the tibial tuberosity.
3. Place additional sutures, if needed, in a fan-like pattern, originating at the fabella and engaging the parapatellar tissue.

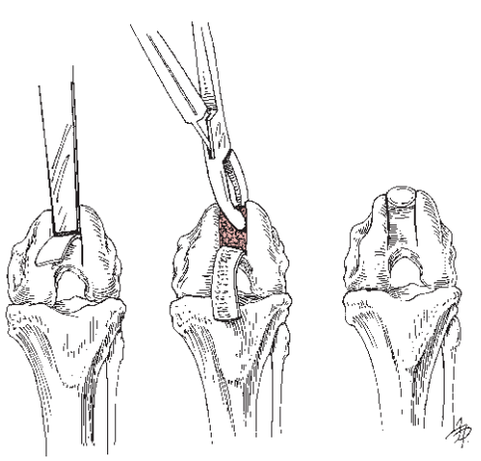

Figure 110-3. Chondroplasty procedure. See text for details.

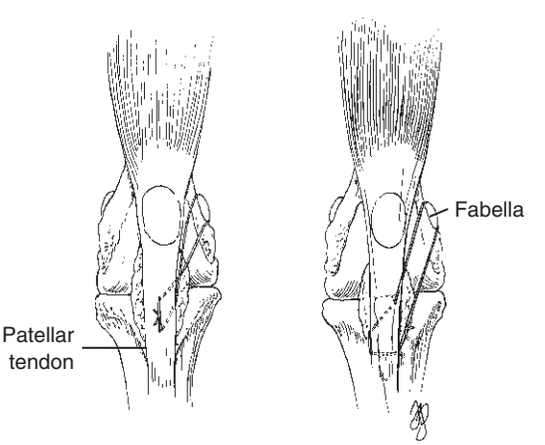

Figure 110-4. Imbrication techniques of DeAngelis *(left)* and Flo *(right)*. These techniques are used for cruciate stabilization and for antirotation purposes with patella luxations.

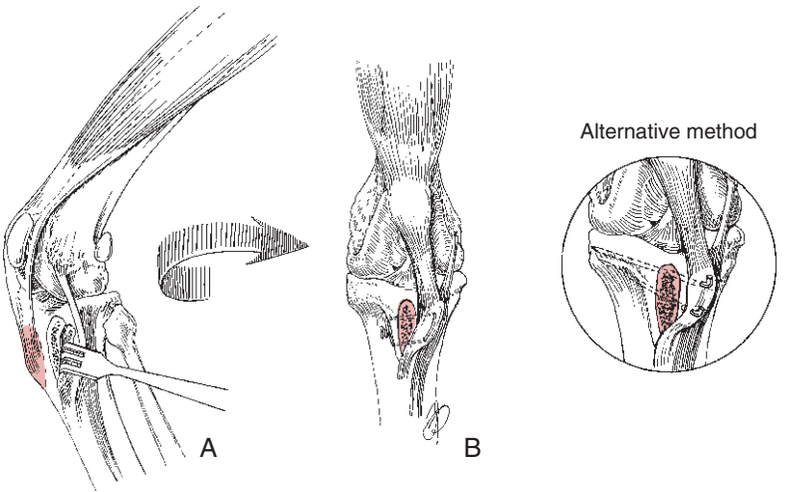

Figure 110-5. Tibial tuberosity transposition: *A,* Area of partial osteotomy of tibial tuberosity is shown in color; the cranial tibial muscle is reflected. *B,* The newly positioned segment is wired in place. Alternate fixation method: (inset) Kirschner wires holding osteotomized tibial tuberosity in transposed position.

4. Alternatively, scarify the retinacular tissue with the scalpel blade and use a Lembert suture pattern to place several bilateral parapatellar sutures.
5. If there is redundant tissue on one side of the patella after reduction, make two elliptical incisions through retinaculum, capsule, and synovia. Remove the redundant tissue and imbricate using routine closure or a vest-over-pants suture pattern.

▼ ***Key Point*** As a rule, when suturing is the main component of imbrication, physical therapy should be gentle to diminish stress upon the suture material and allow adequate time for tissue healing.

Tibial Tuberosity Translocation

Equipment

- Osteotome and mallet or a dental molar cutter
- Orthopedic Kirschner wires

Technique

1. Perform medial and lateral parapatellar arthrotomies. For lateral translocation, reflect cranial tibial muscle.
2. With an osteotome, mallet, or molar cutter, make an osteotomy of the tibial tuberosity, leaving the soft tissue still attached distally if possible (Fig. 110-5, *center*).
3. Hold the osteotomized tibial tuberosity in position with a bone clamp (Synthes 399.07) after creating a bed in the tibia by roughening the site with a rongeur or curette.
4. Using a power or hand drill, make two small holes through the newly positioned osteotomized segment and through the base of the tibial tuberosity (see Fig. 110-5).
5. Place an appropriately sized (20–22 gauge) orthopedic wire through the holes in a mattress pattern and twist tightly medially to secure the bone in the new site. Cut the wire, leaving two to three twists. The new location of the insertion of the patellar tendon should realign the forces to maintain the patella in position, assuming other disruptive forces have been corrected.
6. If the new position is not closely adjacent to the osteotomy site, insert Kirschner wires (Fig. 110-5*B*), a tension band, or a lag screw obliquely for stable fixation.

▼ ***Key Point*** Exercise great care in young animals not to cause physeal growth arrest by inappropriate placement of Kirschner wires through the proximal tibial growth plate.

7. If the wire ends cause skin irritation, they may be removed after bony union has occurred.

▼ ***Key Point*** Because medial and lateral rotary instability and laxity contributes significantly to malalignment of the tibial tuberosity, correction of the laxity by imbrication (Flo technique) may eliminate the need for transposition of the tuberosity.

CRANIAL CRUCIATE LIGAMENT RUPTURE

Diagnosis

- The history usually reveals an acute onset of rear-limb lameness, particularly during exercise.
- Chronic and persistent lameness may also be seen, especially in older, overweight dogs.
- Firm swelling of the medial aspect of the joint can be palpated when a chronic cruciate ligament (CL) rupture is present.

Diagnostic Manipulations

Two diagnostic manipulations can confirm abnormal cranial movement of the tibia at the stifle.

Cranial Drawer

- Position the thumbs on the caudolateral aspect of the stifle so that the lower thumb engages the head of the fibula while the upper thumb is placed in the region of the lateral fabella or the edge of the lateral femoral condyle.
- Wrap the other fingers of the upper hand around the cranial aspect of the lower thigh, keeping the femur motionless and the patella in the trochlear groove.
- Test the cranial laxity of the stifle joint with the tibia in modest flexion (15–30 degrees) (Lachman test) and in 45 to 90 degrees (or more) of flexion (cranial drawer sign).
- Do not test for cranial drawer with the stifle in full extension. The medial and lateral collateral ligaments will tighten in this position, thereby limiting cranial translation of the tibia.
- With complete rupture of both bands of the cranial CL, cranial laxity is detected at each position.
- With partial rupture, laxity may be detectable at only one of these positions.
- Severity of laxity is subjectively ranked in 2-mm increments (e.g., 1+ = 2 mm, 2+ = 4 mm, 3+ = 6 mm, and 4+ = 8 mm) of cranial displacement (translation) of the tibia on the femur.

Tibial Compression

- Use one hand to hold the femur motionless, with the index finger resting on the tibial tuberosity; gently dorsiflex the hock with the other hand.
- The gastrocnemius muscle will tighten and, when cranial CL laxity is present, the tibia can be felt to move cranially under the index finger.
- In our experience, the cranial drawer test is more consistent than the tibial compression test. However, perform both tests. A diagnostic impression is obtainable in 90% of anesthetized dogs if proper positioning and a calm approach are used.

Preoperative Considerations

- Obtain preoperative stifle radiographs to document joint effusion, extent of degenerative joint disease, normal fabellae, and avulsions of the ligamentous attachments.
- To rule out predisposing or concurrent diseases, consider obtaining a routine laboratory database of complete blood count (CBC), serum chemistry profile, and urinalysis.

Comparison of Surgical Techniques for Cranial Cruciate Ligament Repair

Much debate currently exists regarding the optimal method for cranial CL repair. Subjectively, more surgeons are turning to tibial plateau leveling osteotomy (TPLO) for repair due to the perceived earlier return to function and more complete weight bearing. However, objective studies showing a statistically significant difference between the lateral imbrication techniques and the TPLO are lacking. Some studies have shown an improved return to function with the lateral imbrication and TPLO procedures over intracapsular repairs.

The choice of surgical techniques largely depends on surgeon preference, which is related to success with the various techniques and comfort level.

One study showed 36% of surgeons use the lateral retinacular imbrication technique as the primary method of repair, while 13% routinely performed the fascial strip "over-the-top" technique and 25% performed the TPLO.

Surgical Procedures

- The procedures to correct CL rupture are broadly classified as either intracapsular (stabilization from within the joint) or extracapsular (stabilization outside the joint).
- Intra-articular repairs utilize autogenous or synthetic materials to re-create an intact cranial CL. Examples of intracapsular repairs include patellar tendon techniques, over-the-top repairs, and under-and-over repairs.
- While many intracapsular repairs are still performed today, subjective and more recent objective data suggests that these repairs may be inferior to the extracapsular techniques, such as the lateral imbrication technique and TPLO. This is especially true in large-breed dogs.

Objectives

- Visually assess the extent of joint damage.
- Slow the progression of degenerative joint disease by stabilizing the joint.
- Reduce or eliminate the drawer sign.
- Inspect the meniscus for tears (usually caudal horn of medial meniscus).

Equipment

- Standard orthopedic pack and suture
- Intramedullary pin pack
- Orthopedic wire passer

Techniques

Fascial Strip Over-the-Top Technique

1. The fascial strip over-the-top technique is an intracapsular repair and is most suitable for dogs weighing less than 40 lb.
2. Place the dog in dorsal or lateral recumbency and prepare the stifle for aseptic surgery.
3. Make a cranial skin incision extending from 2 inches above the patella to the tibial crest.
4. Perform a craniolateral arthrotomy with formation of a distally based fascial strip. For adequate bio-

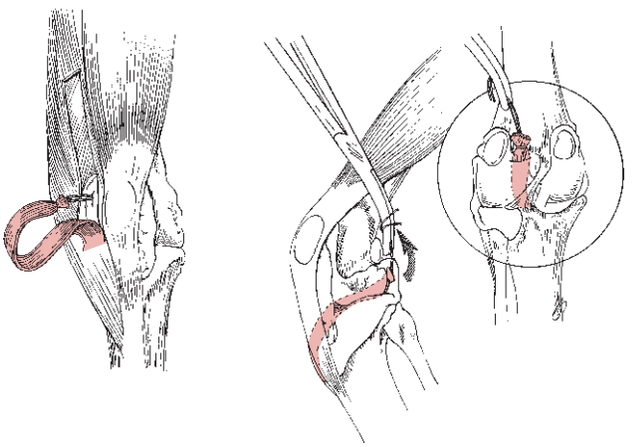

Figure 110-6. Fascial strip over-the-top technique for repair of cranial cruciate rupture. See text for details.

mechanical strength, make the width of the strip 2 to 3 times the width of the patellar tendon. The length needed is twice the distance from the proximal patella to the tibial tuberosity. The base of the strip is at the level of the joint line.

5. Cut the fascial strip proximally and insert it, lateral to medial, through a fat pad tunnel made with a hemostat (Fig. 110-6). Enter the caudolateral joint capsule caudal to the lateral fabella and gently advance the hemostat through the intercondylar notch, keeping the hemostat tip lateral to the caudal CL. Grasp the proximal end of the graft in the joint and pull it through the intercondylar notch lateral to the caudal CL and over the top of the lateral condyle. Make a small incision through the joint capsule, pull the fascial strip through it, and secure it to the capsular reflection onto the lateral femoral condyle with six to eight monofilament nylon sutures (2-0) with the appropriate tension to achieve a minimal drawer sign.
6. Close the arthrotomy incision with interrupted absorbable suture material. Complete closure may not be possible distally, depending on the width of the graft harvested.
7. Routinely close the remaining tissues.

Lateral Retinacular Imbrication Technique

The lateral retinacular imbrication technique is the most common extracapsular technique performed in practice and can be performed in any size patient.

1. Place the dog in lateral recumbency and prepare the stifle for aseptic surgery.
2. Make a lateral parapatellar skin incision.
3. Perform a lateral arthrotomy. The cranial CL and meniscus are evaluated and debrided if torn.
4. Separate the lateral joint capsule from the biceps femoris muscle. Severe the distal insertion, and reflect the biceps femoris fascia caudally as far back as the lateral head of the gastrocnemius muscle.
5. Close the joint capsule using interrupted absorbable suture material.
6. Drill a hole in the tibial tuberosity with an intramedullary pin that is larger than the diameter of the suture material chosen. Drill the hole medial to lateral, just caudal to the tibial insertion of the straight patellar ligament.
7. Pass an orthopedic wire passer (Small Graft Passer, Jorgensen Labs, Loveland, CO) around the lateral fabella. The pointed tip of the wire passer is started between the gastrocnemius muscle and the lateral femoral condyle just distal to the lateral fabella. It is pushed around the fabella and allowed to penetrate through the musculature just proximal to the fabella.
8. Placed appropriately sized nylon leader line (NLL) through the slot in the wire passer, and pull the passer around the fabella, taking the suture material with it. One to two strands of either 80 or 125-lb test NLL are most suitable for elimination of cranial drawer.

▼ ***Key Point*** Use one strand of 80-lb test NLL in dogs <50 lb, two strands of 80-lb test NLL in dogs 50 to 100 lb, and two strands of 125-lb NLL in dogs over 100 lb.

9. Pass the NLL through the bone tunnel created in the tibial tuberosity, from lateral to medial. Then place the NLL behind the straight patellar ligament, just cranial to the intrapatellar fat pad (see Fig. 110-4, *right*).
10. Place the knee in an approximate standing position (about 30 degrees of flexion). Tighten the NLL until cranial drawer is eliminated.
11. The NLL can be tightened by hand then secured using at least two square knots. Alternatively, in order to eliminate the bulky knots, the NLL can be tightened and fixated using the Securos crimp-clamp system (Securos, Charlton, MA).
12. Anchor the biceps femoris fascia back to the patellar ligament using absorbable suture material in either a Lembert or a vest-over-pants suture pattern.
13. Close subcutaneous tissues and skin in routine fashion.

Tibial Plateau Leveling Osteotomy

TPLO is an increasingly popular method of stabilization of the cranial CL–deficient stifle. Both the intracapsular and the extracapsular techniques work at eliminating the cranial drawer sign, which is a passive movement that does not take into account the forces of weight bearing.

TPLO is designed to eliminate tibial thrust. Tibial thrust (see above) is a motion where the tibia translates

forward during active weight bearing in the cranial CL–deficient stifle. Cranial tibial thrust occurs after cranial CL rupture because of contraction of the stifle and tarsal extensor muscles.

By leveling the tibial plateau to nearly perpendicular to the long axis of the tibia, the active forces of the stifle flexors are enhanced so that cranial tibial thrust experienced during weight bearing is eliminated.

One study showed that the cranial tibial thrust is actually converted to a caudal thrust, which requires an intact caudal CL.

The TPLO is applicable to any size or type of patient. In our opinion, TPLO is best suited for large- or giant-breed dogs; hunting, agile, or otherwise very active dogs; and dogs with partial cranial cruciate ligament tears. Subjectively, dogs appear to put weight on the limb earlier and have more complete weight bearing while having a better range of motion than the other surgical techniques at the final recheck examination. However, objective clinical data is lacking.

Disadvantages of TPLO include equipment costs, the large learning curve due to the technical demand of the procedure, and the training involved in certification. TPLO requires specialized equipment and expertise, and its use is largely confined to surgical specialists.

Postoperative Care

Short Term

- Administer analgesics as needed (see Chapter 6).
- Apply a padded bandage for the first 24 to 48 hours if desired to reduce tissue swelling.
- Remove skin sutures and reevaluate the leg 10 to 14 days postoperatively.

Long Term

Fascial Strip Technique

- Protect the leg with a lateral splint, that is, a padded bandage combined with a strip of fiberglass cast material that is molded to the shape of the lateral aspect of the leg and then incorporated into the bandage. Replace this bandage as needed, but use it for the first month postoperatively to prevent stifle motion.
- Restrict exercise to leash walking only for the first 3 months.
- Gradually increase the activity level over the next 3 months, and allow return to normal function after 6 to 9 months.
- Perform physical therapy as needed (see Chapter 95).

Lateral Retinacular Imbrication Technique

- Limit exercise for 6 weeks postoperatively. Do not allow any high-impact activity during this time (e.g., running, jumping, or playing).
- Gradually return the animal to normal activity over the next 2 to 4 weeks.
- Perform physical therapy as needed (see Chapter 95).

Tibial Plateau Leveling Osteotomy

- Limit exercise for 8 weeks postoperatively. Do not allow any high-impact activity during this time (e.g., running, jumping, or playing).
- Obtain radiographs of the leg 8 weeks postoperatively to assess for bone healing. If healing is not complete, re-radiograph at 4-week intervals until the osteotomy is healed. Continue to limit exercise until bone healing is complete, then gradually increase exercise over the next several weeks.
- Perform physical therapy as needed (see Chapter 95).

CAUDAL (POSTERIOR) CRUCIATE LIGAMENT RUPTURE

The importance of the caudal CL is controversial in both dogs and humans. A study in humans (Clancy et al., 1983) indicated severe pathology results with time. In dogs, isolated rupture of the caudal CL without bony avulsion is, in our experience, extremely rare.

Diagnosis

Diagnosis is based on the following:

- History of acute lameness and caudal drawer sign tested at 90 degrees of stifle flexion
- Caudal sag of the proximal tibia, compared with the normal opposite side, viewed on a lateral radiographic projection
- Avulsion of the bony attachment

Surgical Procedure

Objectives

- Similar to those for cranial CL except rupture repair

Equipment

- Similar to that for the patellar tendon procedure for cranial CL rupture

Technique

1. Make a cranial skin incision extending from 4 cm above the patella to 4 cm below the tibial tuberosity.
2. Perform a medial arthrotomy and debridement of the caudal CL.
3. Drill two tunnels. Extend one tunnel from the origin of the caudal CL at the non-articulating portion of the trochlear groove, exiting on the medial side of the medial femoral condyle. Extend the second tunnel from a point approximately 2 cm below the tibial plateau just medial of the midline, directed

caudally to exit just below the centromedial portion of the tibial plateau.

4. Harvest a patellar tendon graft as in the cranial CL patellar tendon procedure; in addition, obtain a piece of tibial tuberosity bone (4 mm wide × 6 mm long × 2 mm thick), including its patellar tendon insertion (i.e., making a free graft). Drill holes in each of the patellar and tuberosity pieces of bone and pass long nylon suture strands through the holes.
5. Using a suture passer, introduce the sutures that are attached to the patellar segment into the tibial tunnel in a cranial to caudal direction and pull the patellar portion of the graft through, leaving the tibial graft segment in the tibial tunnel. Similarly, draw the patellar piece into the femoral tunnel.
6. Insert partially threaded 4-mm Synthes screws, with the far cortex engaged, near the cranial tibial tunnel and at the exit of the femoral tunnel. Use these to anchor the tuberosity and patellar sutures after adjusting the graft to its proper tension.
7. Close the incision and tissues routinely. Place the limb in a Robert Jones bandage (RJB) for 1 month, as described in the patellar tendon procedure for cranial CL rupture repair.
8. An alternate technique for caudal cruciate rupture is to place two imbricating nylon sutures (Fig. 110-7). Place the first suture from the proximal patellar tendon to a drill hole through the proximal head of the fibula. Place the second suture from the proximal patellar tendon through a drill hole in the caudomedial aspect of the proximal tibia. Tighten these sutures with the stifle held in slight extension.
9. For bony avulsion injuries, if the bony portion is large enough, drill holes in the *bony* segment (lag screws or a Bunnell suture pattern can be used). Pass the suture through the ligament using a Bunnell pattern, and pass the suture ends through the bony drill holes. This gives firm fixation of the sutures to the ligament.
   a. Make two drill holes through the avulsion site, exiting on the medial side of the femur or on the cranial surface of the tibia.
   b. Using a suture passer, pass the sutures through the drill holes and tie them securely; this anatomically reduces the avulsion fracture and restabilizes the caudal CL.

Postoperative Care

See "Postoperative Care" under "Cranial Cruciate Ligament Rupture."

MENISCAL PROBLEMS

Preoperative Considerations

- An isolated meniscal tear or laxity is rare in dogs, compared with humans. More commonly, meniscal pathology is associated with a partial or a complete cranial cruciate tear.
- Secondary meniscal damage can occur in the weeks and months following an unrecognized or untreated cruciate injury.
- The resultant craniocaudal and rotational laxity allows the femoral condyles to traumatize the caudal horn of the medial meniscus (Fig. 110-8*A*). A common lesion is a folding cranially of the caudal horn of the medial meniscus.
- Diagnose by palpating a click or clunk during range of motion as the femoral condyle slips over the double thickness of the folded meniscus.

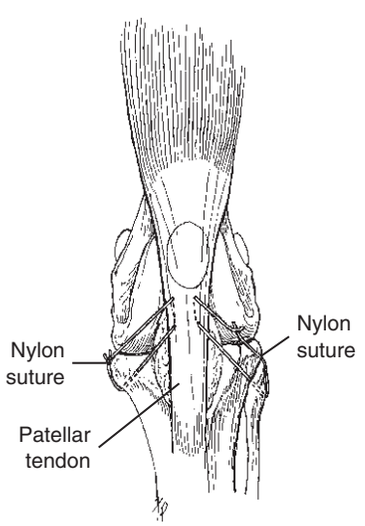

Figure 110-7. Imbrication technique for rupture of caudal cruciate ligament.

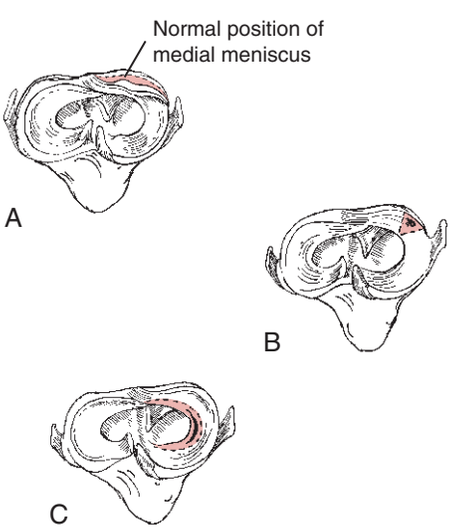

Figure 110-8. Repair of medial meniscal injuries. See text for details.

- Total (complete) meniscectomy is not advised unless there is severe damage of both caudal and cranial horns.

Surgical Procedure

Objective

- Remove or repair damaged portions of the menisci

Equipment

- Standard orthopedic pack and suture material
- Narrow Hohmann retractor (Synthes #399.18)
- Scalpel blade (#15)

Technique

1. Place the dog in dorsal recumbency with the forelegs and unaffected rear limb secured. Perform sterile preparation, stockinette, draping, and suturing in of the stockinette to the skin incision.
2. Because meniscectomy usually is performed in conjunction with CL reconstruction, use the arthrotomy approach (medial or lateral) appropriate for the cruciate technique. Make the arthrotomy of sufficient length to permit adequate retraction and exposure of both menisci.
3. After dislocating the patella from the trochlea, insert a small, sharp Senn retractor behind the fat pad and exert traction cranially. Keep the retractor in position until all internal joint manipulation is completed.
   a. Avoid unnecessary trauma to the fat pad with retractors to prevent damage to the vascular supply.
4. Debride cruciate and meniscal remnants, as necessary, and evaluate all joint structures for damage.
5. Place a second, dull Senn retractor on the medial side of the central Senn retractor to identify the medial meniscus, and then place it laterally to observe the lateral meniscus.
6. To facilitate exposure of the caudal horns, insert a narrow Hohmann retractor or hemostat to gently pry the tibial plateau forward (see "General Principles of Stifle Surgery").
7. Use a probe to determine laxity of the menisci and the extent of any tears.
8. Grasp the partially detached, forward-displaced caudal horn with a hemostat at the midportion. Often, the medial caudal horn is still attached peripherally to the medial collateral ligament and to the caudal tibial insertion.
9. With traction on the caudal horn, use a #15 scalpel blade to make a perpendicular cut to sever the caudal horn from the normally attached cranial horn. The meniscal-medial collateral attachment is usually cranial to the folded caudal horn.
10. Cut the remaining attachment (to the tibia) by placing the blade horizontally under the remaining caudal horn, and remove the caudal horn.
    a. Be careful to avoid cutting into the cartilage of the condyle or tibial plateau or lacerating the caudal CL or popliteal vessels caudal to the meniscus.
11. Flush the joint well with sterile lactated Ringer's solution, reposition the patella, and run the joint through a range of motion. No crepitation or clicks should be felt.
12. Remove any areas of localized injury or tears with a scalpel and create a vascular access channel running from the peripheral synovium (see Fig. 110-8*B*). In "bucket handle" tears (see Fig. 110-8*C*), the vascularity of central area (shaded area of Fig. 110-8*C*) is compromised and therefore is removed by sharp dissection.

Postoperative Care

See "Postoperative Care" under "Cranial Cruciate Ligament Rupture."

COLLATERAL LIGAMENT DISRUPTIONS

Preoperative Considerations

- Collateral ligament injuries usually occur as a result of severe medial (varus) or lateral (valgus) stress to the stifle by blunt force to the joint with the paw fixed during weight bearing.
- Collateral ligament strains are graded as to severity:
  - First degree—Stretching and minor disruption of collagen fibers
  - Second degree—Partial tearing
  - Third degree—Complete discontinuity of the substance of the ligament or avulsion of a bony attachment
- Animals usually are presented with acute lameness.
- Verify joint instability with stress radiographs.
- First- and second-degree injuries respond well to rest, restricted exercise, or a modified RJB.
- Third-degree injuries require surgical repair and partial immobilization for a few weeks using a modified RJB.

Surgical Procedure

Objective

- Restore the integrity of the injured ligament and the stability of the stifle.

Equipment

- Standard orthopedic pack and suture material
- Power drill
- Spiked washers and screws

Technique

1. Surgical approach is directly over the damaged ligament.
2. For complete ligament tears, use a Bunnell, locking loop, or triple-pulley suture pattern (see Chapter 115) for primary repair.
3. For bony avulsion, use a screw and spiked washer (Synthes 219.9, 219.93–95) if the bony portion is large enough to accept a screw. When the bony portion is small, use a ligament fixation plate (Synthes #65.00.1, 65.00.10, 65.00.11).
4. Reinforce a severely traumatized ligament by forming a supplemental fascial strip with two parallel incisions cranial and caudal to the involved collateral ligament: Then suture the fascial strip to the repaired collateral ligament. Alternatively, a fascial strip can be folded down and sutured to the ligament to reinforce the primary repair (see "Fascial Strip Over-the-Top Technique").
5. Alternatively, place screws at the origin and insertion of the collateral ligament and make a prosthetic ligament by looping monofilament nylon (or #1- to 50-lb test, depending on the size of the dog) in a figure-eight pattern around the screws. The wire or nylon usually breaks with time, but enough scar tissue forms to stabilize the joint.

Postoperative Care

See "Postoperative Care" under "Cranial Cruciate Ligament Rupture."

STIFLE LUXATION

Preoperative Considerations

- Severe trauma is necessary for complete stifle luxation to occur. The condition is more common in cats.
- Physical examination reveals total laxity in all directions: cranial, caudal, and rotational; the medial and lateral aspects of the stifle joint open up excessively.
- Usually, the patellar tendon is not disrupted; however, the popliteus and long digital extensor tendons may be torn, as well as both cruciates, both collaterals, and, in varying degrees, the meniscal attachments.

Surgical Procedure

Objective

- Repair ligaments and tendons to reestablish joint stability.

Equipment

- Standard orthopedic pack and suture material
- Power drill and drill bits
- Kirschner-Ehmer pins and clamps

Technique

1. Make a long lateral parapatellar skin and arthrotomy incision and assess the damage to ligaments, tendons, menisci, and cartilage.
2. If possible, stabilize the menisci by suturing peripheral attachments; otherwise, perform meniscectomy.
3. Repair the long digital extensor tendon, popliteus, and collateral ligaments with locking tendon loop, pulley, or Bunnell suture patterns; spiked washer and screw; or fascial reinforcement, as described previously under collateral ligament repair.
4. Cruciate stabilization may be done by intracapsular replacement or extracapsular imbrication techniques, as previously described in this chapter.

Postoperative Care

- To allow adequate healing, place a transarticular external skeletal fixation device, setting pins in the distal femoral and proximal tibia. This device is maintained for 3 to 4 weeks, followed by gradual motion using an RJB for 2 weeks and then a light wrap for 2 weeks. An alternative to the transarticular external skeletal fixation would be a full cast.
- With any form of immobilization of the stifle, place the joint in a functional (partially flexed) position.
- Some limitation of joint range of motion is acceptable and preferable to instability.

▼ ***Key Point*** For complete, multiple, midsubstance ligament disruptions, apposition of ligament ends is important for healing to occur; however, early mobilization also is important for complete biomechanical recovery.

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Chapter

111 Fractures of the Tibia and Fibula

Erick L. Egger

Fractures of the tibia and fibula compose a significant proportion (15–20%) of all long bone fractures in small animals. In addition, the minimal soft tissue coverage of these bones increases the incidence of contamination of open fractures, which may result in infection and healing complications. Proper treatment of tibial and fibular fractures requires

- An understanding of the disruptive biomechanical forces that must be controlled to promote the healing process.
- Selection of a fixation technique that will control these forces.
- Application of fixation without damaging the fracture healing process or compromising the function of the limb.

ANATOMY, FUNCTION, AND BIOMECHANICS OF THE TIBIA AND FIBULA

The anatomy of the tibia and fibula can be divided into regions based on their location, function, architecture, and the forces acting on them.

Epiphysis

- Proximally the epiphysis consists of
  - The tibial plateau, which provides support for the articular cartilage of the distal stifle joint (for information concerning the stifle joint, see Chapter 110).
  - The fibular head, which serves as the distal attachment for the lateral collateral ligament.
  - The tibial tubercle, which is the insertion point of the patellar tendon of the quadriceps muscle.
- Distally, the epiphyseal region consists of
  - The cochlea tibia, which supports the distal articular cartilage and articulates with the tibial tarsal bone.
  - The medial malleolus, which is the proximal attachment of the medial collateral tarsal ligaments.
  - The fibular epiphysis (lateral malleolus), which acts as the proximal attachment of the lateral collateral tarsal ligaments.
- The epiphyseal regions of the tibia and fibula are primarily composed of loosely woven, trabecular bone surrounded by a thin shell of dense cortex. This architecture limits the holding power of fixation implants, requiring extra care in their application.
- The epiphyseal regions that serve as ligament and tendon attachments are subjected to distractive forces. Consequently, repair of avulsion fractures of these areas must control these tensile forces.
- The epiphyseal regions that support articular cartilage are subjected to compressive loads that tend to separate the fragments, resulting in articular incongruity, instability, and eventually degenerative arthritis. Fixation of these fractures must provide anatomic reduction and rigid immobilization so that the fracture will heal with minimal callus formation, and so that early joint motion can be initiated to avoid joint stiffness.
- Because of ample blood supply and preponderance of cancellous bone in the epiphysis, fracture healing tends to be rapid. Consequently, fixation of these fractures usually is not prolonged or robust.

Physis

- The physeal regions of the tibia and fibula are located adjacent to the epiphysis and exist only in growing immature animals.
- The hypertrophied layer and calcifying layers of the physis are relatively fragile, and are commonly fractured with trauma.
- Because the cartilage layers are irregular and transverse, fractures tend to interdigitate well when reduced and require only control of bending forces.
- Because the physis is the origin of long bone growth, injuries to this region can cause premature cessation of growth resulting in shorter bone or angular deformity. Warn clients of this possibility, particularly in very young, actively growing patients.

Metaphysis

- The metaphysis is an indistinct region of bone located between the physis and the diaphysis (central shaft).

- The function of the metaphysis in the mature animal is the gradual alteration of the general construction of the bone from the wide-diameter thin cortex of the epiphysis to the narrow-diameter thick cortex of the diaphysis. The biomechanics and architecture of these regions change along their length.

Diaphysis

- The diaphysis is the central portion of the tibia and makes up the majority of its length.
- The tibial diaphysis is subjected to severe bending and torsional forces, in addition to axial compressive loads. Its hollow tubular construction of relatively thick cortical bone maximizes its effectiveness in resisting these forces.
- Relatively poor blood supply in cortical bone and longer moment arms associated with diaphyseal fractures generally mean these fractures heal slowly and require prolonged robust fixation.

PREOPERATIVE CONSIDERATIONS

General Considerations

- Examine the animal carefully for non-orthopedic injuries.
  - Evaluate cardiovascular status. If cardiopulmonary problems are suspected, radiograph the thorax.
  - Evaluate neurologic status. Determine deep pain perception in the fractured limb for local nerve damage, and proprioceptive and sensory perception in the other limbs for evidence of nerve or spinal cord trauma.
- Examine the animal carefully for concurrent musculoskeletal injuries.

▼ ***Key Point*** Nearly all small animals with tibial and/or fibular fractures are able to support themselves on the remaining three limbs. If not, suspect additional injuries.

- Determine the extent of soft tissue injury and fracture contamination.
  - Cover all open fractures with sterile bandages to prevent further contamination, and debride as soon as possible.
  - Broad-spectrum antibiotics are indicated if the fracture is open. Obtain samples for culture and sensitivity testing from the fracture site before beginning antibiotic therapy.
  - Until definitive treatment is possible, support all tibial fractures with a compressive wrap (Robert Jones bandage) or splint to prevent additional soft tissue injury.

Specific Considerations in Selecting a Fracture Fixation Technique

- Determine the potential axial stability of the reduced fracture based on preoperative fracture radiographs.
  - Stable fractures generally are simple transverse or short oblique. They tend to impact and become more stable upon weight bearing.
  - Unstable fractures have patterns, such as long oblique or comminuted, which tend to override or collapse upon axial loading.
- Perform rigid fixation of extensively contaminated open fractures. However, avoid placing large implants in the fracture site.
- Fractures in immature animals heal quickly, but
  - Premature physeal closure can occur with or without internal fixation.
  - Immature animals rapidly develop joint stiffness with limb immobilization.
  - Implants quickly loosen in the soft bone of immature animals.
- Fractures in very old animals heal slowly.
  - Brittle bone in older animals often splinters when implants are applied.

SURGICAL PROCEDURES

Objectives

- Provide adequate stability for fracture healing to occur while causing minimal damage to the biologic healing process.
- Restore normal limb function by minimizing joint stiffness and muscle atrophy and avoiding subsequent degenerative joint disease.

Pin and Tension Band Wire Fixation

Indications

- Avulsion fractures of the fibular head
- Avulsion fractures of the lateral (fibular) malleolus and medial (tibial) malleolus (Fig. 111-1)
- Avulsion fractures of the tibial tubercle

Equipment

- General orthopedic pack
  - Standard surgical pack
  - Bone and fracture reduction forceps
  - Periosteal elevator
  - Jacob hand chuck
  - Wire pliers and cutters
- Stainless steel monofilament orthopedic wire (18–22 gauge)
- Kirschner wires (0.035–0.062 inch)

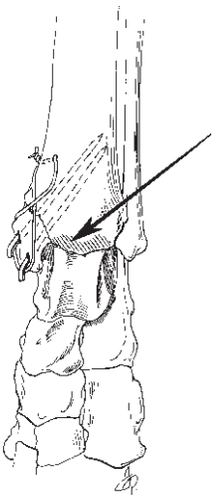

Figure 111-1. Pin and tension wire fixation of a medial malleolar avulsion fracture. Do not violate the cochlear articular surface with the Kirschner wire *(arrow)*.

Technique

1. Incise the skin directly over the affected bone.
2. Reduce and stabilize fracture with small fragment reduction forceps.
3. Create a transverse hole through the intact tibia approximately equidistant from the fracture line with the hand chuck and a Kirschner wire.
4. Insert two parallel Kirschner wires through the fragment, across the fracture, and into the parent bone.

▼ ***Key Point*** In the treatment of malleolar fractures, avoid penetrating the articular surface of the distal cochlea.

5. Pass orthopedic wire (18 gauge for most dogs, 20–22 gauge for small dogs and cats) through the transverse hole, cross the wire over the fracture site, and pass one end under the ligament or tendon attachment.
6. Twist both ends of wire together to form a figure eight. Tighten the wire just enough to compress the fracture (see Fig. 111-1).
7. Cut off excess orthopedic and Kirschner wires. Bend the Kirschner wires over and embed them in the soft tissues to trap the orthopedic wire loop and minimize soft tissue irritation.
   a. In the treatment of tibial tubercle fractures, if the animal still has significant growth potential, do not use tension band wires because this procedure can induce premature physeal closure. If necessary, use additional Kirschner wires oriented perpendicular to the physis for fixation stability.
8. Close soft tissues routinely.

Interfragmentary Lag Screw Fixation

Indications

- Intra-articular fractures of the proximal epiphysis (tibial plateau) and distal epiphysis (tibial cochlea)
- Reconstruction of comminuted shaft fractures prior to neutralization plating (see Fig. 111-7)

Equipment

- General orthopedic pack
- Bone screws and application instrumentation
- Power drill
- Kirschner wires

Technique

1. Manipulate fragments to obtain anatomic reduction of the intra-articular portion of the fracture and temporarily stabilize with fracture forceps.
2. Insert an interfragmentary screw and compress the intra-articular fracture line, using either a partially threaded screw or over-drilling the near fragment to create a gliding hole for fully threaded screws. Orient the screw perpendicular to the fracture line.
3. Insert additional screws or cross pins, depending on the fragment size, to prevent rotation around the first screw and to provide additional support.

Cross Pin and Rush Pin Fixation

Indications

- Transverse fractures of the epiphysis (may be combined with interfragmentary lag screw technique if the fracture extends into a joint)
- Axially stable fractures of the metaphysis (Fig. 111-2)
- Salter I and II fractures of the proximal and distal physis

Equipment

- General orthopedic pack
- Kirschner wires or small Steinmann pins ($^1/_{16}$–$^1/_8$ inch in diameter)
- Pin cutter

Technique

1. Manipulate the fracture and reduce through an open approach. Medial approach to the tibial shaft is preferred owing to relative lack of soft tissues.
2. Select the proper pin diameter (approximately 15% of bone diameter for cross pins, 10% for pins placed in the Rush technique).
3. With a hand chuck (a power drill can be used for cross pins), insert pins from the medial and lateral aspect of the fragment across the fracture into the medullary canal of the parent bone.

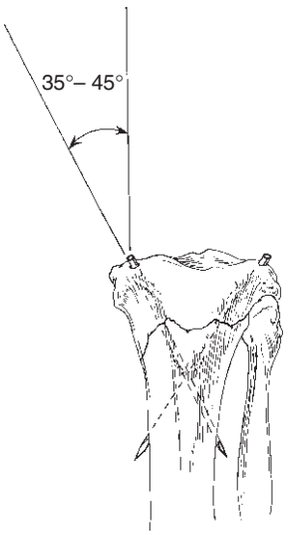

Figure 111-2. Fracture of the proximal tibial metaphysis fixed with cross pins. Note the angle of pin insertion and penetration of the parent diaphyseal cortex.

4. Orient cross pins obliquely to the long axis (35–45 degrees) so that they penetrate the far cortex (parent bone) when inserted (see Fig. 111-2).

▼ ***Key Point*** Cross pins provide excellent fracture fixation, but because they can interfere with normal function of the growth plate, use them with caution in immature animals.

5. Orient pins placed in the Rush technique more parallel (25–35 degrees) to the long axis. During insertion they bounce off the inner cortex of the medullary canal and are driven in to impact into the trabecular bone of the distant metaphysis.
   a. Pins placed in the Rush technique may be preferable for physeal fractures because of their smaller diameter (resulting in less damage to the proliferative zone of the physis) and because of their more perpendicular orientation to the physis (allowing sliding of the physis along the pins as it grows).
   b. Prebend the pins to facilitate reflection of the pins off the inner cortical wall as they are inserted.
6. Cut off excess pin length and countersink the ends below bone level (if the pins will not be removed) or bend the ends over to avoid soft tissue interference.

Intramedullary (IM) Pin and Wire Fixation

Indications

- Simple, axially stable fractures of the tibial diaphysis
- Other selected reducible tibial diaphyseal fractures

Contraindications

- Infected or significantly contaminated open (grade 3) fractures (see Chapter 120)
- Fractures that cannot be reconstructed

Equipment

- General orthopedic pack
- Steinmann pins
- Pin cutter

Technique

IM Pinning Technique for Simple, Axially Stable Tibial Fractures

1. Select a pin diameter 50% to 60% of the smallest medullary canal diameter.
2. Reduce the fracture, usually by manipulation through a medial open approach.
3. Insert the pin at a point midway between the tibial tubercle and medial collateral ligament along the edge of the tibial plateau (slightly distal to the articular surface).
4. Drive the pin distally (normograde) down the proximal fragment and across the fracture to impact into the distal metaphyseal bone.
5. Determine the pin insertion length by comparison with a second pin, identical in length, held along the side of the bone.

▼ ***Key Point*** Avoid driving IM pins through the articular cartilage of the cochlea, because this can result in development of significant arthritis.

6. Remove excess pin length with a pin cutter.
7. Determine rotational stability. If significant rotational motion persists, apply interfragmentary wire or a two-pin external fixator.
   a. An ancillary external fixator is similar to type I external skeletal fixation (described later) but uses fewer fixation pins, one above and below the fracture, which controls rotation but not bending forces.

Technique

Wiring Techniques for Fracture Reconstruction Prior to IM Pinning

With Cerclage Wires

Cerclage wires can be used only on long oblique fracture lines (fracture line length a minimum of twice the bone diameter), which can be very accurately reduced (Fig. 111-3).

1. Use large (18 gauge for medium and larger dogs; 22 gauge for toy breeds and cats) monofilament wire.
2. To control motion, at least two wires must cross the complete fracture line.

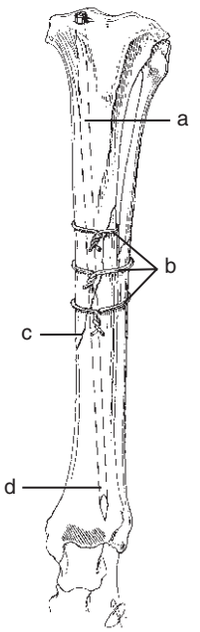

Figure 111-3. Use of cerclage wire to prevent axial collapse of a long oblique fracture stabilized with an intramedullary (IM) pin. (a) Pin diameter equals 50% to 60% of the medullary canal; (b) wires must be perpendicular to bone axis and one-half bone diameter apart; (c) fracture length must be a minimum of twice the bone diameter; (d) stop pin insertion short of cochlea.

3. Orient wires perpendicular to the long bone axis, space apart at least one-half bone diameter, and twist to tighten.
4. Use cerclage wires for fissure fractures as necessary.
5. Always use an IM pin in addition to the cerclage wires to control bending forces.

With Interfragmentary Wires

Use interfragmentary wires to stabilize short oblique patterns (fracture length greater than twice the bone diameter) when only one wire can be applied.

1. Create holes in each bone fragment with a hand chuck and Kirschner wire. Position the holes so the wire crosses the fracture perpendicular to the fracture line, thus providing maximum interfragmentary compression when the wire is tightly twisted.
2. Thread the wire through the holes and incorporate the IM pin that has been inserted to the level of the fracture as described previously.
3. Reduce the fracture, complete the IM pin insertion, and tighten the interfragmentary wire.

External Skeletal Fixation (ESF)

Indications

- Stable, reducible, and non-reducible fracture patterns depending on ESF frame configuration:
- The use of "positive profile" design pins, increased number of fixation pins, new connecting clamp design, and stiffer connecting bar materials has increased the stiffness and decreased pin problems of Type I (unilateral) frames. Therefore, even more unstable fractures can be treated with simpler frame configurations (Fig. 111-4).
- Type II (bilateral) and type III (trilateral) configurations (Fig. 111-5) have axial rigidity comparable to that of plates and newer design aiming devices make pin placement more accurate.
- "Moldable connecting columns" (Fig. 111-6) and biplanar configurations allow placement of an adequate number of pins in short metaphyseal fragments while avoiding significant soft tissue tethering problems by not requiring fixation pin alignment.
- Open fractures with significant soft tissue damage or infected fractures, because rigid fixation can be obtained without large implants (e.g., IM pins, plates) in the fracture site.
- Contraindications:
  - Intra-articular fractures
  - Avulsion fractures of ligament and tendon epiphyseal attachments

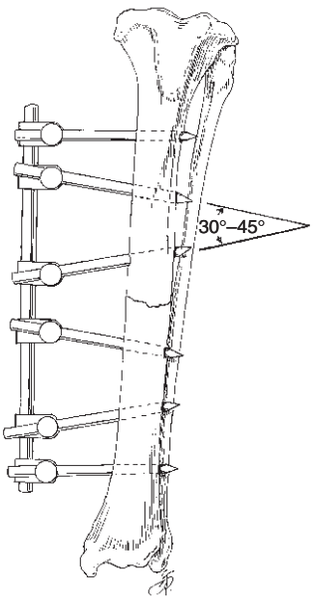

Figure 111-4. A six-pin type I (unilateral) external skeletal fixator applied to the medial side of a relatively stable tibial fracture. Addition of a lateral connecting bar would convert this to a type II (bilateral) fixator.

Equipment

- General orthopedic pack
- Low-speed power drill
- The newer IMEX SK (IMEX Veterinary Inc., 1001 McKesson Dr., Longview, TX) and Securos (Securos, 278 Southbridge Rd., Rte. 169, Charlton, MA) systems provide a wide variety of fixator systems and features for small animal application

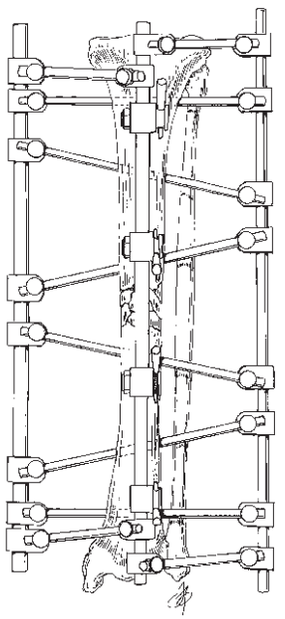

Figure 111-5. A very rigid type III (trilateral) external skeletal fixation (ESF) configuration applied to a non-reconstructible diaphyseal fracture.

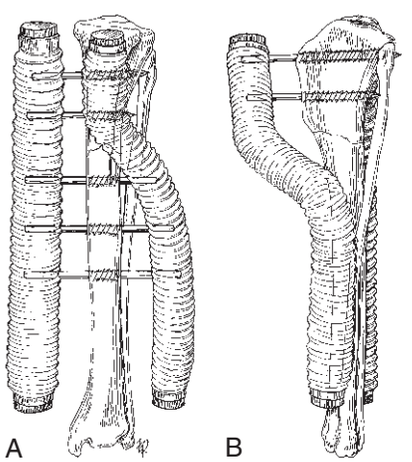

Figure 111-6. Use of a "hybrid" circular-traditional external fixator to stabilize a very distal metaphyseal tibial fracture.

- The acrylic pin external fixator (APEF) system creates "moldable connecting columns" in three sizes.

Technique for Mechanical External Fixator

1. Fixation usually is placed on the medial side of the tibia. However, it can be oriented laterally or cranially to avoid soft tissue injuries.
2. Position the patient in dorsal recumbency with the leg left hanging under tension from a secure attachment to the ceiling (hanging leg prep), to achieve reduction and simplify fixator application.
3. Hold the fracture in approximate reduction, and insert the most proximal and distal fixation pins through small skin incisions into each fragment, using a low-speed power drill. Predrill holes with a drill bit that is 90% of the pin diameter before inserting threaded pins. Threaded pins reduce the incidence of loosening of pins, and preclude need for pin angling.
4. Slide a connecting bar with the appropriate number of clamps onto the end fixation pins (at least three pins in each fragment).
5. Reduce the fracture, using closed manipulation on more comminuted fractures or a limited open approach on simpler fractures, and tighten the end clamps.
6. Insert fixation pins through the remaining open clamps into the bone. The Securos (Securos, 278 Southbridge Rd., Rte. 169, Charlton, MA) aiming device is useful for aligning full pins for Type II and III configurations. Tighten each connecting clamp after placing the pin. If threaded pins are not used, obtain a 30° angle between at least two of the pins in each fragment.
7. For unstable fractures, insert additional pins and bars in other planes to create more rigid frame configurations.
8. Circular fixators are now available for veterinary application from IMEX (IMEX Veterinary Inc., 1001 McKesson Dr., Longview, TX) and use small-diameter Kirschner wires placed at divergent angles and attached under tension to metal rings surrounding the bone instead of traditional fixation. This allows adequate grasp of a very short segment as occurs with distal metaphyseal fractures. Multiple rings can be connected together with threaded rods to create the fixator, or a ring can be combined with traditional fixator components placed in the longer segment in a "hybrid" configuration.
9. Collect autogenous cancellous bone graft from the proximal medial tibial tuberosity, and place it in any bony defects remaining after open fracture reduction.
10. Do not completely close incisions or wounds of open or infected fractures (see Postoperative Care and Complications).

Technique for APEF System Application

1. Insert fixation pins (using positive profile threaded pins for optimal bone-pin integrity) in the bone fragments oriented to best meet the mechanical needs of the fracture and minimize soft tissue tethering.
2. Attach the APEF alignment frame to pins on both sides of the fracture close to the skin level. Reduce the fracture (using closed manipulation or open reduction), and tighten the alignment frame clamps.

3. Close open reduction incisions or pack open wounds aseptically. Adequacy of closed reduction can be checked with radiographs.
4. Cut pins approximately 4 to 5 cm from the skin level.
5. Impale the acrylic column molding tubes on the pin ends and position the tubes adjacent to the alignment frame, parallel to the limb about 2 to 3 cm from the skin.
6. Plug the most dependent end of each molding tube.
7. Premeasured acrylic is mixed for 2 to 3 minutes to a smooth consistency.
8. Cut a corner of the bag with scissors, then pour the acrylic into the open end of each tube.
9. Allow the acrylic to cure (10–12 minutes).
10. Remove the alignment frame, plugs, and excess molding tube.

Plate and Screw Fixation

Indications

- The stabilized limb is needed for immediate weight bearing because of orthopedic or neurologic injuries to the other limbs.
- Restricted activity or adequate postoperative care is not possible.
- Rigid fixation is necessary (e.g., in large, very active dogs).

Equipment

- General orthopedic pack
- Plates, screws, and specialized instrumentation for their implantation
- Power drill

Technique

1. Contour an appropriate-size plate to the shape of the intact bone and apply the plate to the medial (tensile) side of the tibia.
2. If the fracture pattern is axially stable, compress the fracture by applying the plate in the compression mode. When using dynamic compression plates, compression is achieved by drilling screw holes such that the screw slides toward the fracture line.
3. Initially, rebuild long, oblique, and reducible comminuted fractures with interfragmentary lag screws and/or wires. Apply a plate to the tibia without compression to protect the interfragmentary fixation from bending forces (i.e., neutralization mode) (Fig. 111-7).
4. To prevent collapse under loading, apply a heavy plate in the buttress mode for non-reducible fractures.
   a. Add cancellous autograft to the fracture to stimulate rapid formation of load-sharing callus.
   b. Alternatively, remove detached bone fragments (break into small pieces and add to bone graft), transversely osteotomize fragment ends, and collapse the fracture to reestablish good cortical contact and a stable repair. As much as 20% of the tibial length may be removed without causing permanent dysfunction.

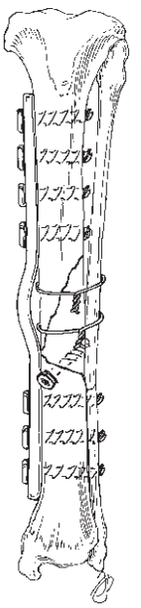

Figure 111-7. Use of a plate to protect a reconstructed comminuted tibial fracture from excessive bending forces. The screw and wires maintain reduction, and the plate "neutralizes" the weight-bearing forces.

POSTOPERATIVE CARE AND COMPLICATIONS

Immediate Postoperative Care

- Apply a compressive wrap (Robert Jones bandage) for 3 to 5 days to prevent soft tissue swelling and to protect the incision.
- Use gauze and tape to cover the connecting bars and clamps of external fixators. This decreases the incidence of the fixator "hanging up" on objects in the environment and protects the opposite limb.

▼ ***Key Point*** Do not primarily close infected and severely open fractures. Lavage and debride the wound q24–48h until healthy granulation tissue covers the wound (7–10 days). Complete wound closure at that time or allow healing by second intention if there is tension at the wound margins.

Implant Removal

- Do not routinely remove small implants such as cross pins, cerclage wires, lag screws, and tension band wires unless they cause problems such as joint interference or chronic drainage.

- Remove large IM pins unless the proximal pin end has been buried by tibial growth.
- Partially disassemble (destabilize or dynamize) rigid external fixation frames to a flexible configuration after early osseous bridging has occurred (about 6 weeks postoperatively). This increases fracture loading, stimulating callus hypertrophy and remodeling while protecting the fracture from excessive forces that might cause refracture. Remove the balance of the fixator when fracture healing is complete.
- Remove bone plates in the following situations:
  - Animal with short hair coat develops pain in limb when exposed to cold ambient temperatures.
  - Stiff plate design induces bone atrophy due to stress protection.
  - Chronic infection and drainage does not resolve.

Complications

Nonunion

- Hypertrophic nonunion:
  - There is exuberant callus proliferation without fracture bridging because of inadequate fracture immobilization. These fractures are biologically active and require only adequate immobilization.
  - Augment existing fixation or replace with a more rigid fixation technique to allow the fracture to heal.
- Atrophic nonunion:
  - There is lack of callus production, bone sclerosis, and bone resorption, reflecting a loss of biologic healing potential. These nonunions usually result from significant vascular damage from the trauma, surgical manipulation, or unstable fixation.
  - Treatment includes resection of non-viable bone, reestablishment of vascularity, control of infection, rigid fixation, and induction of new bone proliferation with an autogenous cancellous bone graft.

Malunion

- Malunion occurs when the fracture heals but poor alignment results in abnormal limb function. This may reflect inadequate initial reduction or loss of reduction owing to inadequate fixation.
- Treatment includes osteotomy, realignment, and adequate fixation.

Infection

- Acute infection of a tibial fracture occurs when bacterial proliferation overwhelms the body's defense mechanisms.
- Clinical signs include pain, swelling, and erythema that reflect the underlying accumulation of exudate and necrotic tissue.
- Immediate aggressive treatment is indicated to avoid progression to chronic osteomyelitis and nonunion:
  - Open the incision and extend the margins, if necessary, to ensure adequate drainage.
  - Culture the wound for aerobic and anaerobic organisms to determine specific antibiotic sensitivity.
  - Repeatedly lavage and debride the fracture site to remove exudate and necrotic soft tissue.
  - Initiate systemic broad-spectrum antibiotic therapy (e.g., cephalothins) until culture and sensitivity testing indicate specific therapy.
- See Chapter 121 for management of chronic osteomyelitis.

Growth Deformities

Growth deformities can result from trauma to the proliferative layer of one of the physes, or from application of fracture fixation that limits physeal elongation. Angular deformities become apparent about 3 weeks after physeal injury; arthritic changes follow if the condition is not corrected. Treatment depends on the cause of physeal dysfunction and the animal's maturity.

- In actively growing animals:
  - Resect the osseous bridge crossing the physis and replace with autogenous fat graft.
  - Remove fixation implants that might be inhibiting physeal growth.
- In mature animals:
  - Perform corrective osteotomy and articular realignment.

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Chapter

112 Luxation, Subluxation, and Shearing Injuries of the Tarsal Joint

Dennis N. Aron

Luxation, subluxation, and shearing injuries of the tarsus involve damage to the supporting ligaments of the joint. Treatment and prognosis of these injuries depend on the location of the ligament damage and subsequent joint instability. Subluxations can be caused by spontaneous overstress or external trauma. Vehicular trauma usually causes luxations and shear injuries. Conservative treatment of most of these injuries with external coaptation is not advised, because continued instability and the development of degenerative joint disease are the likely outcomes.

▼ ***Key Point*** Surgical stabilization and appropriate postoperative rehabilitation gives the most consistent results in repair of luxation, subluxation, and shearing injuries of the tarsus.

ANATOMY AND SPECIAL CONSIDERATIONS

General

- The tarsus consists of the tibia, fibula, metatarsal bones, and seven specific tarsal bones orderly stacked in levels (Fig. 112-1).
- A multiple complex arrangement of ligaments connects the bones of the joint and helps to prevent luxation (Fig. 112-2).
- The *tarsocrural* joint is formed by the tibia and fibula at the proximal level and by the talus and calcaneus at the distal level.
- The *intertarsal* joints are all the articulations between the tarsal bones. Several of these joints are named and include the
  - Talocalcaneal joint—between the talus and calcaneus
  - Talocalcaneocentral joint—between the talus and central tarsal bone (includes a small communication with the calcaneus)
  - Calcaneoquartal joint (proximal intertarsal joint)—between the calcaneus and fourth tarsal bone
  - Centrodistal joint (distal intertarsal joint)—between the central tarsal bone and distal numbered tarsal bones
  - Tarsometatarsal joints—between the distal tarsal and metatarsal bones

Tarsocrural Joint

- Synonyms for this joint are the tibiotarsal, talocrural, ankle, and hock joint.
- Most luxations, subluxations, and shear injuries directly involve this joint.
- The major ligaments providing stability on the medial side of the joint are the long medial ligaments and tibiotalar short component ligament (Fig. 112-3*A*).
- The major ligaments providing stability on the lateral side of the joint are the long lateral ligament and the calcaneofibular short component ligament (Fig. 112-4*A*).
- The components of the medial and lateral ligaments complement each other in maintaining the talus in the mortise provided by the tibia and fibula.
- Certain parts of the ligament complexes are tighter in extension (long lateral and long medial ligaments) or flexion (calcaneofibular and tibiotalar short component ligaments).
- The tibiotalar and calcaneofibular short component ligaments of the medial and lateral sides, respectively, are especially important for maintaining stability of the joint. The joint capsule and malleoli also contribute to joint stability.
- The gross anatomy of the medial and lateral collateral ligament complexes is similar (see Figs. 112-3 and 112-4). The components cross at the tarsocrural joint space, providing the greatest amount of ligament and an advantageous spatial arrangement directly over the joint.

▼ ***Key Point*** In the reconstruction of the collateral ligamentous supporting structures of the tarsocrural joint, consider the complementary nature of ligamentous structure and function.

Intertarsal and Tarsometatarsal Joints

- The most common injury is damage to the plantar ligaments and tarsal fibrocartilage (see Fig. 112-2).
- The plantar ligaments and tarsal fibrocartilage limit extension of the intertarsal joints.

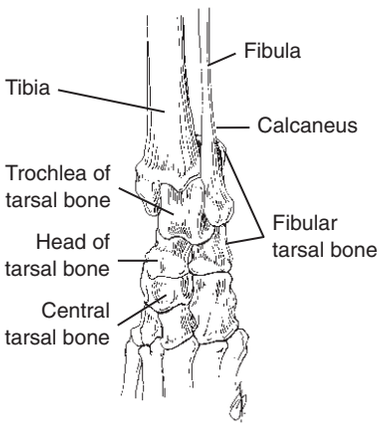

Figure 112-1. Anatomy of the bones of the tarsus.

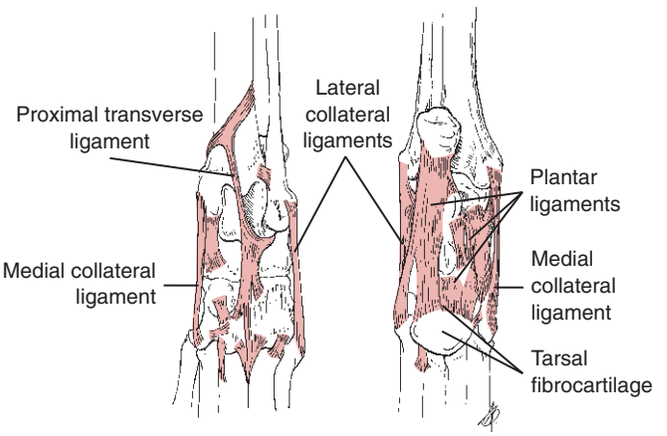

Figure 112-2. Cranial *(left)* and caudal *(right)* views of the ligamentous anatomy of the tarsus.

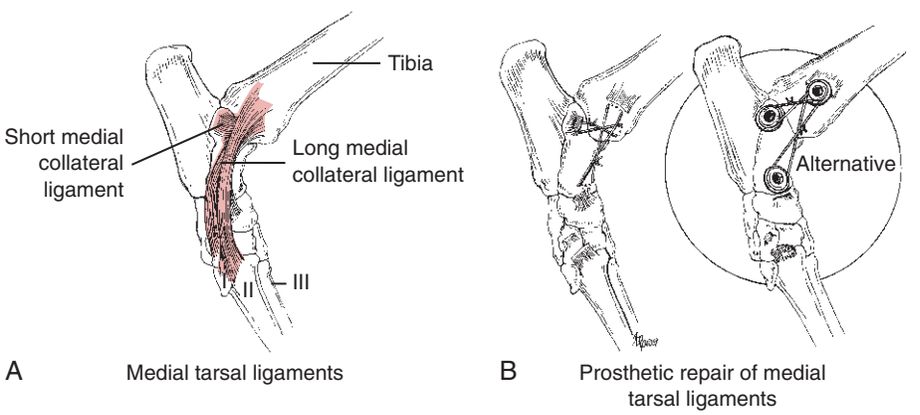

Figure 112-3. *A,* Medial ligamentous anatomy of the tarsus. *B,* Suture prosthesis repair of medial ligament injury. Tunnel sutures through the bones at points where the ligaments attach. Alternatively, place bone anchors or bone screws at these points.

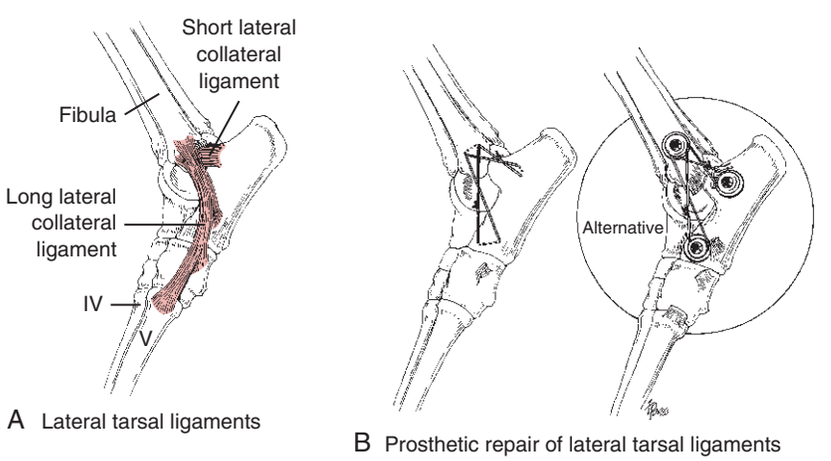

Figure 112-4. *A,* Lateral ligamentous anatomy of the tarsus. *B,* Suture prosthesis repair of lateral ligament injury. Tunnel sutures through the bones at points where the ligaments attach. Alternatively, place bone anchors or bone screws at these points.

- Most of the intertarsal joint stability is provided by three distinct plantar ligaments. These ligaments fuse, with a thickening of the joint capsule (the tarsal fibrocartilage), at the tarsometatarsal joint.
- The first ligament originates from the plantar surface of the sustentaculum tali and attaches to the central tarsal bone and tarsometatarsal joint capsule.
- The second ligament originates from the plantarlateral surface of the calcaneus. It joins with the long component of the lateral collateral ligament complex and attaches to the base of the fifth metatarsal bone.
- The third ligament originates from the body of the calcaneus and attaches to the fourth tarsal bone and the base of the fourth and fifth metatarsal bones.

TARSOCRURAL LUXATION AND SUBLUXATION

Surgical methods are recommended for treatment of luxation or subluxation injuries of the tarsocrural joint. Luxation and subluxation usually are the result of rupture of the medial or lateral collateral ligament complex.

Double-Prosthesis Replacement

- Double-prosthesis replacement (described later) closely reproduces the components of the intact medial and lateral collateral ligament complexes, thus allowing nearly normal joint stability to be maintained throughout a functional range of motion.
- Similar to the components of the normal collateral ligaments, double-suture prostheses become taut and lax with flexion and extension. Because of this, wire is not useful. Certain sutures (see later) give more successful results, most likely owing to the retention of elasticity upon cyclic loading.
- Clinically, double-ligament replacement gives results superior to conservative management with splints or non-anatomic single ligament replacement methods. The prognosis is good for long-term function with most closed luxation and subluxation injuries, depending on timely repair (within 5 days of injury) and absence of articular damage.

Preoperative Considerations

- Tarsocrural luxation results from different combinations of injuries, including
  - Fractures of both malleoli.
  - Fracture of one malleolus and damage to the contralateral ligament complex.
  - Fracture of the fibula and damage to the medial ligament complex.
  - Uncommonly, damage to both the lateral and medial collateral ligament complexes and no fractures.
- Tarsocrural subluxation usually results from complete rupture or avulsion of either the lateral or medial collateral ligament complex.
- In medial ruptures, the paw tilts abnormally toward the lateral direction with a laterally (valgus) applied force.
- In lateral ruptures, the tilt is in a medial direction with a medially (varus) applied force.
- Occasionally, there is rupture of only the long or short components of the medial or lateral ligament complexes. Less joint laxity makes these subluxation injuries more difficult to diagnose. Determine joint laxity using the following methods:
  - Place lateral and medial tilt forces on the hock at different joint angles: Laxity in extension but not flexion suggests major damage to the long medial ligament, or long lateral ligament; laxity in only flexion suggests that most damage is isolated to the tibiotalar or calcaneofibular short components.
  - Make a dorsoplantar (stress) radiograph while applying lateral and medial tilt forces on the hock: Take the stress radiograph at the tarsocrural joint angle that produces the subluxation; for subtle subluxations, compare this radiograph with a similar radiograph of the contralateral (normal) hock.

▼ ***Key Point*** Routine dorsoplantar and lateral radiographic views are always needed to check for concomitant tarsal injuries. Stress radiographs are useful to confirm the diagnosis but are not always necessary.

Surgical Procedure

Objectives

- Stabilize the joint.
- Maintain an adequate range of motion.
- Avoid trauma to the articular surfaces.
- Achieve pain-free weight bearing.
- Minimize patient morbidity and owner expense.

Equipment

- Standard orthopedic instrument pack and suture material
- Gelpi self-retaining retractors
- Small periosteal elevator
- Orthopedic drill (power drill preferred)
- Orthopedic anchors, screws, washers, and insertion equipment
- Kirschner wires (K-wires)
- Assortment of straight and curved needles
- Coaptation splint
- Coated braided polyester or monofilament polybutester (Polydek or Tevdek, Deknatel, Inc., Teleflex Medical, Mansfield, MA)

Technique

1. Clip the injured limb from the level of the proximal femur, extending distally to include the paw. Include the paw in the sterile field to allow direct manipulation.
2. Place the patient in lateral recumbency, with the injured limb up for lateral replacement or down for medial replacement, and prepare the limb for aseptic surgery.
3. Expose the subluxation through a curved skin incision centered over the medial or lateral malleolus.
   a. Begin from the distal one-fourth of the tibia and continue to the proximal metatarsal bones.
   b. Locate the medial or lateral collateral ligament complex along the same line by incising the subcutaneous tissue and deep fascia.
4. Inspect the components of the ligament complexes for damage.

a. To help assess the damage, stress the ligament components with a varus or valgus tilt in both flexion and extension.
b. It is unlikely that there will be a totally isolated injury to only one component of the ligament complex. The ligaments can appear intact but may have lost considerable function owing to internal derangement of the collagen fibers.

▼ ***Key Point*** Usually, the ligament components are too badly damaged to allow primary suturing of the torn ends or reattachment to bone. Replace irreparable ligaments and protect repaired ligaments with prosthetic sutures.

5. Replace or protect the medial or lateral ligament complexes with two figure-eight heavy sutures fastened to the bone directly, with bone anchors (BoneBiter Suture Anchor System, FlexiTwist Suture Anchor, Innovative Animal Products, Rochester, MN; SECUROS Bone Anchor, SECUROS, Charlton, MA), or with bone screws.
   a. Drill bone tunnels in the malleolus in locations similar to the origins of the components of the ligament complex (see Figs. 112-3 and 112-4). Bone tunnels serve as anchors for the suture prostheses.
   b. Secure the suture prosthesis that mimics the lateral or medial short components to tags of the torn ligament at the insertion site. Use a locking loop suture pattern to grip the torn ligament (see Chapter 115). A bone anchor or bone screw (see "Shear Injury") may be needed to fix the prosthesis to the insertion site (see Figs. 112-3*B*, 112-4*B*).
   c. Secure the suture prosthesis that mimics the lateral or medial long components to a drill hole in the tubercle of the distal talus or distal calcaneus (see Figs. 112-3*B* and 112-4*B*). A bone anchor or bone screw (see "Shear Injury") may be used to fix the prosthesis (see Figs. 112-3*B* and 112-4*B*).
6. Use one or two (for large patients) strands of #1 to #5 braided polyester or monofilament polybutester sutures for prosthetic replacement or protection.
   a. Set the sutures in a figure-eight pattern.
   b. Do not use absorbable sutures.
   c. Do *not* use monofilament nylon and monofilament polypropylene for sutures. They tend to stretch permanently and are better suited for primary repair of torn ligaments.
7. Tie the long and short suture prostheses.
   a. Tie the short prosthesis with the tarsocrural joint held in approximately 90 degrees flexion for dogs and 70 degrees for cats.
   b. Tie the long suture prosthesis with the joint in a functional standing angle of 135 degrees for dogs (varies with breed) and 120 degrees for cats.
   c. After the sutures are tied, tighten the screws or bone anchors against the bone.
8. Expose the luxation injury through separate surgical incisions on the medial and lateral sides of the joint.
   a. Fix the malleolar fracture with a tension band technique.
   b. Replace or protect the contralateral ligaments.
9. To manage luxations due to fracture of the fibula and damage to the contralateral ligament complex:
   a. Replace or protect the medial ligaments.
   b. Stabilize the fibula to the tibia with K-wires or bone screws.

Postoperative Care

- Protect the tarsocrural joints but allow weight-bearing mobilization of the limb with a short, three- to eight-layer semi-supple softcast (3M Scotchcast Soft Cast Casting Tape, St. Paul, MN) coaptation splint. The amount of layers used depends on the size and activity level of the animal and amount of microstrain to be allowed.
- Extend the splint from just below the stifle distally to include the digits.
- Place the hock in a functional standing angle.
- Provide semi-supple softcast coaptation as a full circular cast.
- Maintain the semi-supple softcast coaptation splint for 4 to 12 weeks; the length of time depends on the amount of initial trauma, joint instability, and health issues. A longer time is required for luxation and major subluxation injuries and older animals, a shorter time for incomplete tears and partial injuries and younger animals.
- The semi-supple softcast allows for controlled mobilization by progressive unwrapping of layers to increase tissue microstrain as healing advances.
- Once all coaptation is removed, continue progressive controlled mobilization by slowly increasing the animal's activity over another 4- to 12-week period. During this period, if the animal shows signs of increased lameness or pain, progress more slowly with controlled mobilization in a manner that does not create lameness or discomfort.

▼ ***Key Point*** Do not allow immediate uncontrolled activity of an animal after removal of coaptation.

SHEAR INJURY

Preoperative Considerations

- Shear injury usually occurs when an animal is trapped by a moving vehicle, resulting in shearing by the road surface of supporting ligaments, joint capsule, and malleolus.
- The medial side of the joint is injured more commonly than the lateral side of the joint.
- Perform wound management and ligament replacement when the bone and cartilage damage is mostly

isolated to the malleolus. Severe soft tissue damage makes stabilization difficult and prolongs healing.
- Although a successful ligament replacement gives better results than a tarsocrural joint arthrodesis, consider joint arthrodesis if there is extensive bone and cartilage damage.

Surgical Procedure

Objectives

- Prevent infection.
- Anatomically stabilize the tarsocrural joint, eliminate pain, and maintain a functional range of motion.
- Avoid trauma to the articular surfaces.
- Attain wound coverage with strong epithelial tissue.
- Minimize patient morbidity and owner expense.

Equipment

- Equipment is the same as for tarsocrural luxation and subluxation plus
  - Wound dressing materials
  - Coaptation splint materials

Wound Management and Debridement

Technique

1. Before debridement and ligament replacement, cover the shear wound with a temporary sterile dressing (see Chapter 56 for open wound management) and apply a temporary splint to prevent further damage to the unstable joint. Exteriorized material will contaminate deeper recesses if replacement into the wound is attempted.
   a. Do not push or "stuff" extruded soft tissue, bone, or cartilage back into the wound.
   b. Do not soak the wound.
2. Perform debridement as soon as the animal is a stable candidate for surgery, ideally within 6 hours from the time of injury for moderate wounds, and within or less than 1 to 2 hours for severe wounds.

▼ ***Key Point*** Ligament reconstruction and wound closure can be delayed, but do not delay wound debridement.

   a. Anesthetize the animal and remove the temporary splint.
   b. Keeping the wound covered, clip the limb, and cleanse with an appropriate antiseptic.
   c. Remove the dressing and thoroughly irrigate the wound with copious amounts of a prewarmed balanced electrolyte solution (see Chapter 56).
   d. Obtain cultures of the joint surface for identification of contaminating organisms and their sensitivity to antibiotics. A Gram stain may be helpful in identifying bacteria type.
3. After moving the animal to the operating area, perform a final surgical scrub and drape the limb.
4. Debride the wound of all visible necrotic tissue and debris. Be careful to avoid damage to articular surfaces.
   a. During the debridement process, lavage continuously with copious amounts (1 L or more) of a balanced electrolyte solution such as lactated Ringer's, using a moderate amount of pressure, through a 30- to 60-ml syringe and 18- or 19-gauge needle or catheter. Fluid pressure on the tissues should approximate 7 psi. Pulsatile suction and lavage is ideal.
5. Perform ligament replacement at this time or delay for repeat wound debridement or orthopedic referral. If delaying replacement:
   a. Cover the wound with an absorbent dressing to keep the wound moist (e.g., wet-to-dry dressing; see Chapter 56).
   b. Stabilize the joint with a rigid coaptation splint such as a fiberglass slab incorporated into a padded wrap.
   c. Change the dressing once a day or more frequently if necessary.
6. Repeat wound debridement if necrotic tissue is left in the wound after the first procedure. Continue this process until only viable tissue is present in the wound.

Ligament Replacement

The prosthetic ligament replacement technique usually requires three bone anchors or bone screws and figure-eight heavy sutures.

Technique

1. Use bone anchors or 4.0-mm partially threaded cancellous screws or 2.7-mm cortical screws with 2.7-mm spiked washers (Synthes Ltd., West Chester, PA), depending on the size of the animal. Place the screws as close as possible to the origin and insertion of the components of the ligament complex (see Figs. 112-3*B* and 112-4*B*).
2. Position the origin fastener, anchor or screw, in the distal tibia for the medial ligament or the distal fibula and tibia for the lateral ligament. Direct this fastener slightly proximal to avoid penetrating joint cartilage and to obtain maximum bony purchase.
3. Position the insertion fastener for the medial tibiotalar short ligament in the proximoplantar quadrant of the medial trochlear facies of the talus. Direct this fastener slightly distal to avoid the trochlear sulcus of the talus.
4. Position the fastener corresponding to the insertion of the medial long ligament through the tubercle at the plantar base of the talus. Direct this fastener slightly proximodorsally.
5. Position the fastener corresponding to the insertion of the calcaneofibular short ligament proximoplantar to the base of the lateral articular facies of the tuber calcis.

6. Position the insertion fastener for the long ligament through the tubercle at the dorsal extent of the base of the calcaneus. Direct this fastener slightly proximoplantar.
7. Using one or two (for large patients) strands of #1-5 polyester sutures or monofilament polybutester sutures as prosthetic replacements, place suture(s) around the origin fastener and the short insertion fastener, and separate suture(s) around the origin fastener and long insertion fastener.
   a. Set the sutures in a figure-eight pattern.
   b. Tie taut the tibiotalar or calcaneofibular short suture prosthesis with the tarsocrural joint held in approximately 90 degrees flexion for dogs and 70 degrees for cats. Tie taut the medial long or lateral long suture prosthesis with the tarsocrural joint in a functional standing angle of 135 degrees for dogs (varies for some breeds) and 120 degrees for cats.
   c. Tighten the fasteners against the bone.

▼ ***Key Point*** Never perform primary soft tissue closure over a shear injury.

8. If possible, allow second intention healing; alternatively, perform delayed closure or apply a skin graft (see Chapters 56 and 57) after all surfaces of the wound and prosthetic sutures are covered with healthy granulation tissue.

Postoperative Care

- Firmly immobilize the tarsocrural joint until the wound shows healthy granulation tissue and has begun to contract, is sutured closed, or the wound has been covered by a viable skin graft. This can be done several ways such as with a fiberglass slab or aluminum rod incorporated into a padded wrap. This type of wrap will allow frequent bandage changes. Try to avoid using a transarticular external skeletal fixator (ESF) as this rigid form of immobilization is very detrimental to the joint. However, if an ESF is used, maintain it for 2 weeks or less.
- After the firm coaptation is removed, semi-mobilize the hock for 6 to 12 weeks with a 4- to 10-layer short semi-supple softcast coaptation splint. If the wound has not completely been covered by healthy epithelial tissue a "window" can be cut into the softcast. The softcast allows one to progressively increase microstrain to the joint but does not risk failure of the prosthetic sutures.
- During use of the semi-supple softcast coaptation splint, perform controlled mobilization by allowing increasingly longer controlled walks and by progressively unwrapping layers to increase tissue microstrain as healing advances.
- Once all coaptation is removed, continue progressive controlled mobilization by slowly increasing the animal's activity over another 8- to 16-week period. Controlled muscle building techniques are valuable during this stage of rehabilitation. During this time, if the animal shows signs of increased lameness or pain, progress more slowly with controlled mobilization in a manner that does not create lameness or discomfort.

Prognosis

The prognosis is good to guarded for long-term pain-free function if there is no damage to the articular surfaces other than the malleolus. Careful rehabilitation through progressive controlled mobilization is critical to success.

TARSOCRURAL JOINT ARTHRODESIS

Tarsocrural joint arthrodesis can be done by tarsocrural joint fusion or pantarsal fusion.

- Pantarsal arthrodesis includes fusion not only of the tarsocrural joint but also of the intertarsal and tarsometatarsal joints.
- Pantarsal arthrodesis gives more consistent functional results and there is less patient morbidity.

Preoperative Considerations

Indications for performing tarsocrural joint arthrodesis instead of ligament replacement include

- Moderate to severe osteochondral damage to the joint mortise
- Prolonged tarsocrural joint subluxation or luxation causing moderate to severe degenerative joint disease
- Failure of reconstructive surgery or postoperative development of painful degenerative joint disease

Surgical Procedure (Pantarsal Arthrodesis)

Objectives

- Fuse the tarsocrural, intertarsal, and tarsometatarsal joints.
- Fuse the hock at a functional angle.
- Allow pain-free use of the limb.
- Minimize patient morbidity and owner expense.

Equipment

- Standard orthopedic instrument pack and suture material
- Gelpi self-retaining retractors
- Power drill
- Power saw or osteotome and mallet
- Pneumatic surgical bur (optional)
- Bone curettes
- K-wires

- Reconstruction bone plates, screws, and application equipment
- Coaptation splint

Technique

1. Approach the joint laterally from the distal one-third of the tibia, extending over the tarsal bones and ending at the proximal one-third of the fifth metatarsal bone.
2. Using a power saw or osteotome, cut the articular cartilage from the distal tibia and trochlea of the talus.
   a. Cut the distal tibia perpendicular to the longitudinal axis.
   b. Cut the trochlea of the talus at an appropriate angle, allowing the distal tibia to rest flush on the talus and form the proper weight-bearing angle at the hock. Before surgery, use the animal's contralateral limb to determine the correct weight-bearing angle (approximately 140 degrees for dogs [varies with certain breeds] and 120 degrees for cats).
3. Match the tibia to the talus at the appropriate angle and temporarily fix the two bones with K-wires.
4. With a bone curette or pneumatic bur, remove as much cartilage as possible from the intertarsal and tarsometatarsal joints.
5. Obtain autogenous cancellous bone from the ipsilateral greater tubercle of the humerus. Pack cancellous bone into the intertarsal and tarsometatarsal joints and around the tarsocrural joint.
6. Apply a contoured reconstruction bone plate to the lateral surface of the distal tibia, tarsus, and fifth metatarsal bone. Ostectomize the fibula to achieve a good fit. Place at least three screws in the tibia and metatarsasl bones. Alternatively, a standard bone plate can be placed dorsally (Fig. 112-5).
   a. Bend an appropriately sized 8- to 10-hole plate to the proper fit.

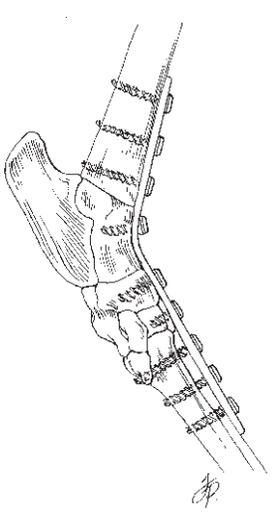

Figure 112-5. Pantarsal arthrodesis by dorsal application of a bone plate.

   b. Fix three cortical screws and the plate to the tibia, three or four screws to the tarsal bones, and three screws to the fifth and fourth metatarsal bones.
7. Maintain or remove the K-wires, pack more cancellous bone around the tarsocrural joint, and perform routine closure.

Postoperative Care

- Apply a short, rigid coaptation splint or full cylinder cast from the foot to just below the stifle until there is radiographic evidence of bone fusion.
- Remove the bone plate after there is complete bone union, usually in 6 to 9 months.
- Protect the arthrodesis for 6 weeks following plate removal with a semi-supple softcast coaptation splint; restrict exercise.

OVERVIEW OF INTERTARSAL LUXATION AND SUBLUXATION INJURIES

- Many intertarsal ligament injuries are a result of daily activity and occur without known trauma.
- Acute loading (e.g., with jumping) can damage plantar ligaments and cause a hyperextension injury.
- Affected animals usually are non–weight bearing or walk plantigrade, have variable swelling in the tarsal region, and have instability of the tarsus.
- Palpation and stress radiographs (see Chapter 4) usually can localize the area of injury.
- Hyperextension injuries are repaired by arthrodesis or tension band wire stabilization.
- Because surgery is performed only on the low-motion intertarsal or tarsometatarsal joints, the prognosis usually is excellent for pain-free normal function.

PROXIMAL INTERTARSAL SUBLUXATION WITH PLANTAR INSTABILITY

Preoperative Considerations

- Injury to the plantar ligaments of the calcaneoquartal and talocalcaneocentral joints results from excessive dorsiflexion; the hock collapses and the animal walks plantigrade.
- A traumatic episode usually is not identified.
- Diagnose by palpation and stress radiographs (see Chapter 4).
- This condition does not respond to conservative management with coaptation splints. Treat surgically by arthrodesis of the calcaneoquartal joint.

Surgical Procedure

Objectives

- Fuse the calcaneoquartal joint.
- Avoid trauma to the tarsocrural joint.

- Achieve pain-free, normal weight bearing.
- Minimize patient morbidity and owner expense.

Equipment

- Standard orthopedic instrument pack and suture material
- Gelpi self-retaining retractors
- Intramedullary pins
- Bone curettes or pneumatic bur
- Bone drill and assorted drill bits
- K-wires
- Orthopedic wire (18 or 20 gauge)
- External coaptation devices

Technique

1. Expose the joint plantar-laterally with medial retraction of the tendon of the superficial digital flexor (SDF). This may entail incising the lateral retinaculum, which normally secures the SDF tendon to the lateral process of the calcaneal tuber.
2. Using a bone curette or pneumatic bur, remove articular cartilage from the surfaces of the calcaneus and fourth tarsal bone.
3. Insert an appropriate-size single intramedullary pin ($^5/_{64}$–$^1/_8$ inch) from the proximal calcaneus down the shaft.
   a. Drill a pilot hole in the (very hard) calcaneus before inserting the intramedullary pin.
   b. Position the pin in the calcaneus.
4. Obtain autogenous cancellous bone from the ipsilateral greater tubercle of the humerus and pack it into the joint space.
5. Reduce the joint, drive the intramedullary pin across the joint, and fix the pin in the distal end of the fourth tarsal bone (Fig. 112-6).

Figure 112-6. Fusion of the calcaneoquartal joint via pin and tension band wire fixation and cancellous bone graft.

6. Retract the intramedullary pin slightly, cut it short, and countersink it beneath the cartilage of the tuber calcis.
7. Drill a transverse hole across the distal portion of the fourth tarsal bone and the middle section of the calcaneus.
8. Place an orthopedic tension band wire (18 or 20 gauge) in a figure-eight pattern through the drilled holes (see Fig. 112-6).
   a. Set the wire directly against the bone under all soft tissue.
   b. Tighten the wire evenly with a double-twist method and bend the twists over to rest against bone.
9. Reduce the superficial digital flexor tendon and suture the lateral retinaculum to stabilize the tendon.
10. Close the subcutaneous tissue and skin routinely.

Postoperative Care

- Place a short (from the proximal tibia to the paw) semi-supple softcast coaptation splint for 4 to 8 weeks. Perform progressive controlled mobilization with the softcast.
- Restrict activity until bony fusion of the joint is evident on radiographs (usually 6–8 weeks).

PROXIMAL INTERTARSAL LUXATION WITH PLANTAR INSTABILITY

Preoperative Considerations

- This condition occurs infrequently, compared with subluxation injury.
- Trauma results in a high-energy hyperextension injury. There is more joint displacement and instability than with subluxation injury.
- Because of the severe instability in this condition, perform arthrodesis of the intertarsal joint with a bone plate rather than with a less rigid pin and wire tension band technique.

Surgical Procedure

Objectives

- Fuse the proximal intertarsal joint. Otherwise, objectives are the same as for proximal intertarsal subluxation.

Equipment

- Standard orthopedic instrument pack and suture material
- Gelpi self-retaining retractors
- Bone curettes or pneumatic bur
- Power drill

- Bone plates, screws, and application equipment
- External coaptation devices

Technique

1. Make a lateral approach from the tuber calcis, extending over the calcaneus and fourth tarsal bone and ending over the proximal one-third of the fifth metatarsal bone.
2. Using a bone curette or pneumatic bur, remove articular cartilage from the bones of the proximal intertarsal joint.
3. Place autogenous cancellous bone in the joint space. Reduce the joint.
4. Place a bone plate on the lateral aspect of the calcaneus, fourth tarsal bone, and proximal fifth metatarsal bone (Fig. 112-7).
   a. Shape the bones slightly to accommodate the plate.
   b. Secure an appropriate-size seven-hole plate with two screws in the calcaneus, one in the calcaneus and talus, one in the fourth and central tarsal bones, and three in the fourth and fifth metatarsal bones.
   c. Alternatively, do not place the screw in the fourth and central tarsal bones, and pack this area with cancellous bone.
5. Close the tissue and skin routinely.

Postoperative Care

- Protect the arthrodesis with a short semi-supple soft-cast coaptation splint. Remove the splint when there is radiographic evidence of bony fusion.
- Remove the bone plate after the arthrodesis is complete. If retained, the plate usually loosens, causing pain and lameness.

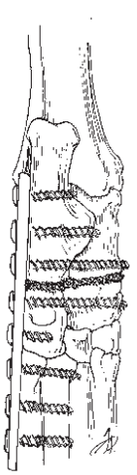

Figure 112-7. Proximal intertarsal joint fusion via lateral application of a bone plate and cancellous bone graft.

DISTAL INTERTARSAL (TARSOMETATARSAL) SUBLUXATION WITH PLANTAR INSTABILITY

Preoperative Considerations

- This condition is less common than proximal subluxation injury.
- The cause is tearing of the plantar tarsal fibrocartilage and usually is associated with trauma.
- A few days after the injury the animal attempts weight bearing and walks plantigrade.
- Consistent with hyperextension injuries, surgical arthrodesis is the treatment of choice.

Surgical Procedure

Objectives

- Fuse the distal intertarsal joint. Otherwise, objectives are the same as for proximal intertarsal subluxation.

Equipment

- See "Proximal Intertarsal Subluxation with Plantar Instability."

Technique

1. Expose the injury by an incision over the plantarlateral calcaneus, fourth tarsal bone, and metatarsal bones.
2. Retract the superficial and deep digital flexor tendons medially and laterally to expose the joints.
3. Remove articular cartilage from the distal intertarsal joint surfaces.
4. Pack autogenous cancellous bone into the joint space.
5. Use a pin and tension band wire technique similar to that described for proximal intertarsal subluxation with plantar instability, but slightly modified.
   a. Insert an appropriate size intramedullary pin ($^{5}/_{64}$–$^{1}/_{8}$ inch) down through the calcaneus; extend through the fourth tarsal bone and continue into the distal half of the fourth metatarsal bone.
   b. Drill transverse holes for the tension band wire (18 or 20 gauge) in the distal one-third of the calcaneus and the bases of two or three of the metatarsal bones.
   c. Place the wire in a figure-eight pattern under the superficial digital flexor tendon.
6. Alternatively, perform the tarsometatarsal arthrodesis with a bone plate. Use bone screws to secure two holes of a five-hole plate to the fourth and central tarsal bones and distal tarsal bones proximal to the subluxation, and three holes to the metatarsal bones distal to the subluxation.

Postoperative Care

- Maintain a short semi-supple softcast coaptation splint until there is radiographic evidence of bony fusion.

OTHER INTERTARSAL-TARSOMETATARSAL SUBLUXATION INJURIES

Proximal Intertarsal Subluxations with Dorsal Instability

- Physical examination findings include
  - Primary damage of the dorsal ligaments and dorsal joint capsule.
  - Frequently, concurrent lateral or medial instability.
  - Usually, no evidence of external trauma.
- The animal places full weight on the limb with only periodic lameness, which is made worse by coincident lateral or medial instability.
- Diagnose by palpation and stress radiographs.
- Slight dorsal swelling and increased flexion and opening of the dorsal joints are seen.
- Lateral or medial instability may be concurrent with dorsal laxity.

Treatment

- If possible, manage the instability with rigid coaptation splints.
- Surgical repair may be necessary if
  - Injuries are severe.
  - The instability does not respond to splinting.
  - Dorsal ligament damage is associated with lateral or medial damage.
  - The affected animal is a large, athletic dog.

Surgical Technique

1. Fix the dorsal instability with a neutralization bone screw placed from the medial side of the head of the talus, diagonally into the distal tarsal bones.
2. Remove articular cartilage before screw placement.
3. Supplement with an appropriately positioned figure-eight tension band wire for concurrent lateral or medial instability; a neutralization screw may not be needed.

Postoperative Care

- Postoperatively, maintain a semi-supple softcast coaptation splint for 6 weeks.
  - Perform progressive controlled mobilization with the softcast.
  - Remove the screw or tension band wire if it loosens.

Distal Intertarsal Subluxation with Dorsomedial Instability

- This type of subluxation can occur alone or combined with other areas of instability involving the tarsus.
- Diagnose by palpation and stress radiographs.
- Valgus deformity and dorsomedial instability are seen.
- Stabilize with a medially positioned tension band wire.

Surgical Technique

1. Place a bone screw in the central and fourth tarsal bones proximally, and a second screw in the second, third, and fourth tarsal bones distally.
2. Secure a figure-eight wire (20 or 22 gauge) around the screws.

Postoperative Care

- Postoperatively maintain a semi-supple softcast coaptation splint below the stifle for 6 weeks. Perform progressive controlled mobilization with the softcast.

Tarsometatarsal Subluxation with Dorsomedial Instability

- Stabilize with a medially positioned tension band.

Surgical Technique

1. Place a bone screw in the central and fourth tarsal bones proximally, and a second screw in the second and fourth metatarsal bones distally.
2. Secure a figure-eight wire around the screws.

Postoperative Care

Postoperatively, maintain a semi-supple softcast coaptation splint below the stifle for 6 weeks. Perform progressive controlled mobilization with the softcast.

Tarsometatarsal Subluxation with Dorsal Instability

- This is a subtle injury that requires stress radiographs to confirm the diagnosis.
- If possible, stabilize with rigid coaptation splints.
- Injury in a large dog or chronic injury may require surgical arthrodesis, using a pin and tension band wire or bone plate technique.
- Alternatively, the arthrodesis can be done by inserting cross-pins from the proximal metatarsal bones into the distal tarsal bones.
- Postoperatively, maintain a semirigid softcast coaptation splint below the stifle for 6 weeks. Perform progressive controlled mobilization with the softcast.

Luxation of the Head of the Talus, the Central Tarsal Bone, and the Talocalcaneus

- These types of luxation occur as an isolated injury or with concomitant tarsal joint instability. Usually, luxation of the head of the talus and the talocalcaneal luxation are the result of relatively high-energy trauma.

Surgical Technique

1. Reduce the luxated tarsal bone(s) and stabilize with a cortical bone screw.
   a. For luxation of the head of the talus or talocalcaneal luxation, insert a neutralization screw from the talus to the calcaneus.
   b. For the central tarsal bone luxation, insert a neutralization screw from the central tarsal bone to the fourth tarsal bone.
   c. Place the screw so that the luxated bones are held in position (neutralized). Do not compress the bones.

Postoperative Care

- Postoperatively, maintain a semirigid softcast coaptation splint below the stifle for 6 weeks. Perform progressive controlled mobilization with the softcast.

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Chapter

113 Orthopedic Disorders of the Distal Extremities

Steven C. Budsberg

Disorders of the extremities distal to the carpus and tarsus usually result from direct trauma. Most abnormalities involve bone fracture and/or ligament damage associated with joint instability. The majority of fractures involve the metacarpal and metatarsal bones. Animals are usually presented with acute, non–weight-bearing lameness. Regardless of the bone being managed, internal fixation, external coaptation, or a combination of both can be used. Most surgeons prefer to use external coaptation whenever possible to manage fractures in these areas. In contrast, ligamentous injuries and associated joint instability rarely respond to external coaptation and often require surgical intervention. If fractures are open, proper open wound management is required before fracture fixation. Follow the generally accepted principles of fracture repair, including adequate reduction, alignment, and stable fixation, for the successful management of these injuries.

METACARPAL AND METATARSAL FRACTURES

Anatomy

The metacarpal and metatarsal bones are numbered 2 to 5, from medial to lateral. There are usually five metacarpal and four metatarsal bones. The third and fourth bones bear most of the forces transmitted through the foot.

Each bone is divided into the proximal base, middle body, and distal head.

Body Fractures

Body fractures may involve one or more bones. Racing animals may develop stress fractures of these bones. Closed reduction and coaptation usually are effective, but internal fixation may be required in cases involving multiple limb trauma, multiple bone fractures, and comminuted, severely displaced, or unstable fractures.

Preoperative Considerations

- Rule out associated injuries with a thorough physical examination and appropriate diagnostic tests.
- Identify the bone and region involved.
- Determine the type of injury (e.g., soft tissue, open or closed fracture, degloving injury).
- The number of bones involved affects treatment.
- Indications for external coaptation include
  - Single-bone fractures.
  - Multiple, non-displaced fractures without other limb trauma.
  - Fractures that have a combination of external coaptation with appropriate internal fixation (e.g., intramedullary pins, screws, plates).
- Indications for internal fixation include
  - Multiple bone fractures with severe displacement.
  - Combined fractures of the third and fourth bones.
  - Additional limb injury.
  - Fracture in working or show dogs.
  - Open fractures.
  - Articular fractures.

Surgical Procedure

Objectives

- Reduce and stabilize the fractures.
- Maintain viable soft tissues.
- Preserve joint function.

Equipment

- Standard surgical pack and suture material
- Kirschner wire (K-wire) (various sizes)
- Mini-fragment plates and screws (1.5, 2.0, and 2.7 mm)
- Small self-retaining retractors
- Small bone-holding forceps

Technique

1. Place the patient in dorsal recumbency, clip the hair, and prepare the extremity for aseptic surgery.

▼ ***Key Point*** Because of the central (metacarpal, metatarsal) and digital pads, surgical approach via the palmar or plantar surfaces of the metacarpal and metatarsal bones is contraindicated.

2. Make a dorsal incision directly over the affected bone or joint.
   a. To approach a single bone, make a longitudinal incision directly over the bone. To expose adja-

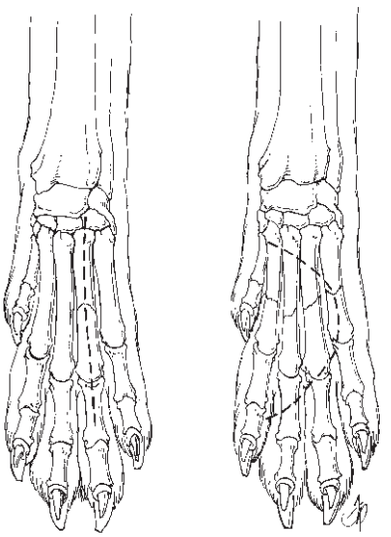

Figure 113-1. Dorsal incision lines for metacarpal fractures of a single bone *(left)* or multiple bones *(right)*.

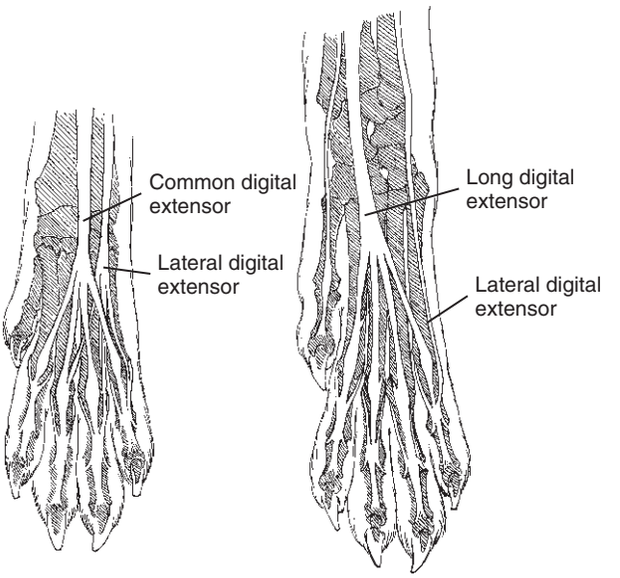

Figure 113-2. Important tendons of the metacarpus *(left)* and metatarsus *(right)*.

cent bones, make the incision between them, if necessary.

b. To approach multiple bones, make two parallel longitudinal incisions or a curved incision incorporating the entire dorsal region (Fig. 113-1).

3. Incise the deep fascia directly over the bone.
   a. In the metacarpus, identify and retract the major tendons (i.e., the tendons of the common digital extensor and lateral digital extensor muscles).
   b. In the metatarsal region, take care to protect the tendon of the long digital extensor muscle (Fig. 113-2).
4. Intramedullary pinning for fracture repair:
   a. Antegrade the pins from distal to proximal through a predrilled hole in the dorsal surface (Fig. 113-3). (Make the predrilled guide hole with a pin one size larger than the intended intramedullary pin.) Bend the pin ends slightly to facilitate removal and to avoid entering the metacarpo(tarso)phalangeal (MP) joint.

▼ ***Key Point*** When passing pins in an antegrade fashion, use a hand drill rather than a power drill to allow the pins to "bounce off" (instead of penetrating) the palmar/plantar cortex.

   b. Alternatively, retrograde the pins from the fracture site to the predrilled hole in the dorsal cortex, reduce the fracture, and seat the pins in the proximal segment (Fig. 113-4).

▼ ***Key Point*** Fixation with single intramedullary pins can accomplish reduction and alignment; however, this procedure does not provide rotational stability to the fracture.

   c. Use supplementary external coaptation of fiberglass (molded half-circumference cast) or metal

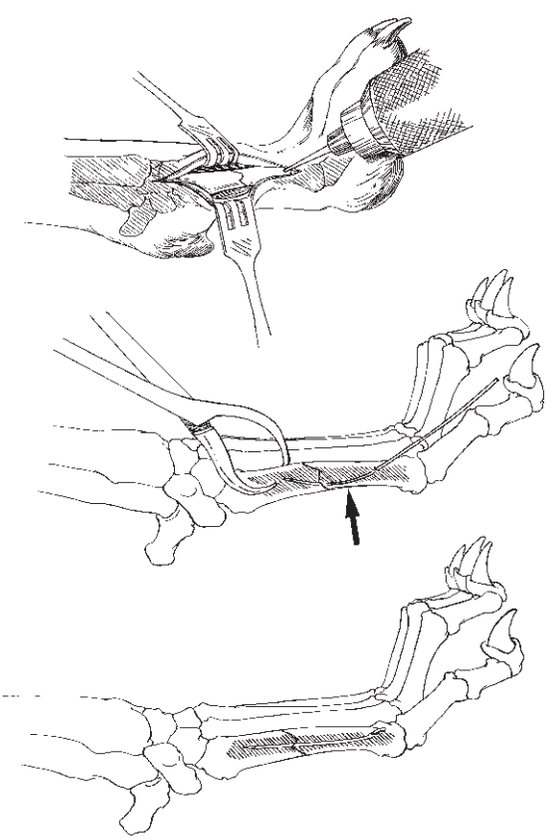

Figure 113-3. Placement of an intramedullary pin for repair of a metacarpal fracture. The center view shows how the pin is "bounced off" the palmar cortex *(arrow)*.

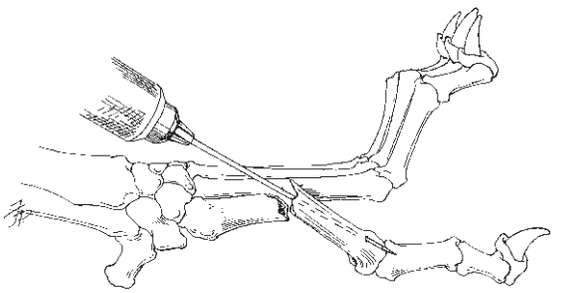

Figure 113-4. Retrograde placement of an intramedullary pin from the fracture site to a predrilled hole in the dorsal cortex.

(palmar/plantar splint) to augment internal fixation.

5. Plate fixation:
   a. For fixation of the third and fourth bones, place the plates on the dorsal surface. For fixation of the second and fifth bones, place the plates on the medial and lateral surfaces, respectively, or dorsally.
   b. A minimum of four cortices of screw purchase above and below the fracture is required.
   c. Perform supplementary external coaptation, as described previously.
6. Lag screw fixation:
   a. Use in oblique fractures, primarily the first, second, and fifth metacarpals and the second and fifth metatarsals.
   b. Perform supplementary external coaptation.
7. Close the incision routinely.

Base and Head Fractures

Preoperative Considerations

- Base fractures usually involve the second and fifth metacarpals, owing to ligamentous attachment; avulsion fractures commonly are seen. Valgus and varus displacement often is noted.
- Internal fixation is strongly recommended.
- Non-displaced fractures may be treated with a palmar splint; however, some displacement usually occurs. Delayed union may be a problem because of the motion from ligamentous attachment.
- Head (articular) fractures usually have concurrent subluxation or complete luxation of the MP joint owing to the collateral ligament attachment.
- Reconstruction of the articular surface is required.

Surgical Procedure

Objectives

- Reduce and stabilize the fracture.
- Repair or reconstruct ligament instability of the joint.
- Reconstruct the articular surface, if necessary.

Equipment

- Same as for body fractures, described previously.

Technique

1. The approach is the same as for body fractures, described previously.
2. In base fractures, fix with lag screws or a tension band technique. Use supplementary external coaptation.
3. In head fractures, use Kirschner and cerclage wires or a combination K-wire and hemicerclage technique. Use supplementary external coaptation.
4. Close the incision routinely.

Postoperative Care and Complications

▼ ***Key Point*** Management of soft tissue injuries in open fractures is as important as internal fixation.

- Maintain external coaptation in combination with intramedullary pins and lag screw fixation until there is clinical union of the fracture. Animals with plate fixation require coaptation for approximately 4 weeks.
- Remove intramedullary pins following clinical bone union. In working dogs, also remove plates. Lag screws and plates in non-working animals may be left in permanently.
- If postoperative bleeding is anticipated, apply a pressure bandage for 48 to 72 hours to minimize hemorrhage.
- In all cases, control and limit exercise until clinical bone union (usually 6–10 weeks).
- Rarely, delayed union and nonunion may result from inadequate stabilization. Excessive proliferative callus formation may cause tendon entrapment and/or pain.
- Valgus or varus deviation may result from undetected or untreated concurrent collateral ligament damage.
- If joint surfaces are involved, degenerative joint disease may develop.
- Treat tissue swelling with warm compresses or hydrotherapy.

PHALANGEAL FRACTURES

Phalangeal fractures are similar to metacarpal and metatarsal fractures. They usually are single injuries; however, they may occur in association with other, more severe multiple injuries to the paw.

Anatomy

- Each digit consists of a proximal phalanx and a distal phalanx. The phalanges are numbered similar to the metacarpals and metatarsals.
- The proximal and middle phalanges are divided into a proximal base, middle body, and distal head.
- The distal phalanges are approximately the same size in all digits and are partially covered by the nails.
- *Dewclaw* is the term applied to the variably developed first digit of the hind paw.
- Polydactyly (extra digits) is common in cats.

Preoperative Considerations

- Same considerations as metacarpal and metatarsal fractures.
- Open, severely comminuted fractures may require digit amputation (see Chapter 114).
- Most fractures can be reduced closed and immobilized in a fiberglass splint.
- Some of the indications for internal fixation include
  - Large working dogs or racing animals.
  - Articular fractures involving the base or head.
  - Failed external coaptation.

Surgical Procedure

Objectives

- See under "Metacarpal and Metatarsal Fractures."

Equipment

- The same as for metacarpal and metatarsal fractures, discussed previously

Technique

1. Make an incision directly over the affected bone.
2. Articular fractures require anatomic reduction and fixation with lag screws, orthopedic wire sutures, K-wire, or a combination of these.
3. Treat body fractures with miniplates or (for oblique fractures) cross pins and lag screws.

Postoperative Care and Complications

- See under "Metacarpal and Metatarsal Fractures."
- External coaptation is required until clinical bone union.

PALMAR AND PLANTAR SESAMOID INJURIES

Fractures of the sesamoid bones of the MP joints usually are seen in racing greyhounds. However, they can cause lameness in any dog, particularly large-breed animals. Signs include sudden lameness with swelling and pain on palpation. Injuries of the second and seventh sesamoids are reported to be the most common.

Anatomy

- The sesamoid bones are numbered 1 to 8 medial to lateral (two for each MP joint).
- The sesamoid bone articulates primarily with the head of the metacarpal/metatarsal bone and secondarily with the palmar tubercles of each proximal phalanx.
- Occasionally, bipartite sesamoid bones are present and may be mistaken for fractures.

▼ ***Key Point*** Old sesamoid fractures or bipartite sesamoid bones may be mistaken as the cause of lameness.

Preoperative Considerations

- An acute injury requires external coaptation. Place the foot in a splint in slight flexion.
- Recurrent lameness requires surgical intervention.

Surgical Procedure

Objective

- Remove the damaged sesamoid.

Equipment

- Standard surgical pack and suture

Technique

1. Make an incision adjacent to the metacarpal/metatarsal pad, with the middle of the incision directly over the MP joint.
2. Slightly undermine the pad to allow retraction and further deep dissection of the affected sesamoid bone.
3. Identify the distal venous arch on the proximal aspect of the incision.
4. Dissect directly over the sesamoid bone and move the flexor tendon to the side if necessary.
5. Transect the sesamoid ligaments and remove the offending fragments.
6. If less than one-third of the total bone is fragmented, leave the larger fragment and remove the smaller one.
7. Close each incised fascial plane with simple interrupted sutures of an absorbable suture material.
8. Close the remainder of the incision routinely.

Postoperative Care and Complications

- Place a snug padded bandage on the paw for 7 to 10 days.
- Limit exercise for 2 weeks and gradually increase to normal by 6 weeks.
- Complications are rare.

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Chapter

114 Amputation of the Digit

Mark C. Rochat

ANATOMY

Distal Phalanx (Cats)

- The proximal end of the third or distal phalanx (P_3) is concave and has a dorsal ungual crest (Fig. 114-1).
- The distal end of P_3 (the ungual process) is covered by a keratinized claw or unguis.
- The ungual crest is a crest-shaped bony shelf that overlies the root of the claw.
- The stratum germinativum contains the germinal cells of the claw and extends into the ungual crest.

Dewclaw (Dogs)

- The dewclaw is the medial or first digit of the rear limb in the dog. The first phalanx and P_2 are often missing, and P_3 and the claw are attached only by skin and fibrous tissue.
- In some breeds, there are two dewclaws. Double dewclaws are breed standard specific in Great Pyrenees and briards and should not be removed.
- The dewclaw articulates with metatarsal bone I, which is often small and may be fused to tarsal bone I.
- If two dewclaws are present, there may be, on occasion, complete duplication of the phalanges and metatarsal bone I. Metatarsal bone I may also exist as two segments united by fibrous tissue or present with a distinct joint between the segments.

Digits (Dogs and Cats)

- The digits consist of three phalanges (P_1, P_2, and P_3) and a nail or claw. The first digit in the front foot does not have a middle phalanx (P_2); the first digit in the rear foot is properly termed the dewclaw.
- The proximal interphalangeal (PIP) and distal interphalangeal (DIP) joints are connected axially and abaxially by collateral ligaments. The DIP joint is also connected by a dorsal elastic ligament that spans from the dorsal aspect of P_2 to the ungual crest of P_3.
- The superficial digital flexor tendon attaches to the proximal (palmar or plantar) end of P_2; the deep digital flexor attaches to a rounded tubercle on the palmar or plantar aspect of P_3; the lateral and common digital extensor tendons attach to the extensor processes of P_3.
- A digital pad is located on the palmar and plantar aspect of the distal interphalangeal joint of each digit, except for the first one. A single large metacarpal or metatarsal pad is located on the palmar and plantar aspects, respectively, of the metacarpophalangeal and metatarsophalangeal joints.
- The blood supply is via dorsal and palmar (or plantar) proper digital arteries; venous drainage is via dorsal and palmar (or plantar) proper digital veins.
- The nerve supply to the digits is the dorsal and palmar (or plantar) dorsal digital and dorsal proper digital nerves. Of more functional significance are the nerves that innervate the foot as a whole, the superficial radial, ulnar, and median in the front foot and the tibial, peroneal, and saphenous in the rear foot. Perform nerve blocks with long-acting local anesthetics whenever foot surgery is performed (see Chapter 6).

ONYCHECTOMY (CATS)

Onychectomy often is performed on house cats as an elective procedure; however, it may be necessary to perform this procedure when a claw is severely traumatized or infected or when neoplasia is present.

Preoperative Considerations

- Kittens and young cats recover from declawing quicker than older cats.
- Many owners are unaware of what a declaw procedure involves. An accurate and frank discussion of the procedure, with anatomic charts, often eliminates confusion and misinformation about the procedure and allows the owner to make an informed decision.
- Inform owners that declawing removes, to varying degrees, the cat's ability to escape or defend itself. This is especially true when all four feet are declawed. Therefore, most cats should be kept indoors as house pets after declawing. Behavioral issues may develop in multi-cat households when some cats are declawed and others are not.
- It is seldom necessary to remove the claws of the rear limbs. If the owner desires declawing of the rear feet, the consequences should be frankly discussed and

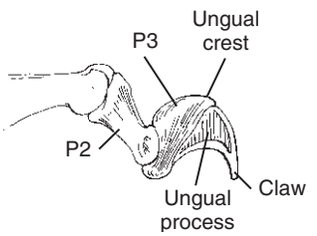

Figure 114-1. Regional anatomy of the distal phalanx of the cat.

other options explored prior to performing the procedure.
- Alternatives to declawing include simple nail trimming on a regular basis, behavioral modification, vinyl caps, and deep digital flexor tenectomy.

▼ ***Key Point*** The germinal cells of the claw extend into the ungual crest. To prevent claw regrowth, completely remove the ungual crest.

Surgical Procedure

Objectives

- Completely remove the claw(s).
- Protect the digital pad.
- Prevent excessive blood loss.
- Prevent nerve and vascular damage to the limb.

Equipment

- Appropriate tourniquet (e.g., Penrose drain)
- Sterile Kocher forceps
- Sterile scalpel blade (#11) and handle (#3 or #7)
- Sterile surgical gloves

Or:

- Appropriate tourniquet
- Sterile Kocher forceps
- Sterile guillotine-type nail trimmers (e.g., Resco); reserve a clean, sharp trimmer for declaws only and replace the blade periodically as it dulls
- Sterile surgical gloves

Or:

- Kocher forceps
- Sterile surgical gloves
- CO_2 laser

General Technique

1. Prepare the entire foot with a germicidal soap followed by solution. Chlorhexidine is preferred.
2. Block the regional nerves with bupivicaine (0.2–0.15 ml of a 0.5% solution at each site).
3. Place a tourniquet below the elbow. Exsanguinate the limb to the level of the tourniquet with an Esmarch bandage or hands prior to tightening or inflating the tourniquet. A Penrose drain and Kelly forceps (with tips curving away from the limb if using curved forceps) work reasonably well. Do not use rubber bands or black rubber tourniquets. Use of a CO_2 laser may eliminate the need for a tourniquet.

Scalpel Technique

1. Extend the claw by grasping the claw with Kocher forceps. Rotate the forceps and claw downward while tractioning the limb towards you.
2. Hold the scalpel like a paintbrush. Orient the blade transversely to the digit. Beginning at the junction of skin and claw, push the skin proximally, tensing the skin over the DIP joint, and press the scalpel blade downward to cut through the skin, dorsal elastic ligament, digital extensors, and joint capsule.
3. Without removing the blade, rotate the blade either laterally or medially to incise the skin from the dorsal incision to the distal aspect of the footpad. Remove the blade and incise the skin on the opposite side of the claw.
4. Further rotate the forceps and claw downward with distal traction to open the DIP joint. While mentally visualizing the shape of the DIP joint, carefully incise the joint capsule and collateral ligaments on either side of the joint. Stressing the joint laterally or medially will make the tissues give way as they are incised and make it easier for you to define the dissection plane.
5. When you reach the caudal aspect of the DIP joint, relax the limb tension to lessen the risk of cutting through the pad. Continue to rotate the forceps and P_3 downward and keep the edge of the blade always directed towards P_3. The attachment of the deep digital flexor tendon to P_3 can make dissection more difficult. Careful filleting of the tendon from the bone is required to avoid cutting downward through the pad (Fig. 114-2).
6. Continue the dissection distally around the palmar aspect of P_3 with the blade directed towards the bone until P_3 is severed. When the dissection is complete the digital pad should be intact and separated from the small hole by a short span of skin.
7. Removal of the claw on the first digit is more difficult because of the way the digit projects medially. While holding the Kocher forceps with thumb and forefinger, the remainder of the paw can be pushed away from the digit (in effect, adducting the digit) with your remaining fingers (right paw for a right-handed surgeon) or with your thumb (left paw for a right-handed surgeon).

Nail Trimmer Technique

1. Position the nail trimmer so the arch encircles the dorsal aspect of the distal interphalangeal joint and the blade rests at the distal margin of the digital pad. The trimmer can be used upright or tuned upside down, depending on the preference of the surgeon.

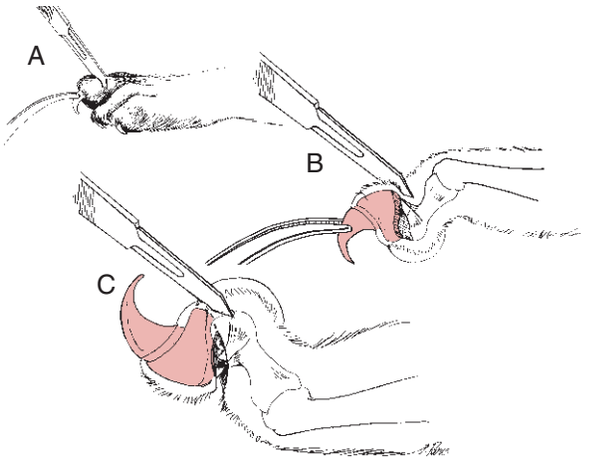

Figure 114-2. Scalpel technique for cat declaw. The deep digital flexor tendon is filleted from its attachment to the base of P_3. See text for details.

2. Use either fingers or forceps to hold the claw.
3. Pull the arch of the trimmer over the ungual crest and into the gap between P_2 and P_3 as much as possible. While holding the trimmers in the gap between P_2 and P_3, close the blades. Slightly release the tension on the blade as you rotate the claw upward to allow the blade to slip proximal to the flexor process. Squeeze the trimmer handle to cut through P_3.
4. When using nail trimmers, it is common to leave a small portion of the flexor process of P_3. This piece of bone, if the trimmers were properly positioned, is usually small and of no functional significance. If the piece seems subjectively large, grasp with forceps and remove with a scalpel.

Carbon Dioxide Laser Technique

1. Grasp the claw with Kocher forceps in the same manner as for the scalpel technique. Use the CO_2 laser in much the same manner as the scalpel. Direct the laser beam towards P_3 to avoid injury to the adjacent condyle of P_2 and the digital pad. Use standard laser safety precautions at all times.

Closure and Bandaging

1. Count all claws when you are finished to make certain all claws have been removed.
2. Leave the incisions open or, alternatively, close the incisions with tissue glue or with a single, absorbable, 4-0, monofilament suture. Tissue glue impedes wound healing and enhances the risk of infection if the glue is placed between the skin edges of the incision. Apply tissue glue on the surface of the skin at the incision site after careful apposition of the incision edges.
3. After completion of the procedure, apply a snug-fitting bandage to the level of the distal antebrachium. Avoid excessive tightness of the proximal portion of the bandage to ensure adequate blood supply to the paw. Declaws performed with a CO_2 laser may not require bandaging.
4. If a bandage is applied, do so prior to removing the tourniquet.

Postoperative Care and Complications

Short Term

- Bleeding after bandage removal occasionally is a problem and is usually self-limiting. Remove the bandages and observe the cat for several hours prior to discharging the cat to its owner. Hemorrhage from the site often appears significant but is usually less severe than it initially appears. If hemorrhage is truly severe, replace the bandage, and then remove in 12 to 24 hours. Do *not* place the bandage too tightly in an effort to achieve hemostasis; tissue necrosis may result.
- Lameness and pain are prolonged if the pad is cut. Careful technique prevents this complication.
- Neuropraxia and/or tissue necrosis may occur if the tourniquet is improperly used. Neuropraxia usually resolves in 4 to 6 weeks but may be permanent. Proper technique prevents this complication.
- Excessively tight bandages can result in tissue necrosis. Proper technique prevents this complication.
- Protrusion of the second phalanx can occur, especially if the skin incision is large or part of the pad has been removed. Debride the bone end if necessary, irrigate and close the wound, and administer oral antibiotics for 7 to 10 days.
- Infection is uncommon if the surgical site is properly prepped, the surgical dissection and operative time are kept to a minimum, and the cat is confined indoors and uses paper litter until the incision is healed. Treat infection by establishing drainage at the distal extremity and administering systemic antibiotics.

▼ ***Key Point*** Keep the cat indoors, and use shredded paper as cat litter for 2 weeks after surgery. Never use commercial cat litter because it will work its way into the wound and create tissue irritation and infection. The cost, lost time, client dissatisfaction, and pain for the cat are often significant and best avoided by stressing the need for paper litter verbally to the owner and in written discharge orders.

Long Term

- Regrowth of a deformed nail can result from incomplete removal of the ungual crest. Perform disarticulation of the distal interphalangeal joint with a scalpel.

- Chronic lameness may result from incomplete removal of P_3 or trauma to the digital pad. Remove the piece of bone with a scalpel.

DEWCLAW REMOVAL (DOGS)

Dewclaw removal is usually an elective procedure, although the claw may become traumatized, especially if it is only loosely attached to the skin.

Preoperative Considerations

- Removal of the dewclaw for cosmetic reasons is best performed in the neonate.

Surgical Procedure

Objectives

- Remove dewclaw and minimize scarring on the medial aspect of the foot.

Equipment

- Standard surgical pack including #3 scalpel handle and #15 scalpel blade, curved Mayo scissors, Kelly forceps, Adson or Brown-Adson tissue forceps, curved Halsted mosquito forceps, needle holders, operating scissors
- Suture material, 3-0 to 4-0 monofilament, absorbable on a cutting needle
- Bone cutters if the metatarsophalangeal articulation exists
- Sterile surgical gloves

Technique

Neonates

1. Surgically scrub the dewclaw and surrounding area.
2. Infiltrate the base of the claw with 0.75 to 0.5 mg/kg of lidocaine (without epinephrine) and 0.5 to 0.25 mg/kg of bupivicaine mixed together in a tuberculin syringe and inject using a 25-gauge needle.
3. Grasp the nail with small forceps and abduct it from the metatarsal bone.
4. With scissors, cut the dewclaw from its attachment to the metatarsal bone.
5. Achieve hemostasis by direct pressure or silver nitrate sticks.
6. Use a single absorbable suture to close the skin or leave the small incision open. No bandage is necessary.

Older Animals

1. Anesthetize the animal and block the saphenous, tibial, and peroneal nerves with 0.2 to 0.4 ml of 0.5% bupivicaine at each site.
2. Prepare the foot for aseptic surgery.
3. Make an elliptical incision around the base of the dewclaw.
4. Ligate the metatarsal and the dorsal proper digital arteries.
5. If only soft tissue attachment exists from the dewclaw to the metatarsal bone, remove the dewclaw and close the skin. If a bony attachment exists, disarticulate P_1 from metatarsal bone I with a scalpel.
6. Alternatively, use bone cutters to transect P_1 close to its base.
7. Close the skin routinely.
8. Place a bandage over the foot for 5 to 7 days.

Postoperative Care and Complications

- Prevent infection by good surgical technique
- Treat infection by drainage and oral antibiotics for 7 to 10 days.
- For adult dogs, treat pain with NSAIDs for 2 to 3 days.
- Hemorrhage is treated by direct pressure and bandaging. Ligate the bleeding vessel if the hemorrhage is severe and uncontrolled by the above methods.
- Scar formation at the site may be caused by the animal removing sutures prematurely, leading to wound dehiscence. Prevent this complication with good surgical technique and an Elizabethan collar and/or a bandage.

DIGIT REMOVAL (DOGS AND CATS)

Digit amputation in dogs and cats usually is performed because of severe trauma, osteomyelitis, or neoplasia. The level of amputation depends on the condition and the site of involvement. The digit may be removed at the metacarpophalangeal joint, metatarsophalangeal joint, PIP joint, or DIP joint or by osteotomy of the bones of the affected digit.

Preoperative Considerations

- Digit amputation proximal to the distal interphalangeal joint may necessitate digital pad removal, but it is preferable to maintain the digital pad when possible.
- The primary weight-bearing digits are the third and fourth, but significant weight is also borne by the second and fifth digits.

Surgical Procedure

Objectives

- Remove the digit.
- Minimize blood loss.

Equipment

- Standard surgical pack including #3 scalpel handle and #15 scalpel blade, curved Mayo scissors, Kelly forceps, Adson or Brown-Adson tissue forceps, curved

Halsted mosquito forceps, needle holders, operating scissors
- Suture material, 3-0 to 4-0 monofilament, absorbable on a cutting needle
- Bone cutters if osteotomy is to be performed

Technique

1. Anesthetize the animal and block the median, ulnar, and radial nerves (front foot) or the tibial, peroneal, and saphenous nerves (rear foot) with 0.2 to 0.4 ml of 0.5% bupivicaine at each site (see Chapter 6).
2. Prepare the foot for aseptic surgery. A hanging limb technique is often helpful.
3. Place a tourniquet below the elbow. Exsanguinate the limb to the level of the tourniquet with an Esmarch bandage or hands prior to tightening or inflating the tourniquet. Non-adhesive bandage material that stretches can be used but may not adequately control arterial inflow and may worsen the hemorrhage at the surgical site. Do not use black rubber tourniquets because there is a greater risk of nerve and muscle damage due to the tight narrow band of compression they create. Do not use rubber bands as tourniquets.
4. For digit removal distal to mid-P_2, make a transverse incision on the dorsal aspect of the digit around to the digital pad.
   a. Ligate the digital arteries and veins.
   b. Disarticulate the digit at the distal interphalangeal joint, after transecting the flexor and extensor tendons. Alternatively, use bone cutters and transect P_2.
   c. Suture the subcutaneous tissue of the pad to the extensor tendon with absorbable suture material and close the skin routinely.
5. For digit removal proximal to mid-P_2, make an elliptical incision at the base of the digit (Fig. 114-3).
   a. Ligate the vessels and disarticulate the digit with a scalpel or cut the bone with bone cutters (see Step 2b previously).
   b. A proximal extension of the elliptical skin incision usually facilitates cosmetic closure of the skin (see Fig. 114-3).
   c. If digit 2 or 5 is amputated, an oblique osteotomy facilitates a tension-free closure and provides a more cosmetic appearance to the foot.
   d. Close the subcutaneous and skin layers routinely.

Figure 114-3. Skin incision for digital removal proximal to mid-P_2.

Postoperative Care and Complications

- Apply a bandage to the foot for 7 to 10 days. Keep the bandage clean and dry.
- Remove skin sutures 10 to 14 days postoperatively.
- Submit the removed tissue for histopathologic examination.
- Hemorrhage is usually controlled with ligation of the associated vessels and direct pressure via bandages.
- Infection is prevented by proper surgical technique. Treat by drainage and oral antibiotic therapy until the infection is resolved (usually 7–14 days).
- Treat dehiscence by proper wound management until the incision is healthy followed by wound closure without tension. Apply padded bandage to reduce the tension on the incision and lessen the risk of dehiscence recurring.
- Neuropraxia and/or tissue necrosis may occur if the tourniquet is improperly used. Neuropraxia usually resolves in 4 to 6 weeks but may be permanent. Proper technique prevents this complication.
- Recurrence of tumor can occur depending on the tumor type and surgical technique. Preoperative review of fine needle aspirates or incisional biopsies will usually identify tumors that are likely to have extended margins. The risk of recurrence of tumor at the surgical margins is best prevented by wide resection of the tumor.

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Chapter

115 Surgery of Skeletal Muscle and Tendon

Matthew Palmisano

Injuries to skeletal muscle and tendon are frequently seen in small animal practice. Injuries to skeletal muscle can either occur secondary to strain from high-impact activity, or result from lacerations, either externally from sharp objects or internally from fracture ends. Injuries to tendons most commonly occur secondary to sharp trauma.

Muscles and tendons heal by the same mechanism found in all tissues of the body. However, muscles and tendons are unique in that they have to be able to generate and resist great tensile forces in order to function properly. Minimizing scar tissue formation is clinically important because it is weaker than healthy muscle and tendon. Apposition of the ruptured ends (i.e., with suture) minimizes scar tissue formation. Early but controlled motion and stress across the wound results in a stronger healed wound. Balancing early motion against protecting the healing tissue from re-rupture is a clinical dilemma that is crucial to optimal healing of the injured tissue.

ANATOMY

Skeletal Muscle

- Skeletal muscle is composed of many muscle fibers, which are very long and cylindrical muscle cells. Each fiber has many peripherally located nuclei. Muscle fibers are grouped into bundles, or fascicles. Each muscle fiber is composed of myofibrils, which are the basic subunit of skeletal muscle.
- The whole muscle is encased in a thick connective tissue called the epimysium. The perimysium binds myofibers into groups to form fasciculi and carries blood vessels and nerves. The endomysium is a sparse, reticulated connective tissue between the muscle fibers and carries blood capillaries and nerve fibers.
- Each myofiber contains a single terminal branch of a motor axon that finishes close to the sarcolemma (muscle cell wall) at the motor end plate.

Tendon

- Tendons are composed of long bands of collagen fibers arranged in parallel rows and are embedded in ground substance and extracellular fluids. The fibroblast (or tenocyte) is the cellular component of tendon fibers.
- Collagen fibers are surrounded by a woven mesh of loose areolar connective tissue called the endotenon. The endotenon allows longitudinal movement of the collagen bundles and carries all of the blood vessels, lymphatics, and nerves. The epitenon covers the entire tendon, and is continuous on its undersurface with the endotenon.
- Free gliding is provided by the outer sheath of the tendon called the paratenon. The paratenon covers and separates tendons from each other. The paratenon forms a synovial membrane in areas of local pressure.
- Blood supply to tendons enters at three locations. Blood vessels entering at the musculo-tendinous junction supply the proximal one-third of the tendon. Blood vessels penetrating longitudinally in the paratenon or synovial sheath supply the middle one-third of the tendon, while the distal one-third of the tendon is supplied by vessels at the bone-tendon insertion.
- Vascular tendons are surrounded by soft tissue, while avascular tendons are surrounded by a tendon sheath. Avascular tendons have the disadvantage of a poor blood supply, which may lead to poor healing and adhesions between the tendon and tendon sheath.

Healing of Muscle

- Muscle can be injured by contusion, ischemia, denervation, sprains, and ruptures. The type and severity of the injury determines whether the muscle will heal with functional myofibers or scar tissue.

▼ ***Key Point*** Healing of muscle by scar tissue is undesirable because it decreases the ability of the muscle to produce tension by 50%.

- The following classification system for muscle injury is based on the severity of the injury and resulting muscle damage:
  - Grade I: Tearing of a few muscle fibers, intact muscle fascia and minimal hemorrhage.
  - Grade II: More severe muscle tearing than grade I, with hematoma formation.
  - Grade III: Tearing of a large amount of muscle. Muscle fascia is torn, so hemorrhage can be diffuse.
  - Grade IV: Complete rupture of one or more muscle bellies.
- Factors that cause an increase in the amount of scar tissue are a poor source of healing myoblasts, poor vascularization or innervation, and excessive stress across the healing wound. Vascular supply is a very important factor for healing. The rate of vascular ingrowth is approximately 0.5 to 1 mm per day. Therefore, large areas that cannot revascularize quickly heal with scar tissue.
- Dense fibrous tissue prevents regeneration of muscle fibers across the wound. Factors causing excessive scar tissue formation include a large gap across the wound and inappropriate stress or motion across the wound during the healing period. Therefore, there is a delicate balance between early return to function versus immobilization. Early motion across the wound promotes desirable parallel orientation of regenerating muscle fibers, but it may also promote excessive granulation tissue formation. This would cause poor penetration of regenerating muscle fibers through the connective tissue scar.
- Conversely, prolonged immobilization decreases scar tissue formation and allows penetration of regenerating muscle fibers, but also causes irregular orientation of muscle fibers, which would cause a decrease in tensile strength.
- Muscle fibers do not go across scar tissue, and only limited myofibril regeneration occurs in directly apposed muscle edges.

▼ ***Key Point*** Approximation of wound edges and duration of wound immobilization are critical for optimal healing of muscle injuries.

Healing of Tendon

- Tendons are often injured by sharp trauma, or the tendon may be surgically cut in order to increase exposure to a joint. Medical conditions, such as Cushing's disease, can cause tendon weakening and tearing. Injections of steroids into or around tendons can substantially weaken tendons for 2 weeks, and weakness persists for greater than 1 year.
- Tendons and ligaments follow the same pattern of healing. Factors affecting the quality of healing include
  - Healing across a gap versus apposition with suture.
  - Early mobilization versus immobilization.
  - Cause and location of the injury.
- Direct apposition of tissues using sutures and <1 mm gap provides optimal tendon healing. Fibroblasts within a wound form collagen by the fourth to fifth day. The border between the undamaged tendon and area of injury becomes indistinguishable by day 21. From 21 days to 1 year, scar tissue progressively recedes toward the site of initial injury until there is a small width of scar tissue interposed between readily distinguished tendon ends. The diameter of healing tendon is greatest at 3 weeks, decreases until week 14, and is unchanged 2.5 years after surgery. Tendons held in apposition with suture heal without interposed scar tissue and are difficult to distinguish from controls.
- Suturing must adequately prevent formation of a gap when the tendon is under tensile load for optimal healing.

Diagnosis of Muscle and Tendon Injury

- Muscle ruptures can be palpated as areas of discontinuity in muscle fibers or sheaths. In addition, there may be bruising or hematoma formation at the injury site. The degree of lameness and pain on palpation varies with the severity and chronicity of the injury. With tendons and ligaments, there may be abnormal laxity with the involved joint.
- Radiographs may show increased soft tissue opacity at the injury site due to swelling and hematoma. In addition, an avulsion fracture may be seen if the tendon has pulled off of the bone. Other imaging modalities that have recently shown promise in characterizing muscle or tendon injury include ultrasound and magnetic resonance imaging.

SURGERY OF SKELETAL MUSCLE

Surgical Procedure

Objectives

- Use gentle tissue handling.
- Preserve blood supply.
- Create a tension-free anastomosis.
- Remove excessive scar tissue or hematoma and perform accurate apposition of the muscle ends.

Equipment

- Standard soft tissue surgical instrument pack
- Self-retaining and hand-held retractors
- Non-absorbable, monofilament suture (e.g., polypropylene)
- Rubber tubing or Silastic buttons for tension relieving sutures

Technique

1. Use large non-absorbable monofilament suture, such as 2-0 or 0 prolene or nylon.

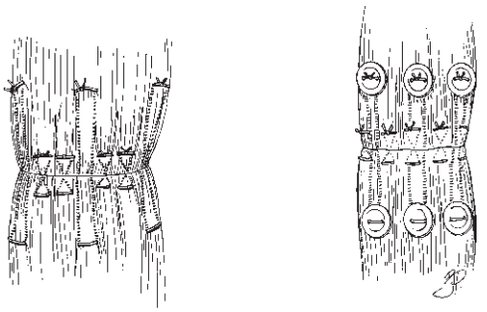

Figure 115-1. Suture patterns for muscle apposition. *Left,* Interrupted cruciate sutures with interposed deeper horizontal mattress sutures. *Right,* Silastic buttons prevent deep tension sutures from pulling out.

2. Use tension relieving suture patterns, such as horizontal mattress or cruciate patterns.
3. Muscle tissue holds suture poorly. Therefore, take large bites of tissue and utilize the dense, outer fascial layer to minimize suture pull-through.
4. If necessary, place plastic stents for greater holding power (Fig. 115-1).
5. Use Penrose drains or closed suction drains (e.g., Jackson-Pratt) if there is excessive dead space. Cover the drain with a soft padded bandage.

Postoperative Care

- Immobilize the limb using cast or splint coaptation for 2 to 3 weeks. After, gradually return to normal activity for another 4 weeks.
- Start physical therapy (see Chapter 95) after the immobilization period. Proper physical therapy is crucial for optimal return to function.

SURGERY OF TENDON

Preoperative Considerations

Many of the same surgical principles apply for surgery of tendon as surgery of skeletal muscle, such as direct apposition of tendon ends, gentle tissue handling, and postoperative immobilization to protect the tenorrhaphy.

Clean dirty or contaminated wounds and manage until tissues are healed enough to perform a delayed primary tenorrhaphy. Debride necrotic tissue. If tendons cannot be sutured at the time of the initial surgery, tag the tendon ends with suture in order to assist in identification later, when delayed primary tenorrhaphy can be performed. Manage open wounds with daily or twice-daily bandage changes. Wet-to-dry bandages may be useful in helping to further debride unhealthy tissue.

Surgical Procedure

Equipment

- Same as for muscle repair, described previously

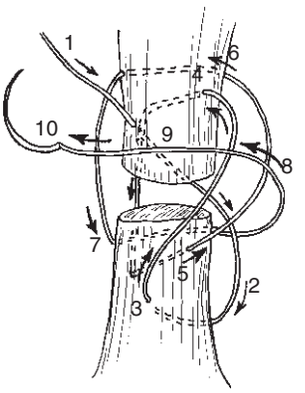

Figure 115-2. Three-loop pulley tenorrhaphy suture pattern. Needle passes follow numbered sequence and alternate in a near-far, middle-middle, and far-near pattern. Loops are oriented in separate planes and rotate approximately 120 degrees from each other.

Technique

1. Remove hematoma and scar tissue. Debride tendon ends to healthy tissue.
2. Two commonly used suture patterns are the locking loop (Kessler) and three-loop pulley. Use the largest diameter, non-absorbable, monofilament suture that will atraumatically pass through the tendon. 2-0 or 0 nylon or prolene is preferred.
3. The locking loop pattern is useful for flat tendons, such as the superficial digital flexor tendon and infraspinatus tendon. Recent studies have shown that more than one locking loop may be placed in order to increase tensile strength.
4. The three-loop pulley suture pattern is applicable to round tendons, such as the common calcaneal tendon. Studies have shown the three-loop pulley suture pattern to be superior to the locking loop pattern in regards to tendon-holding power and resistance to gap formation.
5. With the three-loop pulley suture pattern, place three different loops. Place the three loops, respectively, in a near-far, middle-middle, and far-near pattern. Rotate each loop 120 degrees in a different tissue plane (Fig. 115-2).
6. If the area of tendon injury is close to the bone, consider passing one or more of the suture loops through a bone tunnel in order to increase holding strength of the tenorrhaphy.

Postoperative Care

▼ ***Key Point*** Proper postoperative support of the repaired tendon, and staged return to activity, is critical for a successful repair.

- Place Penrose drains or closed suction drains if there is excessive dead space. Cover the drain with a soft padded bandage.

- Rigidly immobilize the joint involved using either a cast or transarticular external skeletal fixator in order to protect and prevent tension on the tenorrhaphy. Immobilize the joint for the first 4 to 6 weeks.
- After the fixation is removed, allow gradual return to normal activity for another 4 weeks. Consider placing a partial cast or splint during this period to allow partial weight bearing.
- See Chapter 95 for discussion of physical therapy after musculoskeletal injury.

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Chapter

116 Neoplasia of Thoracic and Pelvic Limbs

Matthew Palmisano / Milan Milovancev

Tumors of the appendicular skeleton can occur either as a primary or metastatic lesion. Primary bone tumors occur most commonly in middle-aged and older animals. However, younger dogs 18 to 24 months of age can be affected.

▼ ***Key Point*** Primary bone neoplasms are usually metaphyseal in location, involve one bone, and usually do not cross a joint space.

Metastatic bone tumors may occur anywhere along the bone, and can affect multiple bones. Metastatic lesions can occur with any tumor type, but tumors of epithelial origin are more commonly seen to metastasize to bone.

ETIOLOGY

Primary Skeletal Neoplasms

Osteosarcoma

▼ ***Key Point*** Osteosarcoma (OSA) accounts for approximately 85% of all primary bone tumors in dogs.

- 75% of OSA occurs in the appendicular skeleton.
- OSA is usually an aggressive lesion originating in the metaphysis of long bones.
- The distal radius is the most common site for OSA, making up 40% of all skeletal OSA. Other common sites include the proximal humerus, distal femur, and proximal tibia.
- OSA is a biologically aggressive neoplasm, with a doubling time of 21 days.
- Although 80% to 90% of dogs lack radiographic evidence of pulmonary metastases at time of diagnosis, most dogs are euthanized due to complications associated with metastatic lung disease.
- Large- and giant-breed dogs are over-represented in most studies. Only 5% of OSA occurs in dogs weighing less than 15 kg.
- One study found that OSA in small-breed dogs behaves differently than in their large-breed counterparts, representing less than 50% of all skeletal neoplasms and with no apparent predilection for the distal radius. The proximal humerus is the most common site in the small-breed dog.
- Appendicular OSA in cats behaves less aggressively than canine OSA, with affected cats surviving a mean of 14.8 months following amputation. The hind limb is more commonly affected in the cat.
- Cisplatin, carboplatin, and doxorubicin are chemotherapeutic agents frequently used in treatment of OSA. Survival rates reported with chemotherapy are 45% survival to 1 year, and 30% 2-year survival.
- Poor prognostic indicators in dogs with OSA include a preoperative alkaline phosphatase level greater than 110 U/L, OSA in young patients, high tumor grade, and radiographic evidence of pulmonary metastases.
- Long-term prognosis is poor. Survival rates in dogs diagnosed with OSA are 10% survival at 1 year without chemotherapy. Amputation will achieve local tumor control and relief from pain, but the procedure does not extend long-term life span.

Chondrosarcoma

- Chondrosarcoma represents 5% to 10% of primary tumors of the appendicular skeleton.
- Medium- to large-breed dogs are most commonly affected.
- Unlike OSA, surgical resection of chondrosarcoma is associated with an increased long-term survival when compared to non-surgical management.
- However, long-term prognosis is still guarded, with a 30% 1-year survival seen with treatment.

Fibrosarcoma and hemangiosarcoma are the third and fourth most frequently seen primary tumors of bone, respectively. Both tumors together comprise slightly less than 5% of primary tumors of bone.

See Table 116-1 for biologic behavior, treatment, and prognosis of the most common canine malignant appendicular skeletal tumors.

Table 116-1. COMMON CANINE MALIGNANT APPENDICULAR SKELETAL TUMORS

Tumor Type	Metastatic Rate	Treatment Options	Prognosis
Osteosarcoma	+++	Amputation and chemotherapy Palliative amputation Palliative radiation	MST about 6 months with surgery alone MST 9–12 months with surgery and chemotherapy
Chondrosarcoma	+	Amputation	Good if complete excision
Fibrosarcoma	++	Amputation	Poor
Hemangiosarcoma	+++	Amputation	Poor, MST <5 months

MST, median survival time; +, slow; ++, moderate; +++, high.

Other Primary Skeletal Neoplasms

Other rare bone tumors include osteoma, chondroma, osteochondroma, enchondroma, malignant mesenchymoma, liposarcoma, plasma cell myeloma, lymphosarcoma, and giant cell tumor.

Primary Soft Tissue Neoplasms

Synovial Cell Sarcoma

- Synovial cell sarcomas are tumors that arise from the joint capsule.
- Most commonly seen in middle-aged to older animals.
- The stifle and elbow joint are affected in nearly 75% of cases.
- Radiographs reveal an osteolytic pattern associated with a joint. Classically, this tumor crosses the joint space. This differs from primary tumors of bone, which characteristically do not cross the joint space.
- Histologic grading carries prognostic significance, as tumors with higher biologic grading are more likely to metastasize. The metastatic rate varies from 20% to 70%, depending on histologic grading.
- Recurrence is common after local surgical resection. Therefore, limb amputation is recommended for local tumor control.

Other Primary Soft Tissue Neoplasms

Other primary soft tissue appendicular tumors include hemangiosarcoma, rhabdomyosarcoma, lymphosarcoma, fibrosarcoma, and malignant histiocytosis. These tumors are rarely seen and require histologic analysis for diagnosis and prognosis. Since sarcomas do not exfoliate easily, fine-needle aspiration is generally unrewarding. Therefore, incisional or excisional biopsies are required for diagnosis.

Metastatic Neoplasia

- Metastasis to bone from primary neoplasms located elsewhere in the body is occasionally seen.
- Any neoplasm may metastasize to bone, but carcinomas are more likely to metastasize to bone than sarcomas. In particular, urogenital neoplasms such as prostatic carcinoma, transitional cell carcinoma of the bladder, and mammary carcinomas tend to metastasize to bone.

▼ ***Key Point*** Tumors that metastasize to bone are usually seen in the diaphysis, whereas primary tumors of bone are usually metaphyseal in location.

- A thorough diagnostic workup (bloodwork, three-view chest radiography, abdominal ultrasonography) is essential to determine the primary source of neoplasia.
- Biopsy of both the primary mass and bone lesion is important for accurate diagnosis and staging of disease.

CLINICAL SIGNS

- Clinical signs are variable and range from a subtle lameness and non-painful swelling to a non–weight bearing lameness with obvious limb deformation.
- Occasionally, acute lameness will be seen secondary to pathologic fracture through the diseased bone.
- Rarely, dogs will have respiratory signs at presentation due to metastatic pulmonary disease.

DIAGNOSIS

- A presumptive diagnosis is usually made based on signalment, history, physical examination, and radiographic findings.
- A thorough physical examination, complete blood count, serum biochemical profile, and urinalysis are important to assess the patient's overall health status and check for concurrent conditions that may affect treatment options.

Diagnostic Imaging

- Obtain a three-view thoracic radiographic study (i.e., right lateral, left lateral, and ventrodorsal or dorsoventral views) to evaluate the patient for pulmonary metastasis.
- Chest radiography and nuclear imaging are two modalities that, when used together, detect metastasis in about 18% of cases. Availability of nuclear imaging is limited in private practice.
- Other advanced imaging modalities, such as computed tomography (CT) and magnetic resonance imaging (MRI), are useful in locating metastasis to lung and other extra-skeletal sites. Use of imaging to estimate tumor margins is important in limb-sparing surgeries and in radiation therapy planning.
- Radiographic patterns of both primary and secondary bony neoplasia are very similar, with a combined osteolytic-osteoproliferative pattern seen. Aggressive radiographic features such as cortical lysis, periosteal reaction, and bony proliferation strongly support neoplasia.

Biopsy

- Definitive diagnosis requires representative biopsy performed either using a bone core biopsy (Jamshidi needle, Michel trephine, or open-incisional) in the radiographic middle of the lesion or a wedge biopsy if the mass is soft tissue in origin (Fig. 116-1).
- Jamshidi needle biopsy has an accuracy rate of 91.9% for detection of tumor versus other disease processes and 82.3% for diagnosis of exact tumor type.
- Perform a fine needle aspirate on all enlarged lymph nodes and evaluate cytologically for metastasis.

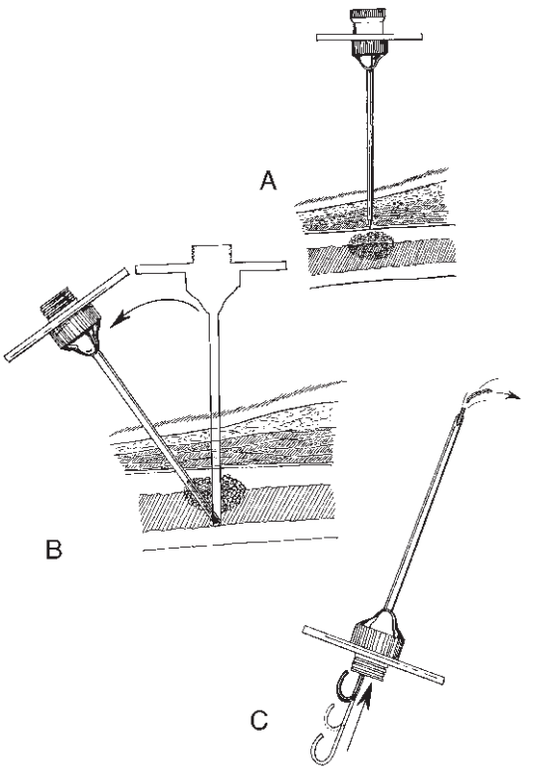

Figure 116-1. *A,* Biopsy of bone by closed technique with a Jamshidi needle. *B,* With the stylet locked in place, advance the cannula through soft tissue until bone is reached. *C,* Remove the stylet and penetrate the one cortex with the cannula. Withdraw the cannula and repeat the procedure with redirection of the needle.

TREATMENT

- Treatment recommendations depend on tumor type and location.

Surgery

- Although some small or benign tumors may be treated by local resection, most appendicular neoplasms require complete or partial amputation of the affected limb, primarily for palliation of pain (see discussion of amputation later in this chapter). Evaluate the patient's other limbs to ensure that adequate function can be carried out with the remaining three limbs.

▼ ***Key Point*** Limb amputation is contraindicated in patients that will have difficulty ambulating with three limbs. This includes overweight and obese patients or patients that have significant orthopedic disease in the other three limbs that will affect postoperative ambulation.

- Some giant-breed dogs have difficulty ambulating initially following amputation due to their large size and require some assistance postoperatively. Most of these patients adjust quickly.

▼ ***Key Point*** Perform the amputation at least one joint above the involved bone.

- Limb-sparing procedures are associated with a higher complication rate than limb amputation, are technically difficult to perform, and require access to a bone bank, which limits its use in private practice.
- Because most malignancies of the appendicular skeleton carry a poor long-term prognosis with amputation alone, follow-up adjunctive therapies are recommended. Adjunctive therapies include radiation therapy to enhance local tumor control and chemotherapy to treat metastatic disease.
- Radiation therapy or chemotherapy can be used alone as palliative therapy for pain control in patients that are not candidates for amputation.

Chemotherapy

- Postoperative chemotherapy is the most important modality for increasing long-term survival for canine osteosarcoma (see Chapter 26).
- Chemotherapy increases survival rates significantly over amputation alone, with reported 45% survival at one year and 30% at 2 years.
- Patients undergoing chemotherapy should have >3,000 neutrophils per µl, >150,000 platelets per µl, and normal renal function.
- Due to potential side effects of chemotherapeutic agents, consult a veterinary oncologist when treating these patients.

Cisplatin and Carboplatin

- Always check for evidence of myelosuppression before administering any chemotherapeutic agent.
- Myelosuppression and nephrotoxicity are dose-dependent, potentially life-threatening complications of cisplatin therapy.
  - Saline diuresis prior to cisplatin treatment helps prevent nephrotoxicity.
- Administer *cisplatin* at a dose of 70 mg/m^2 IV. Start therapy after the skin sutures are removed. Repeat at 21-day intervals for three to six treatments.
- *Carboplatin* is less nephrotoxic than cisplatin, and can be administered intravenously without pre-treatment diuresis, as required for cisplatin.
- Carboplatin is administered at 300 mg/m^2 IV. Start therapy after the skin sutures are removed. Repeat at 21-day intervals for three treatments provided there is no bone marrow suppression.
- In earlier studies, carboplatin had been shown to possess similar antitumor effects to cisplatin. However, recent studies have not found similarly favorable survival times.

Doxorubicin (see Chapter 26)

- Results are mixed in different studies.
- One-year survival rate of 50.5% was reported in 35 dogs treated with doxorubicin.

Combination Chemotherapy

- Few studies are available, but a recent large study reported median survival times greater than 11 months in 102 dogs treated with surgery, doxorubicin, and cisplatin.

Radiation Therapy

- Radiation therapy is an effective treatment modality for relieving pain and dysfunction associated with primary and metastatic bone neoplasia.
- Recently described four fraction treatment protocols for osteosarcoma are effective for palliation of clinical signs (median survival time of 313 days) and may result in a higher response rate than traditional three fraction protocols.
- Certain tumor types (i.e., mast cell tumors) are relatively radiosensitive, so these patients may be better candidates for radiation therapy.
- Development of sarcoma within a previously irradiated site several years after radiotherapy has been reported.

Other Modalities

- Immunotherapy and vehicle-based chemotherapies are currently being investigated as an adjunct treatment modality for canine osteosarcoma. Mixed results have been reported.

LIMB AMPUTATION

Anatomy

A thorough knowledge of limb anatomy is essential to achieve a successful outcome with minimal complications. Blood loss is a significant complication with limb amputation and is minimized with accurate dissection, hemostasis of smaller vessels with cautery, and preemptive ligation of larger arteries and veins.

Thoracic Limb

- The axillary artery extends from the cranial border of the first rib to the joint tendinous insertion of the teres major and latissimus dorsi muscles. It lies deep to the brachial plexus.
- Major veins include the cephalic vein (deep to the cleidobrachialis muscle), the brachial vein, and the axillary vein (caudal and cranial to the axillary artery, respectively).

Pelvic Limb

- The femoral artery lies superficially in the femoral triangle, caudal to the caudal belly of the sartorius muscle, and cranial to the pectineus muscle.
- The femoral vein lies caudal and deep to the femoral artery.

Preoperative Considerations

- Amputation of a limb involves loss of a large amount of fluid and blood. Therefore, use appropriate fluid therapy during and after surgery.
- Have blood products available if excessive blood loss is anticipated during surgery.
- Administer preoperative analgesia (e.g., fentanyl patch) (see Chapter 6).
- Begin antibiotics IV at induction of surgery, and continue postoperatively PO for an additional 3 to 5 days. First-generation cephalosporins (e.g., cephazolin) and amoxicillin/clavulanic acid are the antibiotics of choice.

- Many patients with appendicular neoplasms are older (>8 years of age). Therefore, identify other concurrent diseases and treat accordingly.
- Amputation of a limb is often difficult for owners to accept. Prior to surgery, explain the functional and cosmetic changes resulting from amputation. Most patients function very well after amputation, and cosmesis is acceptable. One study found a direct relationship between owner satisfaction and long-term survival.
- Most clients were happy with their decision to amputate their pet's limb if the pet lived a longer, good-quality life.

Surgical Procedures

Thoracic Limb Amputation with Removal of the Scapula

Use this technique when the tumor involves the humerus or scapula. Scapulohumeral joint disarticulation can be performed when the scapula is not involved, but it is technically harder to perform than amputation with scapula removal. Thoracic limb amputation at mid-humerus is technically easier to perform and causes less blood loss than removal of the scapula because it requires no major muscle belly transection. However, owners often find this procedure cosmetically unacceptable, because both the proximal humerus and scapula are easily visible as the muscles atrophy after surgery.

Objectives

- Complete tumor resection with wide margins of normal tissue
- Minimize blood loss
- Close or drain large areas of dead space

Equipment

- Standard general surgery instruments and suture
- Electrocautery
- Closed suction drainages (preferable) or Penrose drains

Technique

1. Place the dog in lateral recumbency and aseptically prepare the entire leg and chest wall for surgery.
2. Incise the skin along the spine of the scapula to the greater tubercle of the humerus. Carry the incision circumferentially to the medial side of the shoulder joint.
3. Ligate and divide the cephalic vein as it runs deep to the cleidobrachialis muscle.
4. Sharply separate the omotransversarius and the cervical and thoracic parts of the trapezius muscles from the scapular spine (Fig. 116-2*A,B*).
5. Subperiosteally elevate the rhomboideus and serratus ventralis muscles from the medial aspect of the scapula, and abduct the latter from the chest wall (Fig. 116-2*C,D*).
6. Sever the common insertion of the latissimus dorsi, teres major, and cutaneous muscles from the teres tubercle of the humerus. The axillary lymph node can be identified at this location, and should be removed and submitted for evaluation of metastasis.
7. Ligate and divide the thoracodorsal artery and vein and cut the thoracodorsal nerve. Further abduct the scapula and rotate it medially.
8. Ligate and divide the axillary and lateral thoracic arteries and the brachial and axillary veins.
   a. To avoid pooling of large amounts of blood in the limb, double-ligate arteries before veins. Ligate veins first if dissemination of disease is a major concern (Fig. 116-3, *top*).
9. Transect the brachial plexus of nerves with scissors or a scalpel.
10. Complete the amputation by cutting the pectoral and cleidobrachialis muscles away from the humerus (Fig. 116-3, *bottom*).
11. If dead space cannot be closed, place a closed suction drain (e.g., Jackson-Pratt) or passive drain (Penrose). Routinely close the muscles, subcutaneous tissues, and skin (Fig. 116-4). Make sure to eliminate dead space during closure, and do not close tissues under tension.

Pelvic Limb Amputation at Midfemur

Use this procedure when the tumor does not involve the femur. This method provides a stump, which provides lateral protection of genitalia in males.

Objectives

- Same as for thoracic limb amputation.

Equipment

- Same as for thoracic limb amputation, plus
  - Bone cutting instrument (oscillating saw, Gigli wire, bone cutting forceps)

Technique

1. Place the dog in lateral recumbency and aseptically prepare the entire limb and pelvis for surgery.
2. Incise the skin in two connected semicircles; ventrolaterally from the tuber ischii down to the patella and up to the flank and ventromedially from the ends of the lateral incision to midthigh.
3. Transect the caudal belly of the sartorius and gracilis muscles at midthigh.
4. Isolate, ligate, and divide the saphenous nerve and femoral artery and vein.
5. Transect the pectineus muscle at its insertion on the femur, and the cranial sartorius and quadriceps muscles proximal to the patella.

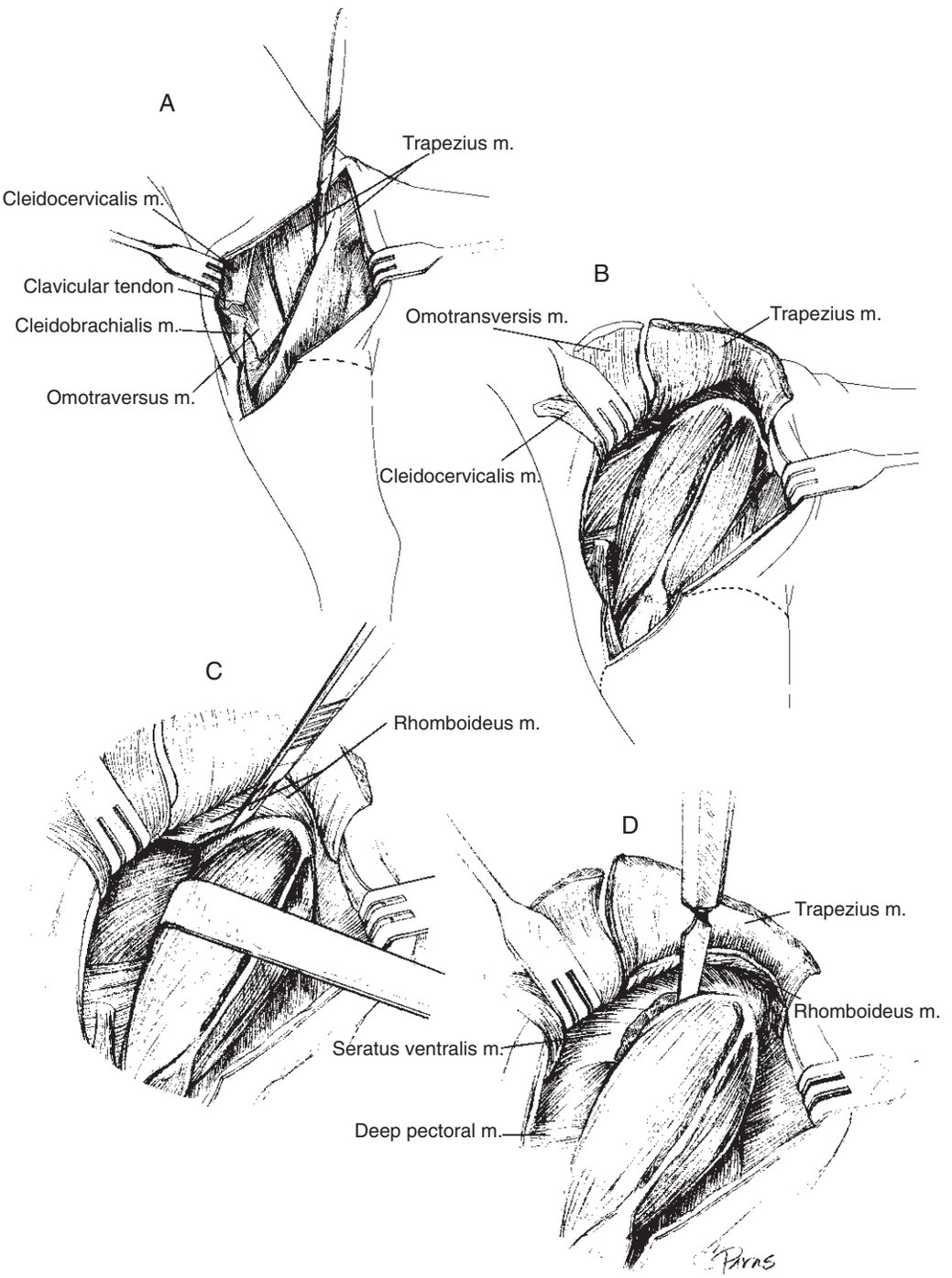

Figure 116-2. Initial dissection of muscles for thoracic limb amputation.

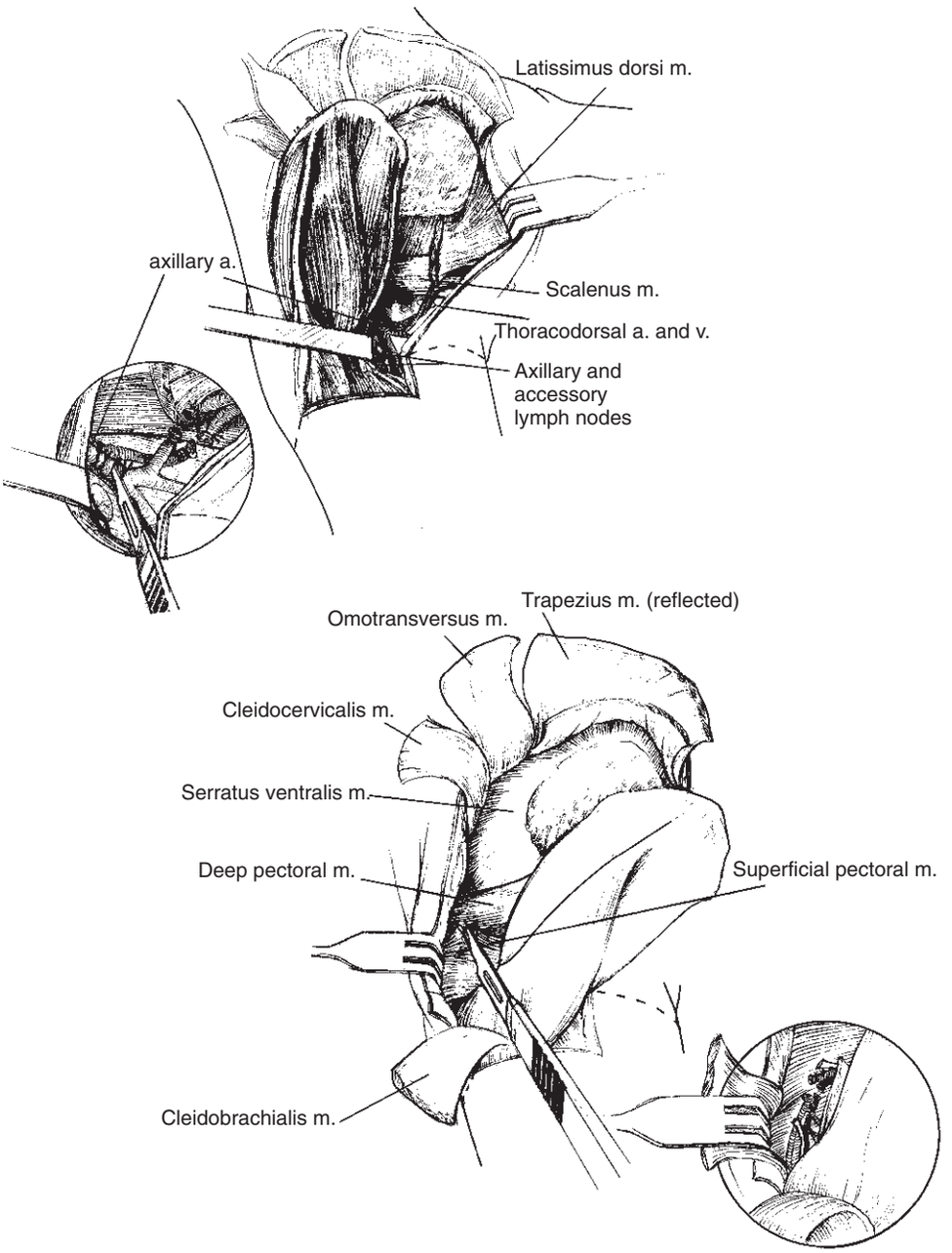

Figure 116-3. Ligation and severing of axillary artery and continued dissection for thoracic limb amputation.

6. Incise the tensor fasciae latae and biceps femoris muscles along the skin incision.
7. Isolate the sciatic nerve trunk and sever it at the greater trochanter.
8. Transect the abductor cruris caudalis, semitendinosus, semimembranosus, and adductor magnus et brevis muscles at midthigh.
9. Complete the amputation by osteotomy of the femur using a Gigli wire or oscillating bone saw, leaving the proximal one-third of the femur. Bone wax is packed into the cut end of the osteotomy.
10. If necessary, place a closed suction drain (e.g., Jackson-Pratt) or passive drain (e.g., Penrose) to drain dead space. Routinely close the muscles, subcutaneous tissues, and skin.

Pelvic Limb Amputation by Hip Disarticulation

Use this procedure when there is tumor involvement of the mid- to distal femur. Tumors of the proximal femur and hip joint may require en bloc resection of the acetabulum and part of the pelvis (subtotal

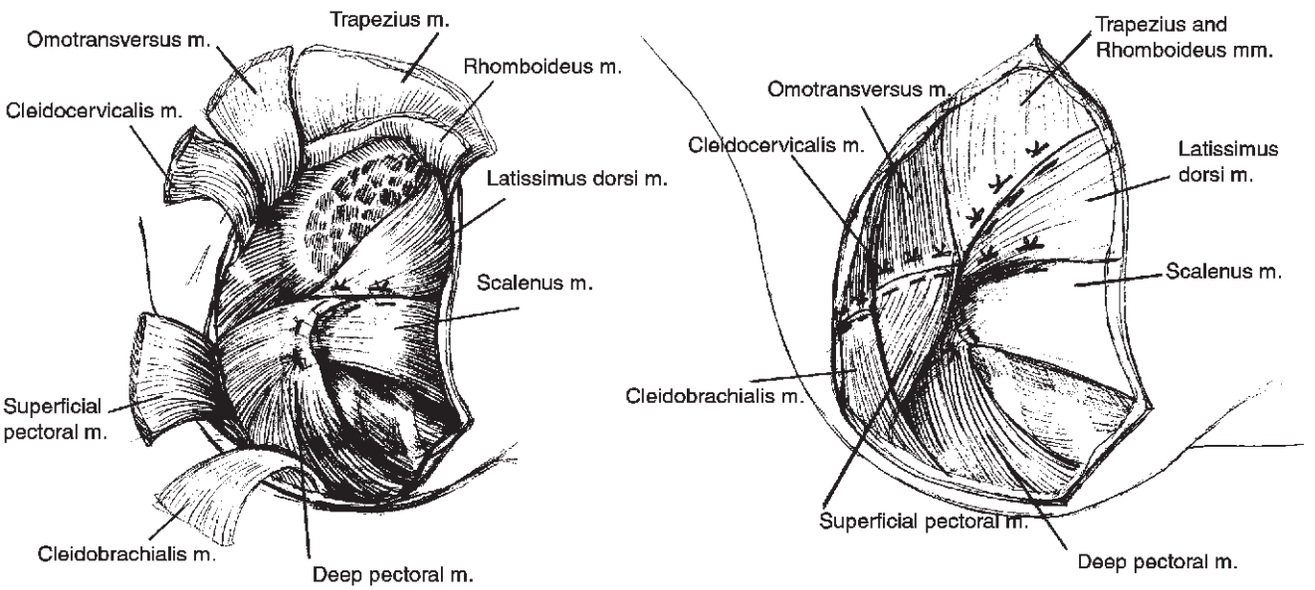

Figure 116-4. Muscle closure after thoracic limb amputation.

hemipelvectomy) with the femur to ensure complete removal.

Objectives

- Same as for thoracic limb amputation.

Equipment

- Same as for thoracic limb amputation

Technique

1. Place the dog in lateral recumbency and aseptically prepare the entire limb and pelvis for surgery.
2. Incise the skin in two connected semicircles, ventrolaterally from the tuber ischii down to the midthigh and up to the flank, and ventromedially from the ends of lateral incision down to the inguinal fold.
3. Isolate, ligate, and divide the femoral and superficial circumflex femoral arteries and femoral vein.
4. Transect the sartorius, pectineus, gracilis, and adductor magnus et brevis muscles 2 cm from their origin (Fig. 116-5*A,B*).
5. Ligate and divide the medial circumflex femoral artery and vein.
6. Elevate the iliopsoas muscles from the lesser trochanter of the femur.
7. Sever the saphenous and femoral nerves.
8. Cut the medial coxofemoral joint capsule and round ligament.
9. Transect the tensor fasciae latae, biceps femoris, abductor cruris caudalis, semitendinosus, and semimembranosus muscles in their proximal one-third.
10. Sever the sciatic nerve distal to its branches to the upper thigh muscles (Fig. 116-5*C*).
11. With the limb in flexion and abduction, sever the hip rotator muscles, including the internal and external obturator and gemellus muscles.
12. Complete the amputation by severing the three gluteal muscles (superficial, middle, and deep), and the lateral joint capsule and by elevating the rectus femoris muscles from the iliopubic eminence (Fig. 116-5*D*).
13. If necessary to drain excessive dead space, place a closed suction drain (e.g., Jackson-Pratt) or passive drain (e.g., Penrose). Routinely close the muscles, subcutaneous tissue, and skin.

Postoperative Care and Complications

Short Term

- Always submit the amputated limb for histopathologic confirmation of the preoperative diagnosis.
- Monitor the patient closely for pain, hemorrhage, hypotension, or electrolyte disturbances.
- Routinely administer analgesics (see Chapter 6).
- With proper surgical technique minimizing dead space, seroma formation should be minimal but can be managed with pressure bandages, warm compresses three to four times daily, or drain placement. Remove drains when drainage is minimal.
- Nursing and supportive care will be required until the patient has recovered and adapted enough to function well on three limbs.
- Start chemotherapy after skin suture removal.

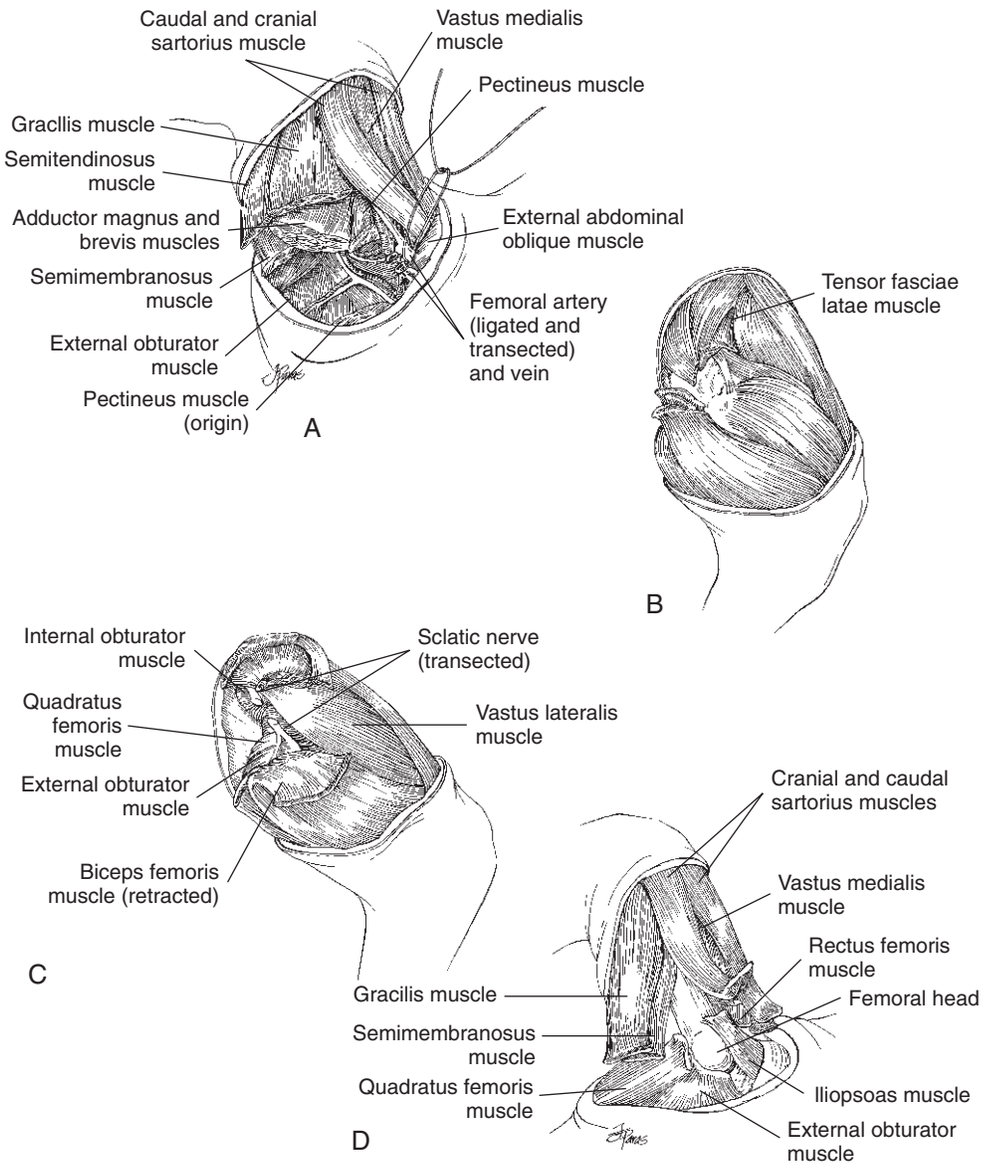

Figure 116-5. Dissection of muscles, vessels, and nerves for pelvic limb amputation by hip disarticulation. *A* and *D,* medial views; *B* and *C,* lateral views.

Long Term

- Evaluate the patient clinically and radiographically every 8 to 12 weeks to look for tumor recurrence at the surgical site and pulmonary metastasis.
- Institute a strict weight loss program, especially with forelimb amputation in overweight patients.

MANAGEMENT OF METASTATIC DISEASE

As a general rule, chemotherapy is ineffective in patients with radiographically detectable pulmonary metastasis secondary to OSA. In some cases, lung lobectomy to remove metastatic tumors can significantly prolong survival time (see Chapter 167). Patients that are candidates for removal of lung metastasis should satisfy the following criteria:

- Primary tumor in complete remission for >300 days.
- No greater than two nodules visible on plain radiographs.
- Metastatic disease restricted to the lung only (negative bone scan or survey radiographs).

Median survival time in 36 dogs after removal of lung metastasis was approximately 6 months.

LIMB-SPARING PROCEDURES

- Limb-sparing procedures are indicated in patients that are not good candidates for limb amputation, or when clients refuse amputation. With this procedure, the affected bone is resected and is replaced with a normal bone allograft. The site that is most amenable to limb-sparing surgery is the distal radius. Other sites (proximal humerus, proximal tibia) are not amenable to limb-sparing surgery because complication rates are unacceptably high. In addition, patients typically have poor limb function because the procedure requires arthrodesis of the joint closest to the tumor.
- Limb-sparing procedures are associated with a higher complication rate than limb amputation, are technically difficult to perform, and requires access to a bone bank, which limits its use in private practice. Consult a surgical specialist.

Indications

- Tumor involving 50% or less of the length of the bone.
- Tumor that does not extend across the joint, into the adjacent ulna, or into the surrounding soft tissues.
- A patient that is free of metastatic or other concurrent diseases.

Complications

- Infection (45–55% of cases)
- Recurrence (25% of cases)
- Plate breakage
- Host bone fracture
- Sequestrum formation

In patients with a failed limb-sparing procedure, limb amputation can be performed as a salvage procedure.

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Chapter

117 Miscellaneous Diseases of Bone

James K. Roush

Some of the diseases affecting bone are discussed in this chapter. See respective chapters for other bone and cartilage diseases, such as hip dysplasia, avascular necrosis of the femoral head, and osteochondrosis.

PANOSTEITIS

Panosteitis is a disease of young large-breed dogs manifested by intermittent lameness of one or more limbs. Onset usually occurs in the first year of life. The disease is self-limiting, but clinical signs may persist in one or more limbs for months. Differentiate panosteitis from other causes of lameness in young dogs, such as hip dysplasia and osteochondritis dissecans.

Etiology

- The etiology of panosteitis is unknown.
- Panosteitis may have a polygenetic origin, because German shepherd dogs are commonly affected.
- Contributing causes include stress, transient vascular abnormalities, metabolic disorders, allergies, hyperestrogenism, and autoimmune reaction following viral infection.
- The characteristic histopathologic lesion is degeneration of medullary adipocytes, followed by stromal cell proliferation, intramembranous ossification, and regeneration of the adipose bone marrow.

Clinical Signs

Signalment

- Panosteitis usually is seen in large and giant-breed dogs, most often 5 to 12 months of age; however, it has been reported in dogs up to 5 years of age, and I have seen it in a 7-year-old dog.
- Male dogs are affected more frequently than females (4:1 ratio). In females, the first episode of the disease often occurs in association with the first estrus.
- Panosteitis has been reported in the German shepherd, Great Dane, Irish setter, St. Bernard, Doberman pinscher, Airedale, basset hound, and miniature schnauzer.

Lameness

- There is acute onset of weight-bearing lameness without a history of recent trauma.

▼ ***Key Point*** Lesions often resolve in one bone and develop in another, resulting in the classic history of "shifting leg" lameness.

- Pain due to the disease is of intermittent duration and severity, but the dog rarely, if ever, is completely non–weight bearing on the affected limb or limbs.
- Lameness or radiographic lesions may occur simultaneously in multiple limbs or bones, or lameness may resolve for a period of time, only to recur in another limb. After a bone passes through the lesion cycle, it is unlikely that it will be affected again, but lameness may occur in that limb if the disease affects another bone in the limb.
- Clinical signs often continue for several months and usually resolve by 18 to 20 months of age.

Diagnosis

▼ ***Key Point*** Diagnosis of panosteitis is established by eliciting pain on firm palpation of a long bone and by characteristic radiographic lesions.

Physical Examination

- Applying firm pressure to the diaphyses of the affected bone results in clinical signs of discomfort.

Laboratory Evaluation

- Hematology and serum chemistry profiles usually are normal.
- Eosinophilia occurs inconsistently (this disease was previously referred to as eosinophilic panosteitis).

Radiography

Confirm suspected cases by survey radiography of the affected bone(s).

Table 117-1. CHARACTERISTIC RADIOGRAPHIC LESIONS SEEN IN DISEASES AFFECTING BONE

Disease	Lesion
Panosteitis	Increased opacity in medullary cavity of diaphysis
Hypertrophic osteodystrophy	Radiolucent metaphyseal line adjacent to physis
Hypertrophic osteopathy	Periosteal reaction beginning on metacarpals or metatarsals, bilaterally symmetric
Craniomandibular osteopathy	Bony proliferation on ventral mandible and skull
Cartilaginous exostosis	Large, smooth bony protuberance in metaphyseal area
Bone cyst	Well-circumscribed, radiolucent metaphyseal defect
Retained enchondral	Longitudinal, linear radiolucent cartilaginous core defect in distal ulna

- Early radiographic lesions are characterized by areas of increased density and accentuated trabecular pattern within the medullary cavity (Table 117-1).
- These areas may be focal or multifocal and commonly occur near the nutrient foramen.
- Bone cortices may be thickened, and progressive mottling and opacification of the medullary cavity occur.
- A smooth, linear periosteal proliferation may develop.
- During resolution, sclerotic areas gradually decrease in size and density. Radiographic signs may persist for several months after lameness resolves.
- There is no correlation between the radiographic lesions and severity of clinical signs.

Differential Diagnoses

- Differentiate panosteitis as a cause of lameness from other diseases that are characterized by onset during or shortly after the rapid-growth phase in large-breed dogs.
- In particular, eliminate hypertrophic osteodystrophy, osteochondritis dissecans of the shoulder or elbow (see Chapter 118), ununited anconeal process (see Chapter 118), and hip dysplasia (see Chapter 108) as a cause of lameness before ascribing clinical signs to panosteitis.

Treatment

▼ ***Key Point*** Panosteitis is a self-limiting disease.

- No specific therapy for panosteitis exists.
- Administer a nonsteroidal anti-inflammatory drug approved for dogs, as needed, to alleviate pain (see Chapter 6).
- Restrict exercise in severely affected animals.
- Inform clients that the lameness may shift to other limbs and that the animal may be intermittently lame for 6 to 18 months.

HYPERTROPHIC OSTEODYSTROPHY

Hypertrophic osteodystrophy (HOD) is a developmental disease of young, rapidly growing large- and giant-breed dogs. Dogs with HOD exhibit lameness in one or more limbs in association with swelling and inflammation of the metaphyseal regions of long bones. Complications related to prolonged recumbency, anorexia, and hyperthermia have been reported in severely affected animals. The overall prognosis for HOD is guarded. Although many dogs recover spontaneously, permanent bone changes and physical deformities may develop.

Etiology

- The etiology of HOD is unknown.
- Historically, the disease has been attributed to vitamin C deficiency, but decreased levels of ascorbic acid in the serum or urine do not appear to be related to the disease.
- Skeletal lesions similar to those of HOD have been produced experimentally by feeding a free-choice diet abnormally high in protein, calories, and calcium.
- Canine distemper virus may be involved as a causative agent.

Clinical Signs

Signalment

▼ ***Key Point*** HOD occurs only in growing animals with open physes.

- Onset of clinical signs usually occurs at 3 to 4 months of age (range, 2–8 months).
- HOD has been reported in the Great Dane, Irish wolfhound, St. Bernard, Irish setter, Labrador retriever, basset hound, greyhound, German shepherd, German short-haired pointer, borzoi, boxer, Dalmatian, Weimaraner, Doberman pinscher, and collie.

Systemic Signs

- The severity of HOD varies, ranging from an absence of systemic signs to severe anorexia, weight loss, fever, and depression.
- Clinical signs are episodic in nature, and lameness often is bilaterally symmetric.

Lameness

- Lameness varies from a mild limp in minimally affected dogs to non–weight bearing lameness in severely affected animals.

- Affected long bone metaphyses are extremely swollen, warm, and painful in animals with severe disease.
- Multiple long bones and limbs are affected, and, in extreme cases, dogs are reluctant to stand or move.

Diagnosis

History/Physical Examination

- The history may include recent weight loss, reluctance to move, and anorexia.
- Affected metaphyses are warm and swollen on palpation.
- Signs of pain may be elicited on palpation of the metaphyseal areas.
- Pyrexia of up to 106°F may be present.

Laboratory Evaluation

- Laboratory data are normal, or mild abnormalities related to anorexia and stress may be present.

Radiography

- Radiographic changes usually occur in the metaphyses of the long bones and are bilaterally symmetric. Other bones, including the mandible, ribs, and scapula, may be affected.
- The characteristic radiographic lesion is generalized sclerosis and enlargement of the metaphysis.

▼ ***Key Point*** Radiolucent areas form in the metaphysis and coalesce to form an area of radiolucency parallel to the growth plate, called a double physeal line (Fig. 117-1).

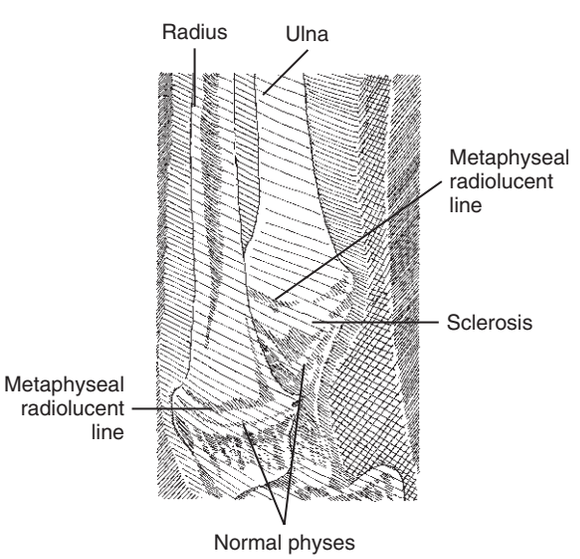

Figure 117-1. Metaphyseal radiolucent lines and metaphyseal sclerosis proximal to distal radial and ulnar physis in a dog with hypertrophic osteodystrophy.

- Irregular widening of the physis may be seen in later stages of the disease.
- Subperiosteal or extraperiosteal bone formation is seen in metaphyseal regions and may involve the diaphysis.

Differential Diagnoses

- Differentiate HOD from other causes of lameness in immature large- or giant-breed dogs.
- Other diseases that result in metaphyseal swelling or in signs of pain during palpation of long bones include panosteitis, bone-associated neoplasms, and hypertrophic osteopathy. Radiographic lesions in these diseases are distinct and allow easy differentiation; the last two diseases are unlikely to be the cause of lameness in young dogs.

Treatment

▼ ***Key Point*** There is no specific treatment for HOD.

- In mild or moderately affected dogs, there is often spontaneous remission.
- Correction of dietary imbalances and decreased caloric intake may be beneficial.
- Good supportive care of severely affected dogs is essential to prevent decubital ulcers, provide nutrition (see Chapter 3), and maintain hydration (see Chapter 5).
- Give nonsteroidal anti-inflammatory analgesics, as needed, to relieve discomfort (see Chapter 6).
- Severely affected animals may require nutritional intake via force-feeding or gastrostomy tube (see Chapter 3). Parenteral fluids may be needed to prevent dehydration in these animals (see Chapter 5).
- There is no evidence that mineral, vitamin C, or vitamin D supplements are beneficial; these substances actually may accelerate the rate of dystrophic calcification.

HYPERTROPHIC OSTEOPATHY

Hypertrophic osteopathy (HO) is a pathologic disease process affecting long bones secondary to a space-occupying mass in the abdominal or thoracic cavities. The disease has been reported in many species, including dogs, cats, and humans. HO is characterized by bilateral symmetric swelling of the distal limbs accompanied by periosteal bone formation. HO has been referred to as hypertrophic pulmonary osteoarthropathy, pulmonary osteoarthropathy, and hypertrophic pulmonary osteopathy. Hypertrophic osteopathy is the term that most accurately reflects the rare joint involvement and the variable site of the primary space-occupying lesion.

Etiology

- Hypertrophic osteopathy occurs secondary to a variety of diseases and occurs in dogs and cats of all breeds and ages.
- HO is most often secondary to metastatic pulmonary neoplasia, although it has been reported with primary pulmonary neoplasia, pulmonary abscesses, pulmonary tuberculosis, chronic bronchopneumonia, spirocercosis, dirofilariasis, rib tumors, bacterial endocarditis, hepatic adenocarcinoma, and various primary bladder neoplasms (neurofibrosarcoma, botryoid rhabdomyosarcoma, and transitional cell sarcoma).
- The pathogenic mechanisms underlying the bone pathology are unknown. Evidence points to an increased peripheral vascular supply secondary to the pulmonary lesion. This increased peripheral blood flow has been observed both in dogs and humans and may be related to irritation of afferent nerve pathways and stimulation of a nervous reflex.

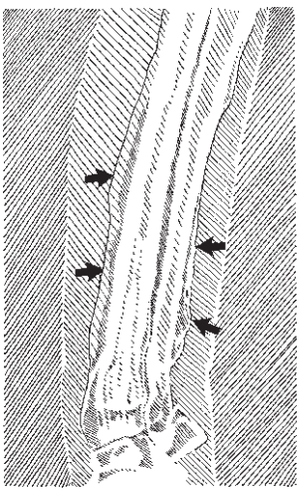

Figure 117-2. Smooth periosteal proliferation *(arrows)* on radius and ulna characteristic of hypertrophic osteopathy.

Clinical Signs

▼ ***Key Point*** Signs of HO may be present months before onset of clinical signs relating to the underlying disease; early recognition is important for diagnosis and treatment of the primary disease.

Signalment

- Dogs and cats with HO may be of any breed and usually are affected late in life.
- A reported increased incidence of the disease in female and large-breed dogs may be due to the increased incidence of mammary tumor metastasis in female dogs, and of primary bone tumors in large-breed dogs.

Lameness

- Most animals present with acute or gradual lameness of all four limbs and with reluctance to move.

Diagnosis

Physical Examination

- The distal limbs are swollen, firm, and warm.
- Signs of pain may be elicited on deep palpation of the long bones.

Laboratory Evaluation

- Laboratory findings reflect the underlying disease process and are not characteristic of HO.

Radiography

- Survey radiographs demonstrate a bilateral, symmetric, generalized periosteal proliferative reaction affecting the long bones of the appendicular skeleton (Fig. 117-2). Endosteal bone proliferation does not occur.
- Distal portions of the limbs, especially the metatarsals and metacarpals, are involved first, but periosteal proliferation eventually may involve the more proximal long bones and occasionally the mandible, pelvis, ribs, and vertebrae.
- In very early cases, periosteal new-bone formation is not evident, but symmetric soft tissue swelling is present.
- If the primary disease resolves, the bony and soft tissue radiographic abnormalities regress.

▼ ***Key Point*** Thoracic and abdominal radiographs are essential to evaluate the underlying disease process and to confirm the diagnosis of HO. Abdominal ultrasound may also be helpful in identifying a mass lesion.

Differential Diagnoses

The bony periosteal reactions of hypertrophic osteopathy are similar to those of panosteitis and hypertrophic osteodystrophy, but HO will not exhibit the increased medullary opacities of panosteitis, nor the radiolucent metaphyseal line characteristic of HOD. It is rare to see HO in a young (adolescent) animal.

Treatment

▼ ***Key Point*** Removal of the underlying primary lesion usually results in regression of the lameness and distal limb lesions.

- Resection of primary or metastatic pulmonary neoplasms provides temporary relief of signs related to

HO, but long-term survival is dependent on the type of neoplasm.
- Appropriate treatment of dirofilariasis, spirocercosis, and primary lung disease may increase the chances for long-term survival.
- Inflammation and clinical signs of pain resolve 1 to 2 weeks after removal of the thoracic or abdominal mass. Periosteal reactions regress in 3 to 4 months, but residual radiographic changes may persist in severe cases. Lameness may persist in some animals even after removal of the mass.
- When resection of the primary mass is not feasible, unilateral vagotomy (on the side of the lesion) may provide temporary regression of clinical signs.

CRANIOMANDIBULAR OSTEOPATHY

Craniomandibular osteopathy (CMO) is a non-neoplastic, noninflammatory proliferative bony disease in growing dogs that affects bones of endochondral origin, most commonly the mandibles, occipital bones, or temporal bones. Bony lesions are bilateral and symmetric. CMO occurs predominantly in terriers, especially Scottish, West Highland white, and Cairn terriers, but the disease also has been reported in the boxer, Labrador retriever, Great Dane, and Doberman pinscher.

Etiology

- CMO is likely of heritable origin, with recent reports of likely autosomal recessive heritance.
- Osteoclastic resorption of mandibular bone occurs, followed by production of woven bone on both the periosteal and endosteal surfaces of the bone. Cyclic episodes of bone resorption and proliferation result in the formation of mature fibrous bone that may remain permanently.

Clinical Signs

- Disease onset occurs at 4 to 10 months of age. Both sexes are affected equally.
- Presenting clinical signs include pain on manipulation or opening of the mouth, mandibular swelling, ptyalism, inability to open the mouth, intermittent fever, and lethargy.

Diagnosis

Physical Examination

Signs of pain are elicited during direct palpation of the swelling or attempts to open the mouth. In advanced cases, the clinician may be unable to open the mouth more than 1 or 2 cm. Dogs may be febrile during the period of bone proliferation. Lymphadenopathy or temporal muscle atrophy may be present.

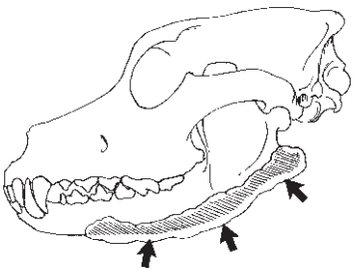

Figure 117-3. Bony proliferation *(arrows)* on the ventral mandible of a dog with craniomandibular osteopathy.

Radiography

Diagnosis of CMO is confirmed by radiographic evidence of the bony proliferative lesions.

- Obtain survey radiographs of the skull and mandible, including oblique, dorsoventral, and lateral views, to assess the extent of the disease.
- A non-neoplastic, bilaterally symmetric bony proliferation is seen projecting from the periosteal surfaces of the mandible or other bones of the cranium (Fig. 117-3).
- Angular processes of the mandible and bullae may fuse and obstruct jaw motion. Lesions may also involve the occipital bone, parietal bone, frontal bone, maxilla, and appendicular bones.
- The proliferation of new bone decreases as growth slows, and becomes radiographically static when the animal is approximately 1 year old. Partial or complete regression of bony lesions occurs, but moderate or severe cases result in permanent bone proliferation to varying degrees.
- The prognosis is poor for dogs with radiographic evidence of partial or complete bony ankylosis of the temporomandibular joints (TMJs).

Differential Diagnoses

- Lesions of CMO in the appendicular skeleton may appear radiographically similar to HOD, but CMO lacks the metaphyseal radiolucent line of HOD.
- Radiographic appearance differentiates CMO from bony neoplasia and osteomyelitis.

Treatment

- There is no specific therapy for CMO.
- Administer nonsteroidal anti-inflammatory analgesic therapy at manufacturer recommended dosage as needed (see Chapter 6).
- Nutritional support by gastrostomy or enterostomy tube or parenteral supplementation may be necessary (see Chapter 3). As the condition stabilizes, most animals have impaired mouth function but are capable of maintaining normal nutritional status.

- Surgical intervention to reduce new bone mass and increase TMJ range of motion has met with limited success.

MULTIPLE CARTILAGINOUS EXOSTOSIS

Multiple cartilaginous exostosis (MCE) is a disease of dogs and cats in which multiple ossified protuberances arise from the bone in metaphyseal regions. Vertebrae, ribs, and long bones commonly are affected. The exostosis ceases to grow when the physis nearest the exostosis ossifies.

Etiology

- MCE probably is heritable in dogs, horses, and humans.
- The accepted pathogenesis is that the exostosis is derived from displaced chondrocytes that separate from the physis during development.

Clinical Signs

- The animal often is presented with a firm, distinct swelling on the involved bone.
- Lameness or limb dysfunction develops only when adjacent structures such as the tendons or nerves are compressed or mechanically distorted by the exostoses.
- Other clinical signs, including pain, lameness, mechanical dysfunction, and neurologic deficits, depend on the structure affected.

Diagnosis

Physical Examination

- A smooth, immovable bony swelling is visible and palpable near a metaphysis.
- Pain may be elicited on palpation of the mass or surrounding soft tissues.

Radiography

- Obtain skeletal survey radiographs of animals with suspected cartilaginous exostosis.
- Radiographic lesions are juxtacortical masses at or adjacent to the metaphysis.
- Large, scattered radiolucent areas of hyaline cartilage may be present within the exostosis. The exostotic growths may involve any bone except the skull.
- Surgical biopsy of the lesion confirms the diagnosis.

Treatment

▼ ***Key Point*** Removal of the exostosis relieves associated pain, mechanical dysfunction, and neurologic deficits.

- Removal of MCE sometimes is requested to improve cosmetic appearance.
- Malignant transformation of exostoses to chondrosarcomas or osteosarcomas has been reported. Continued growth of the exostosis after the animal is mature suggests malignant transformation.
- In general, the prognosis is good after removal of uncomplicated MCE.

BONE CYSTS

Bone cysts are smooth radiolucent cavities found rarely in the long bones of dogs. Flat bones (e.g., mandible, ribs) also may be affected. Four types of bone cysts have been described in dogs:

- Monostotic (affecting one bone)
- Polyostotic (affecting more than one bone)
- Aneurysmal
- Subchondral

Aneurysmal bone cysts are extremely rare in dogs and are locally aggressive. Bone cysts found in young, large-breed dogs usually do not produce clinical signs until they attain a large size.

Etiology

- The etiology of monostotic, polyostotic, and aneurysmal bone cysts is unknown.
- Subchondral bone cysts often are not primary lesions and may be the result of chronic osteoarthritis or diseases leading to osteoarthritis (e.g., rheumatoid arthritis, systemic lupus erythematosus).

Clinical Signs

Signalment

- The age of affected animals ranges from 4 to 30 months, but most animals are less than 1 year of age.
- Breeds reported to develop bone cysts include the German shepherd, Weimaraner, Irish wolfhound, Afghan, saluki, Great Dane, and Doberman pinscher.

Presentation

- Pain, swelling, and stiffness of the nearest joint may be present.
- Acute lameness or swelling may occur at the site of the cyst owing to a pathologic fracture.

Diagnosis

Radiography

- Survey radiographs establish a diagnosis of bone cysts. A benign, expansive, radiolucent area in the metaphysis is characteristic.

- The metaphyseal cortex may be thinned by expanding cysts.
- Pathologic fractures may be evident radiographically.

Histopathology

- The cyst is lined by fibrous connective tissue.
- Aneurysmal bone cysts are filled with blood, and the blood spaces are lined by connective tissue trabeculae. Multinucleate giant cells and mature bone may be present in these cysts.
- Monostotic and polyostotic cysts may fill with blood after pathologic fracture.

Differential Diagnoses

- Differentiate bone cysts from more aggressive lesions such as chondrosarcoma, osteosarcoma, and giant cell tumors.

Treatment

- Curettage of the walls and filling of the defect with cancellous bone is the definitive treatment in most animals.
- Treat pathologic fractures through cysts by debridement of the cyst wall, cancellous graft, and fracture fixation.
- Consider cyst resection if the lesion is located in flat bones (e.g., rib resection or mandibulectomy).

RETAINED ENCHONDRAL CARTILAGINOUS CORES

Retained enchondral cartilaginous cores occur in the distal ulnar metaphysis of young, large-breed dogs. Radiographically, the retained enchondral cartilage is seen as a central, longitudinal radiolucent cone in the distal ulnar metaphysis and usually is an incidental finding of no clinical significance. These lesions, however, may interfere with normal growth of the ulna, resulting in forelimb deformities.

Etiology

- The etiology is unknown.

Clinical Signs

- Signs may include valgus deviation, external rotation of the carpus, and cranial bowing of the radius.

Diagnosis

- Survey radiographs establish the diagnosis in animals with appropriate forelimb deformities.
- The lesion also may be an incidental finding unrelated to clinical lameness if normal growth of the ulna is apparent.

Treatment

- No treatment is necessary for animals without forelimb deformity.
- Immature animals with forelimb deformities may benefit from distal ulnectomy, which may allow spontaneous correction of radial and ulnar deformities during continued growth (see Chapter 105).
- Mature animals require ulnar and radial osteotomies to correct forelimb deformity (see Chapter 105).

LABRADOR RETREIVER SKELETAL DYSPLASIA

Skeletal dysplasia is a heritable disease of Labrador retrievers characterized by forelimb achondroplasia and ocular effects. It demonstrates autosomal recessive transmission of skeletal effects and is linked with an incomplete dominant heritable ocular dysplasia in these dogs.

Etiology

- The skeletal defects are heritable via autosomal recessive transmission.
- Linked ocular defects are heritable via incomplete dominant transmission.
- The disease is only recognized in Labrador retrievers.

Clinical Signs

- The forelimbs of affected immature Labs appear shorter and exhibit achondroplastic conformation. The disease is often first noted during rapid growth phases from 8 to 16 weeks of age.
- Abnormal conformation of the coxofemoral joints also occurs and is visible radiographically.
- Ocular changes include cataracts, retinal dysplasia, and rhegmatogenous retinal detachments. Dogs are often visually impaired at presentation.

Diagnosis

▼ ***Key Point*** The combination of forelimb achondroplasia associated with the linked ocular diseases of cataracts, dysplasia, or retinal detachment in immature animals leads to the diagnosis.

- The history or presence of other full siblings with similar signs is indicative of the heritable condition.
- Radiograph the forelimb to demonstrate the achondroplastic changes of the disease and demonstrate asynchronous growth of the radius and ulna. Comparison of radial length with heterozygote siblings is diagnostic.

Differential Diagnosis

- Differentiate the skeletal lesions from traumatic shortening of the radius and ulna due to previous

damage to the distal radial or ulnar growth plates. In the latter, the radiographic changes will most likely be unilateral and visible evidence of early closure of the growth plates may be evident.

Treatment

- There is no treatment for individual animals affected by the disease.
- Monitor breeding lines of Labrador retrievers for evidence of the disease. Remove probable carriers of the trait from breeding stock.

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Chapter

118 Osteochondrosis

Michael P. Kowaleski

Osteochondrosis refers to a group of diseases that are characterized by aberrant development of the epiphyseal or physeal cartilage in growing animals. The cause of osteochondrosis appears to be multi-factorial; some of the factors that have been implicated include nutrition (overnutrition, excess dietary calcium, excess protein), genetics, exercise, environmental factors, and trauma (excessive mechanical loading), as the lesions frequently occur at the point of greatest loading of the joint.

ETIOLOGY

▼ ***Key Point*** Osteochondrosis is a failure of endochondral ossification, and this term refers to the disease in general. Osteochondritis dissecans (OCD) refers to the combination of dissecting lesions of articular cartilage, communication of synovial fluid into the subchondral bone, and the resulting synovitis. Most commonly large- or giant-breed dogs are affected.

- Osteochondrosis at the physeal growth plate begins as an abnormal accumulation of viable hypertrophic chondrocytes that subsequently fail to undergo matrix mineralization, causing a slowing of growth, not complete cessation. In the dog, this primarily occurs at the distal ulnar physis (retained cartilage core or radius curvus), leading to the characteristic antebrachial deformities seen with asynchronous growth of the radius and ulna, namely shortening of the ulna, cranial bowing of the radius, valgus angulation, external rotation, shortening of the radius, and variable amounts of elbow and carpal incongruity.
- Elbow dysplasia is a collection of diseases presumed to be a result of osteochondrosis, including ununited anconeal process (UAP), OCD of the medial portion of the humeral condyle, and fragmented medial coronoid process (FMCP) (Fig. 118-1).

OSTEOCHONDRITIS DESSICANS OF THE SHOULDER, HOCK, AND STIFLE

In dogs, OCD lesions can occur in the shoulder on the caudal humeral head, in the hock on the trochlear ridges of the talus (medial more commonly than lateral), and in the stifle on the femoral condyle (lateral more commonly than medial).

Anatomy

- See the respective chapters on shoulder, hock, and stifle disorders (Chapters 102, 112, and 110).

Pathophysiology

- A defect in endochondral ossification results in a focal area of abnormal subchondral bone formation.
- The overlying cartilage fails to undergo endochondral ossification resulting in focal retention of cartilage instead of conversion to bone.
- This thickened region of cartilage becomes necrotic and weak, resulting in cartilage breakdown under normal loading conditions or secondary to trauma.
- Early in the disease process, the lesions of osteochondrosis affect only the epiphyseal cartilage, and the animal is asymptomatic.
- Once a fissure occurs in the thickened cartilage, it extends through the necrotic cartilage into the subchondral bone, allowing access of the synovial fluid to the subchondral bone.
  - This stage seems to correspond to the onset of clinical signs, at which time it is called osteochondritis dissecans.
- OCD results in two distinct joint abnormalities: joint incongruity secondary to malformation of cartilage and subchondral bone, and joint mouse formation.
- Cartilage flaps that remain attached may ossify, and the resulting bone remains viable as long as the flap is attached.
  - Detached cartilage flaps may survive in the joint fluid and grow in size.

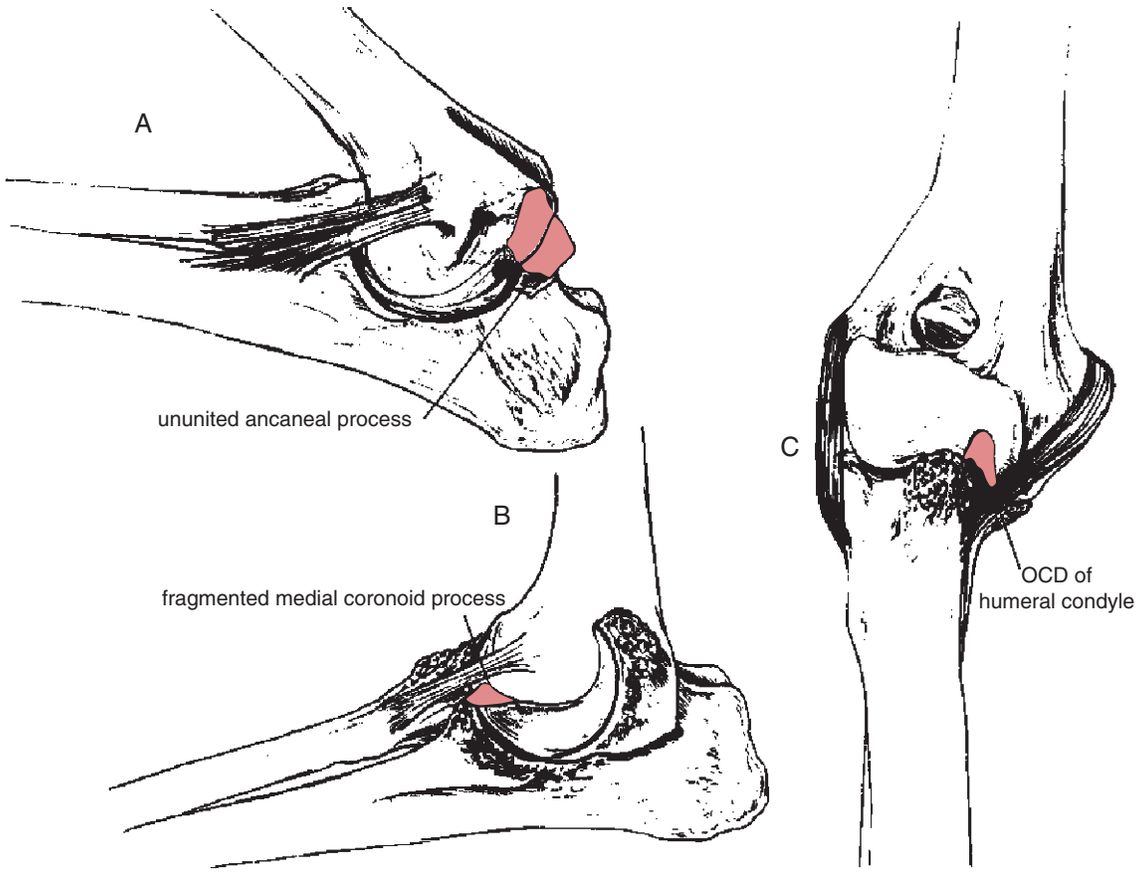

Figure 118-1. The various manifestations of elbow dysplasia include *(A)* ununited anconeal process, *(B)* fragmentation of the medial portion of the coronoid process of the ulna, and *(C)* OCD of the medial portion of the humeral condyle.

- If these cartilage flaps attach to the joint capsule, they may become mineralized or ossified.
- Curettage of the chondral and subchondral lesion stimulates neochondrogenesis; however, the resultant fibrocartilage does not have the same material properties as the original hyaline cartilage, and is not as durable.
- The new cartilage rarely attains the height or density required to reestablish joint congruity.

Clinical Signs

Shoulder

- Large-breed dogs, 4 to 8 months of age, 2:1 to 3:1 male/female ratio.
- Bilateral in 27% to 68% of cases; many are clinically affected in only one limb.
- Lameness is initially noted after exercise or after rest preceded by exercise.
- Pain with shoulder extension, crepitus, deltoid and spinatus muscle atrophy.

Hock

- Large-breed dogs, 5 to 8 months of age, commonly Rottweiler, Labrador retriever, and bullmastiff.
- Lateral trochlear ridge OCD is seen most commonly in the Rottweiler.
- Hind limb lameness characterized by a shortened stride and hyperextension of the tarso-crural joint.
- Thickening of the tarsus especially if the medial trochlear ridge of the talus is involved.

Stifle

- Large-breed dogs, 5 to 7 months of age.
- Lameness varies from mild to severe.
- Joint effusion, muscle atrophy, and crepitus may be evident.

Diagnosis

- The radiographic signs of osteochondrosis are well characterized and easily recognized in most cases;

high-quality, well-positioned radiographs are necessary for an accurate diagnosis (see Chapter 4).
- Normal cartilage is not visible radiographically unless significant dystrophic calcification has occurred.
- Since OCD lesions consist of areas of relatively thicker cartilage than the surrounding cartilage and a failure of endochondral ossification of the underlying bone, the lesion is observed as a flattened or saucer-like "divot" in the subchondral bone.

Shoulder

- Radiographs reveal a flattening of the humeral head in a properly positioned lateral view.
- An arthrogram may be needed of the lesion is not evident or a cartilage has migrated into the biceps tendon sheath.

Hock

- Radiographic identification of the lesion may be difficult due to the location of the lesion on the trochlear ridge.
- Extended dorsoplantar projection may reveal a defect in the trochlear ridge.
- A dorsolateral-plantaromedial 45-degree oblique projection in full extension outlines the medial trochlear ridge of the talus.
- A skyline view of the talus may identify a lesion on the center of the trochlear ridge of the talus.

Stifle

- Slight flattening and sclerosis of the subchondral bone of the femoral condyle is evident in a caudocranial view of the stifle.
- Avoid confusing the extensor fossa for an OCD lesion.

Preoperative Considerations

- As the relative size of the osteochondral defect to the total joint surface area increases, the resulting joint incongruity also increases. Thus, a small defect in a large joint (shoulder) has less of an impact than in a small (hock) or complex (elbow or stifle) joint.

▼ ***Key Point*** Surgical treatment of OCD lesions can result in normal or near-normal function in large joints with relatively small lesions (shoulder); however, function is improved but clinical signs are not always alleviated in complex or small joints (elbow, hock, and stifle).

- The degree of osteoarthritis in the joint prior to surgery has an impact on long-term function; as the degree of osteoarthritis increases, function is diminished.
- Patients with small lesions and minimal osteoarthritis will have the best surgical result; conversely, patients with large lesions and severe osteoarthritis are less likely to benefit from surgery.
- Dogs with OCD of the hock may fare as well with or without surgery; this is likely due the relatively large size of the typical lesion in the hock, as well as the tendency for osteoarthritis to be significant in this joint preoperatively.

Surgical Procedures

Objectives

- The goals of surgery are to debride the osteochondral defect with minimal damage to the joint during the surgical approach and procedure.

Equipment

- Same as for OCD of the humerus, discussed later in this chapter.

Technique

- An arthrotomy or arthroscopy can be employed.
- See respective chapters on shoulder, hock, and stifle disorders for a description of surgical approaches (see Chapters 102, 112, and 110).
- Debride the lesion to the level of subchondral bleeding bone utilizing a curette, a hand bur, or a motorized shaver.
- Debride the edges of the lesion peripherally to normal cartilage, and perpendicular to the subchondral bed.
- Microfracture can be utilized to create vascular access channels from the lesion to the underlying subchondral bone.

Postoperative Care and Complications

- Apply a soft padded bandage for 3 to 5 days from the digits to the mid-diaphysis proximal to the incision to minimize postoperative swelling.
- Remove skin sutures in 10 to 14 days.
- Confine the dog to leash walks only for 6 weeks to allow neochondrogenesis to occur. Allow gradual return to normal activity over the next 6 weeks to allow cartilage remodeling to occur.

Prognosis

▼ ***Key Point*** The prognosis for return to normal function in dogs with OCD of the shoulder is good to excellent; over 95% of patients are sound at 4 to 8 weeks.

- Early treatment of OCD of the hock (4–6 months of age) is indicated; otherwise the prognosis is poor due to a tendency for progressive degenerative joint disease (DJD) to develop.

- OCD of the stifle carries a more guarded prognosis than that of the shoulder OCD; 75% will be normal if treated early.

CANINE ELBOW DYSPLASIA

Elbow dysplasia is a collection of diseases, which were initially presumed to be a result of osteochondrosis. Recently, asynchronous growth or uneven joint loading has been implicated in the pathogenesis of this disorder.

Pathophysiology

- Canine elbow dysplasia (CED) is a collection of developmental diseases of the canine elbow, which is believed to be caused by a primary incongruity between the humerus, radius, and ulna.
- Manifestations include fragmented medial coronoid process (FMCP) of the ulna, ununited anconeal process (UAP) of the ulna, and osteochondritis dissecans (OCD) of the medial portion of the humeral condyle.
- Classically, a decreased radius of curvature of the ulnar trochlear notch was suggested as the cause.
- A second theory is that elbow incongruity in CED is caused by asynchronous growth between the radius and ulna.
- Lagging radial growth and a relatively long ulna may stress the medial coronoid process and humeral condyle, resulting in FMCP and OCD, respectively.
- In an experimental study, surgical shortening of the radius in normal dogs resulted in altered intra-articular contact potentially stressing the medial coronoid process.
- Dogs with unilateral UAP have been shown to have a slightly longer radius on the affected side.

Ununited Anconeal Process

Anatomy

- Ununited anconeal process (UAP) is a failure of the ossification center of the anconeal process to fuse with the proximal ulna by 20 to 24 weeks of age. Thus, a diagnosis of UAP prior to 24 weeks of age may be premature.
- The blood supply to the anconeal process is via the dorsal joint capsule attachment; therefore the bone remains viable and capable of endochondral ossification unless these attachments are disrupted.
- Physeal closure of the anconeal process initially occurs distally, and then progresses proximally along the physis.
- The anconeal process is an important stabilizer of the canine elbow, particularly in extension during the stance phase of the gait. Instability or detachment of the process leads to synovitis and eventually osteoarthritis.

Pathophysiology

- UAP may be secondary to abnormal loading of the elbow joint secondary to elbow incongruity or an abnormal size or shape of the trochlear notch; it has not been definitively proven to be secondary to OCD.
- Physeal closure of the anconeal process initially occurs distally, and then progresses proximally along the physis.
- Incomplete endochondral ossification along the physis can result in foci of retained cartilage within a closed physis mimicking UAP.

▼ ***Key Point*** The anconeal process is an important stabilizer of the canine elbow, particularly in extension during the stance phase of the gait. Instability or detachment of the process leads to synovitis and eventually osteoarthritis.

- In chondrodystrophic breeds, UAP may result from premature closure of the distal ulnar physis and asynchronous growth of the radius and ulna.

Clinical Signs

- Large-breed dogs, especially the German shepherd, basset hound, and St. Bernard, are affected.
- Signs including forelimb lameness, elbow abduction, and external rotation of the foot become apparent at 5 to 8 months of age.
- Crepitus, joint effusion, and peri-articular thickening of the elbow may be noted.

Diagnosis

- Clinical signs, age, and breed form the basis for a provisional diagnosis.
- A flexed lateral radiographic view reveals an irregular radiolucent line between the anconeal process and the olecranon.
- Radiographs of the contralateral elbow may be useful for comparison; bilateral UAP occurs in about 30% of cases.

Preoperative Considerations

- Removal of the anconeal process is an acceptable method of treatment. However, the anconeal process is an important stabilizer of the elbow, and its removal may lead to elbow instability and osteoarthritis.
- Surgical reconstruction, such as procedures that enhance fusion of the anconeal process, may be the preferred method of management, since these procedures preserve the function of this intra-articular stabilizing structure.
- A dynamic proximal ulnar osteotomy alone may be sufficient to allow fusion of the anconeal process in young (6–12 months) dogs, while a dynamic proximal ulnar osteotomy and lag screw fixation may be required in older (over 1 year) dogs, or in dogs

with loose attachment of the anconeal process to the olecranon.

- Four categories of UAP have been defined, and the type of union may be used to guide treatment.
  - *Cartilage retention nest.* In this lesion (usually an incidental finding) the anconeal process is united; however, an area of cartilage remains along part of the fusion site. This lesion is not likely to be a cause of lameness.
  - *Delayed union.* A normal union may occur in young dogs (5–6 months) if cage rest and exercise restriction are employed. If union fails to occur after 4 to 6 weeks of conservative treatment, surgical treatment is indicated.
  - *Non-displaced nonunion.* The anconeal process is apposed to the proximal ulna by fibrous or fibrocartilaginous tissue. Such fragments can be successfully reconstructed if the fragment size, bone density (screw holding power), viability of the tissue interface and fragment, and degree of interfragmentary compression achieved are adequate.
  - *Displaced nonunion.* The anconeal process is physiologically (due to lack of blood supply or viable interface tissue) or anatomically separated from the proximal ulna. These loose fragments act as foreign bodies and interfere with normal joint function, and should be removed.

Surgical Procedures

Objectives

- Remove or reconstruct the anconeal process.
- Identify and treat concurrent conditions such as OCD/FMCP.

Equipment

- Standard surgical pack and suture
- Gelpi self-retaining retractors
- Suction and cautery
- Periosteal elevator
- Drill, drill bits, taps, depth gauge, screws, and screwdriver
- Small bone curette
- Small osteotome and mallet, gigli wire or oscillating bone saw

Technique

The anconeal process may be removed via a caudo-lateral arthrotomy.

1. Place the patient in lateral recumbency, with the affected limb up; prepare for aseptic surgery using the hanging limb technique.
2. Perform a caudo-lateral approach to the elbow, placing the incision in the anconeus muscle at its insertion on the ulna, and elevate the muscle using the periosteal elevator.
3. Retract the anconeus muscle and lateral head of the triceps with the gelpi retractor.
4. Externally rotate the antebrachium and slightly flex the elbow to gain adequate exposure of the anconeal process.
5. Remove the anconeal process and close.

The quality of attachment of the anconeal process can be evaluated with arthroscopy or following an arthrotomy. If the anconeal process is firmly attached, perform a dynamic proximal ulnar osteotomy to normalize loading within the joint; this may allow the anconeal process to fuse spontaneously. If the anconeal process is loosely attached, perform interfragmentary compression with lag screw fixation, and a dynamic proximal ulnar osteotomy can be performed to normalize loading within the joint.

1. Explore the joint and the quality of attachment of the anconeal process with arthroscopy or following an arthrotomy.
2. If the anconeal process is loosely attached, attempt lag screw fixation of the UAP.
   a. Drill a thread hole either freehand from the apex of the anconeal process to the caudal ulna, or from the caudal ulna to the apex of the anconeal process (the latter is facilitated by using an aiming device).
   b. Drill a glide hole in the caudal ulna by overdrilling the thread hole.
   c. Measure the screw length.
   d. Tap the thread hole in the anconeal process.
   e. Insert the screw from caudal to cranial observing the degree of compression (Fig. 118-2).
   f. Do not allow the screw tip to protrude beyond the apex of the anconeal process.
3. Perform a caudo-lateral approach to the ulnar diaphysis by elevating the extensor carpi ulnaris and abductor pollicis longus from the lateral aspect of the ulna, and the flexor carpi ulnaris and deep digital flexor from the medial aspect.
4. Perform an ulnar osteotomy just distal to the level of the radial head, oriented cranio-distal to caudo-proximal 30 to 40 degrees (Fig. 118-3). The angle of the osteotomy prevents caudal tipping of the proximal segment due to the pull of the triceps muscle.
5. An intramedullary pin placed from the olecranon to the distal ulnar diaphysis can be used to increase stability of the proximal segment (see Fig. 118-3).
6. Do not hesitate to remove the anconeal process if
   a. Technical difficulties prevent successful internal fixation.
   b. Bone quality is poor resulting in poor screw purchase or compression.
   c. The shape of the anconeal process results in poor joint congruency following internal fixation.

Postoperative Care and Complications

- Apply a soft padded bandage for 3 to 5 days from the digits to the mid-diaphysis proximal to the incision to minimize postoperative swelling.

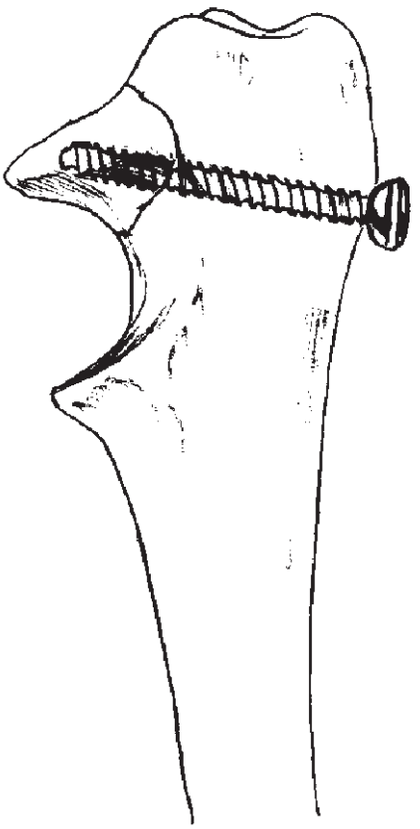

Figure 118-2. Rigid internal fixation of the anconeal process utilizing a screw placed in lag fashion.

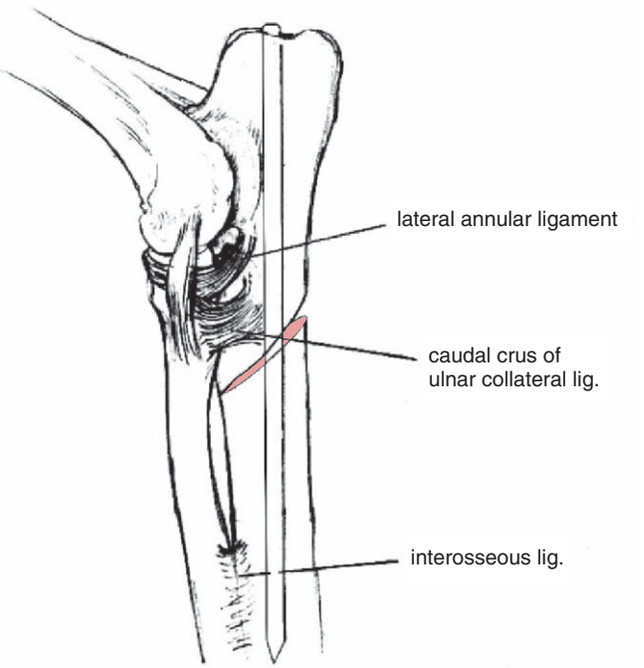

Figure 118-3. An oblique osteotomy of the ulna can be performed to equalize forces within the elbow joint. The placement of an intramedullary pin in the ulna is optional. Perform this technique if internal fixation of the anconeal process is utilized, in order to decrease the likelihood of implant failure due to cyclical stress.

- Remove skin sutures in 10 to 14 days.
- Confine the dog to leash walks only for 6 weeks to allow neochondrogenesis to occur at the site of removal, or anconeal process fusion to occur, depending on the technique that has been performed.
- Repeat radiographs in 4 to 6 weeks to assess fusion of the anconeal process and healing of the ulnar osteotomy if performed.
- Allow gradual return to normal activity over the next 6 weeks to allow cartilage remodeling to occur.

Prognosis

- Good results were obtained with dynamic proximal ulnar osteotomy in a group of young dogs 6 to 12 months old; less favorable results were obtained in a group of dogs 1 to 2 years old.
- In animals with anconeal process removal the prognosis is good to fair; resolution of lameness occurs postoperatively. However, most animals begin to be lame at 6 to 7 years of age secondary to osteoarthritis.
- The prognosis is good to excellent if the anconeal process fuses following surgical reconstruction.

OCD OF THE MEDIAL PORTION OF THE HUMERAL CONDYLE AND FRAGMENTATION OF THE MEDIAL PORTION OF THE CORONOID PROCESS (FMCP) OF THE ULNA

OCD and FMCP affect the distal humerus in the same dog populations that are affected by OCD of the shoulder, and may be bilateral. OCD and FMCP coexist in as many as 37% of cases.

Anatomy

- FMCP is separation of the medial coronoid process from the ulna; the etiology is unknown.
- OCD usually occurs on the medial portion of the humeral condyle.

Pathophysiology

FMCP

- OCD of the medial coronoid may play a role; a defect in endochondral ossification may lead to degeneration of the process and fissure formation.
- Developmental elbow incongruity has also been implicated; a relatively long ulna and short radius may result in an increase of weight-bearing forces on

the medial coronoid process, which may precipitate fragmentation.
- Fragmentation of the coronoid results in a separate piece of cartilage and trabecular bone, which is attached to the annular ligament with fibrous tissue.
- Separation occurs through calcified trabeculae that are then covered, in part, with fibrous connective tissue.
- The end result is joint instability and development of DJD.
- Cartilage on the opposing medial humeral condyle may be eroded by the loose coronoid fragment (kissing lesion).
- Peri-articular osteophytes and soft-tissue fibrosis develop progressively over time.

OCD

- A failure of endochondral ossification results in an OCD lesion in the medial portion of the humeral condyle.

Clinical Signs

- Forelimb lameness, initially evident at 5 to 8 months of age, is seen in retrievers, Bernese mountain dogs, and Rottweilers.
- Clinical signs usually become apparent at 5 to 7 months of age; however, the dog may not be presented until 1 to 2 years of age after development of DJD.
- Lameness is worse after exercise, and joint effusion and peri-articular fibrosis may be palpable.
- Lameness is usually unilateral even if both joints are affected; a stiff or stilted gait may be observed if bilateral forelimb lameness is present due to shortened stride.
- Pain with flexion and extension of the joint is evident, especially with supination or pronation; discomfort may be noted with palpation of the medial coronoid process.
- Avoid shoulder motion during manipulation to avoid mistaking shoulder pain for elbow pain.

Diagnosis

FMCP

- The radiographic findings of FMCP are nonspecific.
- Evaluate both elbows radiographically, as the disease is commonly bilateral.
- A presumptive diagnosis is made based on typical history and clinical signs.

▼ ***Key Point*** The FMCP cannot always be observed, and the diagnosis may be made by inference due to the presence of osteoarthritis.

- Osteophytosis and superimposition of the radial head on the coronoid process make identification of the FMCP difficult.

Radiographs

- Obtain lateral and cranio-caudal views, and a flexed lateral exposed anconeal process to assess for osteophytosis.
- A craniolateral-caudomedial 15-degree oblique with 30 degrees flexion may help visualize the medial coronoid.
- A mediodistal-lateroproximal oblique (MEDLAP) view has recently been shown to enhance visualization of the medial coronoid process.
- Blunting of the coronoid, visible fragments, and osteophytes associated with the coronoid process, anconeal process, or radial head may be visible.
- The earliest radiographic sign is commonly the presence of osteophytes on the anconeal process.
- Later signs include subchondral bone sclerosis, articular and peri-articular osteophytosis, joint space narrowing, joint effusion, and peri-articular soft-tissue thickening indicating secondary DJD.
- Definitive diagnosis can be made with arthroscopy, computed tomography, magnetic resonance imaging, or arthrotomy.

OCD

- Radiographically a triangular subchondral bone defect is evident in the medial portion of the humeral condyle in the cranio-caudal projection.

Differential Diagnosis

- Other conditions affecting the elbows of young dogs produce similar signs, and can be differentiated radiographically.
- Consider UAP, combinations with OCD/FMCP and UAP, and subluxation resulting from premature physeal closure.
- Other diseases of the forelimb in young dogs should be considered such as OCD of the shoulder and panosteitis.

Treatment

Medical Management

- Asymptomatic dogs or those with severe DJD may be treated medically; all surgically treated dogs are also treated with lifelong medical management, as surgical treatment does not halt the progression of DJD.
- Weight loss, exercise moderation, nonsteroidal anti-inflammatory drugs (NSAIDs), and chondroprotective agents are the cornerstones of treatment.
- Rest (2–3 weeks) and NSAIDs are utilized to treat episodes of lameness, followed by return to moderate regular exercise.

Preoperative Considerations

Persistent lameness and mild DJD are indications for surgery; however, some dogs with moderate or severe

DJD may benefit from loose fragment removal. It is important to note that surgical treatment does not halt the progression of DJD.

Surgical Procedure

Objectives

- The goals of surgery are to remove the FMCP and to debride the osteochondral defect with minimal damage to the joint during the surgical approach and procedure.
- An arthrotomy or arthroscopy can be employed.
  - Elbow arthroscopy via medial portals allows identification and removal of the FMCP with graspers or a shaver. Arthroscopy improves intra-articular identification with recognition of cartilage defects, and allows eburnated cartilage to be treated by abrasion arthroplasty and/or microfracture. The ability to treat bilaterally, as well as identify and manage coexistent cartilage defects, supports arthroscopic management.
- See respective chapters on elbow disorders for a description of surgical approaches (see Chapter 105).

Equipment

- Arthroscopy tower, arthroscope and camera, hand instrumentation, and motorized shaver if arthroscopy is to be performed
- Standard surgical pack and suture if arthrotomy is to be performed
- Gelpi self-retaining retractors
- Suction and cautery
- Small bone curette

Technique

- Perform either arthroscopy via the medial portals, or an open approach.
  - If arthroscopy is performed, both elbows may be treated in a single session.
  - If an arthrotomy is performed, operate on the more symptomatic elbow first, followed by the second in 4 to 6 weeks.
- Several open approaches are suitable, including the muscle splitting approach (Fig. 118-4), and osteotomy of the medial epicondyle of the humerus.
- In FMCP, remove the fragment(s) and debride the fragment's bed to the level of subchondral bleeding

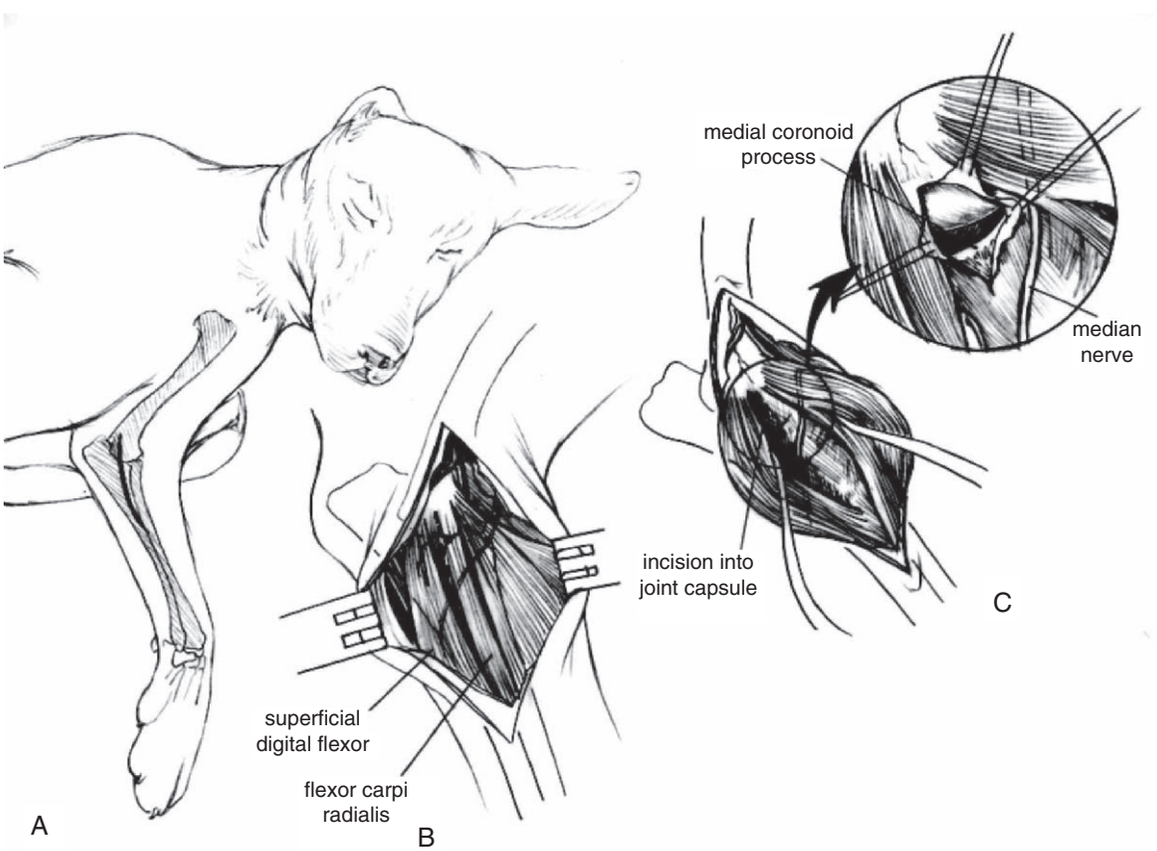

Figure 118-4. Medial approach to the elbow joint by an intermuscular incision. Incise the intermuscular septum between the flexor carpi radialis and deep digital flexor muscles or the flexor carpi radialis and the pronator teres muscles. Retraction of the muscles allows exposure and incision of the joint capsule parallel to the muscles. Note the proximity of the ulnar and median nerves.

bone utilizing a curette, a hand bur, or a motorized shaver.
- In OCD, debride the lesion to the level of subchondral bleeding bone utilizing a curette, a hand bur, or a motorized shaver, ensuring that the edges of the lesion are debrided peripherally to normal cartilage, and are perpendicular to the subchondral bed. Microfracture can be utilized to create vascular access channels from the lesion to the underlying subchondral bone.
- If arthroscopy is performed, identify and treat concurrent conditions such as cartilage eburnation or kissing lesions with microfracture or abrasion arthroplasty.
  - Perform microfracture with specially designed chondropicks. Place the pick within the lesion, and gently tap it into the surface using a mallet. Treat the entire lesion in a grid-like pattern; space the holes 2 to 3 mm apart and 1 to 2 mm deep.
  - Perform abrasion arthroplasty as for an OCD lesion; debride the lesion to the level of subchondral bleeding bone utilizing a curette, a hand bur, or a motorized shaver, ensuring that the edges of the lesion are debrided peripherally to normal cartilage, and are perpendicular to the subchondral bed.

Postoperative Care and Complications

- Arthroscopy:
  - Apply a soft padded bandage for 24 hours.
  - Institute strict exercise restriction for 4 to 6 weeks, followed by gradual return to normal activity.
  - Long-term medical management of osteoarthritis should be employed.
- Arthrotomy:
  - Obtain postoperative and 6-week follow-up radiographs if implants are used (osteotomy of the epicondyle).
  - Apply a soft padded bandage for 5 to 7 days.
  - Institute strict exercise restriction for 4 to 6 weeks, followed by gradual return to normal activity.
  - Administer long-term medical management of osteoarthritis.

Prognosis

- The prognosis for full function is guarded because of progressive DJD regardless of the treatment method.
- Most dogs are functional pets with intermittent lameness.
- Osteoarthritis is usually present and requires lifelong medical management.
- In a recent study of surgical management of 429 dogs, approximately 50% had a resolution of lameness, 30% had a diminished severity of lameness, and in 20% severity of lameness was not affected by surgery.

Chapter

119 Pediatric Fractures

Matthew Palmisano

Fractures occurring in immature animals (<1 year of age) are commonly seen in small animal practice. Immature bone is relatively weaker when compared to the surrounding soft tissues and ligaments, so it is more susceptible to injury. The most common site of fracture in the pediatric patient is in the metaphyseal region of the bone, with 30% of all fractures involving the metaphyseal growth plate (or physis). Fractures may also involve the diaphysis. Special consideration must be made when dealing with these types of fractures in order to ensure a successful outcome.

ANATOMY

- Immature long bone consists of a compact shaft (diaphysis), an intermediate zone (metaphysis), and a terminal portion (epiphysis). Structurally, the metaphysis is weaker than the diaphysis, epiphysis, or its supporting ligaments. The physis lies between the epiphysis and metaphysis, and is responsible for the longitudinal growth of long bones.
- There are two major differences in blood supply in immature and mature bone. First, blood vessels do not cross the actively growing physis, which means that the epiphysis and metaphysis have separate blood flow. Second, the periosteum of young bone requires an extensive blood supply that is not necessary in the mature patient.

Histology of the Physis

The physis is a cartilage that is composed of five developmental zones that are crucial to the longitudinal length of long bones. The zones are, from epiphysis to metaphysis, the reserve zone, the proliferative zone, the hypertrophic zone, the ossification zone, and the metaphyseal zone.

- The *reserve zone* has several layers of randomly arranged chondrocytes. This zone is important in storing nutrients and housing germinal cells.
- The *proliferative zone* is the growth zone of the physis. The germinal chondrocytes are rapidly dividing and forming palisades. Longitudinal growth results from active cell division and matrix production by these chondrocytes.
- In the *hypertrophic zone*, chondrocytes enlarge by accumulation of fluid and calcium.
- In the *ossification zone*, chondrocytes begin degenerating, depositing calcium into the matrix. Metaphyseal capillaries invade the hypertrophic zone and promote mineralization of the matrix and formation of primary and secondary spongiosa in the ossification zone.
- The *metaphyseal zone* is characterized by remodeling of the primary and secondary spongiosa.

CLASSIFICATION OF PHYSEAL FRACTURES

The classification of physeal fractures in young animals is adapted from the human Salter-Harris classification system (Fig. 119-1).

- Type I fractures are characterized by separation of the epiphysis from the metaphysis through the physis.
- Type II fractures occur through portions of the physis and metaphysis.
- Type III fractures occur through portions of the physis and the epiphysis. Therefore, these fractures have an intra-articular component.
- Type IV fractures occur through the metaphysis and the epiphysis. These fractures also have an intra-articular component.
- Type V fractures are crushing injuries, involving all zones of the physis. These fractures are often difficult to see radiographically.
- Type VI fractures are not part of the original classification system. In this type of fracture, the physis is injured resulting in a peripheral closure of one side of the physis.

Early research suggested that the hypertrophic zone is structurally the weakest zone and most susceptible to fracture due to increased cell size and less support matrix. Also, a stress concentration effect may occur in this zone as the tissues of the physis change from softer cartilage to bone. Recent research suggests that the other zones of the physis may be involved with naturally occurring fractures. When the proliferative zone is

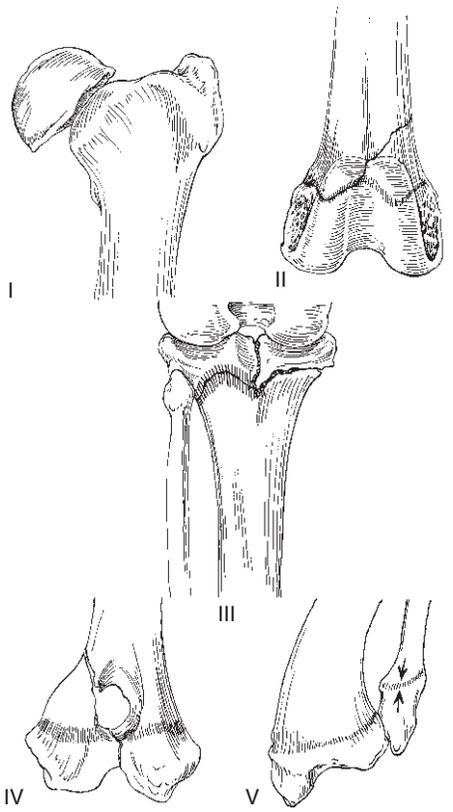

Figure 119-1. Five different types of growth plate fractures. See text for explanation.

involved, the incidence of premature closure of the physis, limb shortening, or angular limb deformity with resultant joint subluxation or luxation is increased. Most growth plates are closed by 12 months of age; physeal injuries are therefore rare in animals >1 year of age.

▼ ***Key Point*** The prognosis for continued growth of the physis with Salter-Harris type I through III fractures may be more favorable than type IV through VI due to preservation of the growing zones of the physis. However, warn owners of the possibility of premature physeal closure with limb shortening or angular limb deformity with any fracture of the long bones involving the physis.

PREOPERATIVE CONSIDERATIONS

- High-quality, orthogonal radiographic views of the fractured bone are a must when characterizing the type of fracture and determining method of repair.
- Consider external coaptation, either by splinting or casting, in fractures that are simple, transverse, minimally displaced, easily reduced, and distal to the stifle or elbow. Some Salter-Harris I and II physeal fractures can be reduced and are amenable to external coaptation.

▼ ***Key Point*** All intra-articular fractures require surgical repair.

- Pediatric bone heals very quickly due to rapid bone turnover and deposition associated with growth. External coaptation has the advantage of preserving blood supply with minimal soft tissue disruption, which will allow a bony union by 3 to 4 weeks.
- Consider open reduction and internal fixation (bone plates, pins, or screws) of fractures with unstable fractures, intra-articular fractures, or fractures >48 hours old.
- Immature bone is very soft and easily fractured with aggressive manipulation. Particular care should be taken with the growth plate. The proliferative zone of cartilage is usually with the epiphyseal segment, so particular care should be taken with this segment so as not to cause premature physeal closure.
- Gentle tissue handling and preservation of blood supply are important. A balance should be made between rigid stabilization of implants and maintenance of the soft tissues.

SURGICAL PROCEDURES

Operative Considerations

- In most physeal fractures, use the smallest Kirschner wires, pins, or screws that will provide sufficient stabilization, while causing the least amount of physeal trauma.
- Refer to the following chapters for specific fixation techniques of commonly seen physeal fractures:
  - Salter-Harris IV distal humeral fracture: Chapter 104.
  - Salter-Harris I or II capital femoral physeal fracture: Chapter 109.
  - Salter-Harris I proximal humeral fracture: Chapter 104.
  - Salter-Harris I or II distal femoral fracture: Chapter 109.
  - Salter-Harris I or II proximal tibial fracture: Chapter 111.

POSTOPERATIVE CARE AND CONSIDERATIONS

Postoperative Care

- Elimination of high-impact activity is a must, since immature bone is soft and implants used in fixation are relatively small and susceptible to bending and loosening.

- If postoperative immobilization is required using a bandage or cast, reevaluate the coaptation weekly. A cast may need to be changed every 2 weeks in young, large- or giant-breed dogs, because they may quickly outgrow the cast.
- Obtain radiographs of the repair every 2 weeks in order to assess healing. Radiograph the contralateral limb for comparison.
- Exuberant callus formation with muscle and tendon entrapment, muscle atrophy, and joint contracture may be minimized using postoperative physical therapy (see Chapter 95).
- In some cases, remove the implants in 4 weeks in order to minimize the potential for premature physeal closure.

Complications

- Exuberant bony callus is a problem in younger patients and is seen in unstable fixations or external coaptation of distal femoral fractures. Bony callus can entrap muscle and tendon.
- Bony callus can also cause fusion between bones. If this occurs between the radius and ulna, asynchronous growth and resultant angular limb deformity can occur.
- Angular limb deformity caused by premature physeal closure should be identified and addressed early. Corrective osteotomies are often required in order to correct the angular limb deformity (see Chapter 105).
- Limb shortening caused by premature physeal closure may alter limb gait, but limb length discrepancies of 25% or less are often well tolerated in dogs and cats due to their relatively flexed stance.

SUPPLEMENTAL READING

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Chapter

120 Open Fractures

Charles E. DeCamp

An open fracture is one that has been exposed to the environment and contaminated by or infected with bacteria. The soft tissue injury that accompanies an open fracture may be a simple puncture wound or a complex injury with vascular compromise and tissue necrosis. Successful management of open fractures depends on proper treatment of soft tissue wounds and fracture fixation. If soft tissue wounds are properly managed, the morbidity of wound infection is reduced and fracture healing can proceed at a normal rate.

CLASSIFICATION OF OPEN FRACTURES

Open fractures are classified as type I, II, or III, based on the mechanism and severity of soft tissue injury (Fig. 120-1). The purpose of classification is to determine the likelihood of serious infection. The type of wound management and the choice of fracture fixation partly depend on the classification.

- Type I develops when a fracture fragment penetrates the skin, exposing the fracture to bacterial contamination. Soft tissue injury is minor, and wound infection is unlikely with proper care.
- Type II develops when an external object forcefully penetrates the skin and soft tissues, creating a fracture and contaminating the wound. Fracture severity is highly variable, but soft tissue injury is relatively minimal and usually is not complicated by vascular compromise and tissue necrosis. Bacterial contamination generally is more extensive than for type I injuries.
- Type III develops when an external object forcefully penetrates the skin and soft tissues, creating a fracture, contaminating the wound, and severely damaging the soft tissues. The ability of the body to combat soft tissue infection commonly is complicated by vascular compromise and necrosis. The risk of bacterial infection is very high.
- Some authors describe an additional class of open fracture, type IV, where the trauma has caused amputation or near amputation of the limb.

▼ ***Key Point*** Type I open fractures are least likely to develop wound infections; type III open fractures almost always have some level of infection.

- In all fracture types, if the wound has been neglected and infection develops, manage the injury as though it were a type III injury.

PREOPERATIVE CONSIDERATIONS

- Perform a complete physical examination to rule out injury to other organs.
- The diagnosis of an open fracture may be made by direct inspection, palpation, and radiography.
- If skin penetration, laceration, or avulsion is present, assume that the fracture is open and contaminated until proven otherwise.
- Cover all open wounds with a sterile dressing.
- Obtain radiographs after dressing placement.
  - Radiographic signs of air within the soft tissues adjacent to a fracture are diagnostic of an open fracture.
- Use aseptic technique when manipulating the wound.

▼ ***Key Point*** Violating the rules of strict asepsis during early wound management increases the probability of nosocomial infection.

- If preparation of the wound cannot proceed immediately, use external coaptation for temporary stabilization of the fracture. Apply a reinforced Robert Jones bandage for injuries below the stifle or elbow. Use a spica splint for open fractures of the femur or humerus.
- To prepare the wound, remove the sterile bandage and carefully clip surrounding hair to avoid contamination. If necessary, cover the wound with sterile gauze sponges moistened with sterile saline or sterile water soluble lubricant gel to prevent introduction of the clipped hair into the wound.

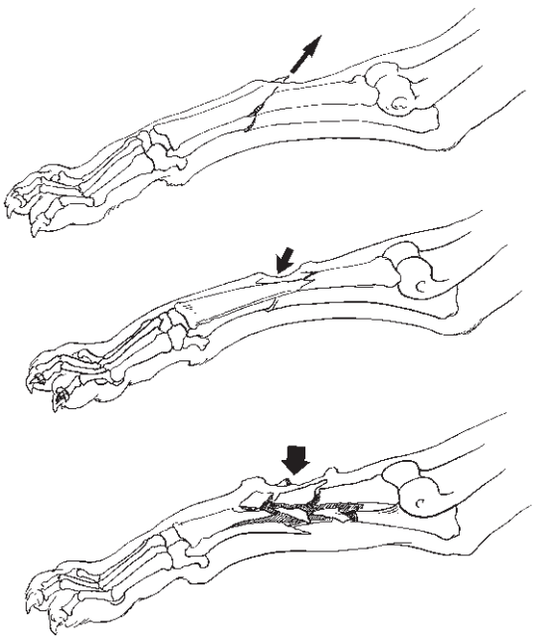

Figure 120-1. Types of open fractures. Type I *(top):* Fracture fragment penetrates skin. Type II *(center):* Penetrating object causes minor injury to soft tissue. Type III *(bottom):* Penetrating object causes extensive damage to soft tissue.

- Lavage the wound with copious amounts of sterile saline or lactated Ringer's solution to remove small particulate matter from the wound interstices (see Chapter 56).
- Betadine and alcohol may be used on the skin surrounding the wound; however, avoid contact of detergents or alcohol with the open wound.
- Remove a sample of fluid from the fracture site for laboratory tests, using a swab if the size and type of wound permit its introduction. Base definitive antibiotic treatment on culture and sensitivity tests. A Gram stain may reveal the organism type and aid the initial choice of antibiotics.
- Consider giving broad-spectrum systemic antibiotics while waiting for results of culture and sensitivity.

▼ ***Key Point*** Systemic antibiotics are less important than proper wound care for prevention and treatment of wound infection.

SURGICAL DEBRIDEMENT, FRACTURE FIXATION, AND SOFT TISSUE RECONSTRUCTION

Objectives

- Improve wound environment to reduce the risk of infection.
- Reconstruct soft tissue to cover bone and provide limb function. It may be necessary to defer this aspect if a large tissue defect or necrosis is present.
- Provide temporary or definitive fracture fixation.

Equipment

- Two standard general orthopedic packs and suture material
- Bone curette and brush
- Sterile saline or lactated Ringer's solution
- Fracture fixation equipment:
  - Materials for external coaptation
  - External skeletal fixation pins and clamps
  - Power drills
  - Bone plating equipment

Surgical Debridement

Techniques

Type I Open Fracture

1. Little or no surgical debridement is required.
2. If the bone is not visibly exposed and the wound is small, copiously lavage the wound with sterile lactated Ringer's solution.
3. Sharply excise necrotic tissue, if present, from the wound before fracture fixation.

Type II Open Fracture

1. Surgical debridement generally is not extensive; however, be careful to remove all non-viable tissue.
2. Copiously lavage the wound with sterile lactated Ringer's solution before fracture fixation.

Type III Open Fracture (Extensive Debridement and Lavage)

1. Prepare the limb and wound for aseptic surgery. If a surgical approach to a bone is anticipated, extend the skin preparation to the appropriate anatomic field.
2. Drape the limb using standard aseptic technique and water-impermeable drapes.
3. Sharply excise necrotic skin, fat, fascia, and muscle from the wound.
4. Remove any loose, dirty, small fragments of bone.
5. To preserve the blood supply and prevent development of bone sequestra, maintain tissue attachments to bone fragments.

▼ ***Key Point*** Clean *large,* attached bone fragments with a bone curette or brush if necessary. *Do not remove them.*

6. Clean, but do not debride, tendons, ligaments, intact blood vessels, and nerves unless they are necrotic.
7. If necessary, extend access to the bone by a surgical approach for fracture fixation. If severe contamina-

tion or infection is present, apply external skeletal fixation with minimal or no surgical approach (see Chapter 111).

Fracture Fixation

- Do not carry out fracture fixation until initial wound management is complete (as described previously).
- If the fracture is stable and non-articular and involves a bone distal to the stifle or elbow joint, external coaptation may be effective. Most other fractures require surgically applied orthopedic fixation.

Techniques

If a surgical approach is made, obtain samples of fluid from the fracture site and submit for culture and sensitivity.

▼ ***Key Point*** To avoid bacterial contamination from debrided tissues, use a new, sterile pack for the surgical approach and fracture fixation.

Type I Open Fracture

1. Repair with the appropriate method of external or internal fixation.
2. If a surgical approach is made to the bone, avoid contact with the traumatic wound to prevent bacterial contamination. Skin drapes may be used.
3. After fracture fixation, close the wound routinely. Penrose drains or delayed wound closure techniques usually are not necessary.

Type II Open Fracture

1. Repair with the appropriate method of external or internal fixation.
2. If a surgical approach is made to the bone, avoid contact with the traumatic wound. Skin drapes may be used.
3. Because bacterial contamination of the wound can be more severe than for type I fractures, provide proper drainage of exudates.
4. If the surgical wound is closed, place Penrose drains to exit the wound at a site ventral to the surgical incision. Alternatively, in medium to large dogs, consider placement of closed suction drains.
5. If bacterial contamination is severe, perform delayed or partial wound closure to ensure proper drainage (see Chapters 55 and 56).

Type III Open Fracture

▼ ***Key Point*** Treatment of most type III open fractures proceed in the following order: wound care, fracture fixation, and skin reconstruction.

1. Carefully choose a method that reduces the risk and severity of wound infection.
2. In general, do not use metallic implants at the fracture site unless adequate wound drainage is assured. Do not use intramedullary pins because of the difficulty in providing surgical drainage from the medullary canal.
3. Bone plates may be used in conjunction with delayed or secondary wound closure techniques, unless severe infection is present.
4. If possible, use external skeletal fixation (see Chapter 111) because a fixator may be constructed that avoids placement of metallic implants directly in the fracture site. However, anatomic considerations may contraindicate their use.

▼ ***Key Point*** Regardless of the type of orthopedic implant, rigid fixation is mandatory for definitive treatment of the fracture.

5. If an external fixator cannot be used, a type I external fixator, transarticular external fixator, or external coaptation may be used as temporary fixation so that local wound care and resolution of infection may proceed. When the wound environment has improved, other methods of internal fixation such as bone plates and lag screws may be applied with less risk of infection.

Reconstructive Soft Tissue Surgery

- Primary, delayed primary, or secondary closure techniques (see Chapters 55 and 56) may be used to treat traumatic wounds in open fractures.
- Wounds may be allowed to heal by second intention.
- Some wounds may not heal because of their large size or because they are located at a site of active motion or a pressure point (e.g., elbow). In these cases, reconstruct the skin wound with a skin flap or graft (see Chapter 57).
- Skin flaps or grafts may be constructed at the time of fracture fixation but often are delayed until a healthy bed of granulation tissue indicates that wound infection is resolved.
- If arthrodesis is the primary method of orthopedic fixation for the carpus or tarsus, perform skin reconstruction 1 month before arthrodesis. This allows full resolution of soft tissue infection and good soft tissue cover over the proposed arthrodesis site.

POSTOPERATIVE CARE

- Administer postoperative analgesics as necessary (see Chapter 6).
- Continue appropriate postoperative wound care to prevent and control infection.
- Keep open wounds bandaged, and replace the bandage daily to prevent accumulation of exudates at the wound site.

- Lavage open wounds daily with sterile saline or lactated Ringer's solution until healthy granulation tissue indicates resolution of infection.
- Restrict activity, depending on the fracture type and method of fixation.
- Use an Elizabethan collar, if necessary, to prevent the animal from licking its wounds or removing the bandages.
- Stage implant removal to provide optimal bone healing and to minimize risk of long-term wound or bone infection.
- Perform a physical examination and obtain radiographs at appropriate intervals to evaluate proper bone healing and resolution of infection.
- Administer postoperative physical therapy as needed to restore function in the affected limb (see Chapter 95).

COMPLICATIONS

- Continued infection suggests the presence of necrotic soft tissue or bone, an unstable fracture site, or unstable orthopedic implants.
- Delayed healing of a fracture may develop from prolonged infection at the fracture site, poor reduction, unstable fixation, or bone loss due to trauma or infection (see Chapters 121 and 122).

▼ ***Key Point*** Most complications can be avoided with proper wound management, orthopedic fixation, and postoperative care. Serial examinations to assess progress are essential to avoid development of major problems.

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Chapter

121 Osteomyelitis

Callum W. Hay

Osteomyelitis is caused by infection of bone and associated structures (soft tissue, periosteum, and endosteum). Osteomyelitis is invariably caused by an infectious agent such as bacteria or fungi. Acute onset osteomyelitis is rare and generally does not show detectable radiographic changes until 5 to 10 days after bone inoculation. Chronic osteomyelitis is seen as a complication from orthopedic surgery, extension of tooth infection into bone (with periodontal disease), or from nail bed infections. Osteomyelitis can mimic other diseases such as panosteitis, hypertrophic osteodystrophy, and neoplasia and should be differentiated from these.

ETIOLOGY

Bacteria

- The common routes of bacterial infection are outlined in Table 121-1.

▼ ***Key Point*** Chronic bacterial osteomyelitis is the most common form seen in veterinary medicine.

- Orthopedic surgical procedures allow introduction of bacteria from the patient's skin or from implants placed in the wound (bone plates, suture). Direct inoculation from the surgeon's skin or apparel is also possible.
- Chronic periodontal disease with extension of infection into the mandible or maxilla can lead to chronic osteomyelitis and bone weakening. The mandible of small dogs can be susceptible to iatrogenic fracture during tooth extraction, if significant osteomyelitis is present.
- Nail bed infections acquired from trauma and the environment can extend into phalanges and digits (see Chapter 63).

▼ ***Key Point*** Osteomyelitis is often propagated by local tissue environmental factor(s), which overwhelm the body's own natural defense mechanisms. These include poor vascularity, necrotic bone or soft tissue, foreign material such as metallic orthopedic implants or methyl methacrylate, and especially fracture instability.

- Beta-lactamase–producing *Staphylococcus aureus* bacteria cause a large majority of infections. Other common bacteria are *Pseudomonas aeroginosa; Escherichia coli;* and *Streptococcus, Bacteroides, Actinomyces,* and *Clostridium* species.
- Bacteria produce a mucopolysaccharide coating called glycocalyx, which protects bacteria from phagocytes, antibiotics, and antibodies. Bacterial colonization of orthopedic implants or necrotic bone allows reinfection once antibiotic therapy is stopped.

Fungi

Fungal entry into the respiratory tract can lead to osteomyelitis from hematogenous spread. Direct contamination through an open wound is possible, but rare. Most infections will occur in the vertebral bodies/disks or in the bones of the skull.

Coccidioides, Blastomyces, Histoplasma, Cryptococcus, and Aspergillus spp. can all cause fungal osteomyelitis.

DIAGNOSIS

History

- Osteomyelitis can be preceded by orthopedic surgery, penetrating trauma, chronic dental disease, injury to the toes/foot pads, or possibly known travel to an endemic fungal region.

Physical Examination

- The patient may have evidence of lameness, inappetence, malaise, elevated body temperature, muscle atrophy, and pain on direct palpation of affected area(s).
- Patients who have had orthopedic surgery may have obvious instability at the fracture site or exterior migration of pins. A draining tract may develop distal

Table 121-1. ROUTES OF INFECTION IN OSTEOMYELITIS

Open reduction and internal fixation of fractures; other orthopedic intervention
Open fractures
Extension from soft tissue infection (periodontal disease, rhinitis, otitis media)
Traumatic injuries and bite wounds
Penetrating foreign bodies, including sticks and grass awns
Gunshot injury
Hematogenous
Prosthetic joint replacement surgery

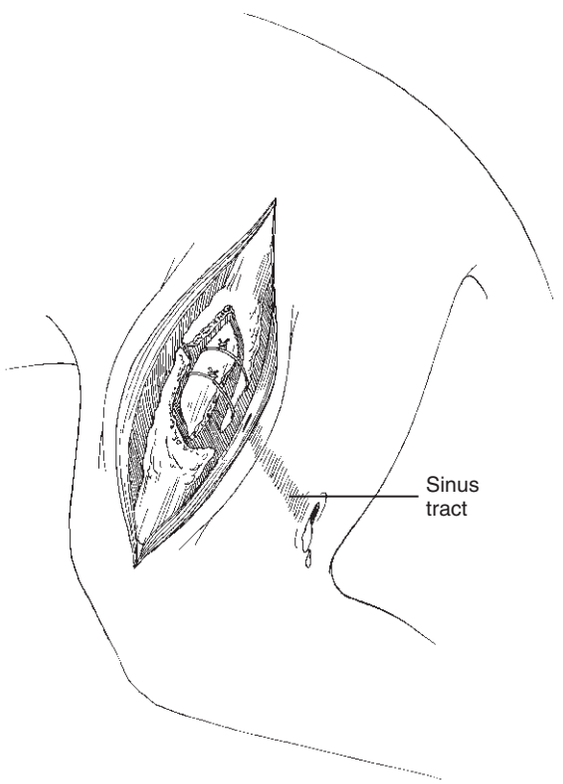

Figure 121-1. Chronic osteomyelitis with sequestrum, loose unstable implants, and involucrum walling off the focus of infection. These conditions favor chronic bacterial infection, and purulent exudate drains through a dependent sinus.

to the surgical site (Fig. 121-1). Exudate from a tract is not necessarily copious and can appear minimal, especially if the patient is frequently licking the site.

- Small-breed dogs with severe dental disease with mandibular involvement may be very painful on oral manipulation. Pathologic fractures (either precipitated iatrogenically from tooth extraction or from trauma) are easily palpable under general anesthesia.
- Swelling, heat, pain, and possibly a draining tract may be seen in patients with digital osteomyelitis.
- Mucopurulent nasal discharge, coughing, or pulmonary crackles/wheezes may be observed in patients with disseminated fungal infections (see Chapter 20).

Hematology

- Acute systemic infection may cause a neutrophilic leukocytosis; however, chronic osteomyelitis may not cause significant hematologic abnormalities.

Diagnostic Imaging

Survey Radiography

- Acute osteomyelitis will not be readily apparent for 10 to 14 days after initial inoculation.
- Focal bone lucencies and aggressive periosteal proliferation may be seen.
- Bone sequestra are diagnostic of chronic osteomyelitis.
- Evidence may be seen of implant migration/failure.
- It can be difficult to differentiate hypertrophic nonunion from chronic osteomyelitis with survey radiographs (also see Chapter 122). Both processes can be associated with an aggressive periosteal response with apparent lucent areas. In the case of mild fracture instability, both can be present simultaneously.
- Fungal osteomyelitis generally involves flat bones and the metaphyses of long bones and may have multiple lytic and proliferative lesions.
- Acute osteomyelitis can be difficult to distinguish from acute postoperative infection because radiographic changes are minimal.

Contrast Radiography

- It may be useful to inject soluble iodinated contrast media (e.g., iohexal) into a draining tract to determine the location and extent of chronic osteomyelitis. This can be especially useful in trying to differentiate the location of necrotic bone encased in more vascular periosteal bone formation.
- Perform the fistulogram by injection of contrast media into the draining tract. Use an appropriate-size rubber feeding catheter, or Foley catheter, and place in the tract under aseptic conditions. Occlusion of the exterior of the tract with digital pressure or using an atraumatic instrument may be necessary to allow proper contrast flow. Try not to allow significant outward leakage, which could hinder the ability to interpret radiographic abnormalities.

Laboratory Evaluation

Cytology

- Smears of aspirates or swabs can be useful for diagnosing fungal infections. They are probably of limited use for presumed bacterial causes since the sensitivity and specificity of cytology is likely to vary widely between cases of osteomyelitis.

Bacteriology

- Obtain samples using appropriate asepsis (clipping, disinfecting skin, and using sterile gloves) with appropriate restraint (heavy sedation or general anesthesia). Submit aspirates of affected tissue for aerobic and possibly anaerobic culture and sensitivity.
- Obtain surgical samples from bone, implants, or tissue; these should be taken preferably before perioperative antibiotic prophylaxis has been administered.
- Obtain samples for fungal cultures. However, these may take weeks to yield results.

Histopathology

- Histopathology is likely to be useful if neoplasia is suspected.
- Specialized fungal stains can be requested on pathology samples submitted to any laboratory.

TREATMENT

The treatment goals in osteomyelitis are to provide a suitable local environment that is conducive to granulation tissue formation, soft callus formation, and ultimately new bone regeneration. Chronic bacterial osteomyelitis is much more common than acute osteomyelitis and fungal osteomyelitis. However, open fractures, acute postoperative orthopedic infection, and deep bite wounds should be considered predisposing factors to acute osteomyelitis, which if inappropriately treated could lead to chronic osteomyelitis.

Surgical Procedures

Objectives

- Identify pathogenic organisms.
- Determine antibiotic sensitivity.
- Drain infected tissue.
- Remove avascular bone (sequestrectomy).
- Stabilize the fracture.
- Implant a bone graft to aid osseous union of fractures.

Equipment

- Standard orthopedic instrument pack and suture.
- Rongeurs to debride bone.
- Fracture repair instruments and equipment (e.g., plates, screws, external fixator, and possibly interlocking nails).
- Orthopedic power equipment.
- Curettes for bone graft collection and debridement.
- Retractors: hand-held or self-retaining, such as gelpi retractors.

Acute Osteomyelitis

▼ ***Key Point*** Open fractures, especially in the upper limbs or with extensive soft tissue loss and bone exposure in any bone, are considered surgical emergencies. Appropriate equipment and experience are necessary to minimize complications. Consider expedient referral to a specialist if these resources are not readily available.

Preoperative Considerations

Antibiotic Prophylaxis

- Administer antibiotics after appropriate samples have been obtained.
- Parenteral use: consider using ampicillin (20 mg/kg q6–8hr IV) with either amikacin (15 mg/kg q24hr IV) or enrofloxacin (5–10 mg/kg q24hr SC). Use metronidazole (15 mg/kg q12hr IV) for suspected anaerobes; however, ampicillin will be effective against most anaerobic organisms. Cefazolin, while effective against *S. aureus*, is generally not effective against *Enterococcus*, which is likely to be present in a wound contaminated from the environment.
- Oral use: consider amoxicillin/clavulanate (20 mg/kg q12hr PO) and/or enrofloxacin (5–10 mg/kg q24hr PO).

Analgesia

- Patients with acute osteomyelitis are extremely painful. Consider using injectable narcotics such as morphine, butorphanol, buprenorphine, or other similar drugs. If not contraindicated, ketoprofen, meloxicam, carprofen, or flunixin can be given parenterally. Consider epidural administration of morphine and/or bupivacaine for hind limbs where there is no involvement of tissue over the lumbosacral junction (see Chapter 6 for discussion of pain management).

Technique

1. Administer general anesthesia and then clip and aseptically prepare the surgical site.
2. While good exposure is necessary, avoid unnecessary disruption of blood supply or soft tissue attachments to bone.
3. Debride necrotic and infected tissue and remove any foreign material involved in the infection.
4. Lavage the wound thoroughly with sterile saline under pressure from a 20- to 60-cc syringe with an 18-gauge needle.

▼ ***Key Point*** Pulsatile pressure with a syringe and needle is more effective at removing bacteria from a wound than simple low-pressure lavage.

5. Replace loose implants and provide rigid fracture fixation.
6. External fixation is useful for temporary and definitive stabilization of open fractures, especially on the tibia, radius/ulna, and mandible. It may be preferable to stabilize the femur and humerus with plates/screws or interlocking nails depending on the surgeon's preferences.
7. Consider leaving wounds on the distal limbs open if there is severe loss of skin, muscle, or bone. With appropriate care these wounds will form granulation tissue and can possibly be closed in a delayed manner.

Postoperative Care and Complications

- If the wound is left open, cover it with sterile petrolatum-impregnated gauze with sterile sponges. Use cast padding, stretch gauze, and a stretch bandage to cover the wound (see Chapter 56 for open wound management).
- Irrigate daily (sterile saline) for 3 to 10 days until there is healthy granulation tissue present.
- Continue with antibiotics, based on the results of culture, for 4 to 6 weeks.
- Obtain radiographs at 3- to 6-week intervals to determine the progression of healing.

Chronic Osteomyelitis

Preoperative Considerations

▼ ***Key Point*** Chronic antibiotic therapy alone will fail unless the other underlying causes are identified and corrected.

Consider amputation of the affected limb if treatment carries a poor prognosis, especially if there is considerable muscle contracture, neurologic damage, soft tissue loss, and financial constraints from the owner. Treat phalangeal osteomyelitis by digital amputation (see Chapter 114). Chronic mandibular or maxillary osteomyelitis can pose a therapeutic challenge due to the lack of bone present in these cases. Obviously infected or necrotic bone should be removed (see Chapter 99); however, iatrogenic fractures created during tooth extraction will generally heal with debridement and antibiotic therapy and will not require stabilization.

▼ ***Key Point*** Bone will heal in an infected environment with internal fixation as long as there is adequate stability.

Technique

1. Expose the fracture site and identify non-viable bone and remove it using rongeurs.
2. Remove and replace implants with either internal fixation (plate/screws or interlocking nail) or external fixation.
3. Irrigate the wound with sterile saline using pulsatile lavage through a 30- to 60-cc syringe and 18-gauge needle.
4. Harvest a cancellous bone graft from the proximal humerus and pack into the bone defect. Larger defects can be filled with a mixture of cancellous bone and cortical/cancellous bone from a rib or ilium.
5. If the wound is to be left open, delay bone graft application until granulation tissue has formed (3–10 days). Manage the wound as outlined in acute osteomyelitis (also see Chapter 56).
6. Highly resistant infections (such as *Pseudomonas aeroginosa* or *E. coli*) can be treated with antibiotic-impregnated methylmethacrylate beads; these can be impregnated with amikacin, gentamycin, or tobramycin and left temporarily in the wound for 7 to 14 days.

Postoperative Care

- Select antibiotics on the basis of microbiologic culture and continue for 4 to 6 weeks.
- Obtain radiographs at 3- to 6-week intervals to assess the progression of healing.
- Consider physiotherapy and swimming to maintain range of motion in joints and to promote controlled use of the limb (see Chapter 95).
- If continued poor healing is present, assess fracture stability, look for sequestra, and reevaluate microbiologic sensitivities. If none of these factors are present, the fracture may be biologically inactive. Place a bone graft in the bone defect to accelerate healing.

Chapter

122 Delayed Union, Nonunion, and Malunion

Randy J. Boudrieau

DELAYED UNION AND NONUNION

Healing times for similar fractures in any single group of patients are fairly uniform; however, a small number of fractures have longer than normal healing times, or may fail to heal at all. The particular type of fracture (comminuted or simple), the bone involved and its location (e.g., distal radius/ulna in small-breed dogs), the age of the animal, and the type of fixation use all influence normal healing times.

- Classification:
  - When the fracture requires longer than normal time to heal but shows definitive signs of progression in healing, it is classified as a *delayed union*.
  - A fracture that does not heal over a similar period and that has no tendency toward further healing is classified as a *nonunion* (Table 122-1).

Other classifications are based on fracture site, fragment displacement, and presence or absence of infection, but are not routinely used.

Definitions

Delayed Union

Radiographic evaluation of the fracture site will reveal callus formation and progressive bone healing, but complete healing has yet to occur over a longer than expected time frame. Delayed union usually needs no other therapy than continuation of ongoing treatment of the fracture. Continued immobilization (assuming stable fixation) allows healing to occur in the majority of cases. A delayed union may, however, be preliminary to a nonunion.

Nonunion

Radiographic evaluation of the fracture site reveals a lack of progression of fracture healing (i.e., bone healing has stopped). Variable amounts of callus may be present depending upon a further subclassification of viable (biologically active) or non-viable (biologically inactive) nonunion (Table 122-2). These nonunions can be classified into two groups: those with callus formation (the hypertrophic viable nonunions) and those without callus formation (both viable oligotrophic and non-viable nonunions).

Most fractures unite within a reasonable time despite systemic factors such as malnutrition, generalized metabolic or endocrine abnormalities, and acute or chronic generalized disease states.

▼ ***Key Point*** Nonunion results from local factors at the fracture site.

Most commonly these local factors can be identified as inadequate fracture fixation, resulting in instability (Table 122-3). Motion within a fracture site creates interfragmentary strain at the site, and if this strain exceeds tissue tolerance, the tissue will not form within the gap. For example, essential fragile capillaries will not be able to cross the fracture gap within the early granulation tissue formation, or later, with the subsequent stages of tissue differentiation (cartilage and bone).

- This concept has mistakenly been thought to be a greater problem in highly comminuted fractures as opposed to simple fractures. The problem has greater significance in a two-piece fracture. This situation most often occurs in transverse fractures, where greater difficulty is encountered in attaining appropriate stability. This is important in fracture fixation and the achieving of stability when anatomically reconstructing a fracture.
- A two-piece fracture has the interfragmentary strain concentrated at the single fracture site.
- A comminuted fracture has this same amount of interfragmentary strain distributed throughout the many fracture sites (or less strain at each individual site).
- The result is that in a single fracture there is high strain, whereas in a comminuted fracture there is low strain at each fracture site.
- Resultant motion in a two-piece fracture will have potentially greater adverse effects on bone healing than in a more comminuted fracture.

Table 122-1. EXPECTED APPROXIMATE HEALING TIMES OF UNCOMPLICATED DIAPHYSEAL FRACTURES WITH MINIMAL LOSS OF CORTICAL BONE

Age of Animal	External Skeletal and Intramedullary Pin Fixation	Bone Plate Fixation*
<3 mo	2–3 wk	4 wk
3–6 mo	4–6 wk	2–3 mo
6–12 mo	5–8 wk	3–4 mo
>1 yr	7–12 wk	5–8 mo

*Fractures stabilized by this method may not be considered clinically healed (have sufficient strength) as early as fractures stabilized by other means of fixation, because direct cortical union (primary bone healing by Haversian remodeling) is not supported by periosteal callus. This is of primary importance when considering timing of implant removal. Clinical function is not adversely affected by this method of fixation because plates provide rigid fixation.

Table 122-2. VIABLE AND NON-VIABLE NONUNION

Viable Nonunion (Biologically Active)
Hypertrophic ("elephant foot," or abundant callus)
Moderately hypertrophic ("horse's hoof," or moderate callus)
Oligotrophic (little or no callus)
Non-viable Nonunion (Biologically Inactive)
Dystrophic (poor vascularity of one or both sides of the fracture)
Necrotic (avascular areas, or bone fragments, within the fracture, i.e., sequestra)
Defect (large bone defect at the fracture)
Atrophic (defect at the fracture with resorption of the adjacent bone)

Table 122-3. FACTORS ASSOCIATED WITH DELAYED UNION AND NONUNION

Local Factors*
Fracture location
Fracture gap
Soft tissue interposition
Bone loss secondary to trauma
Soft tissue trauma
Loss of blood supply as a result of initial trauma
Contamination, infection
Neoplasia
Treatment Factors†
Malposition (inadequate reduction)
Fracture gap
Soft tissue interposition
Distraction (by implants or external fixation devices)
Bone loss due to intraoperative removal
Soft tissue trauma
Loss of blood supply due to surgical trauma
Inadequate Fixation (Internal or External)‡
Instability
Postoperative infection

*Related to the fracture.
†Related to the reduction and fixation.
‡Most common factor.

The most common local factor is a fracture gap (with or without interposition of soft tissues) that exceeds the regenerative capacity of the bone. There is a critical distance over which bone will not form within a gap, resulting in a nonunion.

▼ ***Key Point*** Soft tissue trauma also is an important local factor for bone healing, as damage to the vascular supply will impede healing.

This may occur at the time of fracture, but also at the time of surgery. The importance of the surrounding soft tissues cannot be overemphasized as it is these tissues that are the source for the early revascularization of the bone (transient extraosseous circulation). Therefore, the surgical approaches must be anatomic and atraumatic in nature in order to best preserve this surrounding soft tissue envelope.

Finally, a very common local factor identified in the etiology of nonunions is in miniature or toy breed dogs, where there is a limited vascular supply to the distal radius. Fractures of this bone in these breeds of dogs have a high propensity for developing into a nonunion. Therefore, obtain rigid fixation using bone plates and place cancellous bone grafts.

▼ ***Key Point*** Regardless of the etiology of the nonunion, it requires some form of surgical intervention in order for healing to progress.

Problems Related to Non-healing Fractures

Patients with non-healing fractures may have additional problems related to function, such as disuse muscle atrophy, decreased range of joint motion and stiffness related to scar tissue contraction, neurovascular dysfunction, and limb angulation and/or shortening. These functional deficiencies will be the ultimate determinant of the success or failure of treatment, not whether the bone eventually can be made to unite.

Bone Healing

- Bone heals by either primary (Haversian remodeling) or secondary (periosteal callus) union.
- Secondary bone healing, with formation of visible periosteal callus, begins with connective tissue formation that progresses to form fibrocartilage and finally bone.

- Primary bone healing occurs without formation of connective tissue; bone disposition occurs directly (direct Haversian remodeling, or by gap healing, with fracture gaps <0.8 mm) without any visible callus. Familiarity with these concepts allows accurate sequential evaluation of the healing process.

Histology

- The most notable histologic feature of a delayed union or nonunion is increased periosteal cartilage in the callus in lieu of bone formation.
- Persistent fracture gaps at the bone ends (sometimes greater than that present at the time of the original fracture) are filled with fibrous tissue or fibrocartilage callus.
- The characteristics of a nonunion include chondroid tissue, areas of degeneration with necrosis, and fibrous connective tissue.
- Sclerosis of the bone ends at the fracture site also may occur, effectively sealing the medullary cavity (and access to the medullary circulation).

Clinical Signs

- The patient is usually lame on the affected limb, and may be non–weight bearing.
- Muscle atrophy and joint stiffness are likely sequelae to limb disuse.
- Pain may or may not be present at the level of the fracture.
- Movement (instability) of the fracture may or may not be detected clinically.
- Signs of infection and resultant pain may be present.
- Palpable enlargement of the fracture area may be present.

Diagnosis

Diagnostic Imaging

- Radiographic signs vary, depending on the extent of healing (delayed union versus nonunion); classification of these events is the basis for treatment.
- Radiography allows sequential evaluation of healing.
  - *Delayed union:* There is continued healing, albeit slow, as indicated by progressive callus formation and resorption of dead bone. A persistent fracture line with evidence of some non-bridging callus is characteristic. The marrow cavity remains open without evidence of significant sclerosis of the bone ends.
  - *Nonunion:* There is no evidence of progression of fracture healing (i.e., little or no change on sequential radiographic evaluation over a 3-month evaluation period). Smooth fracture surfaces are typical (no periosteal "irritation"), with evidence of sclerosis at the bone ends and sealed marrow cavities. Sequestra or avascular bone fragments may be observed.
- Radiography may reveal the etiology of the problem.
  - Evaluate the "treatment factors" (see Table 122-3) that may be contributing to the delayed union or nonunion.
  - The fracture fixation is the most common source of the problem, with visible evidence of instability and implant loosening. For example, a small, radiolucent halo around any of the implants (screws, wires, etc.) indicates a loose device. A change in the position of the implants on serial radiographs also indicates implant instability.

Scintigraphic Evaluation

- Scintigraphy may allow for determination between a viable and non-viable nonunion where an absence of callus is present.

Preoperative Considerations

- Always prepare for at least one autogenous cancellous graft donor site.
- Obtain tissue (preferably bone) from the fracture site for aerobic and anaerobic bacterial culture and sensitivity testing.
- Administer perioperative antibiotics (cefazolin, 22 mg/kg IV *after* cultures have been obtained; continue IV administration q2h during the surgical procedure). Continue the antibiotics (cephalexin, 22 mg/kg q8h PO) until culture results and sensitivity testing become available. Further antibiotic therapy depends upon the culture results.
- Decide whether to increase the stability of the fixation without disturbing the fracture site and callus that is present (delayed union, or hypertrophic nonunion) or to debride the fracture site in cases where minimal callus is present (oligotrophic [viable] nonunion or non-viable nonunion).
- Add an autogenous cancellous bone graft in addition to increasing the stability of, or changing, the fixation.
- Note: Treat oligotrophic nonunions (viable nonunion) in the same manner as non-viable nonunions.

▼ ***Key Point*** If in doubt as to the necessary treatment, improve fixation stability and place an autogenous cancellous graft.

- Rigid stability is best achieved with screw and plate fixation. Place the plate under tension in order to compress the fracture fragments and thus use the frictional forces generated at the point of bone fragment contact to increase stability.
- If grossly apparent infection is present (see Chapter 121), consider open wound management (and secondary wound closure with an autogenous cancellous bone graft at a later date) (see Chapter 56).
- If primary closure is performed, consider closed suction drainage of the fracture site.

- Consider options for treatment of soft tissue complications (e.g., joint stiffness, contracture). Use physical therapy to restore functional use (see Chapter 95).

Surgical Procedure

Objectives

- Increase the stability of the fracture site by increasing or changing the fixation (compression plate fixation).
- Debride the fracture site as necessary to provide restimulation for fracture healing.
- Perform autogenous cancellous bone grafting, if gaps are present, to provide further stimulation for bone formation and promote osseous union.
- Restore satisfactory function of the affected limb (*aggressive* physical therapy).

Equipment

- Standard orthopedic pack and suture material
- Implants, usually screws and plates (occasionally may necessitate a separate tension device in order to obtain greater compression at the fracture site)
- Oscillating saw (for making osteotomy cuts)
- Bur set or rongeurs (for debriding fragment ends)
- Appropriate bacterial transport media for tissue cultures
- Curettes for procurement of cancellous grafts
- Closed suction drainage system

Technique

1. Prepare the affected limb for aseptic surgery. Aseptically prepare a separate suitable donor site for harvest of autogenous cancellous bone. Usually the wing of the ilium or the proximal humerus yields a large amount of bone graft.
   a. Plan to procure the graft using a separate set of surgical instrumentation in order to avoid cross-contamination of the donor site and possible infection at the delayed/nonunion site.
2. Make a standard anatomic approach to the affected bone, preserving all soft tissue structures. A large amount of fibrous connective tissue probably is adherent to the overlying muscle bellies; identification of the various tissue planes generally is difficult and requires *sharp* dissection. Exercise caution when approaching sites adjacent to major neurovascular structures.
3. Obtain samples of bone for aerobic and anaerobic bacterial culture and sensitivity testing of the fracture site.
4. *Delayed union, or viable nonunion (with hypertrophic callus formation):* Increase the stability of the fixation with implants such as additional intramedullary pins or an external skeletal fixator (see Chapter 111), or change the implant device (e.g., external skeletal fixator or bone plate placed under tension).

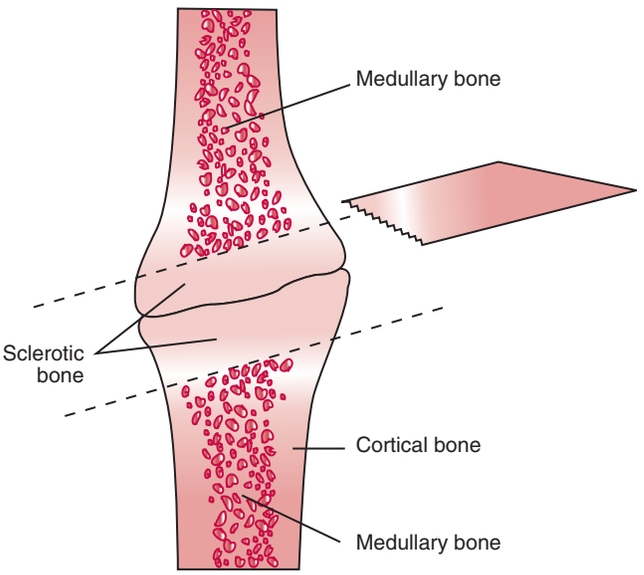

Figure 122-1. Diagrammatic representation of a nonunion with a sealed medullary cavity (sclerotic bone at the fracture margin). Dashed lines indicate level of the osteotomy cut to remove 1 to 2 cm of bone, thus removing the entire nonunion site.

5. *Non-viable nonunion or oligotrophic (viable) nonunion (with minimal callus formation):*
   a. Debride the fracture site. Remove any loose metal, dead bone (sequestra), and infected tissue.
   b. Remove the fibrous connective tissue in the fragment gap by local debridement (bur or rongeurs) or transverse ostectomy (1–2 cm) of the entire nonunion site (Fig. 122-1). *Note:* The latter technique creates a small amount of limb shortening, but this generally is not a functional problem in animals, owing to their flexed joint stance.
   c. Reestablish medullary continuity (and therefore the medullary circulation) by drilling the sclerotic bone ends (Fig. 122-2).
   d. Place an autogenous cancellous bone graft around the debrided fracture site. Ensure a separate sterile operative field and procurement process to prevent possible iatrogenic contamination of the donor site. Bone grafts may not be necessary in cases in which the nonunion site does not have a gap, such as in the osteotomy technique (circumferential fragment contact is ensured under stable, compression plate fixation). Add a cancellous graft if any doubt concerning healing exists.
      - Banked bone may be used, either as an extender for an autogenous cancellous graft or by itself. Banked bone has similar properties to autogenous bone, and is available (Osteo-Allograft, Veterinary Transplant Services, Inc., Kent, WA) as demineralized bone matrix powder, cancellous bone chips (fine or coarse), or a mix of the two.

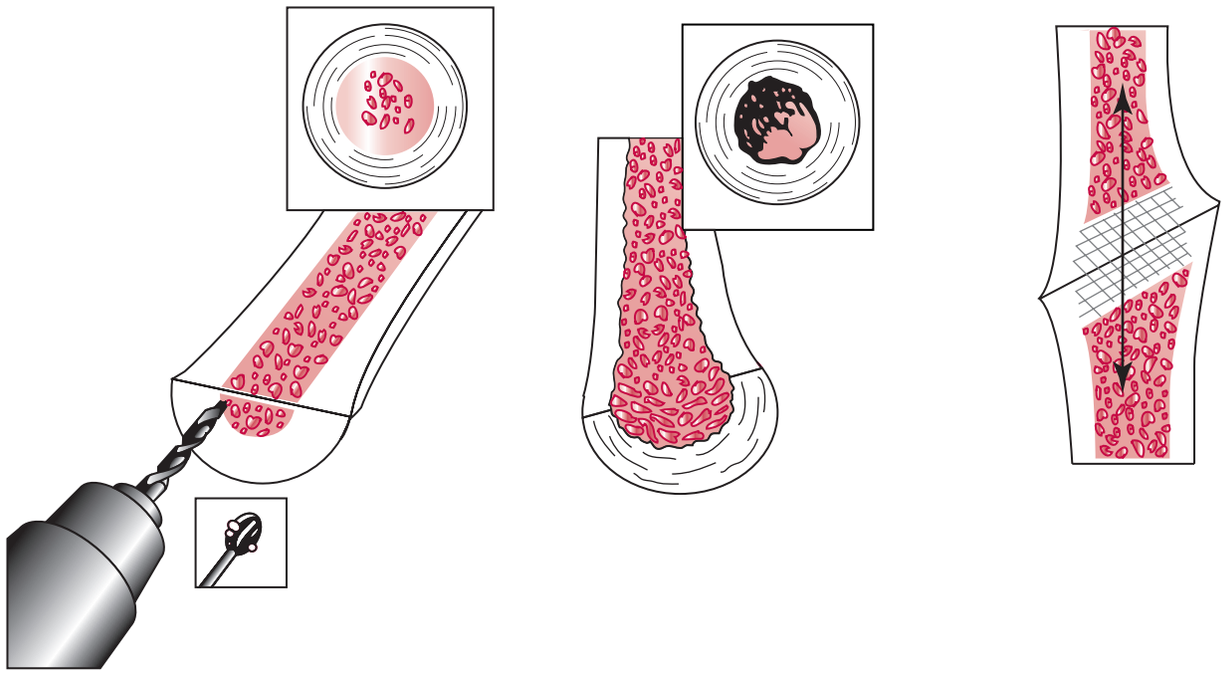

Figure 122-2. After an osteotomy (or local debridement) of the fracture site, the medullary canal may remain sealed by the remaining sclerotic bone at this level. *Left,* Medullary continuity is reestablished by drilling or burring from the fracture site into the medullary canal. *Center,* The medullary canal access has been reestablished. *Right,* Both fracture fragments are reapposed (and compression plate fixation applied), with medullary continuity now reestablished *(arrow). Insets* show cross sections of bone; *hatched area* depicts previous site of sclerotic bone.

- A newer modality is recombinant human bone morphogenetic protein (rhBMP-2) (InFuse Bone Graft, Medtronic Sofomor Danek, Memphis, TN). These substances have had limited clinical use in veterinary medicine as they only recently have become commercially available and are very expensive.

e. When using plate fixation, a separate tension device may be required in order to achieve adequate fragment compression if greater than 4.0 mm of compression is desired. This usually is not necessary, and has not been used with the osteotomy technique.

6. If the tissues grossly appear healthy, routinely close the incision. Place closed suction drains if any question of contamination/infection exists, or if dead space with continued diffuse bleeding is present.
7. Use open wound management if tissues appear grossly infected. Perform delayed primary closure and autogenous cancellous bone grafting at a later date after a healthy granulation tissue bed has developed.
8. Healing *will proceed* in the presence of infection *provided* the fixation is stable.

Postoperative Care and Complications

Physical Therapy (also see Chapter 95)

▼ ***Key Point*** Physical therapy is a key element in successful rehabilitation of these patients.

- Perform passive range of motion of joints adjacent to the surgical site *immediately* after surgery (30–50 flexions-extensions 3–4 times daily). Additional analgesics may be required in the first 2 to 4 days postoperatively. The degree of stability obtained with plate fixation allows this level of activity without major patient discomfort.
- Perform or encourage active range-of-motion exercises (e.g., controlled activity such as short walks and swimming).
- Encourage controlled weight bearing. Limb use favors improved circulation and exercise of the musculature, which in turn improves the local fracture environment.

Open Wound Management

- Change bandage(s) at least once daily and pack the entire wound with wet-to-dry gauze (see Chapter 56). Keep the soft tissues and bone moist. The goal is establishment of a healthy granulation tissue bed to cover both the bone and the implant(s).
- Perform delayed primary closure, usually with the addition of an autogenous cancellous bone graft. Consider using closed suction drains if dead space is present.
- Following successful open wound management of infected wounds, persistent drainage and local or diffuse incisional dehiscence (usually over the implant) may occur. Continued wound management is then required during fracture healing. The

implants are left in position to maintain stability. Subsequent implant removal may be necessary to finally eliminate the infection.

- Note: Metallic foreign bodies (implants) decrease the number of bacteria necessary to establish an infection. Bacterial adherence to the implants with biofilm formation (i.e., glycocalyx) may remain as the nidus for continuing infection.

Prognosis

The prognosis generally is excellent for bone healing. The prognosis is, however, ultimately dependent upon the degree of functional compromise, existing fracture disease, and compromise of joint function due to scar tissue contraction, neurovascular dysfunction, and limb angulation and/or shortening that is present at the time the altered healing is addressed.

MALUNION

Many fractures heal with some degree of deformity without significant effect on function or appearance. Although these technically are malunions, they are not considered true malunions from a practical or clinical standpoint. Clinically, a malunion implies a union with deformity sufficient to cause a functional and/or cosmetic defect. A malunion can occur as a result of untreated or improperly treated fractures.

Malunion may result in angular and rotational deformities, limb shortening, and soft tissue adhesions. These problems may directly affect adjacent joint function by alteration of the articular surfaces and/or supporting ligamentous structures. They also may affect the adjacent joints indirectly through changes in the functional angles placed on the joint and the abnormal stresses thus placed on the ligaments and joint capsule. Joint involvement, either direct or indirect, may result in decreased range of joint motion and degenerative joint disease (see Chapter 123). Correction of the malunion is accomplished by osteotomy through the area of greatest deformity, followed by realignment with stable skeletal fixation.

Precise fracture management can prevent malunion. Serial radiographic evaluation of the fracture throughout the healing period is essential to ensure continued appropriate fragment apposition and alignment. If a deformity is identified early, immediate corrective measures may prevent further complications.

Diagnosis

- Carefully evaluate the entire limb for bone and joint problems. Define the area of the long bone with the greatest amount of deformity: bowing of the bone in the craniocaudal aspect, varus/valgus angulation, or rotational abnormalities along the axis of the bone. For example, a distal radial malunion resulting from premature distal ulnar physeal growth arrest (see Chapter 105) results in cranial bowing, carpal valgus, and external rotation of the distal radius.
- Define the orientation of the adjacent joints. All axes of joint rotation should be parallel to the weight-bearing surface. In the example cited above of a distal radial malunion, the antebrachiocarpal joint surface angles cranially and medially. Depending on the duration of the deformity, severe derangements of the intercarpal joints may be present.
- Assess adjacent structures to the malunion for abnormalities of orientation and function (e.g., degenerative joint disease, joint contraction, altered range of joint motion).

Preoperative Considerations

- Determine the amount of angulation present in the awake, weight-bearing animal and compare with that of the opposite normal limb.
- Determine the amount of angulation observed on radiographic evaluation of the involved limb and compare with radiographs of the opposite normal limb. Carefully determine joint axis orientation. Be aware that radiographs may not reveal the true extent of the deformity, as the stresses of weight bearing are no longer present.
- Compare and collate the information derived from the physical examination and the radiographic evaluation to determine the amount of correction (angle) of osteotomy required.

Preoperative Planning

- Using a duplicate radiograph of the involved limb, draw the limb and joint axes and plot the angle of the correction at the area of greatest deformity.
- Cut the radiograph along the pre-drawn lines and place in the corrected position to evaluate the planned osteotomy cut and the expected result, making adjustments as necessary.
- This two-dimensional radiograph allows correction to be planned in only two planes: craniocaudal and mediolateral. Determine the remaining rotational deformity by observation at the time of surgery. (See Chapter 105 for more information about growth deformities of the radius and ulna.)
- Guide wire technique. In this method all corrections of angulation, rotation, and bending are performed using guide wires placed adjacent to the area of maximal deformity and parallel to the center of motion of the corresponding joint surfaces. Using this orientation, joint surfaces are parallel to the ground and oriented in the transverse plane, to make the respective osteotomy cuts. Although this technique is described for correction of radial ulnar growth deformities, it can be successfully used for any limb deformity.

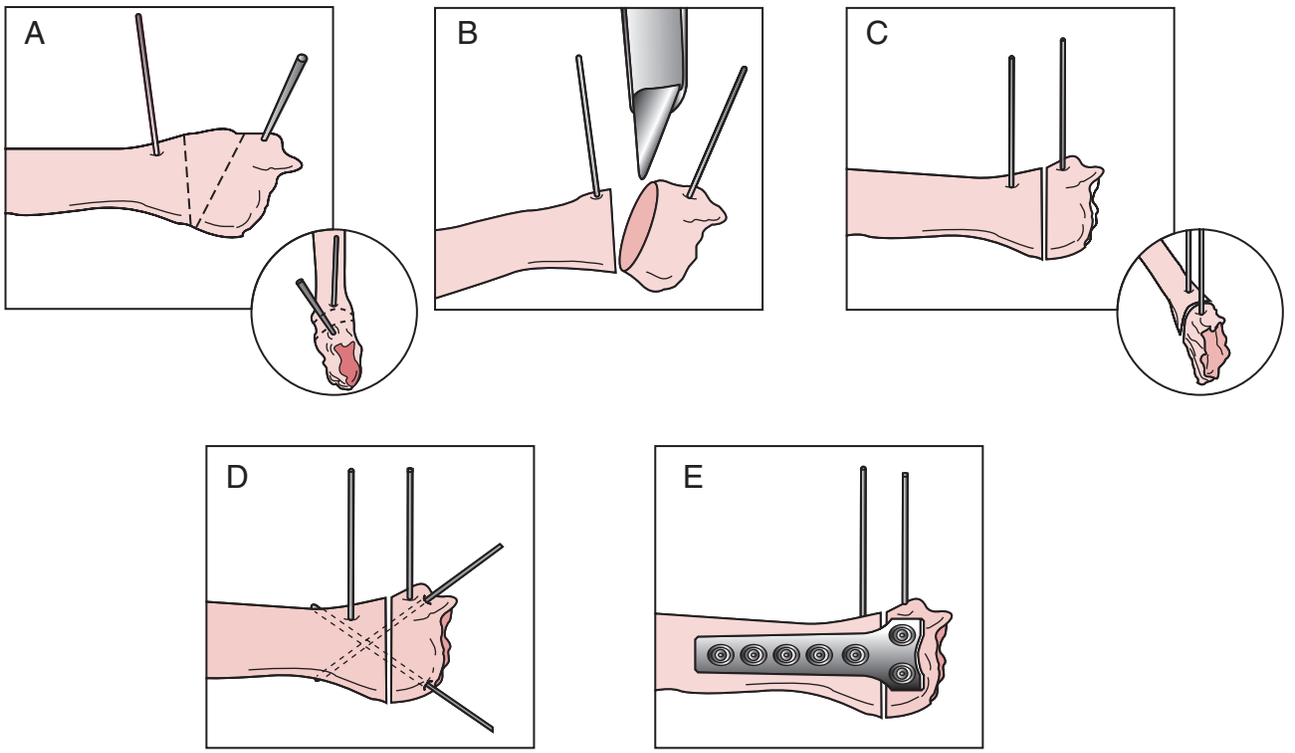

Figure 122-3. Craniocaudal and end-on illustrations demonstrating the guide wire surgical technique for a closing wedge osteotomy (example of right distal radius). (A) Place guide K-wires medial to lateral immediately adjacent to and on either side of the maximal radial deformity. Place proximal K-wire parallel to the elbow joint and its center of rotation. Place distal K-wire parallel to the antebrachiocarpal joint and its center of rotation. The *dashed lines* indicate the angle and placement of the planned osteotomy cuts. These wires address the angulation (varus/valgus) and the rotation of the distal fragment. (B) The osteotomy completed through the distal radius. Orient the cuneiform osteotomy according to the preplaced guide K-wires. Orient the proximal cut parallel to the proximal K-wire and perpendicular to the radial diaphysis. Orient the distal saw cut parallel to the distal K-wire and parallel to the distal radial joint surface. Perform the latter to address the bowing (cranial/caudal) of the distal radius. (C) Reduce the cut ends of the radius so that the K-wires are brought parallel to each other and into the same plane. At this point, correct realignment of the limb has been obtained (the carpal and elbow joints are now all parallel, and the valgus deformity, external rotation, and cranial bowing of the distal radius has been eliminated). (D) Achieve temporary reduction of the cuneiform osteotomy with two cross pins (K-wires). (E) Apply a T-plate to the cranial surface of the radius. Use either 2.7- or 3.5-mm cortical screws with the veterinary T-plate. Achieve compression across the osteotomy site using a compression guide for the eccentric placement of one or two screws in the proximal fragment. Remove the crossed K-wires. (Reproduced with permission from Balfour RJ, Boudrieau RJ, Gores BR: Vet Surg 29:207–217, 2000.)

Surgical Procedure

Objectives

- Straighten the limb by corrective osteotomy.
  - The closing wedge osteotomy is the most versatile and easy to use technique. The loss of bone length is approximately equal to the width of wedge removed.
  - Other osteotomy techniques (reverse wedge, oblique, and dome) are more difficult to perform and/or less precise in the correction of the malunion; furthermore, healing has been shown to occur with a greater number of complications.
  - A technique using distraction osteogenesis with an external skeletal fixator, most often a circular external fixation device, may be used to gradually correct the deformity after a single osteotomy cut. This technique also allows limb length to be maintained as it simultaneously allows bone lengthening.
  - This is a complex technique that requires a great deal of preplanning and expertise/experience. Consider referral to a specialist.
- Provide stable fixation.
  - Apply a plate with bone fragments placed under tension for maximal stability.
  - Alternatively, apply an external skeletal fixator (see Chapter 111).

Equipment

- Standard orthopedic pack and suture material
- Implants (preferably screws and plates, external skeletal fixator, K-wires)
- Oscillating saw
- Goniometer (for measuring and confirming angles of correction intraoperatively)

Technique (Closing Wedge Osteotomy) (Fig. 122-3)

1. Determine the angle of correction, based on the previously evaluated radiographs and physical examination; alternatively, use the guide wire technique (described here).
2. Prepare the affected limb for aseptic surgery; include within the operative field the joints above and below the proposed osteotomy site.
   a. Consider aseptic preparation and full draping of the opposite normal limb within the operative field for use as a comparison. This is especially important with chondrodystrophic-breed dogs.
3. Perform a standard surgical exposure to the bone at the level of greatest deformity.
4. Place guide wires parallel to the center of rotation of the respective joints. These wires are placed adjacent to, and on either side of, the maximal deformity.
5. Perform a closing wedge osteotomy of the affected bone to correct the deformity.
6. Reduce both bone fragments with full contact with both osteotomy surfaces. Use the guide wires to realign the bone fragments, and temporarily secure the fracture with two small cross-pins (K-wires). Make any necessary further adjustments at this time by removing the cross-pins and shaving additional bone as necessary. Draping of the surgical field to include the entire affected limb facilitates this evaluation.
7. Apply plate fixation to both bone fragments under tension. Use standard Association for the Study of Internal Fixation (ASIF) technique, including prestressing of the implant. Then remove cross-pins.
8. Close the surgical wound routinely.

Postoperative Care and Complications

- A soft padded bandage may be applied for the first 24 to 48 hours to control postoperative swelling.
- Provide standard postoperative care as for any fracture fixation, including exercise restriction and physical therapy. Evaluate the postoperative conformation and gait.
- Persistent, mild cosmetic disfiguration requires no further therapy.
- Continued functional problems require further, more precise surgical correction.
- Complications include the following:
  - Undercorrection or overcorrection of the deformity.
  - Continued functional problems due to other previously unrecognized abnormalities (e.g., degenerative joint disease, abnormal range of joint motion).
  - Slightly decreased range of joint motion is to be expected when the fixation device is placed immediately adjacent to the joint. Generally this is not a functional limitation.
  - Slight limb shortening. This generally is not a functional limitation.
  - Infection.
  - Delayed union or nonunion.

Prognosis

- The prognosis generally is good with proper case selection.

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Chapter

123 Osteoarthritis

Callum W. Hay / Paul A. Manley

Osteoarthritis (OA) is the term commonly used in describing the pathologic process of cartilage degeneration in mammalian diarthrodial joints. The term *osteoarthrosis* is preferred by those who wish to stress the non-inflammatory nature of this disease. *Degenerative joint disease* (DJD) is a term used to encompass all changes seen in OA. For practical purposes, the terms can be used interchangeably. Even though aging results in articular cartilage changes of reduced tensile strength, OA is not recognized frequently as a result. The purpose of this chapter is to discuss the etiology, diagnosis, and treatment of small animal OA.

▼ ***Key Point*** Osteoarthritis is diagnosed in dogs far more frequently than cats.

ANATOMY AND PHYSIOLOGY

- Diarthrodial joints consist of articular cartilage lubricated by synovial fluid that is secreted by the synovial membrane lining. The synovial membrane secretes synovial fluid, provides a boundary to the joints, and contains pain receptors. Articular cartilage is aneural and receives nourishment by diffusion from the joint fluid.
- Eighty percent of articular cartilage is composed of water, with most of the remainder composed of type II collagen and proteoglycan matrix, which is synthesized by chondrocytes (Fig. 123-1).

▼ ***Key Point*** In normal articular cartilage, chondrocytes continually synthesize and degrade proteoglycan. Type II collagen is degraded only during disease processes, and then type I collagen is synthesized.

- Proteoglycan consists of many repeating chains of glycosaminoglycans (mainly chondroitin sulfate and keratin sulfate). Glycosaminoglycans are bound to a protein core, which in turn is bound to hyaluronate by a link protein, to form a macromolecular structure called aggrecan (see Fig. 123-1).
- Glycosaminoglycans are negatively charged, causing them to repel one another and maintain the aggrecan in an expanded state. The negative charges bind water and cations, while the expanded state imparts stiffness to the cartilage matrix.

▼ ***Key Point*** As compressive loads move the glycosaminoglycan chains together, displacing water, the negative charge resists further compression. In this way, cartilage is viscoelastic and is able to deform and re-form with normal repetitive loading.

ETIOLOGY

- OA can be caused by primary or secondary disorders. Primary causes are rarely recognized in clinical practice. Secondary causes due to altered joint biomechanics account for most cases of OA in veterinary patients.
- Secondary causes of OA include developmental disorders, such as osteochondritis dissecans or hip dysplasia, and acquired causes, such as cranial cruciate ligament injury, patellar luxation, joint instability due to ligament sprain, and malunion of intra-articular fractures.

PATHOPHYSIOLOGY

▼ ***Key Point*** In dogs and cats OA usually results from a disruption of normal joint homeostasis by an overriding biomechanical force.

- Cartilage derangements observed in OA include increased synthesis and degradation of proteoglycan, increased cartilage hydration, loss of collagen integrity, loss of tensile strength, fibrillation, and eburnation.
- Synovial membrane derangements observed in OA include synovitis, mainly from mononuclear cell infiltration, which releases inflammatory mediators into synovial fluid.

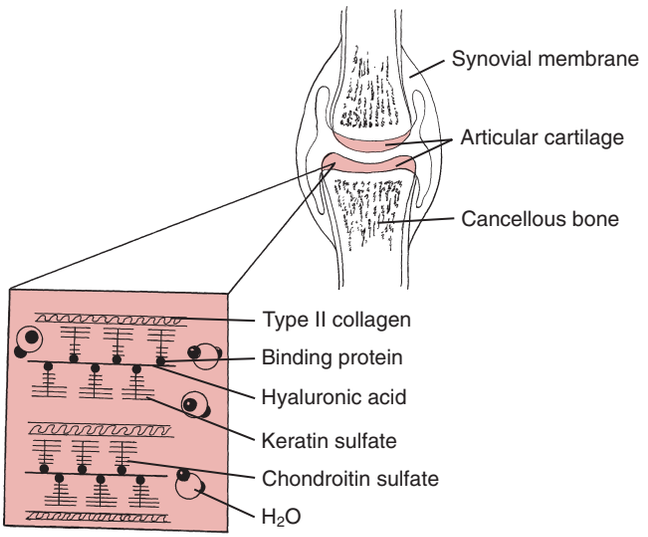

Figure 123-1. Schematic representation of cartilage structure.

▼ ***Key Point*** The release of degradative cartilage enzymes (metalloproteinases) is pivotal in the pathology of OA and results in irreversible cartilage damage. Metalloproteinases can arise from both chondrocytes and synovial membrane.

- Cytokines such as interleukin-1 (IL-1) and tumor necrosis factor-α (TNF-α) cause catabolic cartilage changes by promoting degradative cartilage enzyme production. Other mediators such as insulin-like growth factor (IGF), transforming growth factor-α (TGF-α), and interleukin-6 (IL-6) are associated with increased proteoglycan synthesis.
- The sources of inflammatory mediators include chondrocytes, synovium, and mononuclear inflammatory cells.

▼ ***Key Point*** Although there is increased proteoglycan synthesis in OA, there is increased destruction and a net loss of proteoglycan from matrix, leading to loss of structure and function.

CLINICAL SIGNS

- Morning stiffness, which improves with gentle exercise (animal "warms" out of it).
- Lameness worsens after heavy exercise.
- Lameness in one or more legs, with occasional or persistent non–weight bearing.

DIAGNOSIS

A suspicion of OA will be present after history and physical examination. Radiographs and rarely joint fluid analysis confirm the diagnosis. It is rare to confuse OA with polyarthropathy due to non-infectious or infectious causes.

History and Physical Examination

- Any age, breed, or sex of dog or cat can be affected with OA. Younger animals tend to have developmental disease. Adolescents and older dogs tend to have acquired conditions.
- A history of previous trauma that might lead to joint instability or disturbance of the articular surface is important.
- While the animal is standing, palpate for joint effusion especially in the knees, hocks, elbows, and carpi. Muscle atrophy around the thighs and over the spine of the scapula can also be better appreciated in standing animals.
- Complete the rest of the examination with the animal on its side.

▼ ***Key Point*** Gentle restraint in lateral recumbency works best with sedation, depending on the animal's temperament.

▼ ***Key Point*** Reduced range of motion and joint effusion are good indicators of a joint problem.

- Palpate for pain and crepitus (a grinding feeling when joints are flexed and extended).
- Palpate for joint laxity, which may be especially prevalent in the hip and knee.

Radiographic Examination

▼ ***Key Point*** Good-quality radiographs with correct exposure for bone and joint evaluation and proper developing technique are essential in detecting subtle evidence of OA (see Chapter 4). Radiographic abnormalities include joint effusion, osteophytes at the site of capsular attachment, subchondral bone sclerosis, and bone remodeling.

Joint Fluid Analysis

- Rarely needed in diagnosing OA.
- In most cases of OA, joint fluid yields a noninflammatory, mononuclear cell population.
- See Chapter 124 for a discussion of joint fluid analysis.

TREATMENT

OA is a progressive disease, cannot be reversed, and is generally not arrested by medical therapy. Decide if a particular patient needs to be treated surgically or medically. Many cases of OA can be managed surgically with a good prognosis for improvement in function.

Medical Treatment

There are two general groups of small animal patients that may be treated medically.

Group 1. Dogs with OA in which surgery will not help because OA is advanced or surgery is risky due to concurrent medical problems or those dogs in which surgery is declined by the owners for financial or emotional reasons. (These patients usually have advanced OA in the hips, knees, or elbows.)

Group 2. Dogs in which surgery may be part of the treatment.

▼ ***Key Point*** Often weight loss (in overweight animals) and lifestyle modifications are the only treatments necessary for an animal with OA.

- Gentle exercise is beneficial for maintaining joint mobility. Swimming and controlled leash walks work best. Generally, avoid heavy activity. Counsel owners to identify activities that exacerbate their pet's problem. Such activities are Frisbee catching, rigorous hunting, or excessive agility exercises.
- Supporting joints with external coaptation (i.e., for OA in the carpus or tarsus) may have a short-term benefit for dogs with acute exacerbations. Soft padded bandages or a support splint could be used.

Non-Steroidal Anti-Inflammatory Drugs

- Non-steroidal anti-inflammatory drugs (NSAIDs) are the mainstay of managing OA.
- Some of the pain in OA comes from prostaglandin release. By inhibiting cyclooxygenase, NSAIDs reduce prostaglandin production, alleviating pain and inflammation. Some NSAIDs (e.g., acetaminophen) have anti-inflammatory and analgesic action not attributable to cyclooxygenase inhibition; little is known about these mechanisms. It is likely that some of the NSAIDs used in small animal practice also have analgesic actions not attributable to cyclooxygenase activity.

▼ ***Key Point*** Most NSAIDs used in small animal practice inhibit proteoglycan synthesis and worsen the pathology of OA. Many NSAIDs have undesirable gastric and renal side effects. Management of OA with NSAIDs is a tradeoff between pain relief and deleterious cartilage effects and/or gastric or renal toxicity. Pain relief does not necessarily equate with chondroprotection.

- It is increasingly apparent that at least two categories of cyclooxygenase enzymes exist. Cyclooxygenase 1 (cox 1) is present in vascular tissue and is responsible for normal vascular homeostasis. Cyclooxygenase 2 (cox 2) is induced by cytokines and may have a role in OA.

▼ ***Key Point*** Inhibition of cox 1 leads to gastric ulceration and nephrotoxicity. Different classes of NSAIDs have varying abilities to inhibit cox enzymes, which dictates their efficacy and side effects. The ideal NSAID is one that inhibits cox 2 preferentially and has no deleterious effect on proteoglycan synthesis. Newer NSAIDs have been developed with these principles in mind.

- Use the lowest possible dose of NSAIDs to minimize gastric and renal side effects and minimize cartilage damage.

NSAIDs for Use in All Dogs (Groups 1 and 2)

▼ ***Key Point*** Managing OA in dogs is a balance among effective pain relief, minimal side effects, and owner satisfaction with treatment. Proper owner education about NSAIDs is essential to the harmony of this process.

▼ ***Key Point*** Choosing an NSAID for an individual patient is dictated by factors such as personal experience, relative safety of the product, patient history with NSAID use, and cost.

Buffered Aspirin

- Analgesic dose is 10 to 25 mg/kg q8–12h PO; anti-inflammatory dose is 20 to 40 mg/kg q8–12h PO in dogs.
- Buffered aspirin works better than non-buffered products. Absorption of enteric-coated aspirin can be erratic and may give variable results.
- Inhibits cox 1 more than cox 2, so gastrointestinal (GI) side effects (ulceration) may occur.
- If aspirin is not tolerated due to vomiting, the gastric side effects can be alleviated with misoprostol (a prostaglandin E_2 analog) at 2 to 5 µg/kg q8h PO. Alternatively, change to a less ulcerogenic NSAID.
- Although human buffered aspirin products are not licensed products for animals, we prescribe them commonly. Several preparations marketed for small animals are available.
- Use aspirin with extreme caution in cats. A dose of 10 mg/kg q52h PO is suggested.

Carprofen

- Carprofen may be used as a first choice over aspirin because of its proven effectiveness in pain relief, and less chance of gastric side effects.
- Dose is 2.2 mg/kg q12h PO.
- Carprofen is a carboxylic acid related to ibuprofen, but it inhibits cox 1 less relative to cox 2, so GI side effects are less than aspirin and its relative, ibuprofen.

- Carprofen is licensed for use in dogs but not in cats.
- Rare and reversible hepatic toxicity has been associated with carprofen administration in dogs.

Deracoxib

- Dose is 1 to 2 mg/kg q24h PO.
- Deracoxib has selective cox 2 activity.
- Deracoxib is licensed for use in dogs only, and rare side effects such as vomiting, anorexia, melena, and hepatic enzyme elevation are noted.

Etodolac

- Etodolac is a pyranocarboxylic acid that has selective cox 2 inhibition and possibly direct cellular anti-inflammatory activity.
- Etodolac undergoes extensive enterohepatic recirculation, so administer once daily at 10 to 15 mg/kg PO.

Meloxicam

- Dose is 0.1 mg/kg q24h PO.
- Meloxicam is supplied in an oral liquid and in an injectable form and has selective cox 2 activity.
- Meloxicam is licensed for use in dogs only, and rare side effects such as vomiting, diarrhea, and soft stool have been reported.

Phenylbutazone

- Dose is 10 to 15 mg/kg q8h PO (maximum dose is 800 mg/day regardless of body size).
- Side effects such as GI irritation and bone marrow suppression can occur. Try to taper to lowest possible dose.
- It is licensed for small animal use.
- Do not use in cats, due to adverse side effects.

NSAIDs for Use in Group 1 Dogs

These drugs carry higher risks of GI side effects, but they provide good pain relief and may be necessary for long-term use in patients in which surgery is not an option.

Piroxicam

- Is generally very effective for pain relief.
- Dose is 0.3 mg/kg q24–48h PO. It comes in capsule form, so in smaller patients breakage and division of the capsule contents is necessary to prevent overdosing.
- May not depress proteoglycan synthesis as much as other NSAIDs, based on in vitro studies.
- Gastric ulceration may occur.
- Not licensed for small animal use.

Meclofenamic Acid

- Is generally effective for pain relief.
- Dose is 1.1 mg/kg q24h PO for 4 to 7 days, then 0.5 mg/kg q24h PO.
- Watch for GI side effects.
- Is licensed for dogs.

Ibuprofen

▼ ***Key Point*** Do not use ibuprofen due to potential side effects (such as gastric or colonic perforation) and the availability of suitable licensed alternatives.

Other NSAIDs

- Flunixin and ketoprofen are licensed for small animal use in other countries but were not currently licensed in the United States at the time of publication. The recommended dose of flunixin is 0.5 to 2.2 mg/kg q24h IM or IV or 1 to 2 mg/kg q24h PO for a maximum of 3 days. Do not use in cats or for long-term therapy in dogs due to potential GI or renal side effects.

Other Drugs for Group 1 Dogs

Corticosteroids

- Unlike NSAIDs, corticosteroids severely depress synthesis of proteoglycan, even in normal articular cartilage.
- Use corticosteroids judiciously at the lowest possible dose. Corticosteroids should be used for very short-term (weeks) therapy *only*.
- Combination preparations with aspirin are available, although it is best to administer each drug separately so the dose of steroid can be reduced individually.
- Steroids tend to cause significant pain relief due to their potency; however, this does not equate with long-term benefit to the patient. It also makes it difficult to wean patients with OA off steroids because of the apparent improvement in their condition.
- Steroid therapy in surgical patients (group 2) is not advisable, since steroids may hamper any beneficial outcome of surgery.

Chondroprotective Agents

- The precise mechanism(s) of action of these drugs is still under investigation. They reportedly promote cartilage preservation through stimulation of proteoglycan synthesis and inhibition of degradation.

Polysulfated Glycosaminoglycans

- These have been shown to provide improvement in pain and function in dogs with OA, especially hip dysplasia.
- If needed in group 2 patients, surgery is the best option.
- Dose is 5 to 7 mg/kg IM once every 4 days for 7 injections. Then repeat 1 to 2 times monthly as needed.
- Initially, intra-articular use was recommended but is rarely done now because of the effectiveness of intramuscular administration and the increased

risk of joint infection associated with intra-articular injection.

Glucosamines (Nutraceuticals)

- The hypothesis for their use is that incorporation of glucosamine into glycosaminoglycan is a rate-limited step in OA, and thus by supplementation with glucosamine, more proteoglycan will be produced.
- Most compounds are oral supplements.
- Their use is currently being evaluated and may be beneficial in some cases.
- Be aware that they are licensed as nutritional supplements and not pharmacologic agents.

Shark Cartilage and Fish Cartilage Supplements

- These are marketed similarly to nutraceuticals.
- Many over-the-counter preparations are available.
- Anecdotally, they help some animals and have minimal side effects.

Vitamin C

- This is often used as a treatment for many orthopedic disorders.
- The benefit in OA is questionable, but it appears to do no harm.

Tramadol

- Tramadol is a centrally acting synthetic opioid analgesic. It is supplied in oral form (50-mg tablets) and is licensed for human use.
- The primary author of this chapter has used tramadol in patients with chronic orthopedic pain with very good results. It can be used with or without NSAIDs. The empirical dosage used is 1 mg/kg PO q12h.

Surgical Treatment

- Surgical management of certain cases of secondary OA should be considered. These include osteochondritis dissecans (shoulder, elbow, tarsus, stifle), cranial cruciate ligament disease, patellar luxation, and hip dysplasia. (See respective chapters for more information on these disorders.)
- Surgery can be expected to slow down the progression of OA and improve lameness.
- Salvage surgical procedures, such as total hip replacement and carpal arthrodesis, can provide excellent results.
- Salvage arthrodesis procedures for other joints give variable results.

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Chapter

124 Immune-Mediated Arthritis

Callum W. Hay / Paul A. Manley

Immune-mediated arthropathies are inflammatory, non-infectious, and considered either non-erosive or erosive, depending on the effect on articular cartilage. The arthropathies are characterized by synovitis and articular cartilage damage. Erosive arthritis is characterized by articular cartilage loss, and nonerosive arthritis is not. Nonerosive forms are more common in small animal practice. These conditions are not curable but can be treated to improve quality of life.

ETIOLOGY

▼ ***Key Point*** The initial site for the pathology of immune-mediated arthritis is in the synovium, rather than in the articular cartilage as in osteoarthritis (OA).

- The etiology of immune-mediated arthritis is often unknown.
- Little investigation of cytokines has been done in immune arthropathies in dogs and cats. It is well established that interleukin-1 (IL-1) and tumor necrosis factor-α (TNF-α) activate metalloproteinases and cause cartilage degeneration. These cytokines diffuse from synovial membrane to articular cartilage (and vice versa). Studies in humans have shown higher levels of IL-1 and TNF-α in inflammatory arthropathies compared to osteoarthritis. Future investigation in small animals will probably show that these cytokines are involved in the pathology of both nonerosive and erosive inflammatory arthritis.

Nonerosive Forms

- The nonerosive arthropathies are characterized by antigen-antibody deposition in the synovium.
- Antigen-antibody complexes (type III hypersensitivity reaction) are potent stimuli for inflammatory mediator release, through complement fixation and subsequent infiltration of synovium by inflammatory cells. This inflammatory process releases cartilage-degrading enzymes (metalloproteinases) and leads to a self-perpetuating process of synovial inflammation and cartilage degradation. When such complexes involve antinuclear antibodies, this disease is termed systemic lupus erythematosus (SLE).

Erosive Forms

In rheumatoid arthritis, host IgG becomes antigenic, with rheumatoid factor (IgM antibody) being formed in response. The binding of IgM with IgG triggers inflammatory mediator release, similar to the pathology of the nonerosive forms. It is ill-defined, however, which factor is responsible for the development of articular cartilage erosion.

▼ ***Key Point*** A polyarthropathy is swelling of six or more joints. Swelling of more than one and less than six joints is termed pauciarthropathy.

CLINICAL SIGNS

Canine Nonerosive Arthritis

- This form usually affects larger-breed dogs with an average age of 5 to 6 years.
- The signs may be acute onset of lameness, fever, lethargy, and swelling, especially of the distal joints.
- Initially, the range of motion in the joints may be decreased due to swelling, and later the joints may become unstable due to ligamentous damage.

▼ ***Key Point*** The nonerosive arthropathies are more commonly seen in veterinary patients and have been classified into four groups.

- Type I—These have idiopathic causes and account for 50% of small animal cases.
- Type II—These are associated with remote infection from sites other than joints, for example, bacterial endocarditis or any other focus of infection that could act as a source of antigens. The joints are usually not infected; rather, immune complexes between host antibody and bacterial components cause the problem. Type II accounts for 25% of small animal cases.
- Type III—These are associated with chronic gastrointestinal disease and are also called enteropathic

arthritis. They account for 15% of small animal cases.
- Type IV—These are associated with neoplasia remote to joints and account for the remaining 10% of small animal cases.

Nonerosive Arthritis Syndromes

Several disease syndromes that do not fit in the above classification include:

Systemic Lupus Erythematosus

- Characterized by autoimmunity to body tissues and immune complex disease. Clinical problems include thrombocytopenia, hemolytic anemia, neutropenia, dermatitis, glomerulonephritis, and polyarthritis.

Juvenile-Onset Polyarthritis Syndrome in Akitas

- Affects Akitas less than 1 year of age. Clinical signs include cyclic pain, fever, lymphadenopathy, and occasionally non-septic meningitis. A heritable component is suspected.

Inflammatory Arthritis of Chinese Shar-Peis

- Affects Shar-Peis of any age. The arthropathy is characterized by episodic fever and swelling, mainly of the hocks. It is usually associated with renal amyloidosis and is also known as Shar-Pei fever.

Polyarthritis/Polymyositis

- Affects spaniel breeds. Clinical signs include muscle pain, atrophy, and contracture along with pyrexia and polyarthropathy. High levels of creatine phosphokinase may be seen, due to muscle involvement.

Polyarthritis/Meningitis

- Affects Bernese mountain dogs, beagles, boxers, German shorthaired pointers, and Weimaraners. Clinical signs include cyclic fever and neck pain lasting 3 to 7 days. Joint swelling may be seen but is not the primary feature of the disease.

Idiopathic Drug-Induced Polyarthritis

- Most commonly seen secondary to administration of antibiotics such as sulfonamide drugs and less commonly erythromycin, lincomycin, cephalosporins, and penicillins. Doberman pinschers have been identified as being particularly susceptible to the effects of sulfonamide drugs. The mechanisms of drug-induced polyarthritis could include a hapten reaction or direct immune complexes of host-produced antibody with the drug.

Canine Erosive Arthritis

Rheumatoid Arthritis

- Most commonly recognized canine erosive arthropathy, but is rarer than nonerosive arthropathies.
- This form affects smaller-breed dogs of any age.
- The signs may be more insidious than in the nonerosive forms and may be associated with fever, lethargy, swollen joints, and shifting leg lameness.
- Angular deformities may occur especially in the carpi as a result of ligamentous destruction around the joints.

Greyhound Polyarthritis

- Affects young greyhounds and has been described in Australia and the United States. The cause is unknown, but *Mycoplasma spumans* has been suspected.
- The disease may have an insidious or acute onset characterized by joint swelling, pyrexia, weight loss, pneumonia, and diarrhea. The articular cartilage pathology observed includes erosion and pannus.

Inflammatory Arthropathies of Cats

▼ ***Key Point*** Inflammatory arthropathies in cats are recognized less frequently than in dogs.

Nonerosive Forms

- The Type I to IV classification described in dogs also holds true for cats.
- With polyarthropathy in cats, bone marrow neoplasia (Type IV) should be suspected, with lymphoma or multiple myeloma being the cause.

Feline Progressive Polyarthritis

- This is described in both nonerosive and erosive forms. The nonerosive form, also known as the periosteal proliferative form, is most common.
- The nonerosive form occurs almost exclusively in male cats. Clinical signs include stiffness, pyrexia, and lymphadenopathy. Commonly, the tarsi and/or carpi are affected.
- Feline syncytia-forming virus and feline leukemia virus have been implicated as the causal agent.

Erosive Forms

- This is the less common form of feline progressive polyarthritis.
- Chronic onset of stiffness involving the carpi and/or tarsi may be seen.
- The disease often progresses to subluxation and luxation of the carpi, tarsi, and phalanges.

DIAGNOSIS

Unfortunately, no one diagnostic test is specific for a certain type of immune-mediated polyarthropathy. Extensive diagnostic testing may yield confusing results. Infectious agents such as rickettsiae, *Borrelia burgdorferi,* mycoplasma, bacteria, and fungi can cause polyarthropathy. They may be ruled in or out with a variety of serologic tests and/or cultures.

History/Physical Examination

- Signalment and history help determine if breed-specific causes may be present.
- A thorough physical examination is necessary because of the wide range of causes of polyarthritis.
- Joint swelling and reduced range of motion or laxity, especially of the carpi and tarsi, may be appreciated on physical examination.
- Peripheral lymphadenopathy and splenomegaly may be present.
- About 30% of dogs with the nonerosive form have dermatitis, or focal alopecia.
- Elevated rectal temperature can be present.

Radiography

Nonerosive Forms

- Early-stage nonerosive arthropathies may show joint swelling and minimal radiographic signs of osteophytes. Osteophytes may be present later in the disease.

Erosive Forms

- Erosive arthropathies show small or large lytic areas of subchondral bone and osteophytosis.

▼ ***Key Point*** It may be difficult to radiographically distinguish long-standing nonerosive disease (with secondary joint destruction) from erosive disease.

Laboratory Evaluation

- Obtain a complete blood count, serum chemistry profile, and urinalysis. In conjunction with history and physical examination, prioritize the rule-out list and identify concurrent diseases.
- The presence of an inflammatory leukogram and hyperglobulinemia suggests inflammation.
- Over 50% of patients with nonerosive polyarthropathies are proteinuric, so hypoalbuminemia may be seen as a result of renal damage.
- Consider a rheumatoid factor (RF) test. Dogs with rheumatoid arthritis may periodically have positive or negative RF tests and dogs without rheumatoid arthritis may have a positive RF test.
- Antinuclear antibody (ANA) is helpful in supporting a diagnosis of SLE. A lupus erythematosus (LE) preparation is an in vitro test used to identify polymorphonuclear cells that have phagocytosed nuclear material. This test may be considered when the ANA test is positive and the diagnosis of SLE is elusive.

▼ ***Key Point*** In diagnosing rheumatoid arthritis, the most reliable criteria include the following combination of clinical findings: erosive changes on radiographs, a positive RF test (present in up to 75% of cases), and inflammatory synovial fluid (see Table 124-1). A biopsy to identify histologic synovial membrane changes consistent with canine rheumatoid arthritis may be helpful in elusive cases.

Joint Fluid Analysis

- Aseptic percutaneous needle arthrocentesis under heavy sedation or, preferably, anesthesia is necessary to evaluate joint fluid.
- Clip the hair around the joint and prepare with a disinfectant scrub.
- Use a 20- or 18-gauge needle and 5-cc or 12-cc syringe and aspirate gently. The relevant landmarks for commonly aspirated joints are shown in Figures 124-1 to 124-5.
- Remove the syringe before withdrawing the needle. This prevents iatrogenic blood contamination of the sample from the subcutaneous tissue due to negative pressure in the syringe as the needle is removed.
- Submit synovial fluid (in order of priority) for cytology, total cell count, protein levels, and mucin clot. Save some synovial fluid for aerobic culture. Before submitting to a laboratory by mail, make two slides

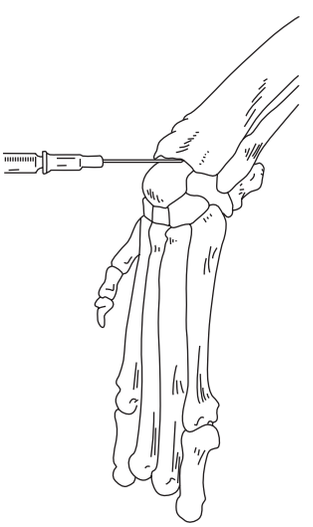

Figure 124-1. Arthrocentesis of the carpal joint. The joint lies on the same level as the base of the accessory carpal bone. With the joint flexed, the needle is introduced at the midline of the joint. (From Piermattei DL, Flo GL: Brinker, Piermattei, and Flo's Handbook of Small Animal Orthopedics and Fracture Repair, 3rd ed. Philadelphia: WB Saunders, 1997.)

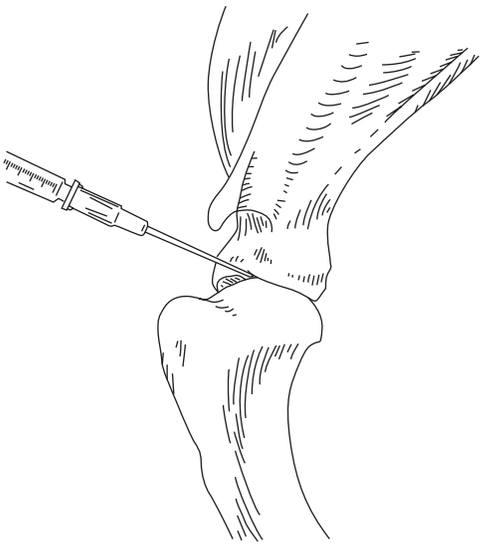

Figure 124-2. Arthrocentesis of the scapulohumeral joint. The needle is introduced about 1 cm distal to the acromion process of the scapula. If no fluid is obtained, an assistant may gently pull the forearm distally to "open" the joint space. (From Piermattei DL, Flo GL: Brinker, Piermattei, and Flo's Handbook of Small Animal Orthopedics and Fracture Repair, 3rd ed. Philadelphia: WB Saunders, 1997.)

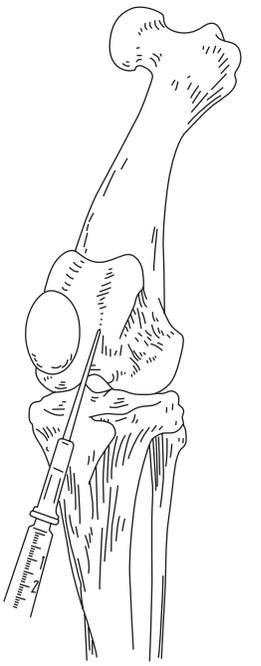

Figure 124-4. Arthrocentesis of the stifle joint. With the knee flexed, the needle is introduced just medial or lateral to the midportion of the straight patellar ligament. (From Piermattei DL, Flo GL: Brinker, Piermattei, and Flo's Handbook of Small Animal Orthopedics and Fracture Repair, 3rd ed. Philadelphia: WB Saunders, 1997.)

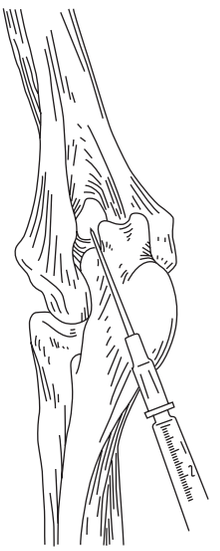

Figure 124-3. Arthrocentesis of the elbow joint. With the elbow in extension, the needle is introduced just lateral to the olecranon. (From Piermattei DL, Flo GL: Brinker, Piermattei, and Flo's Handbook of Small Animal Orthopedics and Fracture Repair, 3rd ed. Philadelphia: WB Saunders, 1997.)

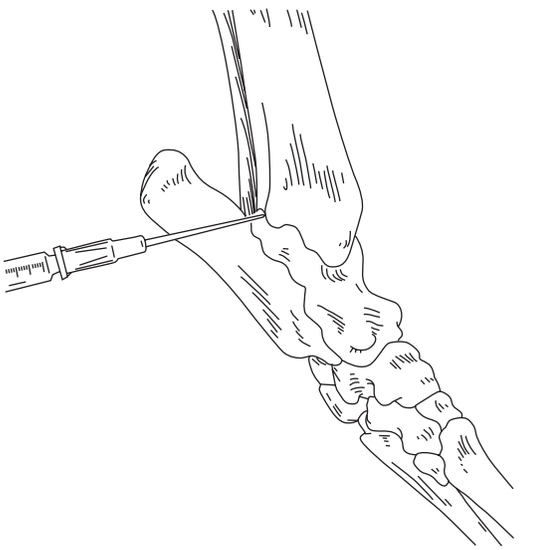

Figure 124-5. Arthrocentesis of the tarsocrural joint. With the hock held in extension, the needle is introduced lateral to the fibular tarsal bone and aimed toward the middle of the joint. (From Piermattei DL, Flo GL: Brinker, Piermattei, and Flo's Handbook of Small Animal Orthopedics and Fracture Repair, 3rd ed. Philadelphia: WB Saunders, 1997.)

Table 124-1. JOINT FLUID ANALYSIS IN DIFFERENT CLASSES OF JOINT DISEASE*

Disease	Mucin Clot	Appearance	WBC Count (mm^3)
Normal	+	Clear	0–2900
Osteoarthritis	+	Clear	<3000
Immune-mediated	±	Turbid	>5000; neutrophils are well preserved
Septic arthritis	–	Very turbid	Usually >60,000; degenerate neutrophils

*Isolation or observation of significant numbers of any microorganism from joint fluid is highly supportive of an infectious or septic etiology, regardless of cell count. Cell counts in immune-mediated and septic joints may be similar in many cases.
WBC, white blood cell; +, positive; ±, can be positive or negative; –, negative.

(one for cytology, one for a Gram stain) and place some synovial fluid in a blood culture bottle to enrich small numbers of bacteria that may be present if sepsis is suspected. Then place the rest of the synovial fluid in a blood tube with ethylenediaminetetraacetic acid (EDTA) shaken out (frequently the synovial fluid volume is small, so there is a relative excess of EDTA). EDTA interferes with the mucin clot test, making interpretation difficult.

- The predominant cell type seen on cytology in immune arthropathy is usually non-degenerate neutrophils, but mononuclear cells can sometimes be predominant.
- See Table 124-1 for comparison of joint fluid analysis in various arthropathies.

Synovial Biopsy

- May be indicated in diagnostically challenging cases of immune-mediated joint disease.
- Requires open biopsy using strict aseptic technique.
- Harvest synovium at the cartilage-bone margin.
- Histology shows plasma cell and lymphocyte infiltration.

TREATMENT

A dilemma in the treatment of polyarthropathy is whether the process is infectious or non-infectious. The treatment for a non-infectious problem (i.e., immunosuppression) exacerbates an infectious cause of polyarthropathy. If intracellular bacteria are seen on synovial fluid analysis or if bacterial culture is positive, the process is likely septic. However, in endemic areas for Lyme disease and ehrlichiosis it can be difficult to distinguish these from immune-mediated joint disease. Some prefer to initially treat with tetracyclines (e.g., for 1 week) and change to corticosteroids if no response is seen, or after results of diagnostic testing are available. The cyclic nature of many of the immune-mediated diseases, however, makes interpreting a response to treatment difficult.

Nonerosive Forms

▼ ***Key Point*** The initial treatment for all nonerosive immune-mediated arthropathies is similar. Use either nonsteroidal anti-inflammatory drugs (NSAIDs) or corticosteroids.

- The lowest dose of drugs to control signs should be used.
- Recurrences are possible after cessation of therapy.

Initial Therapy (2 to 4 Weeks of Therapy)

- Buffered aspirin at the higher (anti-inflammatory) dose range (25–40 mg/kg q8h PO) could be tried. Carprofen (2 mg/kg q12h PO) could be administered as an alternative because of its lower risk of gastrointestinal side effects.
- If sepsis has been ruled out, prednisone at 1 to 3 mg/kg q12h PO may be given.
- It is best to use either NSAIDs or steroids, but not both. The higher doses of these drugs together may potentiate each other's side effects. It is feasible to use prednisone on alternate days with NSAIDs, at low doses.
- Besides clinical signs, repeat aspiration of joint fluid may allow monitoring of the effectiveness of therapy. A cell count of less than $4000/mm^3$ is ideal. In cases in which the cell count does not decrease and the clinical signs are present, other immunosuppressive drugs may be needed (Table 124-2).

Long-Term Therapy (Months to Years)

- Preferably, the patient should be weaned off therapy after 2 to 4 months of treatment.
- If signs reappear after several attempts to discontinue therapy, the patient will likely require long-term corticosteroid therapy at the lowest possible dose. Base the decision to proceed with long-term therapy on the severity of the problem. Cases nonresponsive to glucocorticoids may require more aggressive immunosuppression as outlined in the next section.

Table 124-2. DRUG REGIMENS USED FOR CONTROL OF IMMUNE-MEDIATED ARTHRITIS

Drug	Dose	Action	Comments
Acetylsalicylic acid (aspirin)	25–40 mg/kg q8h PO	Analgesic; anti-inflammatory	Generally more effective for degenerative joint disease
Glucocorticoids (prednisone, prednisolone)	1–3 mg/kg q12h PO until remission achieved; then decrease to lowest effective maintenance dose	Anti-inflammatory; immunosuppressive	First choice for nonerosive forms; can be used alone or in combination with other drugs
Cyclophosphamide* (Cytoxan, Mead Johnson)	1.5–2.5 mg/kg PO q24h 4 days/week	Immunosuppressive	Monitor WBC count; watch for hemorrhagic cystitis
Azathioprine† (Imuran, Burroughs Wellcome)	*Dogs:* 2 mg/kg q48h PO	Immunosuppressive	Monitor WBC count; relatively toxic in cats
Gold sodium thiomalate (Solganal, Schering)	0.5–1 mg/kg IM once weekly	Unknown	Used in erosive forms; limited clinical experience

*Glucocorticoids are commonly administered concurrently with this drug.
†Glucocorticoids are commonly administered on alternating days with this drug.
WBC, white blood cell.

Erosive Forms

▼ ***Key Point*** Canine rheumatoid arthritis usually requires immunosuppression in addition to prednisone for a response.

- Cyclophosphamide is often used along with prednisone in treating rheumatoid arthritis.
- The side effect of hemorrhagic cystitis associated with cyclophosphamide can be devastating to the patient. Discontinuing cyclophosphamide after 4 months of therapy minimizes the chances of hemorrhagic cystitis.
- Note that cyclophosphamide is used for 4 days during each week of therapy.
- Gold sodium thiomalate can be used to maintain remission after cessation of cyclophosphamide. Gold salt is a slow-acting antirheumatic drug and is unsuitable for inducing remission.
- Azathioprine can be used instead of cyclophosphamide to induce remission in dogs only, since it is toxic to cats.
- Additional treatment information is in Table 124-2.

Surgery

- Surgery has a limited role in managing immune-mediated arthropathies.
- Pancarpal arthrodesis could be considered in some patients with localized disease to the carpi (see Chapter 106).
- Surgery for cranial cruciate ligament rupture in immune-mediated polyarthropathies should be considered with a very guarded prognosis due to ongoing joint destruction.

Supportive Care

- As in osteoarthritis, lifestyle modification, weight reduction, and exercise restriction aid in managing immune-mediated arthropathies.

PROGNOSIS

Nonerosive Forms

The prognosis for Type I to III forms is favorable; it is guarded for Type IV due to the presence of neoplasia. The breed-specific diseases differ in prognosis. The arthritis of Akitas and Shar-Peis has a poor prognosis. SLE patients may frequently relapse. The polyarthritis-myositis syndrome of spaniels has a guarded to good prognosis, and the polyarthritis-meningitis syndrome in other dogs has a good prognosis. Drug-induced polyarthropathies usually respond to cessation of drug therapy. The nonerosive form of feline progressive polyarthritis has a guarded prognosis.

Erosive Forms

Canine rheumatoid arthritis can be difficult to treat successfully and may be expensive, especially if gold salt therapy is needed. Greyhound polyarthritis and the erosive forms of feline progressive polyarthritis have poor prognoses.

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Section

9 Nervous System

Philip A. March

Chapter

125 Diagnostic Approach to Neurologic Disease

William R. Fenner / Philip A. March

PRINCIPLES OF NEUROLOGIC EXAMINATION

Objectives

- Confirm that neurologic disease is present.
- Localize the site of any lesion(s).
- Determine the extent to which the nervous system is involved.
- Guide the choice of diagnostic aids.
- Determine the prognosis.

Approach

- Perform the examination in a logical, methodical, and consistent manner.
- Develop a consistent sequence and follow it with all patients.
- Begin with the general and advance to the specific.
- Perform painful portions of the examination last.

PROCEDURES FOR THE NEUROLOGIC EXAMINATION

General Observations

Mental Status

Mental status is regulated by the brain stem and cerebrum and consists of level and content of consciousness.

- Begin by evaluating the level of consciousness. A normal animal is alert; an abnormal animal is depressed, stuporous, or comatose, depending on the severity of the mental depression. Abnormal levels of consciousness may result from lesions of the brain stem or diffuse cerebral disease.
- In addition to the level of consciousness, evaluate the patient for mentational disorders. Behavior of a normal animal is described as appropriate; an animal with abnormal behavior is considered demented.
  - A demented animal is unaware and unconcerned with its surroundings. It may head-press, walk off tables, and in other ways show a complete disregard for its own safety and well-being.
  - Dementia is a sign of a cerebral disorder.

Head Posture

Head posture is regulated by the vestibular system and the strength of neck muscles.

- A normal animal holds its head in a plane parallel to the ground.
- If an animal holds one ear closer to the ground than the other ear, it is described as having a head tilt, which suggests a vestibular injury.
- In some animals, the chin is tucked under or pulled tightly toward the sternum; this postural abnormality (ventroflexion) may be seen in cats with polymyopathies (e.g., hypokalemia) or thiamine

deficiency and in dogs with cervical vertebral malformations.

Coordination of Head Movement

This is regulated primarily by the cerebellum. Disturbances of head coordination appear as head tremors.

Circling

Circling is a nonspecific finding in animals with brain disease.

- A lesion in any part of the brain may cause circling; the animal usually circles toward the diseased side.
- Circling in brain stem and cerebellar injury usually is a result of a vestibular dysfunction; therefore, circling is accompanied by a head tilt.
- Animals with cerebral injury circle, but they rarely have head tilts.

Gait and Stance

Gait

A normal gait requires integration of almost the entire nervous system; therefore, abnormal gaits may result from injury to almost any part of the nervous system.

- Sensory disturbances, such as loss of proprioception, usually result in ataxia or loss of coordination of limb movements. Signs of loss of coordination of the limbs include swaying, veering, crossing over of the limbs, and scuffing of the toes.

▼ ***Key Point*** Ataxia may be seen with disease or injury of the cerebellum, brain stem, spinal cord, and injuries to cranial nerve 8 (vestibular nerve). Cerebral and peripheral nerve lesions rarely cause ataxia.

- Cerebellar lesions cause ataxia in most patients.
- Cerebral lesions may produce mild weakness characterized by intermittent stumbling, tripping, and reluctance to initiate or sustain activity. More obvious signs of weakness may be caused by an injury to the brain stem, spinal cord, or peripheral spinal nerves. When classifying the weakness, also consider the resting muscle tone in the limbs.
  - Spasticity is an increase in muscle tone resulting in decreased flexion of the limbs during movement. The resultant gait is rigid and choppy.
  - Spasticity may be seen with injuries to the cerebrum, the brain stem, and some levels of the spinal cord.

Stance

Normal animals stand with their limbs at about shoulder or hip width, with the weight equally distributed on all four limbs.

- Abnormal posture may be caused by diminished position sense (proprioception), weakness, or pain.
- Many animals present with abnormal posture as a result of pain from orthopedic disorders rather than neurologic disturbances.

Tests of Postural Reactions

Attitudinal and postural (A-P) reactions test the integrity of the interconnecting pathways that regulate posture and movement as an extension of the evaluation of gait and stance. These tests evaluate the proprioceptive fibers of peripheral nerve, spinal cord, brain stem, cerebrum, and cerebellum. Some tests also evaluate special proprioception. The upper motor neurons and their connections to lower motor neurons are also evaluated.

Because so many portions of the nervous system are evaluated, A-P reactions are good screening tools for detecting nervous system disorders but are not very helpful with specific localization.

- With lesions of the cerebrum, the postural deficit normally is seen in the limbs on the opposite side of the body (contralateral) from the diseased hemisphere.
- With brain stem lesions, the clinical signs usually are bilateral but are worse on the same side (ipsilateral) as the brain stem injury.
- With lesions of the cerebellum, spinal cord, and peripheral nerves, the clinical signs are almost always on the same side of the body as the nervous system injury.
- With cerebellar injuries, A-P reactions usually are present but are ataxic.
- With peripheral vestibular injuries, A-P reactions are preserved, but the animal tends to lean, fall, and roll to the diseased side when the maneuvers are performed. Hemihopping may be slightly delayed on the same side as the vestibular lesion.

Proprioceptive Positioning

Abnormally abduct or adduct a limb, or turn the paw so that the animal bears weight on the dorsal surface of its paw (stands knuckled over). If A-P reactions are intact, the animal briskly brings the limb back to a normal resting position.

Hemihopping

Hold the limbs on one side off the ground while the patient is hopped sideways on its other two limbs. A normal animal has no trouble initiating a brisk hopping response without buckling or collapsing on the limb if conscious proprioception and strength are normal in that limb. Hemistanding the animal on one or two limbs can also be used to assess limb strength.

Wheelbarrowing

Hold the thoracic or pelvic limbs off the ground while the patient is walked forward and then backward on its other two limbs. A normal animal has no trouble maintaining itself and walking normally during this test.

Other Attitudinal and Postural Reactions

Additional A-P reactions include the extensor postural thrust reaction, the righting reaction, visual placing reactions, tactile placing reactions, and tonic neck reactions. All these tests evaluate the same basic pathways, although each may test one portion of the nervous system more completely than another. These tests are well described in standard neurology texts.

Cranial Nerve Examination

The cranial nerve (CN) examination tests the function of each CN. Often a CN deficit confirms the presence of a lesion above the foramen magnum. The CN examination allows precise localization of intracranial diseases in many cases. Because many CNs supply only the motor or the sensory component of a CN reflex, the testing of a CN reflex generally involves testing more than one nerve. This is unlike spinal reflexes in which generally the sensory and the motor components of a reflex are carried by the same nerve.

Many of the CN reflexes also are under higher control. Therefore, a CN reflex evaluates the following:

- Two peripheral CNs (one motor and one sensory)
- A central connection (usually the brain stem)
- A higher regulatory center (usually the cerebrum)

A lesion in any one of these sites may cause loss or depression of the reflex being tested. For a more complete review of the neuroanatomy of CNs, consult a neuroanatomy textbook.

Menace Response (see also Chapter 141)

The menace response tests CN2 (sensory) and CN7 (motor) and their central connections in the cerebrum, brain stem, and cerebellum. The test is performed by making a menacing gesture toward an animal. The normal response is an avoidance response (e.g., an eye blink or turning of the head).

- Loss of the menace response normally indicates a lesion in one of the following sites: retina (ipsilateral), optic nerve (ipsilateral), optic tract (contralateral), cerebrum (contralateral), brain stem (ipsilateral), cerebellum (ipsilateral), or facial nerve (CN7) (ipsilateral).
- False-positive menace responses also occur, most commonly when the movement of the hand produces air currents that stimulate the corneal reflex.
- Sounds and other distractions may make the menace response difficult to evaluate. Animals (especially cats) in a stressful environment may have an absent menace (false-negative finding).

Pupillary Light Reflex (see also Chapter 141)

This tests the reflex portion of the optic nerve (CN2) and the autonomic function of the oculomotor nerves (CN3). The test is performed by illuminating the eye with a bright light source. The normal response is rapid constriction of both pupils.

The pupillary constriction in the eye being illuminated is called the *direct pupillary response*. The constriction in the opposite pupil (the one being illuminated indirectly) is called the *consensual response*. Failure of one or both pupils to constrict is an abnormal pupillary light reflex (PLR).

- A lesion of CN2 produces loss of constriction in both pupils when the affected eye is illuminated; however, when the normal eye is illuminated, both pupils constrict.
- If the lesion is in CN3 or the brain stem, the affected pupil fails to constrict regardless of which eye is being illuminated, but the unaffected eye constricts normally when each eye is illuminated.
- Because ophthalmic diseases such as posterior synechia or severe iris atrophy may also produce loss of pupillary responsiveness, a thorough eye examination is essential in any patient with abnormal pupils.
- Other causes of a misleading PLR are increased sympathetic tone and a weak light source, both of which will slow the PLR.

Pupillary Symmetry

In this test the eyes are observed for equal pupil size.

- If CN3 and the sympathetic nerve to the eye are normal, the two pupils will be equal in size.
- If the pupils are unequal (anisocoria), this indicates possible damage to one of these two nerves.
  - If CN3 is abnormal, the large pupil is denervated and the PLR will be absent in that eye.
  - If the sympathetic nerve is abnormal, the small pupil is abnormal and the PLR will be normal in both eyes.
- Cats may have mild physiologic anisocoria if one eye is receiving more light than the other. For this reason, ensure that both eyes receive equal illumination when evaluating for anisocoria.
- A number of ophthalmic disorders may produce anisocoria, including glaucoma, iritis, uveitis, and synechia. Because of this, perform a complete ophthalmic examination on all patients with anisocoria.

Pupillary Size

The size of the pupil is determined by the amount of ambient light (CN2) and the integrity of the innervation of the pupillary muscles (CN3 and sympathetic nerve).

- Abnormally large pupils may be caused by excitement (sympathetic stimulation), bilateral optic nerve injury, CN3 paralysis, or ophthalmic disease.
- Abnormally small pupils may be associated with loss of sympathetic tone, excess parasympathetic tone, or ophthalmic disease.

Ocular Position

In normal dogs and cats, both eyes look in the same direction at any given time (normally straight ahead). This normal resting position is determined by the influence of the cerebrum and CN8 on the extraocular muscles (CN3, CN4, and CN6). If one of these portions of the nervous system is not functioning, deviation of one or both of the eyeballs may occur.

Strabismus is deviation of only one globe.

- Medial strabismus may result from an injury to CN6 (abducens nerve).
- Ventrolateral strabismus may result from injury to CN3 or CN8 (vestibulocochlear nerve).
- A lesion to CN4 (trochlear nerve) results in intorsion (a form of rotation) of the eye, which can be recognized only in animals with oval pupils or on ophthalmic examination.
- Passive deviation of both eyes in the same direction (gaze paresis) is sometimes seen in cerebral injuries.

Ocular Motility

Voluntary Eye Movement

Voluntary eye movement is initiated by cerebral stimulation of CN3, CN4, and CN6. As the animal looks around the examination room, observe to see if it appears unable to move the eyes in one or more directions.

- With a cerebral lesion, both eyes are involved, and there is a tendency for the eyes to look toward the diseased cerebral hemisphere.
- With a lesion of the CNs, only one eye is usually involved. The involved eye will tend to have strabismus at rest and lack the ability to move.

Involuntary Eye Movements: Nystagmus

Involuntary rhythmic oscillations of the eyes, termed *nystagmus,* can be induced by turning the head. This maneuver stimulates CN8, which in turn stimulates CN3, CN4, and CN6, which innervate the extraocular muscles. This involuntary eye movement is called *physiologic nystagmus.*

Physiologic Nystagmus

Physiologic nystagmus is characterized by a "slow phase," in which the eyes move slowly away from the direction in which the head is turning, followed by a "fast phase," in which the eyes rapidly move in the direction of the head turn. This recurring slow-fast, slow-fast oscillation continues as long as the head is moving.

- A lesion of CN8 or its central connections may result in loss of the ability to initiate physiologic nystagmus so that neither eye will move when the head is turned toward the side of the vestibular lesion.
- A lesion of one or more of the CNs that innervate the extraocular muscles (CN3, CN4, or CN6) paralyzes only that eye, resulting in loss of physiologic nystagmus in the paralyzed eye.

Pathologic Nystagmus

When a normal animal's head is not moving, it does not display any involuntary eye movements. If nystagmus is present when the head is at rest, this is a sign of nervous system disease and is called *pathologic nystagmus.* This usually is the result of an imbalance in the special proprioceptive system, which includes CN8, the brain stem, and the cerebellum. A lesion of any of these structures can cause pathologic nystagmus. Features of pathologic nystagmus that may help localize its origin include the *direction, method of induction,* and *persistence* of the nystagmus.

- Direction of nystagmus:
  - In *horizontal nystagmus,* the eyes move in a plane parallel to the head (i.e., the eyes move from side to side).

▼ ***Key Point*** Horizontal nystagmus is most commonly seen in peripheral vestibular disease but can occur in central vestibular disease (see Chapter 61). The fast component of the nystagmus usually is away from the diseased side.

  - In *vertical nystagmus,* the eyes move in a plane perpendicular to the head (e.g., the eyes move up and down).

▼ ***Key Point*** Vertical nystagmus is most commonly seen in central vestibular disease. The fast component of the nystagmus is usually away from the diseased side; therefore, brain stem disease causes up-going nystagmus, and cerebellar disease causes down-going nystagmus.

  - In *rotatory nystagmus,* the eyes rotate in a clockwise or counterclockwise direction in the orbit, with components of both horizontal and vertical movement. This type of nystagmus may occur with a peripheral or central vestibular lesion.
- Method of induction of nystagmus:
  - *Resting nystagmus* occurs when the head is at rest and in a normal position. This type of nystagmus is most characteristic of peripheral vestibular disease but can be seen with central vestibular disease.

  - *Positional or induced nystagmus* occurs when the head is still but is in an abnormal position (e.g., on its side or upside down). Positional nystagmus is most characteristic of central vestibular dysfunction (e.g., brain stem and cerebellar lesions). It is also seen during the recovery phase of peripheral vestibular diseases.
- Persistence of nystagmus:
  - *Permanent nystagmus* persists over time. It may have any direction and method of induction, but it is consistently present. Permanent nystagmus is characteristic of most brain stem diseases and of progressive peripheral vestibular and cerebellar diseases.
  - *Resolving nystagmus* disappears over a period of time (days to weeks). It does not recur unless there is new damage to the vestibular system. Resolving nystagmus is characteristic of nonprogressive peripheral vestibular and cerebellar diseases. In the recovery period of these diseases, nystagmus may become positional.

Facial Symmetry

Facial weakness (CN7) may result from injury to the contralateral cerebrum, ipsilateral brain stem, and ipsilateral peripheral nerve.

- Clinical signs include drooping of the lip, deviation of the nasal philtrum, increases in palpebral fissure size (pseudoptosis), and in some animals, drooping of the eyelid (true ptosis).
- Confirm the diminished muscle function by testing the palpebral and/or corneal reflexes.

Palpebral Reflex

This reflex tests CN5 and its brain stem connection to CN7.

- Initiate the reflex by touching the palpebral margins, which produces an eye blink. Loss of the eye blink reflex is usually complete if there is an injury to CN5 or CN7.
- In some animals with contralateral cerebral disease or myasthenia gravis, lagophthalmos or incomplete closure of the palpebral margins is observed.

Corneal Reflex

Like the palpebral reflex, this reflex tests CN5 and its brain stem connection to CN7.

- Initiate the reflex by lightly touching the cornea, which produces an eye blink.

Retractor Oculi Reflex

This reflex tests CN5 and its brain stem connection to CN6 (abducens nerve).

- Initiate the reflex by lightly touching the cornea, which produces retraction of the eye into the orbit.
- Lack of the reflex usually is a sign of neurologic dysfunction of CN5 or CN6.
- In some animals with loss of the retrobulbar fat pad, the eye may be enophthalmic and incapable of retraction, whereas in others, a retrobulbar mass may prevent retraction.

Facial Sensory Examination

This tests CN5 and its cerebral connections.

- Lightly stimulate the nasal mucosa, which should produce an avoidance response such as head turning or withdrawal.
- The nasal mucosa is a more reliable site for stimulation than the lips, which are relatively insensitive in some animals.

Gag Reflex

The gag reflex, which is easier to test in dogs than in cats, tests CN9 (glossopharyngeal nerve) and CN10 (vagus nerve) and their brain stem connections.

- To initiate the test, lightly stimulate the oropharynx, which should produce a swallowing reflex. Loss or depression of the reflex usually indicates brain stem or peripheral nerve dysfunction.
- Examine the pharynx for evidence of paralysis of the soft palate, and look at the larynx for evidence of laryngeal paralysis (may be difficult in an awake animal). Either condition may result from brain stem injuries or peripheral nerve injuries to CN9 or CN10.

Tongue Examination

- Look for atrophy of the tongue, which can be produced by brain stem or peripheral nerve injury to CN12.
- Also look for deviation of the tongue, which can be caused by cerebral injuries, as well as brain stem and peripheral nerve injuries. The tongue will deviate toward the side of the lesion.

Spinal Reflex Examination

The spinal segmental reflexes directly test the reflex arcs of the spinal cord. They also indirectly test the higher centers in the brain that regulate the spinal reflexes.

▼ ***Key Point*** If an injury occurs within the reflex arc, it will cause loss or depression of the reflex. Such a reflex loss allows precise localization of a nervous system injury. Because a lesion in the lower motor neuron (LMN) is involved, loss of reflexes is called an *LMN sign* or an *LMN reflex change.*

▼ ***Key Point*** If a lesion occurs cranial to a reflex arc, it disconnects the reflex from its higher (brain) regulation. This regulation tends to be inhibitory over specific proprioceptive reflexes such as the patellar and triceps reflexes. Loss of regulation results in exaggeration of these reflexes, especially the patellar reflex. Because this exaggeration reflects a lesion in the central nervous system (CNS) involving upper motor neuron (UMN) pathways, these reflex changes are called *UMN signs* or *UMN reflexes.*

UMN changes are not as precisely localizing as LMN reflexes. Spinal reflexes are classified into three groups:

- Proprioceptive reflexes
- Nociceptive reflexes
- Special (released) reflexes

This division is based on the type of sensory stimulation required to elicit the first two reflexes and on the special conditions required to elicit the third reflex.

Proprioceptive Reflexes

These myotatic reflexes are initiated by stretch of tendons or muscle spindles. The patellar reflex is strongly influenced by UMN pathways and, therefore, may be exaggerated with UMN lesions. Other proprioceptive reflexes either are not influenced or are weakly influenced by the UMN system. Increases and decreases in the force of reflex activity are both components of proprioceptive reflexes; thus, be sure to grade the strength of these reflexes. A standard grading scale is as follows:

0 = Absent reflex
1 = Diminished reflex
2 = Normal reflex
3 = Increased reflex
4 = Increased reflex with clonus

Thoracic Limb Proprioceptive Reflexes

Triceps Reflex

This tests the radial nerve that arises from spinal cord segments C7 to T2.

- Elicit by striking the tendon of insertion of the triceps muscle. A normal response is a slight extension of the elbow.
- This reflex is difficult to obtain in a normal animal. A reflex may be present if a UMN lesion is present.

Extensor Carpi Radialis Reflex

Like the triceps reflex, this tests the radial nerve and spinal cord segments C7 to T2.

- Elicit by striking the muscle belly of the extensor carpi radialis muscle. The normal response is extension of the carpus.
- This reflex is easier to elicit than the triceps reflex, but its significance is often uncertain since it can often be elicited even with lesions of the LMN pathways.

Biceps Reflex

This reflex evaluates the musculocutaneous nerve, which arises from spinal cord segments C6 to C7.

- Initiate by striking the tendon of insertion of the biceps tendon, causing a slight flexion of the elbow.
- This reflex is more difficult to obtain than the triceps reflex and is difficult to interpret.

Pelvic Limb Proprioceptive Reflexes

Patellar Reflex

This reflex tests the femoral nerve and its spinal cord segments (L4–L6).

- Elicit by striking the patellar tendon. This action produces extension of the stifle.
- This reflex is very obtainable and reliable in all animals.
- An exaggerated reflex may be present if a UMN lesion is present.
- When testing this reflex, a phenomenon known as a *false localizing sign* sometimes occurs if a sciatic nerve or L6 to S2 injury is present. Paralysis of the sciatic nerve results in a hyperactive patellar reflex. This may be due to functional loss of the antagonist muscles that oppose the extensor muscles of the stifle.

Cranial Tibialis Reflex

This reflex tests the peroneal branch of the sciatic nerve, which originates from spinal cord segments L6 to S2.

- Initiate by striking the belly of the cranial tibial muscle. The normal response is flexion of the tarsus. This reflex is readily obtainable in most animals.

Gastrocnemius Reflex

This reflex tests the tibial branch of the sciatic nerve, which originates from spinal cord segments L6 to S2.

- Elicit by striking the belly of the gastrocnemius muscle or its tendon of insertion. The expected normal response is extension of the tarsus.
- This reflex is very difficult to obtain in dogs and cats and is considered unreliable.

Nociceptive Spinal Reflexes

The nociceptive reflexes are initiated by nociceptive (painful) stimuli, such as pinching, compression, and pin pricks. These nociceptive stimuli induce withdrawal of the limb or some other reflex action. These reflexes only test the integrity of the spinal reflex arc.

▼ ***Key Point*** The fact that a reflex withdrawal reflex is present tells nothing about the health of the nociceptive pathways traveling cranially to the brain. Loss of a nociceptive reflex indicates an LMN lesion.

These reflexes do not have a large UMN influence; therefore, they do not become exaggerated with UMN lesions.

Thoracic Limb Flexor Reflex

This reflex utilizes all the peripheral nerves of the thoracic limb and tests spinal cord segments C6 to T2.

- Elicit by digital compression. The normal response is withdrawal of the limb from the source of the stimulus.
- Loss of the reflex indicates a lesion in the reflex arc.

Pelvic Limb Flexor Reflex

This reflex tests the sciatic nerve and the L6 to S2 spinal cord segments and nerve roots.

- Initiate by digital compression. The normal response is withdrawal of the limb from the source of the stimulus.
- Loss of this reflex indicates a lesion in the reflex arc.

Perineal Reflex

The perineal reflex tests the pudendal nerve, spinal cord segments S1 to S3, and the cauda equina.

- Initiate by lightly pricking or stroking the perianal skin or perineum area. The expected response is constriction of the anal sphincter and flexion of the tail.
- If mild weakness is suspected, it is best to test the reflex during a digital rectal examination to estimate the strength of contracture of the sphincter.

Special (Released) Reflexes

These are reflexes that are suppressed by the UMN in normal animals. When disconnection between the reflex arc and the UMN occurs, these reflexes become released or uninhibited. Thus, the presence of these reflexes indicates loss of UMN inhibition to a reflex arc.

Babinski Reflex

This occurs only in the pelvic limbs.

- Elicit by lightly stroking the plantar aspect of the metatarsus. In a normal animal, the toes either are unaffected or flex slightly.
- In the presence of UMN disease, the toes may spread apart and elevate (dorsiflex), which is known as a positive Babinski reflex.
- This reflex is often absent even with UMN lesions.

Crossed Extensor Reflex

This abnormal reflex may be seen in any limb.

- Initiate by eliciting a flexor reflex in an animal in lateral recumbency. In a normal animal, the limb being stimulated flexes and the contralateral, paired limb is unaffected.
- In UMN disease, when the stimulated limb flexes, the contralateral limb will involuntarily extend.

▼ ***Key Point*** When present, the crossed extensor reflex is a sign of UMN dysfunction.

Nociceptive Evaluation

Nociceptive evaluation (testing pain responses) tests for cerebral recognition of pain perception after digital compression. Cerebral recognition must be in the form of a purposeful directed response to the stimulus (turning, vocalizing, biting, struggling).

Decreased Pain Perception

A mild loss in pain perception is called *hypalgesia* or *hypoesthesia*. If the loss is total, it is referred to as *analgesia* or *anesthesia*.

- Loss of pain perception is tested by producing enough pain so that cerebral recognition occurs and a reaction is produced.
- To elicit a reaction, compress the digits vigorously. The expected response is turning of the head and/or vocalization.

This evaluation tests peripheral nerves, spinal cord, brain stem, and cerebrum. The cerebellum is not involved in the nociceptive pathways.

▼ ***Key Point*** Peripheral nerve lesions usually cause focal sensory loss, confined to the distribution of the involved nerve(s). Severe spinal cord lesions cause a bilateral, symmetrical sensory loss proceeding caudally from the approximate level of the injury.

- Brain stem lesions rarely produce detectable analgesia, because a lesion of that severity would result in the death of the animal.
- Cerebral lesions produce only hypalgesia.
- The sensory deficit with a cerebral lesion is usually contralateral to the diseased hemisphere.

Increased Sensitivity or Exaggerated Response to Pain

Hyperesthesia refers to increased sensitivity; *hyperpathia* is an exaggerated response to pain. In veterinary medicine these two terms are used interchangeably.

Exaggerated responsiveness to pain is tested by digital manipulation of the dorsal spinous processes

and paraspinal muscles. Alternatively, the paraspinal region can be stimulated with a hemostat or safety pin.

- The objective is to produce a recognizable stimulus that is not normally bothersome to the patient.
- The stimulus is applied up and down the spine, looking for an area where the patient shows an unusually acute response to the stimulus.
- An exaggerated response usually is an indication of an extradural, nerve root, or meningeal lesion (e.g., herniated disc or meningitis).

▼ ***Key Point*** Paraspinal stimulation is valuable for localizing spinal cord lesions because a hyperpathic response indicates that the problem is extramedullary and establishes the location of the lesion.

INTERPRETATION OF THE NEUROLOGIC EXAMINATION

The neurologic examination will usually demonstrate neurologic abnormalities if the patient has neurologic disease. Listing the neurologic abnormalities and then answering the following questions will aid lesion localization (Fig. 125-1).

- Is the disease in the CNS or peripheral nervous system (PNS)?
  - If conscious and unconscious proprioceptive deficits (knuckling, ataxia) are present, the lesion is probably in the CNS.
  - If UMN signs are present (paresis with UMN reflex changes), the lesion is probably in the CNS.
  - If there are lateralizing signs of paresis or proprioceptive loss, the lesion is probably in the CNS.
  - If diffuse weakness and diminished reflexes in all four limbs are present (usually without postural deficits), the lesion is probably in the PNS. (See Chapters 129 and 130 for localization of PNS lesions.)
  - If the animal has CN deficits and limb signs (postural deficits, weakness, ataxia), the lesion is usually in the CNS.
  - If the animal has CN deficits and no other signs, the lesion is probably in the PNS portion of those CNs.
  - If the animal has a history of seizures, a depressed level of consciousness, and/or a head intention tremor, the lesion is probably in the CNS.
- Is the disease above or below the foramen magnum?
  - If the animal has a CN abnormality, a history of seizures, an abnormal head posture, abnormal head coordination, or an abnormal level of consciousness, the lesion is likely to be above the foramen magnum. (See Chapter 126 for localization of brain lesions.)
  - If the lesion involves the limbs alone, the lesion is most likely below the foramen. (See Chapter 128 for localization of spinal cord lesions.)
- After you have localized the lesion (above or below the foramen; CNS or PNS), try to localize the lesion more precisely.
  - Use CN deficits, cerebellar signs, cerebral signs, spinal reflex changes, and areas of spinal hyperpathia to determine a more specific localization (see Chapters 126 and 128).
  - Make every effort to attribute all neurologic abnormalities to one focal lesion. If this is not possible, the lesion is probably multifocal or diffuse.
- Information gained by localizing the lesion includes the following:
  - Ability to rule out etiologies that would not cause lesions at the site of your localization.
  - Improved ability to select appropriate diagnostic tests based on your localization. For example, myelography is appropriate if the lesion localization is in the spinal cord. A cerebrospinal fluid (CSF) analysis would be appropriate if the lesion localization was multifocal since the primary cause of multifocal CNS disease is inflammatory disease.
  - Prognostic information for the animal's likely outcome. For example, UMN tetraplegia with no deep pain sensation after severe trauma has a very guarded to poor prognosis.

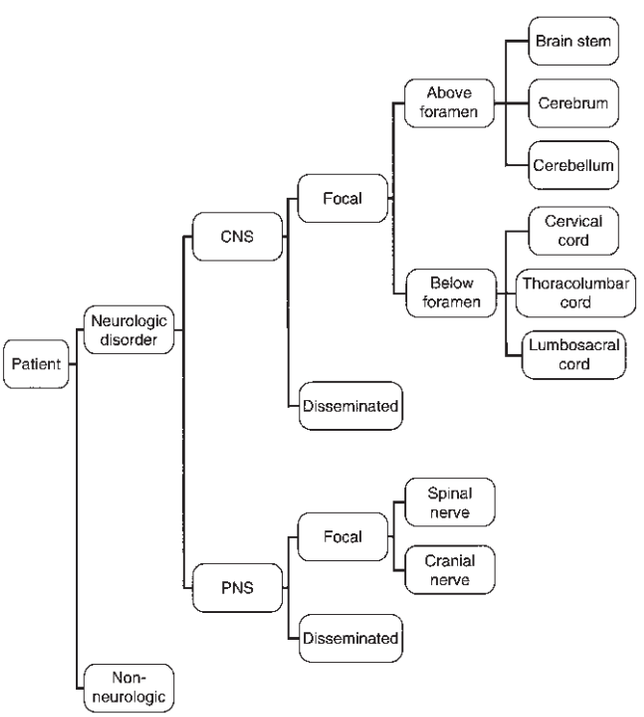

Figure 125-1. Localization flow chart. (CNS, central nervous system; PNS, peripheral nervous system.)

SELECTION OF DIAGNOSTIC AIDS

Diagnostic aids are laboratory tests and procedures that help determine which differential diagnosis is the most likely cause of the patient's signs. The primary purpose of a diagnostic aid is to provide etiologic information. As a consequence of establishing a diagnosis, these tests may also provide prognostic information. In addition, some tests provide anatomic information, allowing "fine-tuning" of the results of the neurologic examination.

Diagnostic aids used in evaluation of the nervous system include general screening tests such as routine serum biochemistries and complete blood counts that identify metabolic and toxic injuries to the nervous system. More specific tests that aid in lesion localization and diagnosis include neuroimaging, CSF analysis, and electrodiagnostic tests. Electrodiagnostic tests will also more specifically localize lesions causing neurologic dysfunction.

To select the most appropriate diagnostic aids, combine historical information with neurologic examination findings. After interpreting results of the diagnostic aids, the diagnosis should be evident.

GENERAL SCREENING TESTS

Hematology

In the majority of patients with nervous system disease, there are minimal hematologic changes. There are exceptions, such as some forms of infectious encephalitis and toxic diseases that secondarily affect the nervous system (e.g., lead poisoning).

White Blood Cell Changes

Elevation of white blood cell (WBC) numbers often indicates an inflammatory disease process; however, a low WBC count may be seen in viral infections.

Red Blood Cell Changes

Anemia, if profound, may result in hypoxia and cerebral signs. An abnormally high red blood cell (RBC) count (polycythemia) with increased serum viscosity can cause diminished blood flow to muscles and produce a myasthenia-like syndrome. It also may result in sludging of CNS blood flow with subsequent CNS infarction.

Biochemical Tests

These tests help evaluate animals with metabolic illness. Because the cerebrum has very high metabolic demands, it is affected by many generalized metabolic disorders. The motor unit also appears susceptible to a wide variety of generalized metabolic insults. Examples of biochemical abnormalities that have an impact on the nervous system include hypoglycemia and hyperglycemia, hypocalcemia and hypercalcemia, hypokalemia and hyperkalemia, hyponatremia and hypernatremia, acidosis and alkalosis, uremia, hyperammonemia, hyperlipidemia, and hyperviscosity from dysproteinemia.

Urinalysis and Urine Culture and Sensitivity

Many metabolic diseases that may affect the nervous system (diabetes mellitus, diabetes insipidus, renal disease, liver disease) produce changes in the urine. An increased urine protein-to-creatinine ratio due to protein-losing nephropathy could predispose the patient to CNS thromboembolic events secondary to hypercoagulability. In addition, some CNS infections (discospondylitis, etc.) are associated with concurrent urinary tract infections; therefore, evaluation of urinalysis and urine culture and sensitivity may be helpful in CNS infections. Urine and blood cultures are recommended if discospondylitis is present.

Ophthalmologic Examination

An ophthalmologic examination is indicated in patients with inflammatory neurologic disease. Many CNS infectious diseases can cause a concurrent anterior uveitis and chorioretinitis. A retinal exam may also be a useful screening test for hypertension (detached retinas and retinal hemorrhage) and raised intracranial pressure (papilledema). (See Chapter 138.)

Blood Pressure Measurement

Hypertension can be associated with hypothyroidism, hyperthyroidism, hyperadrenocorticism, renal insufficiency, hepatic insufficiency, and pheochromocytoma. Hypertension can also be idiopathic (essential hypertension). An elevated blood pressure can predispose the patient to CNS vascular disease. If hypertension is present, appropriate blood tests, especially for underlying endocrine or renal disease, should be performed. (See Chapter 153 for more information on hypertension.)

Thoracic Radiographs and Abdominal Ultrasound

Thoracic radiographs and abdominal ultrasound are often indicated if either neoplastic or infectious conditions of the nervous system are suspected. They may also be indicated if an underlying endocrine or renal disorder exists. Transcranial ultrasonography in young toy breeds with open fontanelles is a useful screening test for hydrocephalus.

Fecal Analysis

Severe parasitism has been reported as a cause of CNS disease in young animals.

Serology

Viral (distemper, feline infectious peritonitis), fungal (cryptococcosis, blastomycosis, histoplasmosis, coccidioidomycosis), protozoal (toxoplasmosis, neosporosis), and rickettsial (Rocky Mountain spotted fever and ehrlichiosis) infections of the nervous system result in the development of antibodies. These antibodies may be assayed in the patient's serum. CSF serology is more reliable than serum antibody assays for some of these infectious disease agents. (See the CSF serology section, Chapter 126, and Section 2 for more specific information.)

Immunofluorescence

Some viral infections that affect the nervous system may be diagnosed by using immunofluorescent techniques to detect antigen in CSF or nervous tissue (the latter is reserved for postmortem examination).

Toxicology

Blood can be assayed for many toxins known to affect the nervous system (e.g., lead poisoning).

NEURORADIOGRAPHY AND SPECIAL IMAGING

Radiography and special imaging can be used to evaluate the supporting structures of the nervous system and in some cases the nervous system itself. These studies provide information about CNS anatomy and can reveal structural abnormalities but generally do not provide information about neurologic function. (See Chapter 4 for additional information about neuroradiography and appropriate radiographic techniques.)

Plain Radiography of the Spine

- Plain radiographs can be very helpful in identifying bony lesions of the spine. Disorders that can cause changes in the vertebrae include vertebral body tumors, osteomyelitis, degenerative joint disease, fractures and luxations, soft tissue tumors that cause secondary bony lysis or pressure necrosis, mucopolysaccharidosis, hypervitaminosis A, and congenital vertebral body disorders (spina bifida, hemivertebrae, atlantoaxial malformation, etc.). Changes in the intervertebral disc space (collapse, calcification, foraminal opacification, discospondylitis) can also be identified (see Chapter 128).
- The major disadvantage of plain radiographs is the inability to image the spinal cord itself and soft tissues that may be impinging on the spinal cord. For this reason, plain radiographs provide minimal information regarding actual spinal cord compression.

Myelography

- For myelography of the spine, positive (radiopaque) contrast material is delivered into the subarachnoid space to outline the spinal cord and radiographs are taken (see Chapter 4).
- Myelography is very useful for imaging extradural or intradural/extramedullary lesions that are causing secondary spinal cord compression. Myelography can be used to localize areas of intervertebral disc herniation, spinal tumors, and other compressive lesions. It is also extremely effective in identifying areas of dynamic spinal cord compression. Post-myelogram computed tomography aids in determining the extent of lesion lateralization in the spinal canal.
- Myelography requires lengthy anesthetic times, provides marginal to no information about intramedullary diseases, is contraindicated in the presence of meningomyelitis, and is contraindicated in the presence of elevated intracranial pressure. Epidural leakage of contrast material can diminish the diagnostic information obtained.
- See Chapter 4 for proper myelographic technique and interpretation.

Skull Radiography

- Skull radiography provides very limited information about potential intracranial lesions. Bony structures of the cranial vault are visualized, but the brain itself is not.
- Loss of convolutional markings (gyral and sulcal markings) on the inside of the skull may be seen with hydrocephalus.
- Foramen magnum occipital dysplasia or "keyhole malformation" can be diagnosed using special rostrocaudal and caudorostral views of the foramen magnum.
- Bony or intranasal tumors and infections may be characterized by focal areas of bony lysis and/or proliferation.
- Occasionally, focal areas of the calvarium will show either hyperostosis (bony thickening) or lysis adjacent to a slowly expanding meningioma.
- Fractures of the skull can usually be identified with the appropriate views.
- Soft tissue or fluid densities within the tympanic bullae, bulla wall thickening and lysis, or a combination of both is usually evidence of chronic otitis media.
- See Chapter 4 for more details of the positioning techniques, imaging procedures, and image interpretation for skull radiography.

Computed Tomography

- Computed tomography (CT) provides adequate imaging of forebrain structures and large space-occupying lesions.
- CT provides excellent imaging of bony lesions such as skull fractures, skull and vertebral tumors, bulla osteitis secondary to otitis media, and discospondylitis. Intraparenchymal brain hemorrhage in the acute stages can also be identified.
- Post-myelogram CT of the spinal cord is very useful for defining axial locations of spinal cord lesions (see Chapter 128).
- Disadvantages of CT include poor resolution of brain stem, cerebellar, and spinal cord parenchyma and limited abilities to image CNS structures in more than one plane. Axial images can be reformatted to provide a limited series of low-resolution images in different planes.
- See Chapter 4 for more details on CT.

Magnetic Resonance Imaging

- Magnetic resonance imaging (MRI) provides superior imaging of brain and spinal cord parenchyma but poor imaging of bony structures. For brain lesions, MRI provides more precise lesion localization than CT (see Chapter 126). Brain edema is also more clearly identified using MRI than using CT. MRI sequences can be manipulated to give more information regarding primary lesions and CSF characteristics. Magnetic resonance images can easily be obtained in three planes to provide additional information about lesion size and extent.
- Extra-axial versus intra-axial location and pattern of contrast enhancement often aid in establishing a tentative diagnosis of brain tumors.
- The precise neuroanatomic information provided by MRI facilitates surgical planning for either biopsy or resection and radiation therapy planning.
- MRI also provides excellent resolution of intramedullary inflammatory, vascular, and congenital lesions. Some neurodegenerative conditions including cerebellar abiotrophy and lysosomal storage diseases may have characteristic MRI features. Syringohydromyelia and caudal occipital malformation syndrome in toy breeds and Cavalier King Charles spaniels are readily identified using MRI (see Chapter 128).
- MRI is less invasive than myelography and is an alternative imaging technique for intervertebral disc herniation and spinal cord tumors. MRI is the imaging modality of choice for peripheral nerve sheath tumors because it enables simultaneous visualization of the peripheral and central (spinal cord) components of the tumor (see Chapters 128 and 129).
- See Chapter 4 for more details on MRI.

CEREBROSPINAL FLUID COLLECTION AND ANALYSIS

Indications

- CSF collection and analysis are indicated if an inflammatory (infectious or non-infectious) CNS condition is suspected. Signs of inflammatory meningoencephalomyelitis may include rapidly progressive focal or multifocal neurologic deficits, recurrent seizures, neck or multifocal spinal pain, and chronic or recurrent "fevers of unknown origin."
- CSF analysis is less useful for non-inflammatory CNS conditions. CSF abnormalities in non-inflammatory conditions are often mild and nonspecific.

Contraindications

CSF collection is contraindicated in the presence of elevated intracranial pressure. Increased intracranial pressure can usually be recognized in the unanesthetized patient as a declining or depressed level of consciousness. In a patient with these signs, MRI is indicated prior to the CSF tap in order to assess the extent of brain swelling and early signs of brain herniation. (See Chapter 126 for a more detailed discussion of signs of brain herniation.) A cisternal or lumber CSF tap in a patient with elevated intracranial pressure can lead to severe brain herniation and death.

Technique

- Perform CSF collection under general anesthesia in dogs and cats. For brain disorders, collect CSF at the cerebellomedullary cistern. For spinal cord disorders, collect CSF at the L4 to L5 or L5 to L6 site. The lumbar space, however, can be more difficult to enter, yields smaller amounts of CSF, and has a higher rate of blood contamination in very small animals.
- The average distance between the skin and the cerebellomedullary cistern varies with the size of the patient. Reported distances for dogs and cats are $^1/_2$ inch for cats and dogs < 4.5 kg, $^3/_4$ inch for dogs 4.5 to 9.1 kg, 1 inch for dogs 9.1 to 22.7 kg, $1^1/_2$ inches for dogs 22.7 to 50.9 kg, and 2 inches for dogs > 50.9 kg.

Cerebrospinal Fluid Analysis

CSF analysis includes gross visual examination, cytologic analysis, biochemical analysis, and culture. In addition, serologic procedures may be indicated. There are slightly different normal values for fluid collected from cerebellomedullary and lumbar spaces; thus, note the

collection site. Fluid from the cerebellomedullary cistern tends to have slightly more cells and lower protein than fluid from the lumbar space.

Gross Examination

Normal CSF is clear and colorless. With inflammation, CSF generally becomes turbid and assumes an off-white to grayish color. Pink discoloration is usually caused by blood contamination. Yellow-orange–colored CSF (xanthochromic) generally indicates either breakdown of hemoglobin from previous hemorrhage or severe elevations of CSF protein (>100 mg/dl).

Cytology

- Cytologic evaluation consists of a total cell count on unconcentrated CSF and preparation of a slide from a concentrated CSF sample for evaluation of cell types and differential numbers.

▼ ***Key Point*** Perform the total cell count quickly (within 1 hour or less of the tap) because cells from CSF begin to degenerate rapidly following collection.

- The type and number of cells may reflect the cause of the inflammation and thus provide etiologic information. Normally there are <5 WBCs per microliter and the WBCs are a mixture of lymphocytes and monocytes.
  - A finding of 5 to 50 WBCs per microliter suggests a mild inflammatory process as seen with viral diseases and some forms of trauma, acute intervertebral disc herniation, vascular disease, and neoplasia; >5 WBCs per microliter are definitively abnormal if no RBCs are present.
  - A finding of 50 to 200 WBCs per microliter suggests a moderate inflammation, as seen with fungal, protozoal, and immune diseases, but this number may also be seen with meningiomas.
  - More than 200 WBCs per microliter indicates a marked inflammatory process, as seen with bacterial meningitis and some immune diseases.

Cerebrospinal Fluid Cytologic Interpretation

Suppurative Meningitis

Suppurative meningitis is diagnosed if the number of cells in the CSF is increased and the cells are predominantly neutrophils. Suppurative meningitis is the most common pathologic response to idiopathic meningitis or vasculitis in young dogs, bacterial encephalitis, feline infectious peritonitis, and some tumors (e.g., meningiomas). Mild increases in CSF neutrophils may be seen following CNS trauma, acute intervertebral disc herniation, fibrocartilaginous embolic myelopathy, and other acute vascular insults.

Mixed Inflammation

Mixed inflammation is diagnosed when the increased number of cells in the CSF are composed of multiple cell types, including macrophages, lymphocytes, neutrophils, and sometimes plasma cells. Although a mixed cytology is generally the result of fungal, protozoal, and idiopathic encephalitis, this cytologic change may also be seen in chronic bacterial infections that are being inadequately treated. Idiopathic granulomatous meningoencephalitis (GME) is typically characterized by granulomatous inflammation (lymphocytes, monocytes, macrophages), but neutrophils may sometimes be present in the acute stages.

Nonsuppurative Inflammation

Nonsuppurative inflammation is diagnosed when the number of cells in the spinal fluid is increased and it is composed primarily of mononuclear cells, especially lymphocytes. It is most characteristic of idiopathic immune-mediated forms of encephalitis, rickettsial infections, and some viral infections. Although this type of CSF abnormality is least likely to be due to an acute bacterial infection of the nervous system, it may occur. Chronic compressive spinal cord lesions may cause a mild elevation of lymphocytes and monocytes.

Eosinophilic Inflammation

Increased eosinophils in CSF may be observed secondary to immune-mediated eosinophilic meningoencephalitis, fungal infections, protozoal infections, and aberrant parasite migrations.

Red Blood Cell Pleocytosis

Increased RBC numbers are usually due to iatrogenic blood cell contamination during the CSF tap procedure. RBCs may also be increased due to previous hemorrhage due to trauma, coagulopathy, or inflammation. Erythrophagocytosis and xanthochromia may be observed if there has been previous hemorrhage.

Tumor Cells, Infectious Agents, and Intracellular Inclusions

Tumor cells are rarely identified in CSF with the exception of neoplastic lymphocytes in some forms of CNS lymphoma. Cryptococcal and other fungal organisms may occasionally be identified (see Chapter 20). Rarely, intracellular rickettsial organisms, distemper inclusions, and bacteria may be observed. Absence of intracellular bacteria and degenerative changes in neutrophils do not rule out a bacterial CNS infection. Some lysosomal storage diseases are characterized by intracellular storage bodies within WBCs. (See Chapters 126 and 128 for further discussion of CSF abnormalities in brain and spinal cord diseases.)

Cerebrospinal Fluid Biochemical Evaluation

When evaluating the chemical composition of the CSF, remember that CSF is produced both by active transport and by ultrafiltration. As a result, CSF contains essentially the same constituents as plasma, but they are present in different concentrations. Generally, the levels of CSF constituents are lower than the serum levels. The two constituents measured most commonly for diagnostic purposes are *protein* and *glucose*.

Protein Levels

The concentration of protein is quite low in CSF compared to plasma. In dogs and cats, protein from a cerebellomedullary cisternal tap is usually less than 25 mg/dl, whereas that from a lumbar puncture may be as high as 45 mg/dl. This difference may be the result of an increase in the permeability of the blood-brain barrier, production of immunoglobulins in the intrathecal space, or a combination of both. Conditions known to elevate CSF protein include encephalitis, meningitis, neoplasms, CNS infarctions, chronic neurodegenerative conditions, and trauma. CSF protein can be analyzed qualitatively and quantitatively by electrophoresis or immunoelectrophoresis. In normal CSF, albumin composes about 75% of the protein, and most of the remainder is globulin. An increase in CSF globulin without a parallel increase in albumin suggests local immunoglobulin production and encephalitis.

Glucose Levels

Normal CSF glucose levels are about 60% to 80% of those in blood. In humans with CNS bacterial infections, the CSF glucose is decreased. There does not appear to be a similar relationship between bacterial encephalitis and decreased CSF glucose in dogs. Plasma glucose can decrease dramatically in the presence of septicemia and bacteremia. A meningitic patient that is also bacteremic will likely have a drop in CSF glucose.

Cerebrospinal Fluid Serologic Examination

The CSF may be tested serologically for antibodies against infectious agents. Cryptococcal antigen can also be measured in CSF. Detection of CSF antibodies may be especially helpful in the diagnosis of canine distemper, feline infectious peritonitis, and toxoplasmosis. Paired or single serum titers are usually sufficient for diagnosis of neosporosis, rickettsial diseases, and some fungal disorders.

- The presence of CSF antibody usually indicates an active CNS infection and production of intrathecal antibody.
- False-positive CSF antibody titers can occur due to either iatrogenic blood contamination or blood-CSF barrier breakdown secondary to inflammation. CSF titer correction formulas are available and can be performed by some diagnostic testing laboratories if both CSF and serum are submitted (see Chapter 126).
- False-negative CSF antibody titers can occur with feline infectious peritonitis and cryptococcosis.

ELECTROENCEPHALOGRAPHY

Electroencephalography (EEG) is the graphic recording of shifts in resting membrane potential of the dendritic network in the cerebral cortex. This network is influenced and modulated by the activity of subcortical nuclear centers such as the reticular formation. Changes in EEG wave frequency and amplitude and occurrence of paroxysmal epileptiform complexes (spikes, sharp waves, and spike-slow wave complexes) are abnormalities that indicate a corticocerebral disturbance.

Indications

- EEG can be a useful screening test for any corticocerebral lesion. The procedure is noninvasive, relatively inexpensive, and can occasionally be performed without chemical restraint in the dog. Sedation or anesthesia is often required to minimize patient movement and to maintain a constant level of consciousness. In the awake state, normal variations in wakefulness can change EEG waveform frequency and amplitude.
- A montage (specific arrangement) of scalp electrodes allows patterns of abnormal activity to be localized to specific cortical areas. Focal slowing and paroxysmal activity suggests a focal neoplastic, infectious, traumatic, or vascular lesion. Diffuse slowing and changes in amplitude are suggestive of diffuse cerebral injury or metabolic disorders.
- EEG can be useful for confirming seizure activity in patients with atypical or subclinical seizures.

Disadvantages

- Disadvantages include recording artifacts due to patient movement, muscle activity, equipment malfunction, electrical interference, and drugs used to sedate or anesthetize the patient. These artifacts can obscure EEG recording and make it difficult to interpret.
- EEG provides little definitive information concerning the etiology of the underlying cerebral lesion. Neuroimaging with CT or MRI provides more definitive information about what is causing the cerebral dysfunction (see Chapter 126).

BRAIN STEM AUDITORY EVOKED RESPONSE

The brain stem auditory evoked response (BAER) tests the nervous system pathways for hearing. A normal

Table 125-1. INTERPRETATION OF ABNORMAL ELECTRODIAGNOSTIC EXAMINATION

Procedure	Abnormal Finding	Interpretation
Electromyography	Increased insertional activity	Neuropathies Myopathies Myotonia Cramp Electrolyte disorders
	Spontaneous activity	Myopathies Neuropathies (axon or cell body) Electrolyte disorders
Motor unit action potentials	Diminished size	Myopathies Acute denervation
	Increased size	Reinnervation Myopathies
Nerve conduction studies	Decreased velocity	Neuropathies (myelinopathies or combined axonopathy and myelinopathy)
Repetitive nerve stimulation	Incremental or decremental response	Junctionopathies

BAER depends on normal function of hearing receptors (cochlear receptors), CN8 (cochlear branch), the cochlear nucleus, and other "relay" nuclei for auditory signal transmission in the brain stem. An audible click produced by headphones or inserts in the ear triggers electrical activity in the structures above. The sequential neural activity is detected by scalp electrodes after each click stimulus. Several hundred amplified responses are "signal averaged," and the averaged waveform is displayed as a consecutive series of four to five waveforms. Wave I is generated by the cochlear receptors and cochlear nerve. Waves II through V are generated by relay nuclei in the brainstem.

Interpretation

- In congenital "sensorineural" deafness, the cochlear receptors degenerate perinatally. The resulting BAER is a "flat line" tracing.
- Injury to the cochlear receptors in the inner ear by otitis interna, neoplastic processes, or ototoxic drugs can also result in sensorineural deafness and an absent BAER.
- Middle ear effusions or soft tissue masses may inhibit normal sound transmission to the inner ear. This can result in lower amplitude, delayed BAER waveforms, or if severe, complete absence of the BAER. This form of hearing loss is called *conductive hearing loss.*
- A brain stem lesion affecting the auditory relay nuclei may decrease amplitudes and delay onset latencies (time to onset of wave) of waves II to V.
- Since the vestibular receptors and vestibular branch of CN8 are close to the cochlear system, the BAER may provide indirect localizing information in patients with vestibular disease secondary to otitis or neoplasia. In idiopathic geriatric vestibular syndrome, the auditory pathways and BAER are not affected.

ELECTRODIAGNOSTIC EXAMINATION OF THE MOTOR UNIT

The electrodiagnostic examination of the motor unit consists of three parts:

- Needle electromyography
- Nerve conduction studies
- Repetitive nerve stimulation

Each test evaluates different aspects of the motor unit. Interpretation of abnormal electrodiagnostic findings is summarized in Table 125-1.

Needle Electromyography

- Electromyography (EMG) provides information about the functional status of motor unit innervation and muscle membrane ion conductance. A recording needle is inserted into a muscle and spontaneous muscle potentials are recorded and evaluated. Electrical activity is "audible," and the sound of the potentials can be amplified to produce characteristic sounds from a loudspeaker. Persistent spontaneous activity in a resting muscle under anesthesia is abnormal. Normal muscle is "electrically silent" in the resting state with the exception of very low–amplitude miniature endplate potentials.
- In veterinary patients, general anesthesia is usually necessary to avoid patient discomfort and minimize patient movement. In humans and in extremely cooperative animal patients, awake studies may be performed to assess motor unit action potentials (MUAPs) normally generated during a voluntary muscle contraction. During sustained contractions, patterns of "recruitment" of these potentials can be observed to determine if they are normal or abnormal. Individual MUAP waveform characteristics

(amplitude, duration, number of phases) can also be altered in neuropathies and myopathies. Neuromuscular junction disorders may cause a reduction in MUAP amplitude.

Interpretation

- Fibrillation potentials, positive sharp waves, and complex repetitive discharges are examples of abnormal spontaneous activity. Fibrillation potentials and positive sharp waves are brief isolated potentials that range from 40 to 1000 μV in amplitude. The presence of any of these potentials indicates a neuropathy or myopathy but does not distinguish between them. Both neuropathies and myopathies cause functional denervation of the myofiber. Myopathic injury and necrosis disrupt normal muscle membrane integrity and the membrane receptors that are post-synaptic to nerve axon terminals.
- Complex repetitive discharges are several-second bursts of high-amplitude potentials (500–1000 μV) that may increment, decrement, or remain consistent in amplitude over time. These potentials may be observed in chronic neuropathies, myopathies, and in congenital myotonia. In congenital myotonia, the high-frequency repetitive discharges that wax and wane in frequency and amplitude are called *myotonic discharges* and may cause a characteristic "dive-bomber" sound.
- Spontaneous activity in neuromuscular junction disorders is rare but can occur sporadically with tick paralysis and botulism.
- In most polyneuropathies and polymyopathies, EMG activity is generalized and can be observed in most muscle groups. With focal nerve or muscle injuries, EMG can be very useful in localizing the distribution and extent of nerve and/or muscle injury.
- Occasionally, the resting EMG will be normal (no spontaneous activity) in peracute neuropathies and in some chronic neuropathies and myopathies. Nerve conduction tests and repetitive nerve stimulation should still be performed in these cases. If nerve conduction studies are abnormal or if clinical signs are suggestive of a neuropathy or myopathy, muscle and nerve biopsies should also be performed.

Nerve Conduction Studies

- Motor nerve conduction studies measure the velocity of action potential conduction between two points along a motor nerve. Conduction velocity is calculated as the difference in distance divided by the difference in conduction latency of the action potential between these two points. Latency is the amount of time that elapses between the stimulus and the onset of the electrical response in the innervated muscle.
- Electrical stimulation of a normal motor nerve proximally results in electrical activation and contraction of the innervated muscle distally. The distal muscle contraction produces a signal called a *compound muscle action potential* (CMAP) that can be recorded with a recording needle placed in the muscle. The CMAP is typically biphasic and approximately 25 mV in amplitude if the nerve is stimulated supramaximally. The CMAP is also called the *M wave*. Amplitude, duration, and number of phases of the CMAP can be altered in different neuromuscular diseases and should be measured and evaluated in all nerve conduction studies.

Interpretation

- The speed of conduction primarily evaluates the health of the myelin sheath. Myelin injury results in slowed conduction velocity and, often, a lower amplitude and polyphasic CMAP due to temporal dispersion. *Temporal dispersion* refers to the prolonged duration of the CMAP due to the presence of nerve fibers that conduct at widely different velocities as a result of varying degrees of demyelination. Conduction block (no conduction) can occur if myelin injury is severe. The amplitude of the CMAP is also affected by the number of healthy motor units (nerve fibers with their respective neuromuscular junctions and myofibers). The greater the number of normal motor units activated, the greater the amplitude of the CMAP.
- With axonal injury that spares the myelin sheath, nerve conduction may be normal or mildly decreased. There is a reduction in the number of available motor units; this reduction leads to the reduced size of the CMAP. As the neurogenic lesion becomes chronic, there is axon sprouting of the terminal branches of surviving neurons. These axon sprouts reinnervate some of the denervated muscle fibers. The evoked potential will then have a prolonged duration (temporal dispersion) and may become polyphasic. This occurs because the axon sprouts conduct more slowly than the normal fibers, so the muscle fibers receive their impulses at different times. In addition, because the motor unit now has more fibers, the evoked potential will be increased in amplitude.
- In most acute and chronic neuropathies, a *combined* axon and myelin injury is the general rule. Furthermore, axonal degeneration will inevitably lead to myelin degeneration over time. For this reason, most neuropathies are characterized by slowed conduction velocity, reduced amplitude of the CMAP, and increased duration and number of phases of the CMAP.
- Myopathic conditions reduce the number of healthy myofibers in the motor unit and thus will result in reduced amplitude of the CMAP. Nerve conduction velocity is normal.
- Neuromuscular junction disorders in which acetylcholine release is reduced (tick paralysis and botu-

lism) are characterized by normal conduction velocity but severely reduced amplitude of the CMAP.
- Sensory nerve conduction is similar to motor nerve conduction testing, except that the stimuli are applied to the nerve distally and the recordings are made directly from the nerve proximal to the site of stimulation.

Repetitive Nerve Stimulation

Repetitive nerve stimulation (RNS) refers to nerve stimulation by 5 or 10 consecutive supramaximal stimuli with concurrent recordings made of the consecutive CMAPs produced by these stimuli. The amplitudes of each CMAP are then compared with the amplitude of the first CMAP. A normal patient will show no changes in the amplitudes of the successive CMAPs in the series. Neuromuscular junction diseases often cause a progressive change in the amplitudes during the first five stimuli. An increase in amplitude is called an *incremental response;* a decrease in amplitude is called a *decremental response.* RNS should be performed at a stimulation rate of <5 stimuli per second.

Interpretation

- An incremental response suggests a presynaptic disease such as botulism, tick paralysis, or hypocalcemia. Most of the disorders that result in incremental responses are characterized by a defect in the release of acetylcholine at the neuromuscular junction.
- A decremental response suggests a postsynaptic disease, especially myasthenia gravis.

OTHER MOTOR UNIT TESTS

Tensilon Test

Edrophonium chloride or Tensilon is a short-acting anticholinesterase drug that will transiently alleviate signs of myasthenia gravis in most affected dogs and cats. Intravenous administration of Tensilon will usually result in a marked improvement in strength in animals with myasthenia gravis. The response to Tensilon is brief (usually about 5 minutes). Other neuromuscular disorders may show a partial response to Tensilon, but obvious signs of exercise-induced weakness are still present (see Chapter 130).

Muscle Enzymes and Metabolic Tests

- Any disease process that results in necrosis of the muscle cell membrane releases muscle enzymes into the systemic circulation. The most significant of these conditions is polymyositis. Because many incidental conditions (e.g., muscle trauma from an intramuscular injection) also release these enzymes, this must be taken into account when interpreting elevated serum levels of muscle enzymes.
- Some metabolic myopathies will cause abnormalities in pre-exercise and post-exercise lactic acid and pyruvic acid plasma concentrations. Specific types of myopathies can alter concentrations of urinary organic acids.

Serologic Tests for Autoantibodies

- Serologic testing for antibodies against acetylcholine receptors is the diagnostic test of choice for acquired myasthenia gravis.
- Serologic testing is also available for autoimmune masticatory muscle myositis. A diagnosis of masticatory myositis can be confirmed by finding increased circulating antibodies against type 2M muscle fiber antigen (see Chapter 130).
- Immune mediated polymyositis may be accompanied by a positive antinuclear antibody titer.

Muscle and Nerve Biopsy

Inflammatory and degenerative diseases of nerve and muscle are best diagnosed by biopsy (also see Chapters 129 and 130). These procedures can be done safely with minimal complications. The tissues require special handling and processing; therefore, arrangements should be made with the laboratory prior to collection of the samples. Analysis by a laboratory that is experienced in handling these biopsies will avoid erroneous results (see Chapter 130).

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Chapter

126 Diseases of the Brain and Cranial Nerves

Philip A. March

The brain may be anatomically and functionally divided into three major compartments, the brain stem, cerebellum, and cerebrum. Cranial nerves have their cell bodies within the brain, but most of their nerve fibers course outside the brain. Diseases of the brain and cranial nerves may be neoplastic, infectious, idiopathic, vascular, traumatic, metabolic, toxic, congenital, or degenerative in origin. These disorders may result in dysfunction of a focal, regionally specific brain area or may produce more diffuse or multifocal deficits. Because many different diseases can affect similar areas causing very similar clinical signs, the first portion of this chapter discusses clinical signs of lesions in each brain region. The remainder of the chapter discusses important brain diseases within each etiologic category. Diagnosis of neurologic disease is discussed in Chapter 125, and management of seizures is discussed in Chapter 127.

CLINICAL SIGNS AND NEUROLOCALIZATION

Refer also to Chapter 125.

Brain Stem Lesions

- The brain stem contains the midbrain, pons, and medulla in the caudal fossa (below the tentorium cerebelli or infratentorial) and diencephalon in the more rostral middle fossa (above the tentorium cerebelli or supratentorial). Signs associated with lesions in the infratentorial brain stem are discussed below. Signs associated with the diencephalic (thalamic and hypothalamic) lesions are similar to those associated with cerebral lesions and so are discussed in the cerebral lesion section.
- Cranial nerve dysfunction is a common sign of brain stem disease. The brain stem contains cranial nerve 3 through cranial nerve 12 (CN3–CN12). Multiple or single cranial nerves may be involved in a disease process; signs are typically asymmetrical. CN5 through CN12 in the pons and medulla are more commonly affected than CN3 and CN4 in the midbrain.

▼ ***Key Point*** Central vestibular signs are usually present in diseases of the brain stem.

- Head tilt, circling, falling, disequilibrium, and nystagmus indicate damage to vestibular nuclei of CN8. Head tilts usually occur toward the side of the lesion. Paradoxical vestibular syndrome is characterized by a head tilt opposite the side of the lesion.
- Dysfunction of muscles of facial expression (CN7) and mastication (CN5) are common. Disorders of swallowing (CN9 and CN10), laryngeal function (CN9 and CN10), and tongue mobility (CN12) can occur but are less common.
- Oculomotor weakness, strabismus, and resting pupillary changes occur with CN3, CN4, and CN6 involvement.
- Injury to ascending white matter tracts in the brain stem results in ipsilateral conscious proprioceptive deficits and other abnormalities in postural reactions. Occasionally, ataxia, dysmetria, and exaggerated postural reactions may be seen.
- Injury to descending upper motor neuron (UMN) nuclei and their tracts in the brain stem causes tetraparesis or paralysis characterized by increased extensor muscle tone and exaggerated reflexes. The weakness or paresis is usually more severe in limbs on the same side as the lesion.
- Severe brain stem lesions can result in disruption of the ascending reticular activating system. Clinical signs of progressively decreasing levels of consciousness (depression, obtundation, stupor, coma) correlate with the severity of the injury.
- Severe brain stem lesions can also affect cardiovascular and respiratory regulation. Altered heart rate (bradycardia, supraventricular arrhythmias) and respiratory patterns (hyperventilation, ataxic respirations, apnea) are evident.

Cerebellar Lesions

- *Ataxia of gait:* Cerebellar lesions produce pronounced limb incoordination during voluntary movements. Exaggerated range and force of limb movement is

common. Hypermetria and limb circumduction can be seen. Strength and conscious proprioception (CP) are preserved. Postural reactions often are preserved but exaggerated.

- *Truncal ataxia:* Truncal swaying and a wide-based stance are typical of cerebellar disease. Affected patients may fall to one side. Dysmetric head bobbing with overshooting and undershooting occurs. Forward and backward movements of the trunk (titubation) may be seen.
- *Intention tremor:* A fine oscillating tremor of the head and sometimes the body is seen during highly controlled movements, such as eating or visually fixating on an object.
- *Menace deficit:* The menace response is lost ipsilateral to the cerebellar lesion. Vision and facial nerve function are intact.
- *Anisocoria:* Mild mydriasis may be seen ipsilateral to the cerebellar lesion.
- *Vestibular signs:* The cerebellum contains the flocculonodular lobe, which is considered part of the vestibular system. Lesions in this area of the cerebellum may produce pathologic (and often positional) nystagmus, head tilt, and circling. Occasionally, a pendular nystagmus (rhythmic but rapid horizontal oscillation of the eyes) is seen with cerebellar disease.
- *Opisthotonus* (extension of the head and neck) and thoracic limb extensor rigidity may be seen with severe cerebellar disease or with cerebellar herniation.
- *Mental status* is normal in patients with isolated cerebellar injury.

Forebrain Lesions

- Forebrain diseases can affect the cerebrum or diencephalon either bilaterally (diffusely) or unilaterally (focally). Both diffuse and focal forebrain disorders can cause the following:
  - Seizures (generalized or partial)
  - Behavior or personality change
  - Dullness, agitation, or otherwise inappropriate responses to environmental stimuli (abnormal mentation or "dementia")
  - Contralateral visual deficits (loss of menace) with intact pupillary light reflexes
- Diffuse diseases of the cerebrum or diencephalon can also cause the following:
  - Generalized conscious proprioceptive deficits (all four limbs)
  - Stupor or coma with decreased to absent responses to painful stimuli
  - Generalized ataxia if an acute injury
  - Bilateral miosis with an intact pupillary light reflex
- Focal diseases of the cerebrum or diencephalon can cause the following:
  - Circling toward the side of the lesion
  - Contralateral conscious proprioceptive deficits and slow postural reactions
  - Contralateral facial sensory deficits (especially nares sensation)
  - Contralateral mild facial weakness
  - Hemi-inattention to stimuli on the side of the body opposite the lesion
- Focal diencephalic lesions may cause lethargy; inappetence; altered mentation and behavior; circling, listing, and/or head turn toward the side of the lesion; and hemi-inattention. These deficits may occur in the absence of proprioceptive, visual, or facial sensory and motor deficits.
- Structural intracranial lesions can produce referred head and neck pain.

▼ ***Key Point*** Cerebral and diencephalic diseases do not cause significant abnormalities of limb strength or weight bearing.

Manifestations of Systemic Metabolic Alterations

The above description of generalized and focal cerebral diseases applies to intracranial or structural disorders. Extracranial diseases (toxic, metabolic, and some nutritional disorders) may not produce actual structural lesions but may alter cerebral function enough to produce cerebral signs. Usually signs are diffuse in nature and mental status is altered. Seizures may be seen and may be either generalized or focal. Between seizures, lateralizing neurologic deficits are not found. Other body systems are often affected concurrently by systemic extracranial disorders.

Herniation from Space-Occupying Brain Lesions

- Space-occupying lesions in the forebrain and cerebellum may grow rapidly, may be accompanied by extensive edema, or may result in acute hemorrhage or infarction due to invasion of local blood vessels. Intracranial tissue and fluid compartments (parenchyma, blood, cerebrospinal fluid [CSF]) can compensate for space-occupying lesions up to a point. Beyond this critical threshold, brain shift or herniation occurs. Sudden changes in clinical signs not referable to the original neurolocalization suggest brain herniation and warrant emergency treatment.
- The two most common types of herniation are caudal transtentorial herniation due to an expanding forebrain mass and foramen magnum herniation due to an expanding cerebellar lesion.
  - Clinical signs of *transtentorial herniation* include extensor rigidity in all four limbs and cervical musculature (decerebrate rigidity), pupillary constriction followed by dilatation or fixed, midrange pupils, loss of the vestibulo-ocular reflex (doll's eye reflex), and a stuporous or comatose state.
  - Clinical signs of *foramen magnum herniation* include opisthotonus (extended head and neck), thoracic limb rigidity (usually without rigidity of the pelvic

limbs), pupillary changes (usually miosis), and either severely irregular respirations or apnea.
- Appearance of these clinical signs indicates a severe brain injury and a need for immediate medical attention.

NEOPLASIA

Primary and secondary brain tumors most commonly affect middle-aged and older dogs and cats and can be located anywhere in the brain. Direct mechanical compression and necrosis of surrounding brain parenchyma, peritumoral edema, and blood vessel invasion with hemorrhage may all contribute to signs of a space-occupying mass. Clinical signs reflect location of the tumor in a specific brain area. As discussed above, when brain compensatory mechanisms are exhausted, brain herniation occurs and rapid clinical deterioration ensues.

Brain tumors can be *extra-axial,* arising from more superficial areas of the brain and compressing or invading the underlying parenchyma, or *intra-axial,* arising deep within the brain parenchyma and invading neural tissue surrounding them. Extra-axial masses tend to have a gradual onset and slow progression of signs. Intra-axial tumors tend to have a more rapid onset and progression.

Etiology

Primary Brain Tumors in the Canine

Primary tumors of the canine brain arise spontaneously and may grow slowly or rapidly.

▼ ***Key Point*** The two most common primary brain tumors in the dog are meningioma and glioma.

Etiologic factors are not well understood. The glioma group includes astrocytomas, glioblastomas, oligodendrogliomas, ependymomas, and choroid plexus papillomas or carcinomas. Meningiomas arise from arachnoid cells of the meninges, whereas gliomas arise from neuroectodermal supporting cells.

Meningiomas tend to occur in dolichocephalic breeds, whereas gliomas tend to occur in brachycephalic breeds. Any dog, however, may develop either tumor. Meningiomas in the dog are often located in the olfactory or frontal lobe or over the convexities of the cerebrum, but they can occur on the floor of the intracranial vault (rostral, middle, or caudal fossae). They often appear to be well-circumscribed masses but invade the underlying neural parenchyma. They may have a cystic component. Astrocytomas and oligodendrogliomas arise mostly from deep intra-axial locations in the brain (usually cerebrum or diencephalon). Ependymomas are relatively uncommon and arise from cells lining any of the ventricular compartments. The lateral ventricles of the cerebrum are the most common sites for ependymoma formation. Choroid plexus papillomas and carcinomas develop in areas of the brain where choroid plexus is present. The most common sites for a choroid plexus papilloma are the fourth ventricle-lateral aperture area and the third ventricle. Obstruction of the third ventricle by a choroid plexus papilloma results in secondary hydrocephalus and intracranial hypertension. Choroid plexus carcinomas, ependymomas, and, occasionally, oligodendrogliomas may metastasize to other central nervous system (CNS) areas using CSF pathways.

Primary Brain Tumors in the Feline

▼ ***Key Point*** The most common brain tumor of aged cats is the meningioma.

Most feline meningiomas are cerebrally located, extra-axial, and well encapsulated. They are frequently multiple and may occur anywhere along the falx, along the tentorium cerebelli, and in the tela choroidea of the third ventricle. Gliomas in the cat are uncommon but do occur. Primary CNS lymphoma may arise from brain structures, but it most commonly arises in thoracolumbar spinal cord locations.

Secondary Brain Tumors in the Canine and Feline

Secondary tumors are either solitary or multiple. The two most common mechanisms of brain invasion are by hematogenous routes and by extension from surrounding tissues. Hemangiosarcoma, malignant melanoma, mammary adenocarcinoma, and pulmonary adenocarcinoma use the hematogenous route to metastasize to the brain. The most frequent metastatic location is the cerebrum. Secondary CNS lymphoma in dogs is usually associated with the multicentric form of lymphoma. Brain, cranial nerve, and spinal cord lesions can occur with concurrent leptomeningeal involvement. Multicentric malignant histiocytosis can secondarily invade the CNS in dogs (especially Bernese mountain dogs, rottweilers, golden retrievers). Forebrain, brain stem, spinal cord, and vertebral body invasion has been reported. Tumors that invade the brain by local extension include nasal adenocarcinoma, pituitary macroadenoma and carcinoma, and bony tumors of the skull including multilobular osteochondroma, osteosarcoma, and chondrosarcoma. Peripheral nerve sheath tumors of CN3 and CN5 also tend to grow up their respective nerve trunks and invade the brain stem. Ganglioneuromas in young dogs behave similarly.

Many of the same tumors that secondarily invade the canine brain also occur in the feline. These include metastatic carcinomas, nasal carcinomas, and pituitary carcinomas. Squamous cell carcinomas can extend into the brain from middle ear locations.

Clinical Signs

- The onset and progression of clinical signs depend on the type of tumor and its location. Extra-axial meningiomas grow slowly and clinical signs are gradual in onset and progression. Intra-axial gliomas grow rapidly and cause a more rapid clinical deterioration. Secondary tumors also tend to progress rapidly. An exception to this is the trigeminal neurofibroma, which exhibits very slow growth (months to years).
- Early clinical signs of forebrain tumors may be vague and include increased irritability, behavior change, pacing, head and neck pain, and increased lethargy. Head pain or headache in dogs can be recognized by gently applying bilateral pressure across the temporal aspects of the head and skull.
- Some forebrain tumors may be clinically "silent" or may only cause seizures. These tumors can be located in the olfactory, temporal, or occipital cerebral lobes.

▼ ***Key Point*** Signs of asymmetrical cerebral involvement include circling and contralateral conscious proprioceptive, visual field, and facial sensorimotor deficits.

- Diffuse cerebral signs may occur secondary to a tumor obstructing CSF flow. This results in fluid accumulation in the lateral ventricles of the cerebrum and secondary hydrocephalus.
- Herniation syndromes may occur with tumors of the forebrain or cerebellum (see under "Herniation from Space-Occupying Brain Lesions").
- Brain stem tumors usually occur in the pontomedullary area and typically cause central vestibular and other cranial nerve and long tract (e.g., limb proprioception and paresis) deficits.
- *Cerebellopontomedullary angle tumors* (choroid plexus papillomas, ependymomas, neurofibromas, meningiomas, and other tumor types) may invade the flocculonodular lobe of the cerebellum or the cerebellar peduncles. If this occurs, a "paradoxical vestibular syndrome" is seen. Signs are head tilt with possible circling and ataxia (rolling, falling, stumbling) *away* from the side of the lesion. The fast phase of nystagmus is often toward the side of the lesion. Long tract signs (e.g., limb proprioception and paresis), however, are ipsilateral to the lesion. If other cranial nerves are involved (e.g., CN5 and CN7), those deficits will be on the same side as the lesion.
- *Cavernous sinus syndrome* is a sporadic syndrome due to a lesion in the cavernous sinus along the floor of the rostral fossa (beneath the forebrain and just caudal to the orbital fissure). Neoplastic masses occupying this area will compress CN3, CN4, CN6, the ophthalmic branch of CN5, and the sympathetic nerve going to the eye. The result is an ipsilateral fixed pupil, absent corneal and eyelid sensation, and ocular immobility.

Diagnosis

Laboratory Testing

- Perform a complete blood count (CBC), chemistry profile, and urinalysis to rule out extracranial causes of brain dysfunction prior to pursuing tests for intracranial disease.
- Because most patients with brain tumors are older, run a geriatric screen of liver and kidney function.
- Perform an adrenocorticotropic hormone (ACTH) stimulation test and a low-dose dexamethasone suppression test if a pituitary mass is suspected.

Ophthalmologic Exam

Perform a complete ophthalmologic examination to check for papilledema (a sign of increased intracranial pressure [ICP]), uveitis, retinal hemorrhage, and other abnormalities.

Electrodiagnostic Testing

- An electroencephalogram (EEG) may detect asymmetries in brain activity or actual epileptiform complexes if a seizure focus is present. See Chapter 125 for a more thorough description of the EEG and its uses.
- A brain stem auditory evoked response (BAER) may aid in localizing a brain stem lesion. See Chapter 125 for additional information.

Radiography

- Perform thoracic radiographs to screen for metastatic disease.
- Skull radiographs are usually not helpful in the diagnosis of a brain tumor.
- Skull radiographs may reveal a nasal or bony tumor with secondary brain invasion.
- An area of bone sclerosis or lysis may be visible in the skull immediately adjacent to a feline meningioma.
- Some feline meningiomas may have an area of dystrophic mineralization that is visible on skull radiographs.

Computed Tomography and Magnetic Resonance Imaging

- Tumor margins and neuroanatomic location can be more precisely defined with computed tomography (CT) or magnetic resonance imaging (MRI). Peritumoral edema is also visible. Parenchyma definition, especially in brain stem areas, is best identified with MRI.
- Intravenous contrast agents (meglumine iothalamate for CT and gadolinium diethylenetriamine pentaacetic acid for MRI) highlight areas of blood-brain barrier disruption. Patterns of enhancement are not pathognomonic for tumor type but aid in making a tentative diagnosis.

- Inflammatory or other non-neoplastic lesions may mimic a neoplastic lesion on both CT and MRI. A CSF tap and biopsy of the mass are sometimes needed to confirm the underlying process.

▼ ***Key Point*** CT and MRI provide the precise neuroanatomic information needed for accurate biopsy, surgical, and/or radiation procedures. (See Chapter 4 for more information on these imaging modalities.)

Cerebrospinal Fluid Analysis

For CSF tap technique and normal values, see Chapter 125.

- CSF analysis may be useful in distinguishing inflammatory from neoplastic processes (see also "Inflammatory Brain Diseases").
- The majority of brain tumors are characterized by no cytologic abnormalities (normal cell count and differential) on CSF analysis. CSF pleocytosis may be seen if the tumor is necrotic and has a secondary inflammatory component. Neoplastic lymphocytes in CSF are typically seen in dogs with CNS lymphoma.
- Protein levels are usually elevated for all tumor types. Elevated protein with a normal cell count is called *albuminocytologic dissociation*.

▼ ***Key Point*** The CSF tap procedure is contraindicated in patients with elevated ICP.

- If clinical signs and/or CT or MRI suggest elevated ICP, the use of mannitol, furosemide, and hyperventilation may lessen the risks of brain herniation.

Brain Biopsy

Brain biopsy can be performed either by open craniotomy or by using stereotactic CT guidance. Cytologic preparations of the biopsy can be examined intraoperatively and may be diagnostic.

Treatment

Corticosteroids

- Corticosteroids primarily help in resolving vasogenic edema and often benefit patients with peritumoral edema. Administer prednisone at a dosage of 0.25 to 0.5 mg/kg every 12 hours as maintenance therapy for peritumoral edema.
- Meningiomas in cats may show a partial clinical response to corticosteroids in the short term (several weeks or months).
- If there is a rapid progression of signs due to a significant edema component, administer methylprednisolone sodium succinate (Solu-Medrol) at 30 mg/kg IV once followed by 15 mg/kg IV every 6 hours for 24 to 48 hours *or* dexamethasone at 1 mg/kg IV every 12 hours for 24 hours.

Hyperosmotic Solutions and Diuretics

- Mannitol therapy is reserved for those patients with signs of increased ICP and/or herniation.
- In the euvolemic patient, mannitol at 1 g/kg IV over 20 minutes will draw fluid out of more normal areas of brain and temporarily lower ICP.
- Furosemide given 20 minutes after mannitol at a dose of 1 to 2 mg/kg IV will help prolong the effects of mannitol. Furosemide may also decrease CSF production.

Anticonvulsant Therapy

Phenobarbital at a dosage of 2.2 to 2.5 mg/kg PO every 12 hours is indicated if seizures are part of the clinical picture (see Chapter 127). Potassium bromide is often required as an additional anticonvulsant if seizures are recurrent.

Specific Chemotherapy

- Controlled clinical trials in dogs and cats have not been done to assess the true efficacy of different chemotherapeutic agents in the treatment of brain tumors.
- Nitrosoureas (lomustine, carmustine) appear to be beneficial in the treatment of some canine gliomas and meningiomas. Longer survival and even temporary tumor regression have been reported. Lomustine is also frequently effective against CNS lymphoma and malignant histiocytosis. Nitrosoureas are unique in that they cross the blood-brain barrier, the limiting factor for most chemotherapeutic agents. Give 50 to 80 mg/m^2 of body surface area every 4 to 6 weeks. For conversion of body weight to surface area (m^2), see Table 26-4 in Chapter 26.
- Cytosine arabinoside reaches therapeutic CSF concentrations after large intravenous doses in normal dogs. Intrathecal and IV infusions of cytosine arabinoside have been used in dogs with CNS lymphoma. A dosage of 300 to 400 mg/m^2 of body surface area intravenously over 4 to 12 hours is recommended.
- Tumor cell heterogeneity with respect to relative phase in the cell cycle diminishes the likelihood of a uniform tumor response to chemotherapeutic agents.

Surgery

- Craniotomy or craniectomy with tumor excision is a treatment option for extra-axial tumors involving the cerebrum or cerebellum. Refer the patient to a neurosurgical specialist.

▼ ***Key Point*** Survival rates are generally good to excellent when feline meningiomas over the cerebral convexities are removed surgically.

- It is usually years before clinically significant regrowth occurs after meningioma excision in cats. Survival periods of 6 months to 1 year are reported following meningioma excision in dogs. Postoperative radiation therapy extends the survival period in the canine (1–2 years).
- Tumors in more intra-axial and brain stem locations cannot be resected completely. Biopsy and radiation therapy (see below) can be performed.

Radiation Therapy

▼ ***Key Point*** External beam megavoltage radiation therapy for brain tumors appears to prolong survival more consistently than other modes of therapy. A well-tolerated treatment protocol appears to be 45 to 48 Gy in 12 to 18 fractions over 3 to 4 weeks.

- Longest survival times for dogs with meningiomas are obtained when radiation therapy is combined with surgery.
- Canine pituitary tumors are radiation sensitive. Long remission times have been achieved.
- Brain metastases may respond to radiation therapy.
- Clinical signs of neurologic dysfunction often improve rapidly (within 2–8 weeks) following radiation therapy. Tumor shrinkage is delayed (>4 months) and is not associated with early clinical improvement.
- Complications of radiation therapy include ocular (conjunctivitis, keratoconjunctivitis sicca, cataracts) and dermatologic (erythema, alopecia, otitis) changes. A potential late, delayed reaction may occur 9 to 24 months after radiation and is characterized by white matter necrosis.

Stereotactic Radiosurgery

- Stereotactic radiosurgery is the application of a single high dose of radiation delivered to a stereotactically defined target volume.
- The procedure utilizes multiple, non-coplanar beams originating from a radiation source that rotates in an arc around the patient's tumor. All beams are focused on the target in non-intersecting planes using a stereotactic image-based system.
- This radiation procedure reduces radiation exposure of normal brain tissue and so avoids adverse effects associated with conventional radiation therapy.
- Delivery of the entire radiation treatment as a single dose minimizes anesthetic events and reduces costly repeat visits associated with conventional radiation therapy.

INFLAMMATORY BRAIN DISEASES

Inflammation of brain parenchyma and its meninges (meningoencephalitis) occurs secondary to infectious or idiopathic insults.

▼ ***Key Point*** Idiopathic inflammatory conditions are more common than infectious conditions in dogs, but the reverse is true in cats.

Idiopathic disorders frequently have an immune-mediated component. Most infectious agents reach the brain hematogenously. Local extension from extraneural sites, usually due to erosion through bone, is a mechanism used by some fungal and bacterial organisms. Other sources of infection include foreign body migration, previous trauma, and iatrogenic contamination during neurosurgery. An unusual but important mode of entry into CNS is that used by rabies and pseudorabies viruses and by *Listeria* bacteria. These agents are inoculated into a peripheral site, enter peripheral nerve axons, and then undergo retrograde axonal transport into the CNS.

The cascade of inflammatory changes that occurs after brain injury leads to a self-perpetuating process of brain tissue ischemia, necrosis, and edema. Inflammatory brain disorders are usually associated with multifocal clinical signs and lesions are often disseminated throughout the CNS. Clinical signs, however, may indicate a focal neurolocalization for the most prominent lesion. Some inflammatory disorders have a predilection for the cerebral cortex, whereas many others have a predilection for brain stem sites and frequently cause central vestibular signs. The onset and progression of clinical signs is usually rapid (days to weeks) but can be prolonged. Infectious diseases may be accompanied by systemic signs, but idiopathic brain conditions are usually characterized by signs referable to the CNS only. As in the case of neoplastic conditions, inflammatory diseases can lead to the formation of large, space-occupying lesions, increased ICP, and herniation of brain structures.

Infectious Meningoencephalitis

Etiology

- Infectious diseases are a common cause of acute to subacute, rapidly progressive neurologic dysfunction in dogs and cats and tend to occur in young adults.
- Major etiologic categories include viral, fungal, rickettsial, and protozoal agents. Bacterial diseases of the CNS can also occur but are less common. *Klebsiella, Escherichia coli, Streptococcus, Enterococcus, Staphylococcus, Pasteurella, Actinomyces, Nocardia,* and various

Table 126-1. INFLAMMATORY BRAIN DISEASE CAUSED BY INFECTIOUS AGENTS IN THE CAT

Disease/Agent	Typical Age of Onset	Onset/ Progression	Typical Neurologic Signs	Typical CSF Characteristics	Serology/CSF Titers	Treatment*
FIP (coronavirus)	Young (<2 yrs)	Rapid or intermediate	Brain stem, cerebral, or spinal cord (may be multifocal)	Suppurative or mixed; very high protein	CSF coronavirus IgG antibody coefficient (some false negatives)	Palliative only (corticosteroids, chlorambucil, cyclophosphamide, melphalan)
Cryptococcosis *(Cryptococcus neoformans)*	Any age	Intermediate to slow	Brain stem (may be multifocal)	Mononuclear or mixed; moderate protein	CSF or serum antigen titer (CSF preferred)	Fluconazole
Toxoplasmosis *(Toxoplasma gondii)*	Adult	Rapid to intermediate	Multifocal or focal brain stem, cerebral, cerebellar, spinal cord, or nerve root signs	Mild to moderate mononuclear; rare eosinophils; moderate protein	CSF antibody coefficient preferred (if serum, need positive IgM or fourfold rise in IgG titer)	Trimethoprim-sulfadiazine +/− pyrimethamine; clindamycin
FIV (lentivirus)	Adult	Slow	Cerebral (behavior change, dementia, roaming)	Mild lymphocytic; normal protein	Positive serum FIV antibody titer	Experimental only (alpha-interferon, PMEA, AZT)
Rabies (rhabdovirus)	Any age	Rapid	Cerebral (behavior change, irritable, seizures) (may be multifocal)	Normal or mild lymphocytic; normal or mild protein	NA (IFA testing of brain tissue most reliable)	None

*Preferred treatment(s) are listed first; other available drugs are listed in parentheses.
CSF, cerebrospinal fluid; FIP, feline infectious peritonitis; FIV, feline immunodeficiency virus; IFA, immunofluorescent antibody; IgG, immunoglobulin G; IgM, immunoglobulin M; NA; not available.

anaerobic species are the most common bacterial isolates. Some of the more important causes of infectious meningoencephalitis and their clinical and clinicopathologic features in the dog and cat are listed in Tables 126-1 and 126-2.

Diagnosis

- Due to frequent multisystemic involvement seen with many infectious brain disorders, diagnostic testing should include ophthalmic exam, CBC, chemistry profile, urinalysis, thoracic radiographs, and sometimes abdominal ultrasound or echocardiography, and ophthalmologic examination. Both anterior uveitis and chorioretinitis are common with toxoplasmosis, rickettsial, and feline infectious peritonitis (FIP) infections. Chorioretinitis and optic neuritis may also be observed with cryptococcal and distemper infections.
- Cytologic evaluation of skin lesions, nasal exudates, liver and splenic aspirates, lymph node and bone marrow aspirates, joint fluid, and CSF can sometimes identify the offending pathogen. Histopathologic evaluation of skin and muscle biopsies may also be useful to diagnose fungal and protozoal infections.
- CSF analysis in CNS infectious diseases frequently reveals a moderate to severe pleocytosis and elevated protein. Bacterial meningoencephalitis typically produces a neutrophilic pleocytosis with or without toxic changes in the neutrophils. Intracellular organisms are rarely observed. Blood, urine, and CSF cultures are indicated when bacterial infections are suspected even though CSF cultures are usually falsely negative. CSF characteristics of other CNS infections are described in Tables 126-1 and 126-2.
- CSF titers are preferred for diagnosis of distemper, cryptococcosis, and toxoplasmosis. An immunoglobulin G (IgG) ratio or intrathecal antibody coefficient for canine distemper virus (CDV) and toxoplasmosis can be determined using CSF and serum samples from affected animals. These methods correct for possible blood-CSF barrier breakdown by comparing CSF-to-serum ratios of pathogen-specific antibodies

Table 126-2. INFLAMMATORY BRAIN DISEASE CAUSED BY INFECTIOUS AGENTS IN THE DOG

Disease/Agent	Typical Age of Onset	Onset/ Progression	Typical Neurologic Signs	Typical CSF Characteristics	Serology/CSF Titers	Treatment*
CDV (paramyxovirus)	Young (<1 yr)	Rapid or intermediate	Cerebral, brain stem, cerebellum, or spinal cord (may be multifocal)	Normal to moderate lymphocytic; mild protein	Positive CSF CDV antibody or antibody coefficient; RT-PCR on CSF	No specific treatment; prednisone in chronic form; AEDs if seizures
Cryptococcosis *(Cryptococcus neoformans)*	Any age; often young (<1 yr)	Intermediate to slow	Brain stem (often multifocal brain stem signs)	Mixed (predominantly mononuclear or eosinophilic); high protein; may see organism rarely	CSF or serum antigen titer (CSF preferred)	Fluconazole
Coccidioidomycosis *(Coccidioides immitis)*	Adult	Intermediate to slow	Cerebrum or brainstem	Mixed; mild to moderate protein	Serum CF titer ≥1:8	Fluconazole
RMSF *(Rickettsia rickettsii)*	Adult	Rapid	Diffuse or multifocal; often central vestibular component; neck pain	Mixed or suppurative; moderate protein	Rising IFA serum antibody titer (paired); PCR if negative titer in acute phase	Doxycycline, (chloramphenicol, enrofloxacin)
Ehrlichiosis *(Ehrlichia canis)*	Adult	Rapid or intermediate	As for RMSF	Mixed or non-suppurative; moderate protein	Positive IFA serum antibody titer at >1:20; PCR	Doxycycline
Neosporosis *(Neospora caninum)*	Young (<1 yr); rarely adults up to 7 years	Rapid	Caudal paresis, arthrogryposis, or tetraparesis (spinal cord); More generalized signs including brainstem and cerebral signs in adults	Non-suppurative; moderate protein	Positive IFA serum antibody (often ≥1:800)	Clindamycin; trimethoprim-sulfadiazine +/− pyrimethamine
Rabies (rhabdovirus)	Adult	Rapid	Spinal cord, brainstem, and/ or cerebral signs (may be multifocal)	Normal or mild mononuclear; normal or mild protein	NA (IFA testing of brain tissue most reliable)	None
Pseudorabies (herpesvirus)	Any age	Rapid	Hyperesthesia; spinal cord and brain stem signs (often multifocal)	Mild mononuclear; mild protein		None

*Preferred treatment(s) are listed first; other available drugs are listed in parentheses.
AEDs, antiepileptic drugs; CDV, canine distemper virus; CF, complement fixation antibody; CSF, cerebrospinal fluid; IFA, immunofluorescent antibody; NA; not available; PCR, polymerase chain reaction; RMSF, Rocky Mountain spotted fever; RT-PCR, reverse transcriptase polymerase chain reaction.

against ratios of vaccine-associated (usually adenovirus or calicivirus) antibodies. Non-paired serum titers for toxoplasmosis are unreliable in the dog and cat due to persistence of high antibody titers long after exposure. The antibody coefficient calculation may also be useful to diagnose CNS FIP, although false-negative cases of CNS FIP have been reported. Cryptococcal antigen-specific titers can be run on serum, but CSF titers provide a more definitive diagnosis of CNS involvement. Cryptococcal antibody titers may be falsely negative due to an inadequate humoral immunologic response to the encapsulated organism. Serum titers are useful for diagnosis of neosporosis and rickettsial diseases. *Neospora caninum* serum antibody titers are usually very high (>1:800) in infected dogs and do not crossreact with toxoplasmosis titers. Dogs exposed to the organism but without clinical signs of infection may also have high titers.

- MRI features of CNS infectious diseases include patchy edema and focal to multifocal contrast-enhancing lesions of the parenchyma. Some fungal and protozoal granulomas and bacterial abscesses can ring enhance. Edema can be severe with bacterial encephalitis. Meningeal enhancement is common, especially with bacterial meningoencephalitis. FIP is

Table 126-3. ANTIMICROBIAL DRUGS FOR CENTRAL NERVOUS SYSTEM INFECTIONS

Drug	BBB Penetration	Bacteriocidal vs. Bacteriostatic	Dose (mg/kg)	Route	Frequency (hrs)	Antimicrobial Spectrum
Amphotericin B	Poor	Static	0.15–0.50	IV	48	Fungi (crypto)
Ampicillin	Intermediate	Cidal	10–20	IV	6	Broad (except BLRSE)
Cefotaxime	Good	Cidal	20–50	IV	6	Broad (except *Salmonella*)
Cefepime	Good	Cidal	40–50	IV	6	Broad (except *Bacteroides, Clostridium, Enterobacter*)
Ceftazidime	Good	Cidal	15–30	IV	6–8	Broad (except *Enterococcus*)
Ceftiofur	Poor to intermediate	Cidal	2.2–4.4	SQ	12	Broad (except *Pseudomonas, Enterococcus, Bacteroides, Bordetella*)
Ceftriaxone	Good	Cidal	15–50	IV, IM, SQ	12	Broad (except *Enterococcus, Salmonella*)
Ceftizoxime	Good	Cidal	25–50	IV	8	Broad (except *Enterococcus, Pseudomonas*)
Cefuroxime	Good	Cidal	30	IV	8	Broad (except BLRSE)
Cephalexin	Poor	Cidal	20–30	PO	8	Gm+ (except BLRSE)
Chloramphenicol	Good	Static	25–50	PO	6–8	Gm– (except *Pseudomonas, Klebsiella*), some Gm+
Clavamox	Poor	Cidal	10–20	PO	8–12	Broad (except *Pseudomonas, Enterococcus*)
Clindamycin	Poor	Static/cidal	12.5–20.0	PO, IM	12	Gm+, anaerobes, protozoa
Doxycycline	Intermediate	Static	5	PO	12	Rickettsial
Enrofloxacin	Intermediate	Cidal	5–10	IV, SQ, PO	12	Gm–
Florfenicol	Good	Static	25–50	IM, SQ	8	Broad
Fluconazole	Good	Static	5–10	PO	12–24	Fungi (crypto)
Flucytosine	Intermediate	Static	50	PO	6	Fungi (crypto)
Gentamicin	Poor	Cidal	2–4	IV, IM	8–12	Gm–
Itraconazole	Poor	Static	5	PO	12–24	Fungi (crypto)
Ketoconazole	Poor	Static	10–20	PO	12–24	Fungi (crypto)
Metronidazole	Good	Cidal	10–15	PO	8	Anaerobes
Penicillin G	Poor to intermediate	Cidal	20,000–40,000 U/kg	IV	6	Broad (except BLRSE)
Pyrimethamine	Good	Cidal	1 (cats: 0.25–1.00)	PO	24	Protozoa
Rifampin	Good	Cidal	10–20	IV	24	Gm+, *Chlamydia*
Tetracycline	Intermediate	Static	22	PO	8	Rickettsial
Trimethoprim-sulfadiazine	Good	Cidal	15–30	PO, SQ	12	Broad (except *Pseudomonas*, anaerobes), protozoa
Vancomycin	Poor to intermediate	Cidal	15	IV	6	Gm+, BLRSE (except Gm–)

BBB, blood-brain barrier; BLRSE, beta-lactamase–resistant *Staphylococcus* and *Enterococcus* species; Broad, broad spectrum including Gm+, Gm–, and anaerobic bacteria; IM, intramuscularly; IV, intravenously; PO, per os; SQ, subcutaneously.

often characterized by periventricular and meningeal contrast enhancement and ventricular dilatation due to secondary hydrocephalus. Fungal granulomas and bacterial abscesses may resemble intracranial tumors due to their patterns of enhancement and perilesional edema.

- Occasionally, a brain biopsy may be needed to make a definitive diagnosis.

Treatment

- Medical therapy for infectious brain diseases is presented in Table 126-3. Protozoal and fungal infections frequently require prolonged therapy. The recommended treatment duration for CNS cryptococcal and coccidioidal infections with fluconazole is 9 to 12 months. In dogs, treatment of cryptococcal infections is stopped after two consecutive negative titers are obtained at least 4 weeks apart. Relapses are common if fluconazole therapy is stopped too early.
- Initial treatment of bacterial meningoencephalitis is most effective if parenteral antibiotics are administered. Parenteral (usually intravenous) administration allows rapid therapeutic CNS and CSF drug concentrations to be achieved. Penicillin or ampicillin in combination with third-generation cephalosporins have a broad antimicrobial spectrum and are bactericidal (see Table 126-3). Many third-generation cephalosporins also cross the blood-CSF and blood-brain barrier in both the presence and the absence of inflammation. Concurrent low-dose dexamethasone therapy (0.15 mg/kg IV every 6–8 hours for 4 days) has been shown to be beneficial in human bacterial meningoencephalitis. After 3 to 5 days of parenteral

therapy, inflammation resolves and the barrier to the entry of many antibiotics is restored. Extended therapy is then instituted with broad-spectrum oral antibiotics that penetrate non-inflamed meninges. These drugs include trimethoprim-sulfonamide, chloramphenicol, florfenicol, and fluoroquinolones. Metronidazole is often added if an anaerobic component to the infection is suspected.

▼ ***Key Point*** Treatment failures usually relate either to delays in antibiotic administration or to selection of antibiotics with an inadequate spectrum, poor CNS penetrating abilities, or lack of bactericidal properties.

Also refer to "Infectious Causes of Vasculitis" later in this chapter. Additional information can be found in the following chapters:

- Feline immunodeficiency virus—Chapter 9
- Feline infectious peritonitis—Chapter 10
- Canine distemper virus—Chapter 13
- Rabies and pseudorabies—Chapter 15
- Rocky Mountain spotted fever and ehrlichiosis—Chapter 17
- Cryptococcosis (and other fungal disorders)—Chapter 20
- Toxoplasmosis and neosporosis—Chapter 21

IDIOPATHIC INFLAMMATORY BRAIN DISORDERS

Most of these conditions have an immune-mediated pathogenesis with clinical signs limited to the CNS.

Granulomatous Meningoencephalomyelitis

Etiology

Granulomatous meningoencephalomyelitis (GME) is an idiopathic, immune-mediated condition in dogs characterized by pronounced inflammatory changes in the CNS. These changes tend to predominate in white matter areas of the brain and spinal cord. Perivascular accumulations of lymphocytes, plasma cells, and histiocytic-like cells are the hallmark of GME. Some perivascular cell aggregates may coalesce to form a space-occupying mass in the brain. GME should be distinguished from neoplastic reticulosis and from B cell lymphoma in which homogeneous populations of neoplastic cells predominate. Whether inflammatory cells in GME eventually undergo neoplastic transformation to these cancerous phenotypes is still unknown. At present, the mixed granulomatous cell response is believed to represent a chronic immune response to a suspected but unconfirmed antigen.

Three forms of GME have been described. The *disseminated form* is characterized pathologically by multifocal perivascular cuffs throughout the brain and spinal cord and clinically by multifocal neurologic signs. The *focal form* is characterized by a focal neurolocalization due to the presence of a granulomatous mass in the brain stem, the cerebrum, or more rarely, the spinal cord. The focal form, however, is probably a variant of the disseminated form since histologic lesions can usually be identified postmortem all throughout the neuraxis. A rare *optic form* with dense optic nerve infiltration by inflammatory cells is also recognized.

Clinical Signs

- GME is primarily a disease of toy and small breeds between 1 and 8 years of age. Large-breed dogs may occasionally be affected (e.g., Airedale terriers).
- Onset and progression of clinical signs may be more rapid (several days) in the disseminated form compared with the focal form (1–3 weeks).
- Initially, mild fever, lethargy, and intermittent anorexia may be the only clinical signs seen.

▼ ***Key Point*** Neurologic signs of GME often indicate a focal brain stem or cerebral lesion.

- Central vestibular signs are common and may be paradoxical (see "Neoplasia"). Long tract signs (proprioceptive deficits and paresis) and other cranial nerve deficits (CN5 and CN7) may be present.
- Neck pain is often present and indicates meningeal involvement.
- Focal or multifocal areas of intramedullary spinal cord inflammation (myelitis) may cause tetraparesis or caudal paresis.
- The optic form is characterized by a sudden onset of bilateral or unilateral blindness.

Diagnosis

- A marked mononuclear pleocytosis consisting of lymphocytes, plasma cells, monocytes, macrophages, and multinucleated giant cells is usually evident on CSF analysis. Neutrophils may be present. Rarely, CSF cytology is normal. Protein is usually elevated.
- CSF titers, cultures, and virus isolation studies are negative for any infectious etiology.
- CT or MRI may reveal focal or multifocal contrast-enhancing lesions (homogeneous or heterogeneous) with edema in white matter adjacent to the lesions.
- GME is a diagnosis of exclusion. A predominant mononuclear CSF pleocytosis and negative tests for infectious agents (rickettsial, fungal, bacterial, protozoal, viral) suggest a diagnosis of GME. If the CSF is normal and a focal lesion is present, a brain biopsy is necessary to rule out neoplasia.

Treatment

- Prednisone at 2 mg/kg every 12 hours for 2 weeks, then 1 mg/kg every 12 hours for 1 to 2 months fol-

lowed by a gradual taper over several months, will usually result in temporary remission of clinical signs in the focal form. The disseminated form has a less favorable response to therapy. The optic form, if treated in the early stages, can result in recovery of vision.
- Other therapies for GME include lomustine, azathioprine, cytosine arabinoside, procarbazine, cyclophosphamide, and cyclosporine. I prefer lomustine as maintenance therapy. The dosage is 60 mg/m^2 of body surface area every 4 to 6 weeks for 12 to 24 months. Lomustine therapy can be initiated early in the course of corticosteroid therapy.
- Radiation therapy for the focal form of GME may be of benefit as adjunctive therapy.

Prognosis

Relapses are common and may occur weeks to months (up to 48 months) following onset of therapy. Upon relapse, patients are often refractory to a second course of chemotherapy.

Necrotizing Encephalitis

Etiology

Necrotizing encephalitis is a brain disease of toy breeds (pugs, Maltese terriers, and Yorkshire terriers). The acute disease bears many similarities to GME and may have an immune-mediated component. Lymphocytes and histiocytes form large perivascular cuffs in cerebrum. Neuronal necrosis and malacia in both gray and white matter are more severe in necrotizing encephalitis than in GME. Multifocal, necrotic, cavitating lesions are commonly observed in the chronic stages. A familial predisposition is probable, but this disorder is considered idiopathic.

Clinical Signs

- Age of onset of clinical signs is 9 months to 5 years of age.
- Seizures, dementia, blindness, neck pain, and ataxia are seen in the acute form. Over 1 to 2 weeks, signs may or may not progress to coma and/or status epilepticus.
- In the chronic form, partial or generalized seizures are initially seen but the interictal neurologic examination is normal. Other forebrain signs and progressive seizure activity develop over the subsequent 4 to 12 months.
- Brain stem and cerebellar signs are also reported.

Diagnosis

- A diagnosis of necrotizing encephalitis is supported by clinical signs and a CSF mononuclear pleocytosis. Small lymphocytes predominate in the majority of affected dogs. More pronounced pleocytosis is seen in the acute form or in the early stages of the chronic form. Protein levels are increased.
- MRI in the acute form shows asymmetrical cerebral edema that affects white and gray matter. Patchy or scant contrast enhancement may be seen acutely. In chronic cases, MRI changes include asymmetrical cortical cavitation, ventriculomegaly, and atrophy. Cavitated, cystic lesions are frequently periventricular. Chronic lesions fail to contrast enhance. Concurrent thalamic, midbrain, and cervical lesions have also been identified in selected cases.
- The primary differential diagnoses are GME, infectious disease, and neoplasia. An additional differential diagnosis for the chronic form is cerebrovascular disease.

Treatment

Use immunosuppressive therapy as for GME and anticonvulsant therapy.

Prognosis

The prognosis is guarded to poor.

Generalized Idiopathic Tremors (Little White Shaker Syndrome) of Adult Dogs

Etiology

An acute onset of tremor in toy- to small-breed dogs with white coat color (Maltese terrier, West Highland white terrier, poodle, Bichon frisé, Samoyed) is recognized. Other breeds with other coat colors (beagle, miniature schnauzer, spitz, Yorkshire terrier, etc.) can also be affected. This syndrome was originally described by some authors as a "non-suppurative encephalitis" or "cerebellitis" due to the occasional finding of a non-suppurative meningoencephalitis involving the cerebellum and other brain areas. A demyelinating disorder, a neurotransmitter defect, and various other mechanisms have been hypothesized but not proven.

Clinical Signs

- Young adult dogs (less than 6 years of age) are affected.
- The onset is acute to peracute.
- Clinical signs are a severe coarse head and body tremor that worsens with stress, exercise, or handling. At rest or during sleep, the tremor diminishes. Continuous shaking makes ambulation difficult, but strength and motor abilities are preserved. The excessive muscle activity may cause hyperthermia.
- Disconjugate, jerky eye movements may be seen (opsoclonus).
- Dogs are alert and responsive and rarely have other neurologic deficits.

Diagnosis

- Differential diagnoses include neurotoxin exposure ("moldy cheese" toxicity, metronidazole toxicity), other inflammatory CNS diseases, and generalized seizures. Generalized tremors in the absence of other signs of neurologic or systemic illness suggest a diagnosis of shaker syndrome.
- CSF may be normal or a mild lymphocytic pleocytosis may be seen.

Treatment

- Cool the patient if hyperthermic.
- Diazepam, 0.5 to 1.0 mg/kg PO every 8 hours, will help alleviate signs in the short term.
- Prednisone, 1 mg/kg every 12 hours for 4 weeks followed by a gradual taper over the next 8 weeks, appears to be the most effective treatment. Some dogs may recover without therapy.

Prognosis

- The prognosis is good for recovery. Relapses may occur.

VASCULAR DISEASES

Vascular Encephalopathies Secondary to Systemic Disorders

Etiology

Vascular encephalopathies can affect the forebrain, cerebellum, or brain stem of dogs and cats. Affected animals are usually older. Signs are peracute and rarely progressive. Focal ischemia or infarction ("stroke") usually occurs due to thrombosis of a brain blood vessel secondary to hypercoagulable states, hyperviscosity syndromes, atherosclerosis, vasospasm (from hypertension), local vasculitis, tumor emboli, or tumor invasion of regional blood vessels. A primary cause may not be found in many cases. Spontaneous hemorrhage in the CNS can occur due to thrombocytopenia, coagulopathies, vasculitis (immune-mediated or infectious), neoplastic invasion of blood vessels (especially from hemangiosarcomas), traumatic or ischemic damage to vessels, or arteriovenous malformations or aneurysms. Traumatic injuries to the brain and its vessels are discussed under "Brain Trauma." Other common causes of vascular disease in small animals are discussed in subsequent sections.

Clinical Signs

- Common zones of ischemia in the dog and cat include those brain areas supplied by the middle cerebral artery (forebrain) and rostral cerebellar artery (cerebellum).
- Signs of focal ischemia are almost always asymmetrical and reflect the areas of the CNS involved. Signs of unilateral forebrain disease (seizures, circling, dementia, aggression, contralateral blindness, and CP deficits) and signs of cerebellovestibular disease (ataxia, head tilt, nystagmus, hypermetria, torticollis) may be seen. Some dogs with cerebellar infarcts may show paradoxical vestibular signs.

Diagnosis

- Hypercoagulable states can occur due to renal disease with protein-losing nephropathy, Cushing's disease, and septicemia. A CBC, chemistry profile, urinalysis, urine protein-to-creatinine ratio, ACTH stimulation test, thoracic radiographs, and abdominal ultrasound are necessary to rule out these disorders.
- Atherosclerosis can occur due to hypothyroidism and is also recognized in miniature schnauzers with hyperlipoproteinemia. A thyroid panel, fasting triglycerides, and a lipid/cholesterol panel are recommended.
- Hypertension in dogs and cats may be associated with hypothyroidism, hyperthyroidism, Cushing's disease, diabetes mellitus, renal insufficiency, hepatic insufficiency, pheochromocytoma, and phenylpropanolamine administration. Idiopathic or essential hypertension is also being recognized with greater regularity. Serial blood pressure monitoring, retinal examination, and appropriate testing to rule out the above disorders are warranted if hypertension is present (see Chapter 153).
- Hyperviscosity syndromes can occur secondary to gammopathies, polycythemia vera, and hyperfibrinogenemia. Protein electrophoresis and coagulation profiles may be indicated.
- MRI is very important in determining the extent of the ischemia or hemorrhage and potential local concurrent conditions (tumor, inflammation, arteriovenous malformation) that could have produced it. Pure areas of ischemia are primarily hypointense on T1-weighted images and hyperintense on T2-weighted and fluid-attenuated inversion recovery images. Secondary edema, especially during reperfusion, can cause a transient mass effect with signs of acute brain swelling, but this is not common and usually no mass effect is evident. Contrast enhancement is minimal to absent in most cases, although a peripheral rim enhancement of the lesion can be seen starting 1 week after onset. Chronically, large areas of infarction "collapse" due to atrophy and loss of parenchymal volume. A paradoxical "mass effect" could be incorrectly diagnosed due to a contralateral shift of the brain midline and ventricles toward the side of the infarction.
- CSF analysis can be normal or show a mild increase in cells and protein. If acute, cells may be predominantly neutrophils.

Treatment

- Treatment for brain ischemia depends on the severity of the event and the correction of an existing underlying cause.
- Severe infarction can cause secondary brain edema that could require mannitol therapy (0.5–1.0 g/kg IV over 20 minutes). Careful but adequate fluid therapy to maintain a euvolemic state is essential.
- Anticonvulsants may be necessary if seizures occur. Anticonvulsant drugs that have fewer sedative properties (felbamate, zonisamide, gabapentin, levetiracetam) will permit better assessment of neurologic recovery.
- Hypertension can usually safely be treated with angiotensin-converting enzyme inhibitors (enalapril) or vasodilators (amlodipine, prazosin). Heparin, warfarin, and aspirin are used routinely in humans after a stroke if atherosclerosis is suspected. Treatment of any predisposing causes of vascular disease is essential.

Prognosis

▼ ***Key Point*** Vascular encephalopathies can cause severe signs initially, but many of the signs improve steadily with time (over 2–3 months) and generally have a good prognosis.

Feline Ischemic Encephalopathy

Etiology

This is an idiopathic syndrome of young to middle-aged cats characterized by a peracute onset of unilateral cerebral infarction due to vasospasm of the middle cerebral artery. The pathogenesis of this disease is not well understood. It is usually *not* associated with thromboembolic disease secondary to feline hypertrophic cardiomyopathy or any other etiology. An association between aberrant *Cuterebra* species migration in brain and possible middle cerebral artery vasospasm has been suggested because of the occasional finding of this parasite in the cranial vault. There is a higher incidence of this syndrome in late summer.

Clinical Signs

- Affected cats often exhibit peracute signs of unilateral cerebral dysfunction. Altered mentation, behavior change, circling, visual field deficits, contralateral postural deficits, seizures, or a combination of these signs may be observed.
- Seizures may be the only clinical sign observed.
- Signs may worsen slightly over 24 to 48 hours but then stabilize.
- If the injury is not fatal, signs may steadily improve over days to months.
- Seizures and altered personality may be long-term sequelae.

Diagnosis

- Rule out other causes of unilateral cerebral dysfunction and peracute vascular disease (cardiomyopathy-associated thromboemboli, hypertension, hypercoagulable states, infectious vasculitis, neoplasia, trauma).
- CSF analysis may reveal a pleocytosis and elevated protein due to inflammatory changes induced by necrotic tissue.
- MRI in acute stages demonstrates cerebral edema, usually without significant mass effect. Chronically, asymmetrical atrophy of cortical regions supplied by the middle cerebral artery will be seen.
- The peracute onset of signs in an otherwise healthy cat aids in making a tentative diagnosis.

Treatment

- There is no specific treatment.
- Corticosteroids do not alter the clinical course.
- Start anticonvulsant therapy (diazepam or phenobarbital) if seizures occur (see Chapter 127).

Prognosis

The prognosis for survival is fair to good. The prognosis for complete recovery is guarded.

Necrotizing Vasculitis of the Beagle, Bernese Mountain Dog, and German Shorthaired Pointer

Etiology

A necrotizing vasculitis of young adult beagles, Bernese mountain dogs, and German shorthaired pointers is frequently associated with neurologic signs. This is an idiopathic condition, but a genetic predisposition is suspected. The typical lesion is a fibrinoid necrosis and thrombosis of small- and medium-sized meningeal vessels with subsequent meningeal fibrosis. A marked inflammatory component to the lesion suggests an immune-mediated basis for the disease. Meningeal artery damage may lead to hemorrhage or to thrombosis or infarction of adjacent neural parenchyma.

Clinical Signs

- Age of onset is 3 to 18 months of age.
- Signs of meningitis (neck pain and stiffness, stiff, stilted gait, fever) are common. "Painful" episodes may wax and wane. Clinical signs of meningitis are very similar to sterile suppurative meningitis of young, large-breed dogs.
- Secondary parenchymal involvement may result in conscious proprioceptive deficits and paresis. Rarely, cranial deficits occur.
- Blindness and seizures are seen secondary to an associated encephalitis in Bernese mountain dogs.
- Beagles may have neutrophilic polyarthritis and coronary arteritis associated with the neurologic disease.

Diagnosis

- CSF analysis is characterized by a marked neutrophilic pleocytosis and elevated protein levels. No infectious agents can be isolated, and titers for infectious causes of meningitis (rickettsial, viral, bacterial, fungal, protozoal) are negative.
- GME can be ruled out based on the CSF findings.
- Intervertebral disc disease is ruled out by the demonstration of no compressive lesions on cervical myelography.
- Antinuclear antibody titers are negative, and there is no evidence of neoplasia or a drug reaction.

Treatment

- Immunosuppressive dosages of corticosteroids (2 mg/kg PO every 12 hours for 2 weeks with a very slow taper over 3–6 months) often result in a clinical response.
- Occasionally patients are nonresponsive and may require other immunosuppressive agents.

Prognosis

The prognosis is fair to guarded. Some patients do not respond to therapy. Relapses can occur.

Infectious Causes of Vasculitis

Etiology

Many of the infectious causes of vasculitis have previously been discussed in "Inflammatory Brain Diseases" (see Tables 126-1 and 126-2). Various fungal, protozoal, and viral agents may create secondary blood vessel inflammation with edema, hemorrhage, or infarction. Rickettsial disorders may produce an immune-mediated vasculitis and direct damage to endothelial cells due to intracellular replication. Bacterial vasculitis occurs most commonly as a sequela to sepsis. Bacterial toxins and inflammatory mediators released by neutrophils increase vascular permeability and cause edema and hemorrhage. Septic thromboemboli lead to multiple areas of infarction.

Clinical Signs

- Diffuse or multifocal vasogenic edema can result in brain swelling and diffuse cerebral signs of dullness, dementia, head pressing, and pacing. Signs of brain herniation may be evident.
- Head and neck pain are common due to accompanying meningitis.
- Multifocal cranial nerve deficits and long tract signs reflect multifocal involvement of the brain stem and spinal cord. Rickettsial diseases are often associated with central vestibular signs.
- Focal or generalized motor seizures and other focal cerebral signs may be seen.
- Systemic signs of fever, lymphadenopathy, polyarthritis, uveitis, and peripheral edema are sometimes present.

Diagnosis

- CSF characteristics will depend on the inciting cause (see "Inflammatory Brain Diseases" and Tables 126-1 and 126-2). The degree of pleocytosis is often determined by the degree of meningitis. Bacterial vasculitis is characterized by normal or neutrophilic pleocytosis and high protein levels.
- Xanthochromia, free blood, and erythrophagocytosis by neutrophils or macrophages are typical CSF findings in patients with previous hemorrhage.
- Gram stains and other special stains may demonstrate organisms.
- Appropriate CSF titers and cultures will often reveal the underlying pathogen.
- A CBC, a chemistry profile, and other blood tests will frequently uncover abnormalities in other organ systems.

Treatment

- Treatment is directed at the underlying etiologic agent.
- See "Inflammatory Brain Diseases" and Table 126-3 for properties of specific antimicrobial agents.

Prognosis

The prognosis will vary depending on the underlying pathogen, its sensitivity to chemotherapies, and the state of disease progression. Aggressive medical therapy is necessary to prevent irreversible brain injury.

BRAIN TRAUMA

Pathophysiology

Severe head trauma can result in acute brain injury. Primary mechanical injury to cell membranes and fiber tracts results in irreversible necrosis. This can take the form of a blunt contusion or a laceration. Secondary events are due to biochemical changes at the cellular level and increased ICP. Excitotoxins, free radicals, prostaglandins, and inflammatory cytokines fuel a self-perpetuating cycle of ischemia and necrosis in the traumatized brain. Intracranial edema and hemorrhage combine to raise ICP, exhaust compensatory mechanisms, and create conditions favorable for brain herniation. Elevated ICP may also lead to bradycardia, systemic hypertension, and neurogenic pulmonary edema. A final immediate or delayed consequence of brain trauma is epilepsy. Seizures can be seen months following head trauma.

Clinical Signs

- The signs of brain trauma will depend upon whether the lesion remains localized or progresses to involve other brain structures. If progression occurs, it will occur within the first 24 to 48 hours after an injury. For this reason, it is critical to perform serial neurologic examinations every few hours in traumatized patients.
- Focal signs may originate from injury to the cerebrum, cerebellum, or brain stem and will reflect dysfunction of the region involved.
- Signs of increased ICP, transtentorial herniation, and foramen magnum herniation are discussed in the first section of this chapter, under "Herniation from Space-Occupying Brain Lesions." An orderly progression of signs due to increased ICP can be graded from mild to severe.
  - Motor activity tends to progress from normal ambulatory status to recumbency with progressive extensor rigidity.
  - Pupils initially appear miotic but soon become mydriatic or midrange and nonresponsive to light.
  - The oculovestibular reflex (doll's eye) is lost in the late stages of transtentorial herniation and is a poor prognostic sign.
  - Level of consciousness deteriorates from the alert state to depression, stupor, and coma. These states are defined by the patient's responsiveness to stimuli, including deep pain.
  - Hyperventilation may be seen with midbrain compression, whereas either an ataxic (irregular) respiratory pattern or apnea may be seen with medullary compression.

Diagnosis

- Clinical signs usually reflect the severity of the injury.
- Use an EEG and BAER can be used to localize areas of brain damage (see Chapter 125). The EEG can also be used to detect seizure foci.
- Consider CT and MRI in those patients with progressive neurologic dysfunction despite medical therapy or if unstable skull fractures are present. Progression of clinical signs may occur secondary to a space-occupying epidural or subdural hematoma or secondary to compression and/or laceration of brain parenchyma by a depressed or displaced skull fracture. CT is often preferred over MRI due to its sensitivity to bony changes and intracranial hemorrhage and also the shorter examination time required compared with MRI.
- A CSF tap is rarely necessary. It is contraindicated in the patient with increased ICP.

Treatment

- Correct hypovolemic shock, pneumothorax, cardiac arrhythmias, and other life-threatening non-neural injuries. When correcting for shock, do not overhydrate the patient.
- Elevating the head will facilitate venous return to the heart, enhance CSF resorption, and help maintain cerebral blood flow. Avoid jugular vein compression when elevating the head.
- Hypercarbia will act to cause cerebral vasodilation and increased ICP. Intubation and hyperventilation will lower blood and brain carbon dioxide concentrations and stimulate vasoconstriction. Vasoconstriction of cerebral vessels will decrease intracranial blood volume, lower ICP, and raise cerebral perfusion pressure.
- Methylprednisolone sodium succinate (Solu-Medrol) may be of some benefit if administered at the time of or immediately following the trauma (within 1 to 2 hours). Administer methylprednisolone sodium succinate at 30 mg/kg as an intravenous bolus, then give repeat boluses of 15 mg/kg IV at 2 hours and then every 6 hours for 1 to 2 days. After this, discontinue the steroids.
- Mannitol and furosemide are administered if signs of impending herniation are present. Administer a single (1 g/kg) IV bolus of mannitol as a 20% solution at a rate of 2 ml/kg/min. Administer 0.7 mg/kg of furosemide IV 15 minutes after mannitol. Furosemide will prolong the effects of mannitol and decrease CSF production.
- Use hypertonic saline (7.5% as a 4 ml/kg IV bolus) with hydroxyethyl starch (20 ml/kg IV) in a patient that presents with both hypovolemic shock and head trauma or cerebral edema. Hypertonic saline will lower ICP as long as there is no bleeding from a major vessel. Hydroxyethyl starch will prolong the effects of the hypertonic saline. Follow these boluses with lactated Ringer's solution at a dosage of 40 to 50 ml/kg/hour. If there is significant bleeding, administer whole blood or plasma at 25 ml/kg over 1 hour (do not use hypertonic saline or mannitol). Follow with lactated Ringer's solution at a dosage 40 to 50 ml/kg/hour. Fluid therapy is discussed in Chapter 5 and management of shock is described in Chapter 156.
- Administer intravenous diazepam to control seizures. Intravenous phenobarbital and other anticonvulsants may be needed in some cases (see Chapter 127). Initiate oral anticonvulsant (phenobarbital) therapy and do not taper or discontinue treatment unless the patient remains seizure free for a minimum of 6 months.
- Monitor supportive fluid therapy to prevent overhydration or dehydration (see Chapter 5). Patients should be turned and kept on padded bedding. Intermittent bladder expressions or catheterizations may be necessary. Initiate parenteral or enteral nutritional support as needed (see Chapter 3).

METABOLIC ENCEPHALOPATHIES

The brain relies on the body's various homeostatic mechanisms to control extracellular osmolality, electrolyte concentrations, acid-base balance, oxygenation, and glucose levels. Potentially neurotoxic metabolites are continuously removed from the body by fully functional hepatic and renal systems. If homeostatic mechanisms are disrupted, normal brain function may be impacted and physical brain injury may occur. The cerebrum is often the major brain region affected by metabolic encephalopathies. Altered behavior, depressed mentation, and seizures are common manifestations of diffuse cerebral dysfunction. Table 126-4 lists important metabolic causes of brain disease, specific regional vulnerabilities, clinical signs, and treatment. Etiologies, pathogenic mechanisms, diagnosis, and further descriptions of each disorder are discussed in detail in other sections of this text and the following chapters:

- Osmotic and ionic imbalances—Chapter 5
- Acid-base imbalances—Chapter 5
- Hypoglycemia—Chapters 34 and 35
- Hypoxia
- Renal failure and uremia—Chapter 77
- Hepatic encephalopathy and liver failure—Chapter 71

THIAMINE (VITAMIN B_1) DEFICIENCY

Etiology

Thiamine is a water-soluble B vitamin that is an essential dietary nutrient. Depleted body stores of thiamine may be a result of deficient thiamine in the diet, a prolonged period of anorexia, or chronic ingestion of all-fish diets containing thiaminase. Thiamine deficiency results in altered energy metabolism, decreased adenosine triphosphate (ATP) formation, and eventual cell death. Neurons in brain stem nuclei are most vulnera-

Table 126-4. IMPORTANT METABOLIC ENCEPHALOPATHIES IN SMALL ANIMALS

Condition	Causes	Brain Region Affected	Clinical Signs	Treatment
Global hypoxia/ischemia	Pulmonary disease, anemia, carbon monoxide, cyanide, shock, cardiac disease or arrest	Cerebrum (occipital region), cerebellum, hippocampus	Blindness, seizures, ataxia, memory loss, coma	Correct underlying cause; give fluids, oxygen, mannitol and furosemide for edema
Hypoglycemia	Juvenile hypoglycemia, insulinoma, sepsis, severe liver disease, Addison's disease	Cerebrum, cerebellum, hippocampus	Ataxia, weakness, collapse, pupillary changes, depressed mentation, seizures, focal facial twitches	Correct underlying cause
Hypocalcemia	Eclampsia, hypoparathyroidism, renal failure, others	Cerebrum (neuromuscular junction)	Muscle tremors, spastic tetraparesis/tetany, behavior change, seizures, myoclonus	0.5–1.5 ml/kg, up to 10 ml total of 10% calcium gluconate, slow IV
Hypernatremia	Diabetes insipidus, severe dehydration, adipsia, primary hyperaldosteronism	Cerebrum	Ataxia, weakness, tremors depression, seizures, coma	Slow correction with normal saline then half-strength saline
Hyponatremia	Diuretics, Addison's disease, inappropriate adh secretion, water intoxication	Cerebrum	Depression, stupor, coma	Slow correction with normal saline then hypertonic saline; will induce pontine or thalamic myelinolysis if corrected too fast
Uremia	ARF, CRF	Cerebrum	*For ARF:* Seizures, tremors, myoclonus, non-fixed muscle twitches *For CRF:* Dementia, depression, coma	Correct underlying cause; use anticonvulsants if seizures, oral phosphate binders, cimetidine
Hepatic encephalopathy	Portocaval shunt, acquired liver disease	Cerebrum	Episodic dementia, head pressing, pacing, ataxia, visual deficits, seizures, ptyalism	IV fluids with potassium, colon evacuation, lactulose or dilute providone enemas, metronidozole PO; low-protein, high-carbohydrate diet; surgery for shunt ligation

ARF, acute renal failure; CRF, chronic renal failure.

ble to this energy deficit. Cats are much more frequently affected than dogs, presumably because of lower body stores of the vitamin.

Clinical Signs

- Signs may be intermittent initially but are rapidly progressive once present. Affected cats are often thin or on a poor diet.
- Head and neck ventroflexion and ataxia may progress to recumbency, extensor rigidity, opisthotonus, and coma.
- Ocular changes include mydriasis, sluggish to no pupillary light reflexes, blindness, and absence of the oculovestibular reflex.
- Positional vertical nystagmus is common. Seizures may be present.
- Sudden death can occur 24 to 48 hours after onset of signs.

Diagnosis

- Rule out other causes of acute brain stem or central vestibular signs in the cat, including FIP, cryptococcosis, toxoplasmosis, and vascular disorders.
- CSF may show a slight pleocytosis and protein elevation and/or xanthochromia due to ongoing necrosis and hemorrhage.
- Erythrocyte transketolase activity may be decreased and blood pyruvate and lactate levels may be increased.
- Blood thiamine levels may be normal or decreased.
- Response to therapy is the usual method of diagnosis.

Treatment

- Give parenteral thiamine at a dosage of 25 to 50 mg per cat intramuscularly or subcutaneously every 12 hours until signs resolve.
- Institute a balanced diet and supplement with B vitamins for at least 2 weeks.
- A dramatic response to thiamine is usually seen in 24 to 48 hours.

Prognosis

The prognosis is good with prompt therapy. If pretreatment signs are severe, the response may be incomplete. The condition is fatal if no treatment is instituted.

NEUROTOXINS

A variety of toxins can affect the CNS in dogs and cats. Multisystemic signs may or may not be present. Any region of the neuraxis can be affected. Those neurotoxins that result in signs of brain dysfunction are discussed below.

For most ingested toxins, general treatment guidelines include the following:

- Induction of vomiting with 2 ml/kg of 3% hydrogen peroxide (except in comatose or obtunded patients or in the case of petroleum distillate or alkali ingestion) if it has been less than 2 hours since ingestion.
- Gastric lavage under anesthesia if it has been less than 2 hours since ingestion. Use 5 to 10 ml/kg of water for each lavage and lavage several times. Leave activated charcoal in the stomach after the final lavage.
- Administration of activated charcoal 2 g/kg orally by stomach tube.
- Administration of a cathartic (usually magnesium sulfate) at the same time as or 30 minutes following activated charcoal administration.
- Colonic lavage and enemas (especially for heavy metals).

Lead Poisoning

Etiology

Lead poisoning is a sporadic problem caused by ingestion of lead-containing paint chips, plaster board and sheetrock, grease, crankcase oil, linoleum, battery parts, solder, putty and caulking material, roofing material, and occasionally lead-contaminated soil. Younger animals are more frequently affected than older animals due to chewing tendencies, increased gastrointestinal absorption, and increased blood-brain barrier permeability. Acute toxicity is generally seen, but chronic exposure to low levels of lead may lead to a cumulative toxicity. Within the CNS, lead causes endothelial cell damage, edema, hemorrhage, and cerebrocortical laminar necrosis.

Clinical Signs

- Acute systemic signs of vomiting, diarrhea, anorexia, and abdominal pain may be seen. A rare finding is megaesophagus.
- Neurologic signs include hysteria, behavior change, pica, vocalization, and blindness.
- Either generalized or focal motor seizures may be present. “Chewing gum” seizures and myoclonus may be observed.

Diagnosis

- A blood lead level greater than 40 µg/dl is suggestive of lead poisoning. A level greater than 60 µg/dl is diagnostic for lead poisoning.
- Urinary lead levels will be elevated approximately 24 hours after the start of chelation therapy.
- Abdominal radiographs may reveal radiopaque material in the gastrointestinal tract.
- Nucleated red blood cells and basophilic stippling are often evident on stained blood smears.

Treatment

- If lead is visible in the gastrointestinal tract, administer cathartics and enemas.

- Use any one of the following chelating drugs:
  - Calcium disodium ethylenediaminetetraacetic acid at 25 mg/kg SC every 6 hours for 5 days. Prepare a 1% solution in 5% dextrose in water. Side effects are anorexia, diarrhea, and nephrotoxicity.
  - D-penicillamine at 110 mg/kg/day PO divided into three or four doses every 6 to 8 hours for 2 weeks. Gastrointestinal side effects are common.
  - 2,3-Dimercaptosuccinic acid at 10 mg/kg/day PO for 10 days. Side effects are rare.
- Administer anticonvulsants for seizures (diazepam, phenobarbital) (see Chapter 127).
- Treat suspected cerebral edema with mannitol and corticosteroids.

Prognosis

The prognosis is fair to good if neurologic debilitation is not severe. Residual neurologic deficits and seizures may be long-term sequelae.

Metaldehyde Poisoning

Etiology

Metaldehyde is a molluscide that can produce signs of neurotoxicity after oral ingestion. Metaldehyde produces a severe metabolic acidosis. Levels of the CNS neurotransmitters gamma-aminobutyric acid (GABA), norepinephrine, and serotonin are decreased in affected animals. The exact mechanism of neurotoxicity is unknown.

Clinical Signs

- Seizures, tremors, depression, salivation, tachycardia, hyperesthesia, hyperthermia, vomiting, and diarrhea are seen peracutely. Cats may also have nystagmus and ataxia. Respiratory failure may develop within 24 hours.
- If animals survive the initial toxic insult, hepatic failure occurs 3 to 4 days after ingestion.

Diagnosis

- Compatible signs, acidosis, and a history of exposure are suggestive of metaldehyde intoxication.
- A definitive diagnosis can be made by chemical analysis of stomach contents, urine, or liver tissue.

Treatment

- Perform gastric lavage and administer activated charcoal if it is within 2 hours of ingestion.
- Use sodium bicarbonate to treat the acidosis.
- Anticonvulsants are indicated for seizure control (see Chapter 127).

Prognosis

The prognosis for recovery is poor.

Methylxanthine Toxicosis (Caffeine, Theobromine, etc.)

Etiology

Ingestion of stimulants containing caffeine, theophylline, aminophylline, or theobromine may produce signs of methylxanthine toxicosis. Chocolate contains both caffeine and theobromine. Ingestion of 1 ounce of baker's chocolate per kilogram of body weight can be lethal in the dog. Although it is known that methylxanthines inhibit phosphodiesterases, increase calcium influx into cells, and enhance catecholamine release, the mechanism of its neurotoxicity is unknown.

Clinical Signs

- Tachycardia, cardiac arrhythmias, vomiting, polyuria and polydipsia, hyperthermia, respiratory paralysis, and cyanosis.
- Acute signs occur within several hours of ingestion and include seizures, hyperactivity, muscle tremors, ataxia, and coma.

Diagnosis

- Drug or chocolate exposure and clinical signs allow a tentative diagnosis of methylxanthine toxicosis.
- Serum, stomach contents, and urine can be analyzed for methylxanthine levels.

Treatment

- Administer activated charcoal and promote diuresis with aggressive fluid therapy.
- Treat cardiac arrhythmias with antiarrhythmic agents (see Chapters 145 and 146).
- Use diazepam for muscle tremors and seizures.

Prognosis

The prognosis is fair to good if treatment is instituted early.

Organophosphate and Carbamate Poisoning

Etiology

Both organophosphates and carbamates inhibit acetylcholinesterase, the enzyme that breaks down acetylcholine at muscarinic and nicotinic sites of the autonomic and somatic nervous systems. Usually signs of parasympathetic stimulation predominate, but signs of somatic, sympathetic, and CNS overstimulation may also be present. Delayed organophosphate neurotoxicity can cause an irreversible central-peripheral axonal degeneration. Chlorpyrifos, dichlorvos, fenthion, carbaril, methonyl, aldicarb, and carbofuran are just a few of the insecticides that can be toxic after dermal application or following oral ingestion. Many of these insecticides are found in dips and sprays, flea collars, and wormers.

Clinical Signs

- Muscarinic signs include salivation, vomiting, diarrhea, bronchial secretion, miosis, and bradycardia.
- Nicotinic signs may be delayed in onset and include muscle tremors, neuromuscular weakness, exercise intolerance, and respiratory paralysis.
- CNS stimulation results in hyperactivity and seizures.
- Organophosphate toxicity in cats is characterized by pronounced muscle weakness, mydriasis, twitching, and anorexia, which may last for weeks.

Diagnosis

Exposure history, clinical signs, and low whole-blood cholinesterase activity (less than 25% of normal) suggest toxicosis.

Treatment

- Induce vomiting if ingestion has occurred within 2 hours of presentation and the patient is asymptomatic. Provide a meal prior to giving an emetic. Follow with activated charcoal and a cathartic (may need to repeat every 8 hours).
- Bathe the animal in dishwashing detergent and water if exposure was by skin contact.
- Start anticonvulsants (IV diazepam, phenobarbital) if seizures occur (see Chapter 127).
- Administer 0.2 mg/kg atropine (0.05 mg/kg IV, 0.15 mg/kg SC); repeat as necessary for bradycardia, bronchoconstriction, respiratory depression, and other muscarinic signs.
- Use pralidoxime chloride (10–15 mg/kg IM or SC) for muscle tremors and nicotinic signs.
- Intravenous fluids, nutritional support, frequent turns, and padded bedding are recommended.

Prognosis

The prognosis is good with early treatment.

Ivermectin Toxicity

Etiology

Ivermectin is an avermectin used as an anthelmintic in large and small animals. The blood-brain barrier of normal animals normally prevents ivermectin entry into CNS tissues. A P-glycoprotein pump in brain endothelial cells transports any ivermectin that enters the CNS back into the systemic circulation. A subpopulation of collies, Shetland sheepdogs, Australian shepherds, and Old English sheepdogs are homozygous recessive for a specific P-glycoprotein gene mutation that results in a nonfunctional P-glycoprotein molecule. Ivermectin and other P-glycoprotein substrates are able to freely enter the brain of these affected individuals. Single oral doses of 100 to 500 µg/kg of ivermectin can be neurotoxic in these breeds.

Clinical Signs

- Ivermectin has inhibitory actions in the brain similar to GABA.
- Signs of neurotoxicity include ataxia, muscle tremors, symmetrical or asymmetrical tetraparesis, dullness, and sometimes coma.
- The more rapid the onset and progression of clinical signs, the more likely that signs will progress to coma.
- Mydriasis and apparent blindness have also been reported.

Diagnosis

Ivermectin exposure and compatible clinical signs in a breed with known sensitivity to ivermectin is strongly suggestive of ivermectin neurotoxicosis.

Treatment

Treatment is supportive only (there is no definitive way to remove the neurotoxin). Use fluid therapy, parenteral or enteral nutrition, turns, bladder and fecal management, and other supportive care for the recumbent, nonresponsive patient.

Prognosis

The prognosis is good with appropriate supportive care, but recovery can take several weeks.

Metronidazole Toxicity

Etiology

Metronidazole (Flagyl) toxicosis is seen in the dog and cat following oral dosages of 66 mg/kg/day for more than 7 days. The mechanism of toxicity is unknown. Lesions of the vestibular nuclei and Purkinje cells of the cerebellum are recognized.

Clinical Signs

- Severe ataxia, positional vertical or rotary nystagmus, opisthotonus, seizures, asymmetrical upper motor neuron tetraparesis, and spastic muscle tremors may be seen acutely.
- Affected animals may exhibit a crouched posture in the pelvic limbs that is accentuated during ambulation.
- Many animals are weakened and disoriented to the point that they are recumbent, non-ambulatory, and anorexic.

Diagnosis

Drug exposure and compatible clinical signs are suggestive of the diagnosis. Tests for inflammatory, neoplastic, or other causes of multifocal CNS disease are negative.

Treatment

Discontinuing the drug will result in gradual resolution of clinical signs over 1 to 2 weeks. Provide supportive care as necessary.

▼ ***Key Point*** Diazepam (0.5 mg/kg IV or PO every 8 hours) reduces mean recovery time to less than 24 hours in most cases of metronidazole toxicity.

Prognosis

The prognosis is good if the drug is withdrawn.

Bromethalin Poisoning

Etiology

Bromethalin is a pelleted anticoagulant rodenticide that uncouples oxidative phosphorylation in CNS mitochondria. This results in a cellular ATP deficit, a sodium-potassium pump failure, and mild cerebral and spinal cord edema. Cats are more susceptible than dogs to the neurotoxic effects. Histopathologic lesions are mild, indicating a functional deficit at the cellular level.

Clinical Signs

- Acute hyperexcitability, muscle tremors, hyperthermia, running fits, and focal or generalized seizures may be seen in dogs. Thoracic limb rigidity, nystagmus, anisocoria, and depressed levels of consciousness are also part of the acute syndrome in dogs. Death occurs within 10 hours if the amount of bromethalin ingested is >5 mg/kg of body weight.
- Chronic signs (1–4 days after ingestion) in dogs include depression, pelvic limb ataxia, paresis, and hyperreflexia. This progresses to paraplegia and loss of deep pain. Cats exhibit very similar clinical signs 3 to 7 days after ingestion.

Diagnosis

- Exposure history and appropriate clinical signs suggest bromethalin toxicity.
- Tissue chemical analysis is definitive but not widely available.

Treatment

- Induce vomiting, perform gastric lavage, and administer activated charcoal if it is less than 2 hours after ingestion. Activated charcoal and a cathartic are recommended every 4 to 8 hours for at least four doses.
- Mannitol and dexamethasone do not appear to alleviate clinical signs.
- Control seizures with IV diazepam or phenobarbital (see Chapter 127).
- Provide supportive care; avoid overhydrating the patient with IV fluids.
- Monitor for 48 hours to evaluate for continued absorption or delayed onset signs.

Prognosis

The prognosis is poor once neurologic signs are seen.

Ethylene Glycol Poisoning

Ethylene glycol is a potent neurotoxin that can cause marked CNS depression. See Chapter 77 for additional information.

CONGENITAL MALFORMATIONS AND ANOMALIES

Most developmental defects of the brain affect either the cerebrum or the cerebellum. Clinical signs are usually present at birth and are nonprogressive. Congenital hydrocephalus can worsen postnatally with a gradual or sudden exacerbation of clinical signs. Although the majority of congenital malformations have a suspected genetic basis, a small number of disorders are due to in utero viral or toxic insults.

Hydrocephalus

Etiology

Primary hydrocephalus is a congenital disorder characterized by a pathologic accumulation of CSF within the ventricular system of the brain. Congenital hydrocephalus is recognized in the Maltese terrier, Yorkshire terrier, Chihuahua, Manchester terrier, Pomeranian, toy poodle, Cairn terrier, Shih Tzu, English bulldog, Boston terrier, Pekinese, Lhasa apso, and other breeds. Decreased CSF absorption at arachnoid villi and occlusion of the mesencephalic aqueduct are potential causes, but frequently an underlying structural abnormality cannot be identified. Congenital hydrocephalus may also be associated with other nervous system anomalies, including caudal occipital malformation syndrome, cerebellar hypoplasia, and meningomyelocele.

Clinical Signs

- Signs are usually seen in dogs less than 1 year of age, but trauma may precipitate signs in older dogs.
- Altered consciousness, head pressing, dementia, behavior changes, seizures, visual deficits, and ataxia are observed.
- Acute intraventricular hemorrhage can cause a sudden deterioration in neurologic status.
- Affected animals are frequently stunted, unthrifty, and poor doers.
- Associated signs are an open fontanelle, a thinned and domed calvarium, and a bilateral ventrolateral strabismus (“setting sun sign”).

Diagnosis

- Differential diagnoses include hepatic encephalopathy due to a portosystemic shunt, encephalitis due to

infectious or idiopathic causes, and toxin exposure (lead).
- Skull radiographs may demonstrate a large, thinned calvarium with loss of gyral markings.
- Ultrasonography through an open fontanelle allows visualization of dilated ventricles.
- Optimal visualization of ventricular dilatation and subcortical white matter atrophy is obtained by CT or MRI. There may be mild to moderate asymmetry in ventricular size.

▼ ***Key Point*** The presence of acute to subacute forebrain signs in conjunction with marked ventricular dilatation is strongly suggestive of hydrocephalus.

- Affected animals have normal (normotensive) or elevated (hypertensive) CSF pressures.

Treatment

- Provide therapy only if the patient has clinical signs of cerebral dysfunction. Many animals with ventriculomegaly are clinically normal and do not require therapy.
- Corticosteroids with or without furosemide benefit many patients in the short term.
- Mannitol is helpful if patients are exhibiting signs of acute ICP elevation.
- Anticonvulsant therapy is used for seizures (see Chapter 127).

Ventriculoperitoneal or ventriculovenous shunts can be placed to promote drainage of CSF. This procedure has alleviated clinical signs in some cases; however, referral to a neurosurgery specialist is required.

Prognosis

The prognosis is fair with early diagnosis and treatment.

Lissencephaly

Etiology

Lissencephaly is a migration defect of neural cell precursors in the telencephalon characterized by an absence of cerebrocortical convolutions, thickened cortical gray matter, and thinned cortical white matter. It is presumed to be an inherited defect in the Lhasa apso, wirehaired fox terrier, and Irish setter. Affected wirehaired fox terriers and Irish setters often have concurrent cerebellar hypoplasia.

Clinical Signs

- Neurologic signs are usually present at birth or within the first year of life.
- Behavioral changes, visual deficits, dementia, and seizures are seen.

Diagnosis

- Differential diagnoses are the same as for hydrocephalus (see above).
- CT or MRI reveals absence of gyri and sulci, thickening of the gray matter, and thinning of the white matter. Ventricular size is usually normal.

Treatment

- There is no specific treatment for this condition.
- Treat seizures symptomatically with anticonvulsants (see Chapter 127).

Prognosis

The prognosis is fair to poor. Seizures may be refractory to therapy.

Congenital Arachnoid Cysts

Etiology

- Congenital arachnoid cysts, also called subarachnoid cysts, are developmental anomalies characterized by cystic accumulation of fluid in the subarachnoid space. The cyst wall is composed of several layers of arachnoid cells.
- Arachnoid cysts can occur at any location along the neuraxis including the brain. Intracranial arachnoid cysts most frequently form between the cerebellum and the tentorium cerebelli and often are associated with the quadrigeminal cistern.
- Over time, the cyst can slowly enlarge to compress adjacent neural tissue.

Clinical Signs

- Signs are usually seen in young adults.
- Seizures, paresis, abnormal behavior, and cranial nerve deficits may be observed. If the cyst is causing secondary hydrocephalus, diffuse forebrain signs may be evident.
- Arachnoid cysts may be incidental findings associated with no clinical signs.

Diagnosis

- MRI or CT will reveal a well-circumscribed cystic structure compressing underlying brain tissue.
- Secondary hydrocephalus may be present if the cyst is compressing CSF outflow pathways.

Treatment

Surgical fenestration of the cyst wall and partial excision will result in decompression of underlying neural tissues and prevent further damage to these tissues. Medical therapy with glucocorticoids and diuretics can be attempted but is usually only effective in the short term.

Prognosis

The prognosis is good if surgery is performed before significant irreversible brain atrophy has occurred.

Cerebellar Hypoplasia in Cats

Etiology

Cerebellar hypoplasia refers to a defect in cerebellar development leading to decreased neuronal numbers with or without a gross reduction in size. This condition in kittens is usually due to an in utero or early postnatal panleukopenia viral infection (see Chapter 14). Vaccination of pregnant queens with modified live panleukopenia virus vaccine may also produce this syndrome. Rapidly dividing cells in the developing cerebellum are killed by the virus.

Clinical Signs

▼ ***Key Point*** Severe ataxia, falling, hypermetria, head intention tremor, head bobbing, and loss of menace response are usually seen at 3 to 4 weeks of age when kittens begin to ambulate.

- Signs are nonprogressive.
- There may be fewer clinical signs with lesser degrees of cerebellar damage.
- Littermates may or may not be affected.

Diagnosis

- Differential diagnoses are other infectious causes of cerebellar disease, cerebellar abiotrophy, or lysosomal storage disease.
- Clinical signs of a nonprogressive, purely cerebellar disorder in kittens are strongly suggestive of a diagnosis of cerebellar hypoplasia.
- CT or MRI will often reveal a small cerebellum.

Treatment

No treatment is available.

Prognosis

The prognosis is poor for clinical improvement. Many cats with cerebellar hypoplasia make functional pets.

Cerebellar Hypoplasia in Dogs

Etiology

Most of the canine forms of cerebellar hypoplasia have a genetic basis. An exception to this is cerebellar hypoplasia secondary to postnatal herpesvirus infection. Breeds affected include the chow chow, Airedale, Irish setter, wirehaired fox terrier, Boston terrier, bull terrier, Weimaraner, dachshund, and Labrador retriever. The Irish setter and wirehaired fox terrier have concomitant lissencephaly. Selective involvement of the cerebellar vermis (vermian hypoplasia) is observed in the Boston terrier and bull terrier.

Clinical Signs

- Nonprogressive cerebellar signs are obvious at the time of ambulation, but subtle deficits can be detected from birth.
- Truncal ataxia, disequilibrium, dysmetria, falling, intention tremor, and an absent menace response are seen to varying degrees.

Treatment

No treatment is available.

Prognosis

Strength, CP, and personality are maintained. If coordination is not incapacitating, affected dogs can make acceptable pets.

DEGENERATIVE BRAIN DISEASE

Inborn errors of metabolism can lead to neural cell degeneration after normal differentiation and maturation. Neuronal or glial cell degeneration is termed *abiotrophy*. A metabolic defect has not been identified in the vast majority of abiotrophies in animals. Neurodegenerative changes may occur within either the cell body or its processes. Although most abiotrophies affect the cerebellum, others may affect neurons in multiple brain regions. Neurodegenerative changes also occur with aging in some dogs and cats. Neuronal and glial changes are most severe in the cerebrum of older animals with this disorder.

Lysosomal storage diseases are autosomal recessive neurodegenerative disorders in which the cellular defect has been identified in most cases. Homozygous recessive individuals often exhibit a specific lysosomal hydrolase defect that leads to a cascade of structural and biochemical changes at the cellular level. The most obvious change is the accumulation of undegraded material within lysosomes, giving neurons a foamy, vacuolated, and swollen appearance. Other abnormalities include neuroaxonal dystrophy (axonal swellings), changes in synaptic connections, neurotransmitter and calcium imbalances, and occasionally cell death. Neuronal ceroid lipofuscinosis is unique in that massive neuronal cell loss and atrophy occurs in both the cerebrum and the cerebellum. Other lysosomal storage diseases do not share this feature.

▼ ***Key Point*** Animals affected with lysosomal storage disorders are normal at birth and weaning, but at a few months of age they develop a slowly progressive neurologic disease with multifocal cerebellar, brain stem, and spinal cord signs.

For reasons poorly understood, the cerebellum is especially vulnerable and will often show the most severe pathologic changes early in the disease course. Consequently, early clinical signs in the majority of lysosomal storage diseases are predominantly cerebellar in origin. Differential diagnoses for cerebellar signs in young cats and dogs include infectious diseases (FIP, cryptococcosis, toxoplasmosis, CDV, etc.), cerebellar hypoplasia, or cerebellar abiotrophy. With the exception of globoid cell leukodystrophy, lysosomal storage diseases are also characterized by visceral storage of undegraded material. Storage in liver, pancreas, spleen, kidney, bone marrow, adrenal glands, ocular structures, and lymph nodes is commonly found but rarely causes organ dysfunction. Globoid cell leukodystrophy results in storage within cells of the nervous system only and eventually produces central and peripheral demyelination.

Cerebellar Abiotrophies

Etiology

Cerebellar abiotrophies have been identified in many canine breeds and in the cat. Breeds affected include the beagle, Samoyed, Irish setter, Kerry blue terrier, Gordon setter, American Staffordshire terrier, rough-coated collie, Airedale, Finnish harrier, Bern running dog, Bernese mountain dog, Labrador and golden retrievers, cocker spaniel, Cairn terrier, Great Dane, Australian kelpie, Brittany spaniel, English springer spaniel, bull terrier, and German shepherd. Normal cerebellar formation is followed by premature degeneration and cell death. Cerebellar Purkinje and granule cell loss usually occurs. Pathogenic mechanisms are largely unknown. An autosomal recessive mode of inheritance is proven in some breeds.

Clinical Signs

- Age of onset is usually between 4 and 10 weeks, but some breeds show an earlier or later onset. Most dogs are normal at birth.
- Progression may be slow or rapid.
- Cerebellar signs of intention tremor and progressive ataxia and dysmetria are characteristic.

Diagnosis

- Other causes of progressive cerebellar disease in young dogs (infectious diseases, lysosomal storage disease, myelin disorder, medulloblastoma) should be ruled out.
- CT or MRI may reveal a smaller-than-normal cerebellum, but usually the cerebellum is normal in size.

Treatment

No treatment is available.

Prognosis

The prognosis is guarded to poor due to the progressive, debilitating nature of these disorders.

Multisystem Neuronal Abiotrophies

Etiology

Multisystem neuronal abiotrophies are characterized by overt cell loss or chromatolytic change in multiple brain compartments. Breeds affected include the Kerry blue terrier, rough-coated collie, miniature poodle, cocker spaniel, and Cairn terrier. The primary lesion in Kerry blue terriers, rough-coated collies, and miniature poodles is cerebellar abiotrophy, but multiple brain stem nuclei, spinal cord neurons, and cerebrocortical neurons also degenerate. Affected cocker spaniels have cell loss in multiple regions and neuroaxonal dystrophy in cerebellar and cerebral white matter. Multisystem chromatolytic degeneration in Cairn terriers is characterized by chromatolysis of neurons in spinal cord, brain stem, and cerebellum. An autosomal recessive mode of inheritance has been demonstrated in some breeds.

Clinical Signs

- Onset of signs is between 4 and 16 weeks of age, and clinical progression may be rapid (over weeks) or slow (over months).
- Kerry blue terriers and rough-coated collies exhibit primarily cerebellar signs.
- Miniature poodles have early cerebellovestibular signs from 3 to 4 weeks of age followed by upper motor neuron tetraplegia at 4 months of age.
- Cocker spaniels show both cerebellar and cerebral signs at 1 year of age.
- Signs in Cairn terriers include cerebellar ataxia, paresis, and cataplexy.

Diagnosis

- Differential diagnoses include lysosomal storage disease and inflammatory CNS disease.
- A tentative diagnosis is based on signalment, clinical signs, and progression.
- A definitive diagnosis can only be made postmortem.

Treatment

No treatments are available.

Prognosis

The prognosis is poor.

Multisystem Neuroaxonal Dystrophy

Etiology

Primary neuroaxonal dystrophy refers to an inherited error of metabolism resulting in swellings or spheroids along any region of the axon. The distal axon and axon

terminal are the most common cellular sites affected by this neurodegenerative disease. Any region of the CNS may be affected, including the cerebellum, cerebrum, and brain stem. Neuroaxonal dystrophy has been reported in the rottweiler, Jack Russell terrier, Chihuahua, collie-sheepdog mixed breed, bullmastiff, Labrador retriever, and domestic shorthaired cat. An autosomal recessive mode of inheritance is known or suspected in these breeds.

Clinical Signs

- Clinical signs are primarily cerebellar in origin in the majority of affected breeds.
- Cerebral signs are seen in the Labrador retriever.

Diagnosis

- Differential diagnoses include inflammatory, metabolic, toxic, and other congenital causes of cerebellar or cerebral disease.
- No specific diagnostic tests are available.

Treatment

No treatment is available.

Lysosomal Storage Disorders

See Table 126-5 for information about the more important lysosomal storage disorders.

Neurodegenerative Changes Associated with Aging and Cognitive Dysfunction

Etiology

- Canine cognitive dysfunction is a neurodegenerative disease of the forebrain characterized by a very gradual onset and progression of cognitive decline in dogs greater than 11 years of age.
- The cause of cognitive dysfunction is not fully understood, but certain morphologic and functional changes are recognized in association with this syndrome.
- Cortical atrophy due to neuronal loss (apoptotic cell death), amyloid plaques and perivascular amyloid, myelin degeneration with perivascular macrophage infiltration and gliosis, and intraneuronal lipofuscin accumulation are commonly observed. Changes in the frontal and temporal lobes are most severe. The density of amyloid plaques shows a correlation with the severity of cognitive decline.
- Functional changes hypothesized to occur include decreased levels of norepinephrine and dopamine in frontal cortex, increased monoamine oxidase activity with increased norepinephrine and dopamine breakdown (with free radical formation), alterations in post-synaptic receptor numbers and function, and decreased mitochondrial energy production.

Clinical Signs

▼ ***Key Point*** The clinical course of canine cognitive dysfunction is often 18 to 24 months or longer. Behavior problems are "newly emergent" and should not resemble previous behavior patterns in the pet.

Behavior changes include decreased spatial orientation (staring, wandering, getting lost, resisting confinement), decreased responsiveness and social interaction (no seeking of affection, loss of owner recognition, resistance to handling), loss of house training, and altered sleep-wake cycles (active at night and sleeping during the day).

Diagnosis

- A tentative diagnosis can be made based on a compatible history and clinical signs and by ruling out disorders that may mimic the signs of cognitive dysfunction.
- The neurologic examination is normal with the exception of abnormalities of mentation that include resisting restraint, agitation, increased startle, blank stare or shifting eye movements, and aimless pacing and wandering. Lateralizing deficits and seizures are not observed.
- Affected dogs should be screened for concurrent disorders such as vision and/or hearing loss and for metabolic and endocrine imbalances that may impact normal brain function.
- MRI or CT will rule out a brain tumor or vascular lesion as the cause of the dementia. Corticocerebral atrophy with secondary ventriculomegaly is a common finding.

Treatment

- Cognitive dysfunction secondary to neurodegeneration is not a traditional behavior disorder. Since manifestations of dementia are due to a neurodegenerative process, behavior modification strategies are usually not effective.
- Steps that modify the pet's environment, such as providing adequate space and footing, building ramps, and fencing outdoor areas, are useful. Frequent attention, close monitoring of nutrition, and "timed" feeding and exercising are also advised.
- Medical therapy that has been approved for use with this disorder is selegiline. Improved sleep-wake cycles, activity levels, and house training have been reported after administration of 0.5 to 1.0 mg/kg PO every 24 hours (given in the morning). Selegiline inhibits the breakdown of several monoamines, including dopamine, norepinephrine, and 2-phenylethylamine, and facilitates dopaminergic transmission and activity.

Table 126-5. LYSOSOMAL STORAGE DISEASES IN DOGS AND CATS

Disease	Enzyme Defect	Breeds	Age of Onset	Clinical Signs	Diagnosis	Treatment
GM1 gangliosidosis	Beta-galactosidase deficiency	Portuguese water dog, English springer spaniel, Siamese cat, DSH	2–4 months	Early cerebellar signs, UMN tetraparesis, dementia, seizures, cranial nerve deficits, visual deficits +/− hepatomegaly, skeletal deformities, corneal opacities	Enzyme assays on WBC, plasma, other tissues; vacuolated WBCs	BMT with limited effect
GM2 gangliosidosis	Beta-hexosaminidase deficiency	Japanese spaniel, mixed-breed dog, DSH, Korat cat	2–4 months (18 months in dogs)	Cerebellar signs, UMN tetraparesis, blindness, seizures, dementia +/− skeletal deformities, corneal opacities	WBC, plasma, tissue assays; WBCs with heterochromatic granules	BMT with no clinical effect
Niemann-Pick disease type A	Sphingomyelinase deficiency	Balinese cat, Siamese cat, miniature poodle	4–5 months	Cerebellar signs, LMN tetraparesis +/− hepatomegaly	WBC, plasma, tissue assays	Not attempted
Niemann-Pick disease type C	Cholesterol transport defect	DSH, boxer	2–4 months	Cerebellar signs, UMN tetraparesis, mentation changes +/− hepatomegaly	Cholesterol esterification assays on cultured fibroblasts	BMT with limited effect
Mucopolysaccharidosis I	Alpha-L-iduronidase deficiency	DSH, Plott hound	3–6 months	No neurologic signs, skeletal deformities, stunted growth, corneal changes	WBC, other tissue assays; urine screening test	BMT with moderate to marked effect
Mucopolysaccharidosis VI	Arylsulfatase B deficiency	DSH, Siamese cat, miniature pinscher	2–6 months	See MPS-I; paraparesis due to cord compression	WBC, other tissue assays; urine screening test	BMT with moderate to marked effect
Alpha-mannosidosis	Alpha-mannosidase deficiency	DSH, DLH, Persian	2–7 months	Cerebellar signs +/− cataracts, hepatomegaly, limb deformities	WBC, other tissue assays	BMT with marked clinical effect
Fucosidosis	Alpha-fucosidase deficiency	English springer spaniel	6–12 months	Behavior change, cerebellar signs, dementia, visual deficits, jaw chomping	WBC, plasma, CSF, or tissue assays	BMT with moderate effect
Neuronal ceroid lipofuscinosis	Defect unknown (mitochondrial subunit accumulates)	English setter, dalmation, border collie, Australian cattle dog, others	1–2 years	Behavior change, dementia, visual seizures +/− cerebellar signs	Brain biopsy or not attempted deficits,	BMT not effective in many breeds
Globoid cell leukodystrophy	Galactocerebrosidase deficiency	West Highland white terrier, Cairn terrier, miniature poodle, bluetick hound, beagle, others	2–4 months	Cerebellar signs, paraparesis to tetraparesis	WBC, tissue assays; peripheral nerve biopsy	BMT not attempted in dogs (moderate success in mice)

BMT, bone marrow transplantation (allogeneic); DLH, domestic longhaired cat; DSH, domestic shorthaired cat; MPS, mucopolysaccharidosis; LMN, lower motor neuron; UMN, upper motor neuron; WBC, white blood cell.

Prognosis

This condition can be managed but not cured. Response to medical therapy is variable. Neurodegenerative changes will continue, and response to therapy is often transient at best.

CRANIAL NERVE DISORDERS

Disorders of the peripheral portions of cranial nerves may occur secondary to neoplastic, inflammatory, idiopathic, congenital, and endocrine diseases. The most common cranial neuropathies affecting CN5, CN7, or CN8 are discussed below. Horner's syndrome is discussed in Chapter 141. Laryngeal paralysis is covered in Chapter 161. Megaesophagus is discussed in Chapter 65.

Idiopathic Disorders

Trigeminal Neuritis (Idiopathic Trigeminal Neuropathy, Dropped Jaw Syndrome)

Etiology

The etiology is unknown. A bilateral, nonsuppurative neuritis of CN5 and its ganglia is seen histologically. There is no breed predilection. Most dogs are middle aged.

Clinical Signs

- An acute to peracute onset of a dropped jaw and inability to close the mouth are seen. The signs are nonprogressive and muscle atrophy rarely occurs.
- Animals have difficulty prehending and chewing food. Food and water fall out the sides of the mouth. Swallowing abilities are usually maintained if food is placed in the back of the mouth.
- A unilateral or bilateral Horner's syndrome may be seen in association with trigeminal neuritis.
- Sensation to the face is usually normal, and there are no long tract signs or changes in mentation.
- Pain may be elicited upon palpation around the jaw.

Diagnosis

- Acute, severe mandibular paralysis in the absence of other neurologic deficits is usually pathognomonic for this disease.
- Lymphoma and other myelomonocytic leukemias with nerve root involvement may rarely produce similar signs.

Treatment

- Therapy is strictly supportive. Maintaining hydration and nutrition is critical.
- Corticosteroid therapy is of no benefit.

Prognosis

▼ ***Key Point*** Idiopathic trigeminal neuritis is a self-limiting disorder with recovery taking place within 2 to 4 weeks after the onset of signs. The prognosis is excellent with adequate nutritional support.

Idiopathic Facial Paralysis or Palsy

Etiology

An idiopathic paralysis of the facial nerve occurs in dogs. There may be unilateral or bilateral involvement. Histologically, there is axonal degeneration with secondary demyelination of the facial nerve. There appears to be a high incidence in cocker spaniels.

Clinical Signs

- Signs are acute in onset and nonprogressive.
- Complete paralysis of the facial nerve results in a unilateral facial droop (lips, ears, etc.) and an inability to blink the eye. The palpebral fissure may be wider than normal.
- Food, water, and saliva tend to fall out the side of the mouth that is paralyzed.
- In the acute stage, the nasal philtrum is deviated slightly toward the unaffected side due to unopposed nasal muscles.
- Denervation of the lacrimal gland may lead to decreased tear production.
- Facial contracture (lip retraction, deviation of the lip and nose toward the affected side) can be seen chronically.
- No other neurologic signs are usually present, but involvement of the opposite facial nerve is not uncommon.

Diagnosis

Differential diagnoses include otitis media or interna (see Chapter 61), hypothyroid neuropathy (see this section and Chapter 31), a neuropathy associated with pituitary lesions, lead poisoning, neoplasia, and trauma.

Treatment

There is no treatment. Artificial tears may be needed to prevent corneal lesions (see Chapter 139).

Prognosis

The prognosis for recovery of function is guarded to fair. Many dogs may recover partial function only.

Canine Idiopathic Vestibular Disease (Old Dog Vestibular Syndrome)

Etiology

This is a disease of older dogs (average age of 12–13 years) of any breed. The pathogenesis is unknown. This condition can also occur in the cat at any age, but it usually occurs in young adult cats.

Clinical Signs

- Signs of vestibular imbalance are peracute and include head tilt, ataxia, circling, falling, rolling, and nystagmus (usually rotary) with a fast phase away from the side of the head tilt.
- Affected dogs are disoriented and frequently agitated.
- Postural reactions and strength are preserved, and there are no other cranial nerve deficits.
- Anorexia with or without vomiting is common.
- Signs are most severe at the onset and gradually improve over days to weeks.

Diagnosis

- Otitis media or interna, hypothyroidism, trauma, vascular disease, and neoplasia are differential diagnoses.
- Otic examination, bulla radiographs or CT, thyroid testing, blood pressure measurement, and other screening tests for vascular disease may be performed to exclude the above differential diagnoses.

Treatment

- There is no specific treatment.
- Steroid therapy is not beneficial.

- Nutritional and fluid support may be necessary if persistent nausea and anorexia are present.
- A padded, confined area may be needed to prevent self-injury.

Prognosis

▼ ***Key Point*** The prognosis is good to excellent for recovery in dogs with idiopathic vestibular disease. Improvement is usually seen over the first 2 to 3 days after onset, and resolution of the majority of signs is observed 10 to 14 days after onset. Recurrences can occur but are uncommon.

Endocrine Diseases

Hypothyroidism

Etiology

Thyroid hormone deficiency can cause an unusual combination of peripheral and central vestibular signs. Other cranial nerves may be affected, especially CN7 and CN10 and the sensory branches of CN5.

Clinical Signs

- Middle-aged to older dogs of any breed may be affected, and there may be no other signs of hypothyroidism.
- The onset may be rapid or chronic and the clinical course may be static or progressive.
- Vestibular signs are usually unilateral (head tilt, etc.) but signs can be bilateral. The character of the nystagmus is vertical, horizontal, rotary, or direction changing. Vestibular ataxia is usually present with listing and falling toward one side.

Diagnosis

- Differential diagnoses include otitis interna, idiopathic vestibular disease, vascular disease, infectious disease, or neoplasia.
- Otoscopic exam, CSF analysis, and imaging studies (CT or MRI) are typically normal.
- A complete thyroid panel is necessary to distinguish non-thyroidal illness from true hypothyroidism (see Chapter 31).

Treatment

Treatment is thyroid supplementation (see Chapter 31). Resolution of signs can occur but is gradual over 1 to 4 months.

Prognosis

The prognosis is good for eventual return of vestibular function.

Neoplasia

Trigeminal Neurofibroma (Schwannoma, Nerve Sheath Tumor)

Etiology

The most common tumor that may involve CN5 is the neurofibroma or schwannoma. Lymphoma and meningioma may involve the trigeminal nerve less commonly. Trigeminal neurofibromas are invariably unilateral and usually originate peripherally with eventual encroachment on brain stem structures in the region of the cerebellopontomedullary angle. Nuclei of CN7 and CN8 may secondarily be affected. This neoplastic disease occurs in middle-aged to old dogs.

Clinical Signs

- The onset and progression of signs are slow (over months).
- Marked unilateral temporalis and masseter muscle atrophy is seen initially.
- Jaw weakness is not clinically apparent.
- Muscle atrophy is followed by facial sensory loss.
- Brain stem involvement is indicated by the onset of ipsilateral vestibular signs, facial muscle weakness, and occasionally long tract signs with ipsilateral hemiparesis and conscious proprioceptive deficits.

Diagnosis

- The main differential diagnosis is trauma to CN5. The progressive course of this disorder helps rule out trauma.
- Electromyography and temporal muscle biopsies reveal signs of denervation.
- Contrast-enhanced MRI scanning is most sensitive in detecting the tumor location and extent.

Treatment

- Surgical excision is the treatment of choice, but the surgery is technically demanding and rarely achieves complete excision.
- Radiation therapy appears to slow progression of the tumor, but further clinical studies are needed to confirm this observation.
- MRI aids surgical and radiation planning and may improve outcome.

Prognosis

The prognosis is guarded to poor, especially if brain stem involvement has occurred.

Primary and Secondary Neoplasia Involving Cranial Nerve 8

Etiology

Primary neurofibromas of CN8 are rare. Meningiomas in the caudal fossa may affect the extradural, intra-

cranial portion of CN8. Secondary tumors affecting CN8 usually originate in the temporal bone or bullae and invade the nerve or its peripheral receptors by local extension. Squamous cell carcinoma, ceruminous gland adenocarcinoma, osteosarcoma, and chondrosarcoma are tumors in this category and do occur in the dog and cat. Middle ear polyps in cats may also secondarily involve vestibular and cochlear structures in the inner ear (see Chapters 61 and 62).

Clinical Signs

- Slowly or rapidly progressive vestibular signs are observed.
- Horner's syndrome and other cranial neuropathies (especially of the facial nerve) may be seen concurrently.

Diagnosis

- Rule out otitis media and interna (see Chapter 61), idiopathic conditions, and endocrine-related neuropathy.
- Otic examination and biopsy may reveal a neoplastic process.
- Bullae radiographs detect soft tissue opacities or bony lysis.
- CT is useful in identifying both bony and neural parenchyma involvement.
- MRI is the imaging modality of choice for determining the extent of neural parenchymal involvement.

Treatment

Total surgical resection is usually not possible, except in the case of a benign inflammatory polyp.

Prognosis

The prognosis is usually poor.

Congenital Degenerative Disorders

Congenital Sensorineural Deafness

Etiology

Postnatal cochlear hair cell and spiral ganglion degeneration occurs in many breeds, including dalmatians, English setters, bull terriers, Old English sheepdogs, English bulldogs, Australian heelers, border collies, collies, Australian shepherds, Australian cattle dogs, Catahoulas, Norwegian dunkerhounds, pointers, rottweilers, and white cats with blue irises. Cochlear structures develop normally, but degeneration of the stria vascularis is soon followed by loss of cochlear hair cells. The pathogenesis is unknown. The method of genetic transmission is also poorly understood in most breeds.

Clinical Signs

- Owners may not recognize a deaf puppy for several months.
- Poor response to verbal commands and loud noises often indicates bilateral deafness.
- Unilaterally deaf pups may not orient to sounds properly or may appear completely normal.

Diagnosis

- Clinical signs may or may not be definitive.
- The BAER will accurately detect unilaterally and bilaterally deaf animals.

Treatment

There is no treatment for this degenerative disorder.

Prognosis

The prognosis is poor for recovery of hearing. Special behavioral training is often necessary for dogs with bilateral deafness.

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Chapter

127 Seizures

Michael Podell

Any animal may be prone to having a seizure, often with little indication of when, why, or how often the seizures will occur. Moreover, the veterinarian never observes most clinical signs of the disease. This unpredictability and lack of direct connection with the disease is challenging to veterinarians trying to determine the appropriate diagnostic and therapeutic plan. The purpose of this chapter is to provide a perspective on how to identify and treat dogs and cats with a seizure disorder.

TERMINOLOGY

Classification of seizures and epilepsy into a universally accepted, coherent, and relevant scheme for clinicians has been an ongoing dynamic process in human epilepsy over the past 2 decades. The standardized classification scheme for seizures and epilepsy, established by the International League against Epilepsy (ILAE) in the 1980s, provided the first basis for a taxonomic foundation to an analytic approach in the diagnosis and treatment of epilepsy. This classification scheme, however, is restricted by the following limitations: (1) the reliance on the clinician's ability to classify seizure types based on the presence of "impaired consciousness"; (2) the reliance on electroencephalographic features to classify seizure type; and (3) the difficulty in distinguishing between an *idiopathic* disorder of confirmed undetermined etiology and a *cryptogenic* cause of highly suspect morphologic disease of the brain. Considering these limitations and that, as veterinarians, we may not always have the opportunity to perform a complete battery of neurodiagnostic tests (including brain imaging), it is no wonder that confusion arises when we try to describe, classify, and categorize seizures and epilepsy in our patient population.

My goal is to piece together a rationale categorization for use in small animal epileptic patients adapted from the recent recommendations of the ILAE Task Force on Classification and Terminology. The purpose is to establish a common mode of communication to allow diagnostic and therapeutic data to be tabulated for clinical outcome measures. The proposed new diagnostic scheme consists of five levels, or axes, as proposed by Engel (Table 127-1; for review see Engel, 2001 and Podell, 2004).

Axis 1: Ictal Phenomenology

- A *seizure* can be defined as a nonspecific, paroxysmal, abnormal event of the body.
- An *epileptic seizure* is the clinical manifestation of excessive and/or hypersynchronous abnormal neuronal activity in the cerebral cortex. Thus, an epileptic seizure has a specific neural origin.
- *Epilepsy* is present if the animal has a chronic brain disorder characterized by recurrent epileptic seizures. Note that neither the term seizure nor the term epilepsy connotes the underlying etiology of the disorder.
- *Non-epileptic episodes* are paroxysmal events with severe consequences to the body but without any epileptic electroencephalographic activity (e.g., syncope).
- *Status epilepticus* can be defined as a state of continuous seizure activity lasting 30 minutes or longer or repeated seizures with failure to return to normalcy within 30 minutes. *Epilepsia partialis continua* is a continuous focal seizure involving the motor cortex. Although not well documented by electroencephalography in animals, the typical manifestations include facial muscle movements with "chewing gum" activity, repetitive eye or lip twitching, or myoclonic jerking of limb muscles.

Clinical Stages of Epileptic Seizures

- The *prodrome* is the time period prior to the onset of seizure activity. Owners report that they can "predict" the onset of their pet's seizures by behaviors exhibited during this time, such as increased anxiety-related behaviors (attention seeking, whining, etc.), reluctance to do normal activity patterns, or increased hiding (in cats).
- The *aura* is the initial manifestation of a seizure. During this time period, which can last from minutes to hours, animals can exhibit stereotypic sensory or motor behavior (e.g., pacing and licking), autonomic patterns (e.g., salivating, urinating, and vomiting), or even unusual psychic events (e.g.,

Table 127-1. PROPOSED DIAGNOSTIC SCHEME FOR DOGS AND CATS WITH EPILEPTIC SEIZURES

Axis 1: Ictal Phenomenology
Seizure
  Epileptic seizure
  Non-epileptic episodes
Epilepsy
Status epilepticus

Axis 2: Seizure Type
Self-limiting
  Focal
    Sensory
    Motor (elementary; automatism)
  Generalized
    Tonic-clonic
    Clonic
    Myoclonic
    Atonic
Clustered or continuous (status epilepticus)
  Focal
    Motor: epilepsia pars continua
    Sensory: aura continua
  Generalized
Reflexive: precipitating stimuli present

Axis 3: Syndrome
Familial
Idiopathic
  Focal
  Generalized
Symptomatic
Probably symptomatic
Reflex
Epileptic encephalopathies (progressive neurologic dysfunction)
Myoclonus

Axis 4: Etiology
Idiopathic
Symptomatic
Probably symptomatic

Axis 5: Impairment from Epilepsy
Temporary
  Motor
  Sensory
  Other
Permanent
  Motor
  Sensory
  Other

Adapted from Engel JJ: A proposed diagnostic scheme for people with epileptic seizures and epilepsy: Report of the ILAE Task Force on classification and terminology. Epilepsia 42:796, 2001.

excessive barking and increased or decreased attention seeking).

- The *ictal* period is the actual seizure event manifested by involuntary muscle tone or movement and/or abnormal sensations or behavior lasting usually from seconds to minutes.
- The *postictal* period is the time immediately following the ictal phase and can last from minutes to days. During this time, an animal can exhibit unusual behavior, disorientation, inappropriate bowel or bladder activity, excessive or depressed thirst and appetite, and/or actual neurologic deficits of weakness, blindness, and sensory and motor disturbances. The latter problems are known as Todd's paralysis and are often an indicator of a contralateral cortical epileptic focus. Often owners only observe the postictal period as evidence that their pet has had a seizure. Thus, careful questioning is needed by the clinician to decide if an animal did experience a seizure.

Axis 2: Epileptic Seizure Types

Self-limiting: Isolated (Single Event Only) Seizures

- *Focal seizures* are the manifestation of a discrete, epileptogenic event in the cerebral cortex. The focal nature of this seizure type is associated with a higher incidence of focal intracranial pathology.
- *Focal elementary motor seizures* are either commonly seen as facial muscle twitching or manifested by more abnormal behavioral disorders. Progressive involvement of the facial, neck/shoulder, and/or limb muscles is known as a *Jacksonian march seizure event.*
- *Automatism, or automotor seizures,* were previously termed complex partial or psychomotor seizures (Engel, 2001). Animals may show "fly-biting" behavior patterns, become aggressive without provocation, howl incessantly, become restless, or exhibit a variety of motor disturbances. Cats may show a variety of abnormal behaviors and/or motor signs, including drooling, hippus, excessive vocalizations, or random, rapid running behaviors in the house.

▼ ***Key Point*** Whenever a focal seizure is suspected, the clinician should be suspicious of a focal cerebral disturbance and plan the diagnostic workup accordingly.

- *Generalized convulsive seizures* are the most common seizure type seen in veterinary medicine. These seizures are characterized by impaired consciousness coupled with bilateral motor signs of a tonic-clonic, tonic, or myoclonic nature.
- *Generalized non-convulsive seizures* are less common and are either atonic (complete loss of voluntary movement with collapse) or absent (ability to stand or pose but without the ability to perceive or respond). These terms replace the previously used terms convulsive *(grand mal)* and non-convulsive *(petit mal)* seizures.
- Generalized seizures originate from both cerebral hemispheres from the start or progress secondarily from focal seizures. Unlike focal seizures, generalized seizures are not necessarily associated with focal cerebrocortical disease.

Clustered or Continuous Focal Seizures

Clustered seizures are two or more seizures within a 24-hour period.

- Motor: Epilepsia pars continua
- Sensory: Aura continuous
- Generalized: Status epilepticus

Axis 3: Syndrome

- Epilepsy syndromes are not well defined in veterinary medicine, although familial epilepsies are now being identified with segregation analysis.
- A number of purebred dogs have been identified with either proven or highly suspect familial epilepsy: Belgian Tervuren, keeshonds, retrievers, Shetland sheepdogs, and a variety of other breeds.
- The vast majority of epileptic syndromes in dogs will be idiopathic in nature.

Axis 4: Etiology

Epilepsy represents a heterogeneous disease consisting of diverse etiologies, electrophysiologic and behavioral seizure patterns, and responses to therapy. Genetically determined "seizure susceptibility factors" play a crucial role in the brain's response to triggering or precipitating factors. Seizures in these individuals may be activated from unrecognized changes in neuronal activity, by intrinsic neurochemical transmission, or by environmental stimuli that do not cause seizures in the normal brain.

▼ ***Key Point*** A basic mechanism of epilepsy is an imbalance in excitatory and inhibitory neurotransmission.

- A seizure develops when the balance shifts toward excessive excitation. Recruitment of a critical number of areas in the brain with synchronized depolarization will lead to a seizure. Reasons for the progressive nature of epilepsy include the following:
  - Conditions leading to excessive excitation or loss of inhibition result in depolarization of neurons without normal regulatory feedback mechanisms.
  - The number of cells with an intrinsic pattern of high spontaneous firing activity (pacemaker cells) increases in the epileptic focus.
  - A mirror focus of actively firing epileptogenic neurons may develop in a similar region on the opposite hemisphere. This enables the number of epileptic foci to multiply rapidly. As an animal continues to have seizures, an increased number of areas of the brain are randomly and spontaneously able to initiate a seizure.
- Refer to Chapter 126 for information regarding specific diseases of the brain.
- The differential diagnosis of epileptic seizures due to underlying brain disease can be divided into three main etiologic categories: Idiopathic, symptomatic, and probably symptomatic (previously termed cryptogenic) epileptic seizures.
  - *Idiopathic epilepsy* implies that no underlying structural brain lesion is present, and the epilepsy is presumed to be genetic in origin.
  - *Symptomatic, or secondary, epilepsy* is the result of an identifiable structural lesion of the brain.
  - *Probably symptomatic, or cryptogenic, epilepsy* is believed to be the result of a structural lesion of the brain that is not identified. While this sounds like a nebulous disease category, it has particular implications when understanding why certain animals may be refractory to therapy. Examples of cases that may fit into this category would be prior head trauma in patients with normal imaging, postencephalitic seizures developing at a later date, undetected hypoxic or vascular events of the brain after anesthesia, and birth trauma.
- Reactive epileptic seizures are due to metabolic disease and therefore are not classified as an etiology for epilepsy, as the brain returns to normal once the underlying inciting change in metabolism is corrected. The differential diagnoses for these categories are presented below.

Axis 5: Impairment from Epilepsy

Inclusion of signs that are associated with epilepsy allows veterinarians to evaluate for persistence of functional and/or structural neurologic changes with associated seizures. The majority of signs in cats and dogs are transient, including disorientation, visual impairment, salivation, incontinence, and altered behaviors. Dogs have been found to demonstrate transient structural changes with cerebral edema of the temporal lobe on magnetic resonance imaging (MRI) scans of the brain, along with altered cerebral metabolism with proton magnetic resonance spectroscopy after seizures. Symptomatic temporal lobe epilepsy with associated hippocampal neuronal loss, however, appears not to be present in idiopathic epileptic dogs. More permanent neuropathologic deficits can occur, especially in dogs or cats with very prolonged seizure activity.

CLINICAL SIGNS

A thorough and accurate history is essential for diagnosis of seizure patients.

▼ ***Key Point*** Suspicion of an epileptic seizure should be made with any event that has a sudden onset with a finite period of abnormal behavior and/or motor activity followed by some change in behavior or orientation.

- Obtain historical information concerning pedigree information, vaccination status, travel, trauma and toxin exposure potential, previous medical and surgical problems, and drug history.
- Organize information about the actual seizure episode(s) by stage into the prodrome, aura, ictal, postictal, and interictal periods.
- Record dates, times, duration, and description of each abnormality to assess progression and allow a comparison if medication is started.

▼ ***Key Point*** Evaluate the status of the pet's cerebrocortical function between seizures (after the postictal period) by asking questions concerning the animal's behavior, vision, gait, and sleep-wake patterns.

- Take a thorough neurologic history. For example, question if the dog is more withdrawn or attention seeking, shows any unusual episodes of aggression or

irritability, or fails to follow simple commands. These would suggest a structural cerebral problem. Likewise, determine the presence of subtle gait abnormalities (stumbling up and/or down the stairs), visual disturbances (occasionally bumping into objects on one side), and restless sleep patterns that may indicate cerebral problems.
- Classify seizure type as focal or generalized (see "Axis 2: Epileptic Seizure Types" and Table 127-1).
- Subcategorize focal seizures into elementary or automatisms.
- Subcategorize generalized seizures into convulsive and non-convulsive seizures.
- Characterize postictal abnormalities.
- Characterize as either isolated (one per 24 hours) or clustered (two or more in 24 hours). As a consequence of severe or prolonged seizure events, animals can develop detectable neurologic deficits during the immediate and extended postictal period. More severe immediate postictal abnormalities include vision loss, circling, paresis, profound disorientation, aggressive personality changes, and other dementing behaviors. Some of these changes may last several days to weeks, a condition known as Todd's paralysis when sensorimotor localizing deficits are found. Fortunately, practically all of these abnormalities are reversible.
- Characterize seizure-related interictal abnormalities.
- With chronic seizure activity, changes in cellular physiology of the brain can lead to actual changes in neurologic function, especially persistent behavior disturbances. Dogs with recurrent epileptic seizures may also exhibit changes in personality. Lack of obedience, withdrawal activity, changes in socialization with other animals or people in the household, and unprovoked aggressive behavior can all occur as interictal manifestations of a chronic epileptic condition in the dog. Attributing these changes to the disease or the treatment can be difficult to discern.

DIAGNOSIS

Differential Diagnosis

Dogs

▼ ***Key Point*** Carefully evaluate for an underlying identifiable etiology for seizures when dogs present from <1 or >5 years of age, have an initial interictal interval of <4 weeks, or have a focal seizure as the first observed seizure.

When approaching a differential diagnoses list (Table 127-2), consider the signalment, history, physical and neurologic examination changes, and laboratory abnormalities.

- For dogs <1 year of age, seizures are most commonly secondary, in particular, caused by developmental, metabolic, and inflammatory diseases (see Table 127-2). Specific diseases to include are hydrocephalus, portosystemic shunts, and canine distemper encephalitis, respectively. Specific breeds prone to congenital hydrocephalus are Maltese dogs, Chihuahuas, Yorkshire terriers, and the brachycephalic breeds. Any breed of dog, however, may suffer from this disease.
- For dogs between 1 and 5 years of age, the most common cause of seizures is idiopathic epilepsy. However, a proportion of dogs in this age category may suffer from a congenital brain anomaly that may be progressive in nature.
- For dogs >5 years of age that start to experience seizures, consider specific structural (symptomatic) and metabolic diseases (e.g., reactive). In particular, dogs are more prone to primary brain tumors and cerebrovascular disease as they age.

Cats

▼ ***Key Point*** Idiopathic epilepsy is rare in the cat.

The diverse genetic background of cats has fortunately made idiopathic epilepsy an uncommon diagnosis. Practically all cats have an underlying etiology for their seizure disorder. The differential diagnoses of seizure etiology for cats are listed in Table 127-2.

Diagnostic Approach

Refer to Chapter 125 for information on diagnostic evaluation of the patient with neurologic disease, and Chapter 126 for diagnostic parameters of specific diseases of the brain.

▼ ***Key Point*** The decision to pursue diagnostic testing should not be based on the number or severity of prior seizures. Rather, the decision should be based on the signalment, history, and initial neurologic examination.

Dogs

The goals of a diagnostic evaluation in a patient with seizures are to determine the underlying etiology, evaluate the prognosis for recurrence, and establish if antiepileptic medications are necessary for treatment. Most dogs have already suffered from more than one seizure by the time they are presented to a veterinarian. Furthermore, many dogs appear normal when examined during interictal periods. In a dog with a history of seizures, try to determine if the seizure will recur and whether a more serious underlying disease exists.

Table 127-2. DIFFERENTIAL DIAGNOSES OF SEIZURES IN THE DOG AND CAT

Idiopathic
Channelopathies
Other genetic diseases

Symptomatic (or Secondary)

Developmental anomaly
Hydrocephalus
Cortical dysplasia
Lissencephaly

Inflammatory Diseases (Encephalitis)
Infectious
- Viral
- Fungal
- Bacterial
- Parasitic

Immune-mediated
- Granulomatous meningoencephalitis
- Eosinophilic meningoencephalitis
- Breed-specific meningoencephalitis
- Other corticosteroid-responsive inflammatory diseases

Vascular
Ischemic
- Thromboembolic
- Idiopathic feline ischemic encephalopathy

Hemorrhagic
- Hypertension-related
- Coagulopathy

Neoplasm
Extra-axial: Meningioma, bone tumors
Intra-axial: Glial tumors, metastasis
Intraventricular: Ependymoma, choroids plexus tumors

Traumatic
Toxicity

Probably Symptomatic (or Cryptogenic)
Prior head trauma in patients with normal imaging
Postencephalitic seizures developing months to years later
Undetected hypoxic or vascular events of the brain after anesthesia
In utero or birth trauma

Reactive Epileptic Seizures
Organ failure
- Hepatic
- Renal

Electrolyte imbalance
- Hyponatremia or hypernatremia
- Hypocalcemia

Energy deprivation
- Hypoglycemia
- Thiamine deficiency

- A diagnosis of idiopathic epilepsy is more likely when the following are true:
  - The dog is between 1 and 5 years of age at the first seizure.
  - The dog is a large breed (>15 kg).
  - The interval between the first and the second seizure events is long (>4 weeks).
- A diagnosis of secondary epilepsy is more likely when the following are true:
  - A dog is <1 or >7 years old at the first seizure.
  - The first seizure is a focal seizure.
  - The interval between the first and the second seizure events (an event being all seizures within a 24-hour period) is brief (<4 weeks).
  - The neurologic examination is abnormal.
- A diagnosis of reactive epileptic seizures (metabolic etiology) is more likely when the following are true:
  - The interval between the first and the second seizure events is brief (<4 weeks).
  - The animal is showing signs of systemic illness.

Diagnostic Testing

Dogs

- Evaluate a minimum database consisting of noninvasive blood pressure, complete blood count (CBC), serum chemistry profile, urinalysis, and thoracic radiographs to rule out possible metabolic causes. In younger dogs, a serum bile acid study is recommended to rule out a portosystemic shunt. Unfortunately, these tests have a very low yield of positive findings in most seizure patients.
- If symptomatic epileptic seizures are suspected, consider MRI of the brain. This test offers the best opportunity to diagnose either an intracranial anomaly or a primary neoplasia, which are the prevalent causes of seizures in dogs <1 or >7 years of age, respectively. If negative scan results are found, then cerebrospinal fluid (CSF) should be collected for analysis.
- Collect CSF first if a multifocal disease or meningeal inflammatory process is suspected after the neurologic examination.
- Perform additional diagnostic testing in any dog with persistent interictal neurologic abnormalities. Select tests according to the history and clinical suspicions—for example, serum bile acids to evaluate liver function, serial fasting blood glucose paired with insulin levels to diagnose hyperinsulinemia, plasma lead concentration, and specific serum antibody titers for infectious diseases.

Cats

▼ ***Key Point*** Always consider that an underlying cause for seizures is present in cats, until proved otherwise.

Consider the following diagnostic tests in cats:

- Evaluate a minimum database consisting of noninvasive blood pressure, complete blood count, serum chemistry profile, urinalysis, baseline thyroid level, retrovirus testing, *Toxoplasma* antibody titers, and thoracic radiographs to rule out possible metabolic or infectious causes. Serum feline infectious peritonitis (FIP) antibody titers are poorly correlated with the central nervous system form of infection.

- Collect CSF first if a multifocal disease or meningeal inflammatory process is suspected.
- Perform MRI brain scanning in all cats >7 years of age and/or in those cats with an abnormal neurologic exam. The combination of MRI scanning and CSF analysis is often the most direct approach to a definitive diagnosis in any age cat with normal laboratory testing.
- Also consider specific serologic tests for infectious diseases (e.g., fungal) and serum bile acids to evaluate liver function.

TREATMENT

This section describes seizure control therapy. Refer to Chapter 126 for treatment of specific diseases of the brain.

Goals of Therapy

Prior to starting antiepileptic drug (AED) treatment, owners and veterinarians should have a realistic expectation of what to expect over the course of therapy.

- Foremost, seizure control does not equal elimination.
- Realistic goals are a decrease in the number and severity of seizures, fewer post-ictal complications, and an increase in the interictal period.
- Inform clients that this may be a lifetime, daily treatment regimen; there will be frequent reevaluations; there is a potential for emergency situations to arise; and there are inherent risks from the drugs.
- Single-drug therapy for treating epilepsy is preferred because it reduces possible drug–drug interactions and adverse effects.

▼ ***Key Point*** The ultimate goal of antiepileptic therapy is to maintain a seizure-free status with acceptable or no adverse effects.

Limitations of Antiepileptic Drugs

Unfortunately, several limitations exist in the selection of AEDs for use in veterinary medicine:

- *Toxicity*—Drugs with hepatic metabolism have the potential for hepatotoxic effects.
- *Tolerance*—This can be metabolic in origin in that progressively more drug is needed over time to maintain the same therapeutic serum concentration, or it can be functional in that cellular adaptations occur that prevent full efficacy of the drug.
- *Inappropriate pharmacokinetics*—Certain AEDs are metabolized too rapidly to allow a steady-state concentration to be achieved with normal-interval dosing (2 to 3 times per day).
- *Expense*—Lifetime drug administration and monitoring can be prohibitively expensive for some owners.

Deciding When to Start Treatment

▼ ***Key Point*** Instruct the owner to document seizures and other problems in a written log. This record provides the basis for initiating and adjusting AED therapy and for determining the benefits of therapy.

Base the decision to initiate AED therapy on the underlying etiology, seizure type and frequency, and diagnostic evaluation. Initiate phenobarbital therapy in the following situations:

- An identifiable intracranial disease process is present.
- Status epilepticus has occurred.
- Two or more isolated seizures have occurred within a 6-month period.
- Two or more cluster seizure episodes have occurred within a 12-month period.
- The first seizure was within 1 week of trauma.
- Severe or prolonged post-ictal effects are present (e.g., prolonged blindness and aggressive behavior).

Phenobarbital Administration

Phenobarbital is the initial AED of choice because it is a relatively inexpensive, well-tolerated drug that effectively prevents seizures in animals when administered 2 to 3 times per day.

Phenobarbital in Dogs

▼ ***Key Point*** In the dog, give phenobarbital initially at least every 12 hours at a dose of 2.5 mg/kg PO with subsequent increases in dose most likely within 30 days to maintain a trough therapeutic serum concentration.

- In the dog, phenobarbital has a high bioavailability (between 86% and 96%). The drug is rapidly absorbed within 2 hours with a maximal plasma concentration obtained within 4 to 8 hours after oral administration. Almost one-half of the drug is protein bound. The majority of phenobarbital is metabolized by the liver, with approximately one-third excreted unchanged in the urine. Phenobarbital is an autoinducer of hepatic microsomal enzymes (P450 system), which can progressively reduce the elimination half-life with chronic dosing. Elimination half-lives have been reported to range from 42 to 89 hours, with a significantly shorter half-life in beagles (32 hours). Thus, initial steady-state serum phenobarbital concentrations (Css) are achieved within a maximum of 18 days in dogs with the longest elimination half-life (five elimination half-lives). At 5.5 mg/kg/day, Css and total body clearance are stable by 30 days.

Phenobarbital in Cats

▼ ***Key Point*** In the cat, give phenobarbital initially every night at a dose of 2.5 mg/kg with subsequent increases in the dose or frequency most likely within 30 days to maintain a trough therapeutic serum concentration.

- As in the dog, phenobarbital has a high bioavailability with rapid gastrointestinal absorption in the cat. Unlike the dog, the cat does not have significant autoinduction of the p-450 system with phenobarbital treatment. Thus, the elimination half-life of 40 to 60 hours does not appear to change significantly over time. This long half-life makes it possible to start once-a-day therapy. However, a wider fluctuation between the peak and the trough daily serum concentrations with once-a-day dosages may not provide adequate seizure control, necessitating dosages to be given in twice-daily intervals in some cats.

Intravenous Phenobarbital Loading

▼ ***Key Point*** Phenobarbital has the dual advantage of achieving high serum concentrations and reducing the cerebral metabolic rate following intravenous (IV) dosing.

- The advantage of IV administration is the ability to achieve a therapeutic concentration in the brain very rapidly (see "Hospital Emergency Treatment for Seizures"). IV phenobarbital is rapidly distributed within 10 minutes in the dog and the cat; therefore, it provides a rapid, high drug concentration to stop seizures while serving as a cerebral protectant.
- To achieve a serum concentration of 20 µg/ml in the dog:

$$\text{Total IV loading dose (mg)} = (\text{Body weight [kg]}) \times (0.8\ \text{L/kg}) \times (20\ \mu\text{g/ml})$$

- To achieve a serum concentration of 15 µg/ml in the cat:

$$\text{Total IV loading dose (mg)} = (\text{Body weight [kg]}) \times (0.9\ \text{L/kg}) \times (15\ \mu\text{g/ml})$$

- Give the total dose at a rate of <100 mg/min.

Serum Monitoring of Phenobarbital

▼ ***Key Point*** Monitor trough serum concentrations of phenobarbital to determine if a therapeutic level is maintained when the lowest serum concentration is present (i.e., immediately before the next dose). Animals will be most susceptible to seizure at this time.

Overall, phenobarbital is well tolerated at therapeutic serum concentrations in the dog and cat. My recommended trough therapeutic concentration range of phenobarbital is between 20 and 40 µg/ml in the dog and between 10 and 20 µg/ml in the cat.

- The goal of any AED therapy is to achieve serum concentrations within the established therapeutic range for that drug. The major advantage of monitoring serial serum trough phenobarbital concentrations is to individualize treatment by documenting that an adequate amount of drug is being given while minimizing the potential for toxic effects.
- The lower limit of the therapeutic range is the minimal concentration at which 50% of animals will have any therapeutic benefit. Conversely, the upper limit is the maximal concentration at which 50% of animals will not have toxic adverse effects. Monitor the serum concentrations only after steady-state levels are reached. Furthermore, wide variations in serum concentration can occur in dogs and cats on similar oral doses of phenobarbital.

▼ ***Key Point*** Optimal seizure control with minimal toxicity can be obtained by maintaining the trough serum concentration of phenobarbital between 20 and 30 µg/ml in dogs and between 10 and 20 µg/ml in cats.

- Measure trough serum concentrations of phenobarbital according to the following guidelines:
  - At 14, 45, 90, 180, and 360 days after the initiation of treatment
  - At 6-month intervals thereafter
  - Any time the pet has more than two seizure events between these times
  - Any time cluster seizures or status epilepticus occur
- Adjustments of the trough concentration can be calculated with the following formula:

$$\text{mg of phenobarbital per day} = \frac{\text{Desired concentration}}{\text{Actual concentration}} \times \text{Total mg of phenobarbital PO per day}$$

  - This new value can then be divided either twice daily or 3 times daily. The only advantage of administration 3 times a day is less fluctuation between the peak and the trough serum concentrations, which may be important in animals requiring tighter therapeutic windows. Note that no adjustment is made according to weight and no upper-limit dosage is present. Each animal is treated as an individual with allowances for individual variations in metabolism.
- If concern arises about toxicity, obtain peak levels by measuring the concentration 4 to 6 hours after pill ingestion with once-daily or twice-daily administra-

tion and 4 hours after pill ingestion with 3-times-a-day dosages.
- Evaluate complete blood counts and serum chemistry profiles at 3 months and at 6-month intervals thereafter for evidence of toxicity.

Adverse Effects of Phenobarbital

▼ ***Key Point*** Do not lower the initial phenobarbital dose if signs of sedation or behavior changes are seen after starting treatment. These signs are transient adverse effects that typically disappear in 10 to 14 days.

Adverse effects of any AED can be broadly categorized into predictable and unpredictable (idiosyncratic) complications. Further subclassification can be based on transient versus chronic or progressive problems. Despite the long historical use of phenobarbital in veterinary medicine, few reports exist documenting the adverse effects of the drug in dogs and cats. Lack of reportable information may be due to overall safety of the drug, difficulty in accurately documenting clinical adverse reactions, delay in detection of problems after onset of therapy, or a combination of these.

Idiosyncratic Drug Reactions

Idiosyncratic drug reactions to phenobarbital are usually associated with unusual behavioral changes after starting the drug. Hyperexcitability and restlessness are infrequent problems that do not appear to be dose related. Acute toxic hepatopathy is infrequently associated with phenobarbital administration in the dog and cat.

Transient and Mild Effects

More predictable, dose-related, transient adverse effects of a non–life-threatening nature can be categorized as follows:

- *Behavior changes*—Owners may complain that their pet is acting more sedate and lethargic after starting phenobarbital therapy. This change often dissipates after 1 to 2 weeks of treatment. Other potential transient complaints are polydipsia, polyuria, and polyphagia. On physical and neurologic examination, animals may demonstrate excessive somnolence, ataxia, and disorientation. Higher oral and IV doses can produce more profound behavioral changes. Polydipsia and polyphagia can also occur. Dogs may develop psychogenic polydipsia with associated polyuria. The polyphagia can lead to intense scavenging and begging behavior. This can lead to dietary indiscretion with subsequent serious problems of gastroenteritis, pancreatitis, or foreign body obstruction. Some owners also complain that their dog "just isn't the same pet" after phenobarbital therapy.
- *Physical examination changes*—The most common change with chronic phenobarbital therapy is weight gain. Most likely this is the result of increased appetite (with an increased food supply) coupled with a more sedentary lifestyle. Some dogs may develop splenomegaly and/or hepatomegaly. Persistent neurologic deficits without underlying intracranial pathology are extremely uncommon.
- *Clinical laboratory changes*—Transient clinical laboratory changes are minimal. Urine specific gravity may decrease. The most common clinical laboratory change associated with chronic phenobarbital therapy is elevation of serum alkaline phosphatase (ALP) in the dog. This can occur as quickly as 2 weeks after therapy. Neither endogenous adrenocorticotropic hormone (ACTH) nor exogenous response to ACTH is altered by phenobarbital. Moreover, phenobarbital does not interfere with a low-dose dexamethasone suppression test regardless of dose or treatment time. However, baseline serum thyroxine concentration is depressed in 60% to 70% of dogs on phenobarbital. These dogs have a normal response to thyroid-stimulating hormone (TSH). Thus, use TSH response to diagnose hypothyroidism in dogs on phenobarbital.

Life-Threatening Complications

Three serious and potentially life-threatening complications can occur with long-term phenobarbital therapy:

- *Physical dependence*—Such dependence on the drug develops over time. Withdrawal seizures can develop as serum phenobarbital concentration declines, especially during precipitous drops below 20 µg/ml (dog) or 10 µg/ml (cat).
- *Functional tolerance*—The loss of drug efficacy despite adequate serum concentration can develop as the result of altered transport of the drug through the blood-brain barrier, down-regulation of receptors in the brain, and progression of epilepsy resulting in multiple seizure foci or changes in neurotransmission. The degree of functional tolerance to phenobarbital in the dog is not clear. In my experience, phenobarbital is less in dogs with predominant focal epileptic seizure types.
- *Drug-induced toxicity*—Chronic phenobarbital therapy can also lead to hepatotoxicity, especially if serum trough levels are maintained at or above 35 µg/ml. Hepatotoxicity to primidone (which is metabolized predominantly to phenobarbital), either alone or in combination with other AEDs, occurs in dogs. A more serious idiosyncratic reaction is development of immune-mediated neutropenia, anemia, and thrombocytopenia in dogs. Typically, this reversible blood dyscrasia will occur within the first 6 months of dosing.

Treatment of Refractory Epilepsy in Dogs

Approximately 20% to 50% of dogs treated for epilepsy at referral veterinary institutions are reported to be poorly controlled with medical management and thus become classified as refractory epileptics.

Criteria for Refractory Epilepsy

My criteria for classifying idiopathic canine epileptics as refractory are as follows:

- An etiology of seizures has not been identified.
- Phenobarbital has been administered for at least 3 months with all serum trough concentrations between 20 and 40 µg/ml and a trough steady-state concentration between 25 and 30 µg/ml without a subsequent change in dosage for at least 1 month.
- Seizure number and severity have not improved or have worsened for at least 3 months despite phenobarbital and/or other AED treatment.
- Status epilepticus has occurred.
- Hepatotoxicity is present.

▼ ***Key Point*** Consider adding a second AED for dogs whose seizures continue despite persistent trough serum phenobarbital concentrations > 30 µg/ml for 1 to 2 months.

Bromide Therapy

The recommended add-on AED of choice in the dog is bromide (Table 127-3). Concomitant bromide and phenobarbital decreased seizure numbers and severity in the majority of dogs in two studies, with seizure-free status ranging from 21% to 72% of all treated dogs. In general, many canine refractory idiopathic epileptics may benefit from bromide despite prior seizure history onset or duration. By allowing a reduction of the use of drugs metabolized by the liver, bromide therapy may also reduce the incidence of hepatotoxicity.

Table 127-3. SUMMARY OF ANTIEPILEPTIC DRUG THERAPY IN THE DOG

ANTIEPILEPTIC DRUG	CLINICAL PHARMACOLOGY $T_{1/2}$ (hour)	Tss (days)	Vd (L/kg)	Prot Bd (%)	THERAPEUTIC RANGE	INITIAL DOSAGE	EFFICACY	MAJOR POSSIBLE ADVERSE EFFECTS
Phenobarbital*	40–24	10–14	0.80	40	20–40 µg/ml	2.5 mg/kg q12h	Generalized seizures	Sedation, polydipsia, liver disease; induces P450 system
Bromide*	15–20 days	100–200	0.40	0	Monotherapy: 2000–3000 µg/ml With phenobarbital: 1500–2500 µg/ml	40 mg/kg q24h	Generalized seizures	Sedation, weakness, polydipsia, polyphagia
Felbamate*	5–6	1–2	1.00	25	25–100 µg/ml	20 mg/kg q8h	Partial seizures	Blood dyscrasia, liver disease; induces P450 system
Gabapentin*	2–4	1	0.20	0	4–16 µg/ml	30–60 mg/kg/day[t] (divide bid or tid)	Generalized and partial seizures	Sedation
Clorazepate*	5–6	1–2	1.60	85	20–75 µg/L (nordiazepam)	2–4 mg/kg/day (divide bid)	Add on: Generalized and partial seizures	Sedation, withdrawal seizures
Topiramate	20–30	3–5	0.65	15	2–25 µg/ml	2–10 mg/kg q12h[t]	Add on: Generalized and partial seizures	Gastrointestinal upset, irritability
Zonisamide*	15–20	3–4	1.50	50	10–40 µg/ml	5–10 mg/kg/day (divide bid or tid)	Add on: Generalized and partial seizures	Sedation, ataxia, loss of appetite
Levetiracetam*	4–6	1–2	0.50	<10	10–37 µg/ml	500–4000 mg/day[t] (divide bid or tid)	Add on: Generalized and partial seizures	Sedation, inappetence

*Clinical pharmacology data presented for dogs.
Prot Bd, protein binding; t, gradual incremental dosing recommended; $T_{1/2}$, elimination half-life; Tss, approximate time to steady state; Vd, volume of distribution.

Although its exact mechanism of action is not completely understood, bromide appears to have a competitive interaction with chloride to hyperpolarize neuronal membranes in the brain. Thus, bromide is expected to have a synergistic effect with drugs that enhance chloride conductance, such as phenobarbital.

Bromide is administered as the inorganic salt, potassium bromide, typically as a 200- to 250-mg/ml solution dissolved in doubled distilled water. Bromide is a known mucosal irritant, and while capsular formulation is available, this dosing method may result in gastric irritation due to the direct contact of a concentrated amount of bromide with the gastric lining.

At a starting dosage of 40 mg/kg/day, bromide is slowly metabolized in the dog, with a median elimination half-life of 15.2 days resulting in achievement of median steady-state concentrations of 2450 mg/L. Apparent total body clearance was 16.4 ml/day/kg and volume of distribution was 0.40 L/kg. Steady-state concentrations fluctuate among dogs, most likely due to individual differences in clearance and bioavailability. Dietary factors also alter serum bromide concentrations, with high chloride diets resulting in excessive bromide renal secretion and lower serum concentrations.

The protocol for potassium bromide administration and monitoring is as follows:

- *Preparation*—Dissolve analytic-grade potassium bromide in double distilled water as a 200-mg/ml solution.
- *Administration*—The initial dosage is 30 mg/kg/day PO in food (with concurrent phenobarbital administration) or 40 mg/kg/day as monotherapy. The solution can be placed directly on the dog's food. Give the drug once per day or divided every 12 hours. Dividing the dose allows better adaptation to the sedative effects of the drug.
- *Monitoring*—Obtain trough serum concentrations of bromide at 30 days, 90 days, and every 6 months after initiation. The therapeutic range is 150 to 200 mg/dl (1.5–2.0 mg/ml) with concurrent phenobarbital administration (maintaining trough serum phenobarbital concentration from 20–30 µg/ml). Decrease the phenobarbital if hepatotoxicity occurs or if the dog is seizure free for >6 months.
- *Dosage adjustments*—The dosage is adjusted according to the following formula:
  - For concomitant phenobarbital- and bromide-treated patients, the new maintenance dose can be calculated with the following formula:

(Target Css – Actual Css) × (Clearance/Bioavailability) =
(2000 mg/L – Actual Css) × 0.02 =
added mg/kg/day to existing dose

  - Here, Css is the steady-state concentration at day 75 after treatment.
- Bromide is indicated as a single-agent AED in the following situations:
  - Underlying liver disease (e.g., hepatotoxicity or portosystemic shunting), which prevents the use of phenobarbital
  - Prolonged seizure-free status (>1 year) on combined phenobarbital and bromide therapy
  - Unacceptable quality of life on combined phenobarbital and bromide therapy with a seizure-free status period of >3 months
  - Infrequent initial seizures (<4 per year)
- *Dosing and monitoring*—The oral monotherapy starting dosage is 40 mg/kg/day. Oral loading dosing can be accomplished with a dose of 900 mg/kg divided into equal doses every 4 hours over 1 day, but this may result in gastric upset. The IV loading dose is described under emergency treatment of seizures (see below). Dogs treated with subsequent monotherapy bromide should have bromide concentrations at or above 2500 mg/L for optimal seizure control. Gradual increases in the dose allow better adaptation to the drug. Doses are adjusted according to the following formula:
  - For monotherapy bromide-treated patients, the new maintenance dose can be calculated with the following formula:

(Target Css – Actual Css) × (Clearance/Bioavailability) =
(2500 mg/L – Actual Css) × 0.02 =
added mg/kg/day to the existing dose

  - Again, Css is the steady-state concentration.
- *Adverse effects*—Bromide is generally well tolerated in the dog. The most common adverse effects seen with combination bromide and phenobarbital therapy are polydipsia, polyphagia, increased lethargy, and mild ataxia with increasing serum concentration. Pancreatitis and gastrointestinal intolerance have also been reported. Bromide intoxication to the point of stupor is rare, but pelvic limb ataxia, weakness, and altered behavior are more likely with serum concentrations >3000 mg/L. Caution should be used in treating dogs with underlying renal insufficiency, due to reduced renal elimination of bromide. Therapy of bromide intoxication consists of IV normal saline administration to enhance bromide renal excretion. Careful monitoring is advised as dogs may become more susceptible to seizure activity with lowering of the serum concentration.

New Antiepileptic Drugs with Potential for Use in Dogs

Several AEDs that have recently been approved for use in people offer exciting potential for use in dogs. Unfortunately, complete information is unavailable on the pharmacokinetic or therapeutic properties of these

drugs in controlled studies in dogs. Most of these medications are still quite expensive. The drugs are listed in alphabetical order and not in preference of use.

Felbamate (Felbatol)

Felbamate is a dicarbamate with proven ability to block seizures induced by a variety of methods. Felbamate is believed to increase seizure threshold and prevent seizure spreading by reducing excitatory neurotransmission in the brain. Neuroprotective effects have also been shown through this ability to alter excitatory neurotransmission. In clinical trials in people, felbamate has been shown to be most useful as monotherapy in the treatment of uncontrolled partial epilepsy. The drug is metabolized by the hepatic microsomal P450 enzymes and with increased clearance in younger dogs. In dogs, the drug has a high bioavailability and protein-binding capability.

- Effective control of focal seizure activity with documented therapeutic serum concentrations has been shown with felbamate therapy in dogs.
- The recommended dosage in dogs is 20 mg/kg q8h PO initially; increase as necessary up to a maximum of 3000 mg/day.
- Felbamate is a non-sedating drug but has been reported with a higher incidence of aplastic anemia and liver toxicity in people. These adverse effects have not been documented in dogs.
- Avoid concurrent use of felbamate and phenobarbital due to the possibility of increased hepatotoxicity and alteration of serum phenobarbital concentrations (felbamate increases serum phenobarbital concentration by 25%).
- Serial monitoring of the complete blood count and chemistry panel is recommended at 1 month and then every 3 months during treatment for the first year and then every 6 months thereafter.
- Trough serum drug concentration is typically done 1 to 2 weeks after initiation of treatment, with a therapeutic range between 25 and 100 mg/L.

Gabapentin (Neurontin)

Gabapentin is a novel AED whose mechanism of action is still not fully understood. Initially designed to mimic gamma-aminobutyric acid (GABA) in the brain, gabapentin can readily pass through the blood-brain barrier. Once in the brain, however, gabapentin does not mimic the pharmacologic properties of GABA, nor does it bind to GABA receptors. In preclinical studies, gabapentin effectively blocked seizures induced by a variety of proconvulsant methods. New evidence suggests that gabapentin may facilitate the extracellular transport of GABA out of cells to act on the GABA-alpha receptor. The dog is the only known species to partially biotransform the drug to N-methyl-gabapentin.

▼ ***Key Point*** A major benefit of gabapentin is that there is minimal hepatic metabolism thus it will not induce drug–drug interactions with other AEDs with hepatic metabolism (e.g., phenobarbital).

- Dosage: 30 to 60 mg/kg/day (divided every 8–12 hours). Gradual increase in dose over 1 to 2 weeks is recommended to allow adaptation to the sedating effects. Reduced doses may be needed in patients with renal insufficiency.
- Serum monitoring is not recommended, as the drug has a very high therapeutic index and little drug–drug interactions.
- Gabapentin is particularly useful in epileptic dogs with underlying hepatic disease.

Levetiracetam (Keppra)

Levetiracetam is the S-enantiomer of the ethyl analogue of piracetam that has broad-ranging, unique, and not completely known mechanisms of action against seizures. The drug is well absorbed but is more rapidly metabolized in people as compared with other drugs. The pharmacodynamic effect (i.e., the effect of the drug at the target organ) is believed to outlive the known half-life of the drug. Levetiracetam was the best tolerated of all new AEDs currently in human clinical trials, with adverse reactions equal to that of the placebo. Overall, this drug is proven to be an effective adjunctive therapy to control partial seizures previously refractory in treatment in people.

- Initial dosage: 500 to 1500 mg/day divided every 8 to 12 hours with gradual incremental dose titration.
- In my experience, the best response to this drug has been in dogs exhibiting automatisms and generalized seizures as an add-on medication to phenobarbital and/or bromide.
- The serum trough therapeutic range in epileptic people is reported to be 3 to 37 µg/ml.

Topiramate (Topamax)

Topiramate is a sulphamate-substituted monosaccharide with a mechanism of action of blockade of seizure spread by rapidly potentiated GABA activity in the brain. In people, topiramate is well absorbed and is primarily renal excreted as an unchanged drug. With a relatively long half-life of 20 to 30 hours, twice daily dosing is recommended. With a relatively broad-spectrum activity against many seizure types and minimal adverse effects, topiramate is approved for use in both adult and pediatric human patients. The dosage range is between 25 and 50 mg/kg/day, but gradual dose titration is better tolerated.

- Initial dosage: 2 to 10 mg/kg q12h with gradual incremental dose titration.
- I have used topiramate most successfully in dogs with partial and generalized seizures unresponsive to phenobarbital and bromide therapy.
- The serum therapeutic range is unknown in dogs but is between 2 and 25 mg/L in people.

Zonisamide (Zonegran)

Zonisamide is a substituted 1,2-benzisoxazole derivative that works by both blocking the propagation of epileptic discharges and suppressing focal epileptogenic activity. Pharmacokinetic information on the dog is limited to a very small population of normal beagles. In general, zonisamide is well absorbed, has a relatively long half-life, and has high protein-binding affinity. The drug is highly concentrated in red blood cells due to high binding to carbonic anhydrase and other red cell protein components. Zonisamide is hepatic metabolized and thus is influenced by concurrent administration of similarly metabolized drugs. Broad-spectrum antiepileptic activity has been reported against a variety of seizure types, with particular improvement in the treatment of adult myoclonus epilepsy. Major adverse effects in people include a higher incidence of renal calculi formation, sedation, and gastrointestinal disorders.

- Initial dosage: 5 to 10 mg/kg/day divided every 8 to 12 hours with gradual incremental dose titration.
- In my experience, zonisamide can be an efficacious and well-tolerated drug in the dog with recurrent generalized seizures refractory to phenobarbital and/or bromide therapy. The major adverse effects include sedation, ataxia, and inappetence. Phenobarbital dosages should be reduced by 25% at the time of starting zonisamide.
- The serum trough therapeutic range is reported from 10 to 40 µg/ml.

Drugs with Increased Risk or Inappropriate Pharmacokinetics in the Dog

▼ ***Key Point*** Since both primidone and phenytoin have been proved not to provide effective seizure control and are potentially hepatotoxic in the dog, do not use these drugs to treat seizures in the dog.

Lamotrigine (Lamictal)

The drug is converted to a cardiotoxic 2-N methyl metabolite in dogs, which is not found in people.

Phenytoin (Dilantin)

- There is a high risk of hepatotoxicity with this drug.
- It is difficult to maintain adequate steady-state serum concentrations due to the very rapid elimination half-life (approximately 2 hours).

Diazepam (Valium)

- Functional tolerance develops very quickly to diazepam, which results in inability to use diazepam as an effective emergency drug to stop cluster seizures or status epilepticus.
- There is potential for causing physical dependence and withdrawal seizures.
- It is difficult to maintain adequate steady-state serum concentrations.

Gamma-vinyl-gamma-aminobutyric acid (Vigabatrin)

- Potential for causing hemolytic anemia
- Potential for causing central nervous system vacuolation with chronic use
- Ineffective for stopping seizures

Carbamazepine (Tegretol)

It is difficult to maintain adequate steady-state serum concentrations due to the very rapid elimination half-life (approximately 2 hours).

Benzodiazepines

Benzodiazepines are a class of AEDs that interact with specific central nervous system benzodiazepine receptors, which activate the GABA-alpha chloride channel to hyperpolarize neuronal membranes.

- Diazepam is the most widely used benzodiazepine in veterinary medicine and is best used for the treatment of emergency seizures by IV and per rectal administration (see below).

▼ ***Key Point*** Chronic oral administration of diazepam is not recommended in the dog due to lack of effectiveness to stop seizures, very short half-life, potential for increased hepatic enzyme inhibition, physical dependence, and cross-tolerance to prevent effective use of IV diazepam to stop emergency seizures.

- A long-acting benzodiazepine, clorazepate, is a diazepam prodrug with more suitable pharmacokinetic properties for chronic use in the dog. However, similar problems may arise as with chronic oral diazepam, especially the potential for severe withdrawal seizure activity.

Treatment of Refractory Epilepsy in Cats

Since cats have an extremely high prevalence of symptomatic epileptic seizures, epileptic cats may not respond to phenobarbital alone. Moreover, the often focal nature of the underlying pathologic condition (e.g., meningioma or cerebrovascular accident) may predispose cats to focal seizure activity, which can be difficult to control with phenobarbital, in my experience. Unfortunately, cats are quite sensitive to the sedative

effects of many of the AEDs. Therefore, most combination therapies require a delicate balance of drug dosing. The following drugs may be tried in addition to or as replacement of phenobarbital therapy in cats.

▼ ***Key Point*** Adding a second AED or changing to a different therapy should be considered in cats whose seizures continue despite persistent trough serum phenobarbital concentrations above 20 μg/ml.

Benzodiazepines

Diazepam

- Cats appear to be resistant to developing functional tolerance to diazepam.
- Initial dosage: 0.5 mg/kg PO divided every 8 to 12 hours.
- Serum concentrations of nordiazepam can be monitored, but a therapeutic range has not been determined for the cat.

Clorazepate

Clorazepate is a long-acting benzodiazepine, similar in action to diazepam.

- Initial dosage: 2 to 3.75 mg total dose per cat q12–24h PO. Start at a low dose (1–2 mg per cat) and gradually increase over time.
- Serum concentrations of nordiazepam can be monitored, but a therapeutic range has not been determined for the cat.

Clonazepam

Clonazepam is a long-acting benzodiazepine, similar in action to diazepam.

- Initial dosage: 0.5 mg total dose once to twice daily.

Gabapentin (Neurontin)

Gabapentin is a useful AED in the cat due to its predominant renal excretion, similar to the dog. Cats, however, may exhibit increased sedation and will benefit by a gradual increment in dosing over 1 to 2 weeks.

- Initial dosage: 5 to 10 mg/kg daily for 3 to 5 days, then increase to every 12 hours. Further increases are dependent on response to therapy.
- Both solution (250 mg/5 ml) and capsular formulations of the drug are available. The drug can be used as both a monotherapy and an add-on medication.

Topiramate (Topamax)

In my experience, a number of cats with focal seizures, exclusive or with secondary generalization of seizures, will improve with the addition of topiramate to phenobarbital therapy. The key to success is gradual adaptation and eventual lowering of the phenobarbital dosage. The latter should be performed to acquire a trough level of approximately 10 μg/ml.

- Initial dosage: 12.5 mg total dose per cat per day, with incremental dosing up to 25 mg every 12 hours.
- Both breakable tablet (25 mg) and sprinkle (15 mg) formulations are available.
- Metabolic acidosis has been associated with chronic dosing in people. Periodic venous blood gas monitoring is recommended in addition to routine evaluation of complete blood counts and serum chemistry panels.

Drugs with Increased Risk or Inappropriate Pharmacokinetics in the Cat

Benzodiazepines

Fatal, acute idiosyncratic hepatotoxicity after diazepam administration has been reported in the cat. Thus, obtain a liver chemistry panel in all cats 3, 7, and 14 days and then every 3 to 6 months after initiation of therapy.

Bromide

Bromide therapy in cats is not recommended as a standard therapy due to the relatively high prevalence of adverse respiratory problems. Cats can develop cough and more severe respiratory signs suggestive of an allergic asthmatic disease. I no longer recommend the use of bromide in cats.

Hospital Emergency Treatment for Seizures

▼ ***Key Point*** A reliable protocol for rapid treatment is necessary for the emergency management of seizuring patients.

The physiologic sequelae of clustered or continuous seizure activity (status epilepticus) leading to increased intracranial pressure and neuronal necrosis include systemic arterial hypertension, loss of cerebrovascular regulation, disruption of the blood-brain barrier, and cerebral edema. If not treated appropriately, the seizuring patient may develop serious neurologic complications due to these events.

Guidelines for When to Administer Emergency Therapy for Seizures

- A single seizure that persists >5 minutes from the time the seizure is identified
- Status epilepticus
- More than one seizure per hour, regardless of seizure length
- Three or more seizures per day, regardless of seizure length

Protocol for Emergency Management of Seizures

A protocol for the emergency treatment of seizures in the dog and cat is outlined in Table 127-4. Two main

Table 127-4. PROTOCOL OF THE MEDICAL MANAGEMENT OF STATUS EPILEPTICUS AND CLUSTER SEIZURES IN THE DOG AND CAT

Phase 1

The goals of this initial phase are to stabilize the patient, institute short-acting AEDs with minimal adverse effects to immediately control active seizures, and to rapidly establish serum concentrations of a maintenance AED to preserve seizure control.

1. ABC: Establish a patent airway, maintain adequate breathing, and provide circulatory support.
2. Start a continuous IV infusion of 0.9% saline at a dosage of 5 to 10 ml/kg/hour.
3. Evaluate STAT blood glucose, PCV/TP, BUN, and AED serum concentration (if appropriate). Treat for hypoglycemia only if the blood glucose is ≤60 mg/dl.
4. Administer a bolus dose of DZ 0.5 mg/kg IV if a seizure episode lasts ≤1 minute, there have been at least two seizures (regardless of duration), or an intracranial etiology is suspected (regardless of duration).
   a. Alternate treatment: DZ per rectal injection (5 mg/ml of parenteral DZ)
      (1) No prior PB therapy: 1 mg/kg
      (2) Prior PB therapy: 2 mg/kg
5. Administer PB after DZ to provide a sustained antiepileptic effect as serum levels of DZ decline.
   a. Drug-naïve patients:
      (1) Give a loading dose of PB to rapidly establish therapeutic drug levels. Use this formula: **Loading dose (total mg) = Desired serum level (µg/ml) × Body weight (kg) × 0.8 L/kg.** Use an IV injection at a rate of ≤100 mg/min.
      (2) Desired serum concentration: Dogs = 20 µg/ml, cats = 10 µg/ml.
   b. PB-treated patients:
      (1) Give 1 mg/kg IV for each microgram per milliliter of desired increase in patient serum level.
      (2) Dogs: Raise serum concentration at increments of 5 µg/ml up to 30 µg/ml.
      (3) Cats: Raise serum concentration at increments of 3 µg/ml up to 20 µg/ml.
6. Alternative treatment with BR after DZ in dogs only:
   a. Drug-naïve patients:
      (1) Oral loading (NaBr or KBr): 200-mg/ml solution
      Target Css × Vd = Total dose administered = 2000 mg/L × 0.45 L/kg = 900 mg/kg/day divided into equal doses every 4 hours for 24 hours
      (2) IV loading (NaBR): 3% NaBR in sterile water
      Target Css × Vd = Total dose administered by continuous rate infusion in a central vein = 2500 mg/L × 0.45 L/kg = 900 mg/kg every 24 hours
   b. BR-treated patients:
      (1) New added oral dose over 24 hours: (Target Css − Actual Css) × Vd L/kg = (Target Css − Actual Css) × 0.45 L/kg = mg/kg doses in 4 equal doses every 6 hours
      (2) Target Css: Monotherapy BR treatment = 2000 mg/L; BR plus PB = 1500 mg/L

Phase 2

The goals of this phase are to institute maintenance AED therapy and monitor for further seizures activity.

1. Institute maintenance PB either PO or IM.
   a. Drug-naïve patients: After IV loading dose, initiate oral therapy at 2.5 mg/kg q12h starting in 12 hours.
   b. Established epileptic patients: Increase dose to an amount higher than that being administered on admission.
      (1) New total mg/day = (Desired concentration/Established concentration) × Total mg current dose
   c. Dogs: Increase the desired concentration in the maintenance dose formula at increments of 5 µg/ml up to 30 µg/ml.
   d. Cats: Increase the desired concentration in the maintenance dose formula at increments of 3 µg/ml up to 25 µg/ml.
2. BR therapy (dogs only) if BR is to be used as *monotherapy:*
   a. Drug-naïve patients:
      (1) Maintenance dose: Target Css × (Clearance/Bioavailability) = mg/kg/day = 2000 mg/L × 0.02 = 40 mg/kg/day divided bid
   b. Previous BR-treated patients:
      (1) New maintenance dose: (Target Css − Actual Css) × (Clearance/Bioavailability) = mg/kg/day = (2500 mg/L − Actual Css) × 0.02 = added mg/kg/day
3. BR therapy (dogs only) if BR is to be used as *combined therapy with PB:*
   a. Drug-naïve patients:
      (1) Maintenance dose: Target Css × (Clearance/Bioavailability) = mg/kg/day = 1500 mg/L × 0.02 = 30 mg/kg/day given daily or divided BID
   b. Previous BR-treated patients:
      (1) New maintenance dose: (Target Css − Actual Css) × (Clearance/Bioavailability) = mg/kg/day = (2000 mg/L − Actual Css) × 0.02 = added mg/kg/day
4. If seizures continue:
   a. At a rate of less than one per 3 hours: Use DZ 0.5 mg/kg IV bolus up to three doses and then proceed to phase 3.
   b. At a rate of more than one per hour: Proceed to phase 3.

Table 127-4. PROTOCOL OF THE MEDICAL MANAGEMENT OF STATUS EPILEPTICUS AND CLUSTER SEIZURES IN THE DOG AND CAT—cont'd

Phase 3

The goal of this phase is to treat recurrent seizures in patients that fail to respond to an initial course of IV bolus doses of DZ and PB.

1. Begin continuous rate IV infusion of DZ at an initial rate of 0.25 mg/kg/hour in a 0.9% NaCl (or 0.45% NaCl/2.5% dextrose if on BR) at a maintenance fluid rate.
2. If seizures continue (less than three total), increase the rate up to 0.5 mg/kg/hour.
3. If a total of three or more seizures occur while on the DZ infusion, administer one of the following for 6 hours:
   a. For pentobarbital: Initial bolus to induce general anesthesia at 2 mg/kg IV slowly to effect (if patient has been on PB prior to admission, a higher dose may be needed due to induction of the hepatic P450 system). Continuous infusion of approximately 5 mg/kg/hour to effect.
   b. For propofol: Initial slow infusion of 4 to 8 mg/kg IV to effect, followed by continuous infusion to maintain general anesthesia (8 to 12 mg/kg/hour).
      (1) Advantages: Primarily renal excreted (safer to use in dogs with liver disease), rapidly metabolized to allow rapid recovery, and does not induce biochemical changes.
      (2) Disadvantages: Can induce apnea, cause hypovolemia, and is relatively expensive for prolonged use.
4. Maintenance PB therapy should be administered IM throughout the anesthesia to provide sustained therapeutic serum concentration upon emergence from anesthesia.
5. Appropriate supportive care and monitoring should be provided for general anesthesia.
6. After 4 to 6 hours, if any further seizures occur, proceed to phase 4.

Phase 4

The goal of this phase is induction of prolonged general anesthesia.

1. Barbiturate
   a. Maintain general anesthesia as established in phase 3 for an additional 12 hours, followed by a tapering of anesthesia every 2 to 4 hours.
2. Gas anesthesia
   a. Indications: Refractory seizures to above steps or contraindication to use of benzodiazepine or barbiturate drugs (hepatotoxicity or hepatic encephalopathy).
   b. Isoflurane offers the following advantages: Rapid induction and adjustable anesthetic depth with smooth emergence from anesthesia, no hepatotoxicity, less perfusion problems, and less effect on elevation of intracranial pressure than halothane.
   c. Obtain arterial blood gases every 4 to 8 hours to ensure adequate oxygenation.

AED, antiepileptic drug; BR, bromide; BUN, blood urea nitrogen; Css, steady-state concentration; DZ, diazepam; PB, phenobarbital; PCV/TP, packed cell volume and total protein; Vd, volume of distribution.

components are listed in this protocol: restoring homeostatic conditions and providing specific seizure treatment. Many drugs used to control seizures have the potential to cause serious adverse effects, including death. Specific seizure treatment is divided into four successive phases.

- Phases 1 and 2 involve using a short-acting AED to stop immediate seizure activity and a long-acting AED to prevent further seizures. Diazepam is currently the drug of choice in treating prolonged seizures, including status epilepticus and cluster seizures.
- Phases 3 and 4 outline steps to follow if a dog continues to seizure despite prior treatment.
- To implement this protocol, be sure to have injectable diazepam, phenobarbital, pentobarbital, propofol, and a 24-hour monitoring facility.

At-Home Emergency Treatment for Seizures Using Diazepam per Rectum

Financial and emotional constraints of recurrent emergency therapy are often the limiting factor in an owner's decision to continue treating an animal. Per rectal administration of diazepam is a safe, affordable home treatment for cluster seizures that can reduce owner cost, decrease patient morbidity, and contribute positively to the overall AED therapy.

Per rectum administration of the IV formulation of diazepam allows rapid absorption of active drug into the bloodstream through the rectal mucosa in <15 minutes. Antiepileptic plasma concentrations are maintained for several hours after administration. In comparison, an intramuscular injection of diazepam results in an erratic absorption of the drug and may take up to 30 minutes for peak concentrations to appear in the blood. Use rectal administration of diazepam for the emergency treatment of seizures in the dog according to the following recommendations. No information is available for the cat.

- *Indications:* History of generalized cluster epileptic seizures, status epilepticus, and underlying cerebral disease.
- *Administration:* Use a syringe through a plastic application tip ($1^1/_3$ inch J-12 teat infusion cannula) lubricated with a water-soluble jelly.
- *Dosage:*
  - If not on phenobarbital: rectally administer 1 mg/kg of diazepam parenteral solution (5 mg/ml).
  - If on phenobarbital: rectally administer 2 mg/kg of diazepam parenteral solution (5 mg/ml).

- Do not exceed a maximum dose of 100 mg.
- Administer at the onset of a seizure up to 3 times in 24 hours but no closer than 15 minutes apart.

- *Toxicity:* Increased sedation and rectal mucosal irritation.

NON-EPILEPTIC SEIZURES DUE TO NARCOLEPSY AND CATAPLEXY

Non-epileptic seizures or episodes can be categorized into non-neurogenic and neurogenic causes. Many events may mimic epileptic seizures. Distinguishing non-epileptic seizures or episodes is important, because failure to do so could lead to failure to identify another serious medical condition, administration of unnecessary medication to the animal, and undue emotional and financial strain on the owner. This section discusses the non-epileptic seizures associated with sleep disorders: narcolepsy and cataplexy.

Etiology

- *Cataplexy* is a brief, sudden episode of muscle weakness without loss of consciousness. The signs are due to motor inhibition only.
- *Narcolepsy* is a disorder of daytime somnolence characterized by excessive sleeping episodes. Narcolepsy and cataplexy can occur together.

Pathophysiology

- A deficient hypocretin or orexin system is the underlying mechanism in narcolepsy.
  - Hypocretin or orexin neurons are restricted to the tuberal region of the hypothalamus, with extensive cortical projections that function to enhance brain excitation for arousal control.
  - Loss of hypocretin or orexin output results in a failure to regulate critical sleep-wave pathways.
  - Breeds documented to have an autosomal inheritance are the Doberman pinscher, Labrador retriever, miniature poodle, and dachshund.
  - The genetic mutation is due to the *canarc-1* deletion mutation of the hypocretin or orexin receptor-2 gene, resulting in a nonfunctional receptor.
  - The *canarc-1* gene is transmitted as an autosomal recessive trait with full penetrance that is not associated with the dog leukocyte antigen system.
- Several other breeds reported with narcolepsy or cataplexy include the Airedale, Afghan, Irish setter, malamute, Saint Bernard, rottweiler, English springer spaniel, Welsh corgi, and giant schnauzer.
- Autoimmune destruction of hypocretin-containing cells in the hypothalamus has been proposed as another common cause of narcolepsy in humans with the adult-onset form of the disease.
- The characteristic finding in this acquired form of the disease is low concentrations of hypocretin in CSF.
- Hypocretin-deficient narcolepsy or cataplexy has recently been described in a 3-year-old Weimaraner.
- This disease is rare in cats.

Clinical Signs

In practically all instances, dogs with non-epileptic seizures do not exhibit postictal effects. Possible exceptions are dogs that exhibit autonomic release phenomena (e.g., urination) after a syncopal episode and dogs with vestibular disease that continue to appear disoriented from their vertigo. The typical history and clinical signs of narcolepsy-cataplexy consist of the following:

- Onset usually by 6 months of age
- Sudden, paroxysmal generalized muscle atonia lasting seconds to 10 to 20 minutes
- Episodes often precipitated by excitement
- Intact respirations and cough and swallow reflexes
- Possibly aroused by external stimuli
- Possible signs of rapid eye movement (REM) sleep with ocular motility, facial or eye muscle twitching, and whining

Diagnosis

Differential Diagnoses

Non-neurogenic Episodes

- Syncope of cardiac origin (see Chapter 148)
- Arrhythmias (see Chapter 145)
- Right-to-left shunts (reverse patent ductus arteriosus, tetralogy of Fallot) (see Chapter 154)
- Cardiomyopathy (see Chapter 150)
- Metabolic disturbances
- Polycythemia (see Chapter 22)
- Hypoglycemia (see Chapter 35)
- Hypoadrenocorticism (Addison disease)
- Pheochromocytoma

Neurogenic Episodes

- Narcolepsy and cataplexy
- Vestibular disease (see Chapter 126)
- Myasthenia gravis (see Chapter 130)

Diagnostic Testing

Food-Elicited Test

The purpose of this test is to create an environment of excitement to induce an attack.

- *Protocol:* Place 10 pieces of palatable food approximately 1 cm^3 in size in a row about 1 ft apart from each other. Record the time required to eat all pieces and the number, type, and duration of the attacks.
- *Interpretation:* The normal dog will eat the food in <1 minute and have no attacks.
- *Abnormal responses:*

- The dog will take >2 minutes to eat the food and have two or more attacks.
- The animal drops to the ground with flaccid paralysis (complete attack).
- Thoracic and/or pelvic limbs drop to the ground but the head does not (partial attack).

Pharmacologic Testing

The purpose of these tests is to induce or reduce attacks with various central-acting drugs.

- *Yohimbine response test:* Give a 50-µg/kg IV bolus of yohimbine. A positive response is a 75% reduction in the number or severity (time reduction) of attacks. Response occurs within 30 minutes and may last up to 4 hours.
- *Physostigmine challenge test:* Give 0.025 mg/kg of physostigmine salicylate as an IV bolus. Follow each injection with a food-elicited test in 10 minutes. Repeat the test with additional 0.025-mg/kg increments up to 0.100 mg/kg. In affected animals, signs increase in severity and frequency in a dose-dependent manner. The total effect of each dose will last 15 to 45 minutes.

Electrophysiologic Testing

The purpose of these tests is to confirm loss of muscle activity during an attack and absence of epileptic activity in the brain.

- Electroencephalographic recordings are consistent with acute onset of REM sleep during an attack without epileptiform activity.
- Concurrent electromyographic recordings from appendicular muscles show complete loss of activity during an attack.

Genetic Analysis

Genetic analysis in dogs has been performed at the Center for Narcolepsy, Department of Psychiatry, Stanford University, School of Medicine, Stanford, CA 94305.

Treatment

- Modafinil is the drug of choice for narcolepsy and cataplexy.
  - Novel wake-promoting agent
  - Dosage: 1 to 5 mg/kg/day
  - Adverse effects: Excessive stimulation and wakefulness, decreased appetite, tachycardia, and hypertension
- Methylphenidate (Ritalin)
  - Dosage: 0.25 mg/kg q24h or q12h PO
  - Adverse effects: Potentially inappetence, irritability, or altered sleep patterns

Prognosis

Overall, the prognosis for a good life is fair to good. Dogs may improve as they age. Alterations of lifestyle may be necessary to avoid precipitating events, such as reducing excitement or stressful events as much as possible.

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Chapter

128 Disorders of the Spinal Cord

Patricia J. Luttgen / Paul A. Cuddon

The term *spinal cord disorders* (see Table 128-1 for classification and examples) broadly refers to all diseases affecting the spinal cord. Clinically, spinal cord disorders may cause dysfunction in one or more limbs. Urinary and fecal incontinence and tail dysfunction may also be seen.

▼ ***Key Point*** Disorders of the spinal cord do not cause signs referable to diseases above the foramen magnum, such as mentation changes, cranial nerve deficits, and vestibular ataxia.

ETIOLOGY

Spinal cord disorders can arise from numerous insults and may be associated with particular signalments (breed, age, sex) and neuroanatomic localizations. Many of these disorders cause relatively predictable patterns of onset (acute versus chronic) and clinical signs (progressive versus nonprogressive).

Anomalies

Anomalies of the spinal cord usually are first recognized when ambulation begins and are nonprogressive. Examples include spinal dysraphism in Weimaraners and sacrocaudal dysgenesis with spina bifida in English bulldogs and Manx cats.

- For some anomalies, traumatically induced "decompensation" may be required for minor lesions to be recognized clinically. An example is atlantoaxial subluxation of toy breeds in which ligamentous and dens malformations create C1-C2 instability and an increased risk of C1-C2 luxation.
- Some anomalies slowly worsen over the life of the animal to cause progressive worsening of signs. Dogs with congenital arachnoid cysts show slowly progressive spinal cord signs as the cavitating lesion expands in size. In dogs with caudal occipital malformation syndrome (COMS), progressive foramen magnum compression causes disruption of cerebrospinal fluid (CSF) flow and syringohydromyelia formation. Signs of slowly progressive spinal cord dysfunction can be seen at almost any age.
- Vertebral anomalies that compromise the stability of the vertebral column or the canal size may cause spinal cord dysfunction secondary to compression. For example, hemivertebra may lead to vertebral body luxation, and malarticulation/malformation of articular facets may lead to spinal canal stenosis.

Degenerative Disorders

Degenerative conditions are usually insidious in onset and chronically progressive.

- Many of these conditions are inherited and are seen in young animals. Examples include lysosomal storage disorders such as globoid cell leukodystrophy and Niemann-Pick disease, spinal muscular atrophy of Brittany spaniels, and hereditary ataxia of Jack Russell and smooth-haired fox terriers.
- Other neurodegenerative disorders are age-related and may be familial. Examples include degenerative myelopathy seen in older, large-breed dogs, particularly the German shepherd. In this disorder, white matter degeneration is most severe in the T3-L3 region.
- Some age-related degenerative disorders affect bony and soft tissues surrounding the spinal cord and result in spinal cord compression. Examples include cervical spondylomyelopathy in Doberman pinschers, intervertebral disc disease (discussed under spinal cord trauma below), lumbosacral spondylopathy/stenosis of German shepherd dogs, and mucopolysaccharidosis in cats.

Trauma

- Trauma can arise from external sources (e.g., being hit by a car or a bullet) or from internal sources (e.g., disc herniation or a pathologically collapsed vertebra).
- Clinical signs are usually acute and nonprogressive. However, progressive signs may be seen.
- Pathologic vertebral body fractures can occur secondary to vertebral body neoplasia or osteomyelitis.

Table 128-1. CLASSIFICATION AND EXAMPLES OF SPINAL CORD DISORDERS

Category	Examples
Degenerative	Globoid cell leukodystrophy
	Degenerative myelopathy of German shepherds
	Hereditary spinal muscular atrophy of Brittany spaniels
	Hereditary ataxia of smooth-haired and Jack Russell terriers
	Caudal cervical spondylomyelopathy
Anomalous	Spinal dysraphism
	Spina bifida
	Myelodysplasia
	Atlantoaxial subluxation
	Hemivertebrae
	Spinal arachnoid cysts
	Caudal occipital malformation syndrome with syringohydromyelia
Neoplastic	Intramedullary ependymoma
	Intramedullary astrocytoma
	Intramedullary oligodendroglioma
	Extramedullary intradural meningioma
	Extramedullary peripheral nerve sheath tumor
	Lymphoma
	Extradural vertebral osteosarcoma
Infectious	Feline infectious peritonitis
	Canine distemper myelitis
	Rabies
	Cryptococcosis
	Rickettsial diseases
	Neosporosis
	Toxoplasmosis
	Discospondylitis
Immune-mediated	Granulomatous meningoencephalitis
	Steroid-responsive meningitis/vasculitis
Toxic	Tetanus
	Strychnine
Traumatic	Intervertebral disc herniation
	Fracture/luxation of spinal column
Vascular	Fibrocartilaginous embolization
	Progressive hemorrhagic myelomalacia
	Caudal aortic embolization

Intervertebral Disc Disease

- *Type I intervertebral disc disease* is characterized by sudden disc extrusion. Signs of spinal cord compression are usually acute and may progress over a few hours or days.
- *Type II intervertebral disc disease* is characterized by slow protrusion of a slowly degenerating disc. Signs are usually gradual in onset and progression.

Inflammation/Infection

Numerous infectious agents can affect the spinal cord and surrounding structures of animals of all breeds and ages. Clinical signs vary depending on the inciting agent, the location of the lesion, and the degree of spinal cord involvement. Signs are usually rapid in onset and progression. Often inflammatory disease of the central nervous system (CNS) is not confined to the spinal cord, and clinical signs of brain involvement will also be present (see Chapter 126).

Bacterial

- Primary bacterial meningitis or meningomyelitis is infrequently diagnosed in dogs and cats. Bacterial infection is most commonly introduced secondary to infection of surrounding tissues or to trauma.
  - For example, bacterial discospondylitis causes discomfort from disc and vertebral body infection and may cause neurologic deficits if secondary compression of the spinal cord occurs.

Viral

Viral myelitis is a relatively common problem in dogs and cats. Clinical presentation and neuroanatomic localization vary.

- Typically, encephalitic signs are associated with rabies infection, but this virus may also cause signs of myelitis (see Chapter 15).
- All ages of dogs are susceptible to canine distemper virus (CDV; see Chapter 13). Previous vaccination does not preclude "breaks" in immunocompetency due to other illnesses or disease states. Signs of spinal cord disorder without associated encephalitic signs may occur.
- In cats, coronavirus (feline infectious peritonitis) and retrovirus (feline leukemia virus and feline immunodeficiency virus) infections may cause signs of spinal cord dysfunction with or without signs of brain involvement (see Chapters 8, 9, and 10).

Fungal

- Fungal myelitis has been reported in patients with cryptococcosis, blastomycosis, histoplasmosis, and coccidioidomycosis.
- Multiple levels of the nervous system usually are involved simultaneously (e.g., eyes, brain, spinal cord); however, signs are limited to the spinal cord in some patients.
- Systemic mycoses are discussed in Chapter 20.

Rickettsial

- In addition to other clinical signs, tickborne rickettsial diseases such as ehrlichiosis and Rocky Mountain spotted fever may cause myelitis, meningitis, and encephalitis (see Chapter 17).

Protozoal

- *Neospora caninum* may cause pelvic limb rigidity followed by a rapid ascending tetraparesis/tetraplegia due to a severe myelitis (see Chapter 21).

- Toxoplasmosis can also cause spinal cord myelitis and radiculitis, especially in cats (see Chapter 21). Encephalitis, ocular involvement, and myositis may also be present.
- We recommend testing for both organisms if protozoal myelitis is suspected.

Granulomatous Meningoencephalomyelitis (GME)

- This is believed to be an immune-mediated disorder of the brain and spinal cord.
- Signs of spinal cord myelitis and meningitis may predominate. The cervical area seems to be the preferred site of involvement in the spinal cord.
- GME primarily affects the white matter of the CNS and consists of perivascular accumulations of lymphocytes, plasma cells, and reticuloendothelial cells. Perivascular cuffs can coalesce to produce granulomas.
- The disease is invariably progressive in nature (see Chapter 126).

Immune-Mediated Disorders

- Immune-mediated steroid-responsive meningitis and/or meningeal-vasculitis have been reported in young dogs of many breeds. Boxers are commonly affected with this disorder. A more severe form of this syndrome (necrotizing vasculitis) has been reported in beagles, Bernese Mountain dogs, and German short-haired pointers.
- Clinical signs are typical of spinal meningitis including neck stiffness, hyperesthesia, and fever.

Toxins

- Strychnine and tetanus directly affect the spinal cord in dogs and cats. These toxins act in a similar manner.
- Tetanus toxin decreases the release of the inhibitory neurotransmitters, γ-aminobutyric acid and glycine in the spinal cord, whereas strychnine competitively blocks the inhibitory effect of glycine.
- Clinical onset is usually acute, and the disease progresses to a state of severe tetany.

Vascular Disorders

- Vascular conditions resulting in ischemia of the spinal cord most often cause peracute to acute nonprogressive spinal cord dysfunction. Intramedullary spinal cord lesions are nonpainful.
- The lesion may affect any area of the spinal cord.

▼ ***Key Point*** In adult large-breed dogs, fibrocartilaginous embolization is the most common cause of vascular injury to the spinal cord. Lesions are often asymmetrical and may affect several spinal cord segments in a continuous or discontinuous distribution.

- In cats, caudal aortic embolization secondary to cardiomyopathy is a common cause of spinal cord vascular injury.

Neoplasia

- Neoplasia of the spinal cord can affect animals of all ages and breeds. Initial clinical signs vary, depending on the type and location of the tumor. Signs usually are progressive over weeks to months. Two major types of tumors affect the spinal cord: intramedullary and extramedullary.
  - Intramedullary tumors such as astrocytoma and ependymoma arise from the spinal cord itself, causing damage by derangement of the normal anatomy. Hemangiosarcoma, lymphoma, and other tumors may metastasize to intramedullary sites in the spinal cord.
  - Extramedullary tumors arise from tissues surrounding the spinal cord and cause damage by compression. Extramedullary tumors can be located intradurally (e.g., meningiomas and nerve root tumors) or extradurally (e.g., vertebral osteosarcomas and multiple myeloma). Extradural lymphoma is a common cause of caudal paresis in cats.
- See Chapter 101 for discussion of neoplasia of the axial skeleton.

CLINICAL SIGNS

Characteristic clinical signs of spinal cord injury include spinal pain or hyperpathia, proprioceptive deficits, paresis or plegia, and nociceptive (pain) loss.

Hyperpathia

- Involvement of nerve roots, dura, and other extradural structures adjacent to the spinal cord will result in hyperpathia (exaggerated response to a painful stimulus).
- Spinal hyperpathia can be assessed by observing for pain on spinal palpation, neck guarding or stiffness, or signs of a root signature (holding/favoring the limb at rest).
- Extradural and extramedullary lesions are often painful. This can be helpful in lesion localization.

Postural Deficits and Ataxia (Proprioceptive Dysfunction)

- Ascending sensory tracts in cord white matter convey proprioceptive information from the limbs to the brain.
- Conscious proprioceptive (CP) tracts convey signals concerning limb position at rest to the cerebral cortex.
- Unconscious proprioception (UP) tracts convey signals concerning limb position during locomotion to the cerebellum.

- Injury to CP tracts causes knuckling and slow postural reactions (as during the hopping test).
- Injury to UP tracts causes ataxia ("drunken" gait with crossing over, wide-based posture, truncal sway, circumduction, and, occasionally, hypermetria). Ataxia is usually observed in the limbs caudal to the lesion.

▼ ***Key Point*** Ascending proprioceptive fibers in the spinal cord are the most sensitive to compressive lesions. Therefore, CP deficits and incoordination (sensory ataxia) of one or more limbs is commonly the initial sign of spinal cord disease.

Paresis and Plegia

- Descending upper motor neuron (UMN) tracts in cord white matter originate in brain and terminate in the spinal cord. The UMN system modulates functions of the thoracic and pelvic limb lower motor neurons (LMNs) located in the gray matter of cord segments C6-T2 and L4-S2, respectively.
  - UMN inputs facilitate limb strength and motor abilities and inhibit some spinal reflexes and limb extensor muscle tone.
  - LMNs also facilitate strength, relay locomotor signals from the UMN system, are part of the reflex arc for spinal reflexes, and provide trophic support to limb muscles.
- Injury to either UMN or LMN pathways will cause varying degrees of *paresis* (weakness) or *plegia* (weakness with loss of locomotor abilities) of the limbs.

▼ ***Key Point*** UMN injury results in paresis to limbs caudal to the level of the lesion, and LMN injury results in paresis to limbs at the level of the lesion.

- Injury to UMN pathways results in retention of spinal reflexes and increased extensor muscle tone when animals are recumbent.
- Injury to LMN pathways results in depression of spinal reflexes, decreased muscle tone, and muscle atrophy.

Affected Spinal Segment

- *C1-C5 injuries* can potentially cause signs of UMN tetraparesis or tetraplegia if damage to UMN pathways occurs.
- *C6-T2 injuries* can cause signs of LMN paresis in the thoracic limbs and signs of UMN paresis in the pelvic limbs.
- *T3-L3 injuries* can cause signs of UMN paresis in the pelvic limbs.
- *L4-S3 lesions* can cause signs of LMN paresis in the pelvic limbs, incontinence due to urinary bladder, urethral sphincter, and anal sphincter dysfunction.

Nociceptive (Pain) Loss

- Ascending nociceptive tracts in the spinal cord white matter convey nociceptive (pain) signals from the limbs to the cerebral cortex.
- Injury to these tracts results in depressed or absent detection of noxious stimuli.
- Nociceptive perception is usually assessed by testing the digits for superficial and deep pain sensation.
- Nociceptive tracts in cord white matter are very resistant to injury and are affected by only very severe spinal cord injuries.

▼ ***Key Point*** The ascending spinal cord pain fibers are the most resistant to compressive lesions. Therefore, lack of deep pain perception as demonstrated by no visible response to a noxious stimulus (i.e., the animal does not appear to be consciously aware of the pain) applied to a limb or tail caudal to a compressive lesion indicates severe damage to the spinal cord.

Other Features of Spinal Cord Lesions

- As compressive (extradural or extramedullary) lesions worsen, CP, UP, UMN (limbs and then bladder/sphincter), and then nociceptive functions are lost in that order. Examples include intervertebral disc disease, discospondylitis, vertebral body tumors, and vertebral malformations. Predictable and sequential signs of CP deficits, sensory ataxia, and then paresis are observed.
- Neurologic deficits are ipsilateral to the lesion.
- Extramedullary lesions that "lateralize" cause asymmetrical signs.
- Intramedullary lesions such as some spinal cord tumors, degenerative conditions, myelitis, and some spinal cord anomalies tend to cause symmetrical neurologic deficits (exception is asymmetrical fibrocartilagenous infarction) that may progress in a less predictable fashion.
- Intramedullary lesions without concurrent extramedullary involvement are nonpainful.
- Intramedullary cervical cord lesions may lead to cervical torticollis (lateral deviation of the neck).
- The ratio of spinal canal to spinal cord diameter is much greater in the cervical region than in the thoracolumbar region. For this reason, extramedullary lesions in the cervical region can be quite large without causing severe neurologic deficits. Conversely, smaller extramedullary lesions in the thoracolumbar area can be associated with severe neurologic deficits due to the small amount of space around the spinal cord.

DIAGNOSIS

History

- In spinal cord disorders, key aspects of the history are signalment, nature of onset, and progression of clinical signs. Knowledge of breed, age, and progression of signs can usually aid in narrowing down the list of most likely differential diagnoses.
  - For example, chronic progressive disease in an older German shepherd suggests degenerative myelopathy, neoplasia, or chronic type II disc herniation.
  - Acute nonprogressive disease in a young dog suggests trauma, acute type I disc herniation, or fibrocartilaginous embolization.

Lesion Localization (Neurologic Examination)

- The neurologic examination establishes the presence or absence of neurologic dysfunction (see Chapter 125).
- See previous discussion under "Clinical Signs" for localizing lesions in animals with paresis and/or plegia.
- Many of the diseases described above (myelitis, tumors, fibrocartilagenous infarction, degenerative disorders) can affect any segment of the spinal cord.
- Other diseases target specific areas of the spinal cord. Examples include atlantoaxial subluxation (C1-C2), hemivertebrae (thoracic spinal cord), degenerative myelopathy (T3-L3), spina bifida (lumbosacral area), and cervical spondylomyelopathy (C5-C7). Knowledge of these predilection sites can aid in choosing appropriate diagnostic tests to perform.
- As discussed above, spinal hyperpathia usually suggests an extramedullary lesion while absence of hyperpathia suggests an intramedullary lesion. This information may influence choice of imaging modality (magnetic resonance imaging [MRI] versus myelography).

Minimum Database

- Establishing a minimum database (MDB) is essential for assessment of the animal's overall health prior to general anesthesia for neurologic testing. The MDB also aids in ruling out systemic inflammatory, metabolic, and endocrine disorders that may be contributing to the neurologic state.

▼ ***Key Point*** The MDB for neurologic patients consists of a complete physical examination (including neurologic, otic, and ophthalmic evaluation), complete blood count (CBC), serum biochemical analysis, urinalysis, fecal analysis, thyroid panel (T4, free T4, thyroid-stimulating hormone) and electrocardiogram. Routinely test for heartworm in endemic areas.

Specialized Laboratory Examinations

- Specialized tests may be indicated, based on physical examination findings and/or MDB results.
- Examples include endocrine function tests, fine-needle aspiration cytology of enlarged lymph nodes, tests for infectious diseases (e.g., feline leukemia, feline immunodeficiency, feline infectious peritonitis, canine distemper, toxoplasmosis, neosporosis, rickettsial disease, and fungal infections; see appropriate chapters in Section 2, Infectious Diseases).
- Urine and blood cultures are recommended if discospondylitis is present.

Electrodiagnostic Tests

- Electrodiagnostic tests useful in the diagnosis of spinal cord disease include electromyography (EMG), motor and sensory nerve conduction velocity studies (MNCV and SNCV, respectively), dorsal and ventral nerve root studies (cord dorsum potentials [CDPs] and F waves, respectively), spinal cord evoked potentials (SCEPs), and somatosensory evoked potentials (SSEPs). These evaluations generally require specialized equipment and referral to a veterinary neurologist.
- Epaxial and limb EMG is useful for localizing areas of denervation secondary to a lower motor neuron lesion (see Chapter 125).
- MNCV and SNCV studies of peripheral nerves, and nerve root evaluation (CDPs and F waves), help to rule out peripheral nerve, nerve root, and muscle diseases that present with many of the same clinical signs as spinal cord disease (see Chapters 129 and 130 for discussion of peripheral nerve and muscle disorders, respectively).
- SCEPs and SSEPs evaluate the integrity of the ascending spinal cord tracts to determine the extent of functional damage.

Imaging Techniques

Plain Spinal Radiography

- Plain radiography is often sufficient to diagnose problems such as atlantoaxial subluxation, vertebral fracture/luxation, vertebral neoplasia, vertebral anomalies such as spina bifida and hemivertebrae, and discospondylitis.
- Discospondylitis is characterized by lytic, irregular end plates with sclerosis of adjacent vertebral bone. Avoid causing further injury to the animal during these procedures.
- Refer to Chapter 4 for positioning and technique.
- When plain radiographs are inconclusive, use specialized procedures.

Myelography

- Myelography remains a useful diagnostic procedure in small animals (see Chapter 4).

- Disadvantages compared to MRI include greater invasiveness (intrathecal contrast injection), longer anesthetic times, lack of imaging of intramedullary lesions, and inability to image in the axial plane.
- Myelography has certain advantages for imaging extradural lesions, especially those involving bony structures or those that may dynamically compress the spinal cord. Post-myelogram computed tomography allows excellent imaging of the axial spinal canal and bony structures and provides accurate information concerning localization of lateralized lesions.
- Myelography is contraindicated in the presence of CNS inflammation (encephalitis, myelitis, meningitis) or if increased intracranial pressure is suspected.

Magnetic Resonance Imaging (MRI)

- MRI is a very useful and effective technique to image the spinal cord (see Chapter 4).
- MRI provides excellent soft tissue resolution and is the imaging modality of choice for characterizing intramedullary spinal cord lesions, nerve sheath tumors, and lumbosacral spondylopathy in the German shepherd.
- MRI has increased our awareness of the prevalence of syringohydromyelia in certain breeds. It also provides imaging in the sagittal, axial, and horizontal planes for improved lesion localization.

Computed Tomography (CT)

- If the goal is to evaluate a suspected bony lesion, CT is the preferred imaging modality (see Chapter 4).

Cerebrospinal Fluid (CSF) Analysis

▼ ***Key Point*** CSF analysis is the test of choice for establishing an inflammatory cause of spinal cord disease; furthermore, it provides nonspecific information that is helpful in the diagnosis of degenerative, neoplastic, and vascular conditions, including the following:

- Degenerative, neoplastic, and occasionally vascular problems may cause increased protein levels in the presence of normal cell counts in CSF.
- Inflammatory conditions of the spinal cord cause increases in CSF protein and variable increases in cell numbers and type, depending on the specific etiologic agent causing the insult.
- Sterile suppurative or steroid responsive meningitis is characterized by a predominance of neutrophils in CSF.
- GME is characterized by increased numbers of lymphocytes, monocytes, and macrophages in CSF.
- Etiologic agents (e.g., bacteria, rickettsiae, protozoa, fungi) are sometimes identified in CSF by culture (bacteria) or cytology.
- Comparative titers on simultaneously collected CSF and serum are also helpful for identifying active CNS infection by canine distemper virus and toxoplasmosis.
- Neoplastic cells are rarely seen in the CSF of patients with CNS neoplasia. However, globoid cells may be identified in cases of globoid cell leukodystrophy.
- For further details concerning CSF collection technique and abnormalities in specific infectious and inflammatory conditions of the CNS, see Chapters 125 and 126.

TREATMENT

The management of spinal cord disorders depends on the etiology and the severity of the spinal cord injury. Medical treatment, surgery, radiation therapy, or a combination of these treatment modalities may be indicated.

Medical Therapy

Degenerative Disorders

- Glucocorticosteroids at anti-inflammatory doses are recommended for degenerative conditions that cause secondary compression of the spinal cord. These disorders include cervical spondylomyelopathy, type II intervertebral disc disease, and lumbosacral spondylopathy. In each of these disorders, avoid long-term corticosteroid therapy. Surgical intervention is usually indicated due to the progressive nature of these conditions.
- For most of the neurodegenerative diseases, no specific therapy is available and only supportive treatment can be provided. Various treatments have been attempted in degenerative myelopathy, all without proven effect. Bone marrow transplantation has shown some efficacy is some lysosomal storage diseases (see Chapter 126).

Spinal Cord Trauma

- Medical therapy to combat the effects of acute spinal cord trauma (e.g., edema, ischemia) is based on the use of glucocorticosteroids.

Glucocorticosteroids

- Best results in spinal cord trauma are obtained when large doses of corticosteroids are administered immediately after injury, followed by rapid dosage tapering.
- Base the total dosage and tapering of dosage on the patient's response to therapy. Evaluate the patient's neurologic function at least every 8 hours to determine if another dose is necessary.
- The maximum amount of time that glucocorticosteroids are beneficial following spinal cord injury

appears to be 2 to 3 days; longer administration is of little benefit and enhances the likelihood of gastric ulcers, gastroenteritis, and pancreatitis. Use a concurrent H_2-blocker and sucralfate therapy to reduce the potential for gastric ulceration (see Chapter 67 for dosages).

▼ ***Key Point*** The most beneficial glucocorticosteroid for acute spinal cord trauma, including that from acute intervertebral disc herniation, is methylprednisolone sodium succinate (MPSS or Solu-Medrol, Upjohn).

- In experimental studies, MPSS administered intravenously during the first 8 hours following injury has shown remarkable sparing action on the spinal cord compared with dexamethasone, mannitol, dimethyl sulfoxide (DMSO), naloxone, and thyrotropin-releasing hormone.
  - Give an initial dose of 30 mg/kg IV followed by dosages of 15 mg/kg IV at 2 hours and then every 6 hours for a minimum of 24 hours. Alternatively, give the initial 30 mg/kg dose followed by a continuous infusion of 5.4 mg/kg/hr IV for 24 to 48 hours. The above protocols have been shown to be effective in human and experimental animal models of spinal cord injury if provided within 1 to 6 hours of the injury. Controlled clinical trials in veterinary medicine have not been performed.
- If additional glucocorticosteroid therapy is necessary, substitute with dexamethasone, prednisolone, or prednisone.

Hyperosmotic Solutions

- Hyperosmotic solutions, such as mannitol, have been widely used to combat post-traumatic brain edema, but their use in cases of spinal cord trauma is ineffective.

Other Drugs

- Other investigated drugs for adjunctive therapy of spinal cord trauma, such as antioxidants, calcium channel blockers, and vasodilators, are not routinely recommended at this time.

Infection

Antimicrobial Drugs

- Antimicrobial drugs may be indicated if specific infectious agents are identified or suspected. Treatment of systemic mycoses, protozoal, and rickettsial infections are discussed in detail in Chapters 20, 21, and 17, respectively. Also, see Chapter 126 for treatment of CNS infections.

Spinal Meningitis and Myelitis

- In cases of meningitis or myelitis, select antimicrobials that are known to cross the blood-brain barrier readily (i.e., highly lipid soluble in the non-ionized state, such as trimethoprim-sulfonamide combinations, rifampin, metronidazole, chloramphenicol, and certain imidazoles such as fluconazole).
- Drugs with intermediate penetrating abilities in the normal CNS may have improved penetrating abilities when the CNS is inflamed. These include the penicillin family (e.g., amoxicillin, carbenicillin), quinolones (e.g., enrofloxacin), the newer-generation tetracyclines (e.g., doxycycline, minocycline), clindamycin, and certain cephalosporins.
- Avoid drugs that penetrate poorly such as the aminoglycosides, amphotericin B, and ketoconazole.

Discospondylitis

- Treatment of discospondylitis presents a unique challenge because of the difficulty of presenting sufficient antimicrobial concentrations to the affected disc space and vertebral bodies.
- *Staphylococcus* is the organism most frequently reported. *Brucella canis, Nocardia, Streptococcus canis, Corynebacterium diphtheroides,* and various fungi also have been isolated.
- If possible, base selection of antimicrobial drugs on positive culture results (blood, urine, or the affected disc space) or a positive *Brucella* agglutination test. Otherwise, assume that the causative organism is coagulase-positive *Staphylococcus* and administer beta-lactamase–resistant antibiotics that reach sufficient therapeutic levels in bone and purulent exudates.
- Clinical signs may improve within a few days, but long-term therapy of several months is usually required to prevent relapses.
- In some cases, antimicrobials alone are not effective, and surgical intervention is required. When surgery is required, remove the infected vertebral end plates and associated disc structures. Use a vertebral body bone plate to stabilize the area and fill in the defect with cancellous bone. (See Chapter 100 for more information on spinal surgery.) Administer intralesional antibiotics.

Immune-Mediated Disorders

- Both GME and immune-mediated meningitis syndromes are treated via immunosuppression. Initially give prednisone (1.0–2.0 mg/kg q12h) and consider using it in combination with other immunosuppressive agents (cytosine arabinoside, azathioprine, procarbazine, lomustine). With combination therapy, the prednisone dosage often can be decreased to once daily or every other day therapy. In some dogs, prednisone therapy can be eliminated over time.

- Radiation therapy has been shown to have a beneficial effect on encephalitis caused by GME.

Toxicities

Tetanus

- For tetanus, initially administer penicillin G (20,000–100,000 IU/kg q6–12h IV or IM). Tetracycline (22 mg/kg q8h PO or IV) is recommended as an alternative because of the variable effect of penicillins on vegetative forms of the organism. Metronidazole (dog, 15 mg/kg q8h PO; cat, 250 mg total, q12–24h, PO) has shown excellent efficacy. It is bactericidal against most anaerobes and reaches effective levels in necrotic tissues.
- Equine tetanus antitoxin (100–1000 IU/kg IV, usually administered only once) may combat the neurotoxin if given early enough. However, anaphylactic reactions are common, necessitating an initial test dose (0.1–0.2 ml) given SC or intradermally (ID) 15 to 30 minutes prior to IV dosing.
- Chlorpromazine (0.5–2.0 mg/kg q8–12h, given IM, IV, or PO) is effective against the hyperexcitability sometimes observed.
- Diazepam (dog, 5–10 mg total, q2–4h, given PO, IV, or IM; cat, 2.5–5 mg total, q2–4h, PO) blocks the effect of the toxin on the spinal cord but has a very short duration of action.
- Barbiturates also may be used to combat the tetany. Phenobarbital (16–18 mg/kg, IV) can be given to immediately control seizure activity and generalized body stiffness, followed by oral maintenance therapy (2–4 mg/kg q12h PO). Pentobarbital therapy may be needed if muscle spasms are severe and nonresponsive to diazepam, methocarbamol, and phenobarbital therapy.

Strychnine

- For strychnine intoxication, chlorpromazine, diazepam, and barbiturates are used as for tetanus above. In order to block further gastrointestinal absorption, perform gastric lavage followed by oral administration of binding agents, such as activated charcoal.

Neoplasia

- Most antineoplastic drugs do not cross the blood-brain and blood-CSF barrier.
- Lomustine does penetrate CNS tissues and, in conjunction with prednisone, can be useful for treatment of CNS lymphoma. Cytosine arabinoside penetrates into the CNS when given intravenously at high concentrations (up to 400 mg/m^2). Use of cytosine arabinoside at induction followed by long-term lomustine therapy can be used in conjunction with traditional chemotherapy protocols for multicentric lymphoma with CNS involvement (see Chapter 27).
- Lomustine and glucocorticoid therapy can also be used effectively for malignant histiocytosis in the CNS.
- Radiation therapy has been beneficial in the treatment of some types of neoplasia. Remission times of 1 to 2 years for tumors such as meningiomas, nerve sheath tumors, and lymphoma must be weighed against the significant risk of radiation-induced spinal cord injury.

Surgical Treatment

Principles

- The primary goals of neurosurgical intervention are to decompress the spinal cord and nerve roots and to stabilize the vertebral column. Surgical intervention is most frequently effective in cases of compressive extramedullary spinal cord disease such as intervertebral disc herniation. It is possible to debulk some intramedullary tumors, but surgery has no application in the majority of intramedullary diseases (i.e., degenerative, anomalous, and infectious disorders; traumatic lacerations; vascular accidents).

Criteria for Surgery

- The decision for neurosurgical intervention is based on the historical progression of spinal cord signs, the localization and extent of neurologic deficits, and the likelihood that decompression and/or stabilization will be effective for the disorder diagnosed.

Timing of Surgery

- When indicated, surgical intervention is most valuable in the early stages of a problem, especially in acute compressive conditions such as acute type I disc herniation in which the functional outcome often parallels the speed with which surgical decompression is performed.
- Prompt surgical decompression for acute compressive lesions is indicated if neurologic deficits are progressive over 24 hours or if the patient is plegic or has lost deep pain. See "Prognosis" (next page) for prognostic indicators of outcome.
- In chronic progressive conditions, such as caudal cervical spondylomyelopathy and type II intervertebral disc disease, surgery performed in the early stages of disease is far more rewarding than surgery performed after significant dysfunction has been allowed to develop. Chronic compression causes irreversible damage to the spinal cord that surgery cannot correct and may even worsen by decompensating a chronically compensated condition.

▼ ***Key Point*** When recommending spinal cord surgery for a paralyzed animal, warn the owner that

extensive postoperative physiotherapy and nursing care may be necessary.

Surgical Techniques

- Cervical cord decompression for disc herniation usually is performed via a ventral slot procedure (through the vertebral body). Dorsal decompression of the cervical cord is used less frequently for cases of stenosis, malformation, malarticulation, dorsal ligamentous hypertrophy, and lateralized disc extrusion.
- Surgical decompression of the thoracolumbar or lumbosacral spinal cord usually is performed via hemilaminectomy, foramenotomy, or dorsal laminectomy, depending on the site of the lesion.
- Disc fenestration is routinely performed by some neurosurgeons as a prophylactic procedure to prevent recurrence of disc herniation. Disc fenestration does not decompress the spinal cord.
- For COMS, a subtotal occipital craniectomy with durotomy decompresses the foramen magnum and has been shown to improve CSF flow in humans.
- See Chapter 100 for details on treatment of spinal fractures and luxation.
- Spinal cord surgery requires advanced skills and equipment, and can cause significant harm to the animal if improperly performed. Refer the patient to a surgical specialist.

Physiotherapy and Nursing Care

▼ ***Key Point*** Regardless of the nature of the spinal cord disorder, physiotherapy and good nursing care are extremely important to avoid secondary problems and to hasten return to a functional state.

Physiotherapy (also see Chapter 95)

- Thermal applications—cold and hot packs
- Soft tissue mobilization—muscle massage
- Joint mobilization—limb manipulations
- Functional exercise training—towel walking, sit-to-stand
- Electrical stimulation of muscles
- Hydrotherapy—swimming

Nursing Care

- Perform frequent evacuation of the bladder (q4–6h) to prevent urinary tract infections and secondary bladder dyssynergia.
- Use clean padded bedding or pet waterbed to prevent decubital ulceration.
- Give daily baths to prevent secondary dermatitis.

PROGNOSIS

- In general, the more severe the neurologic deficits, the more guarded the prognosis.
- As discussed under Clinical Signs, severe clinical signs of compressive spinal cord lesions include plegia and loss of deep pain. Loss of deep pain for greater than 24 hours indicates a poor prognosis for recovery of normal function. If deep pain is still present and surgery is done immediately, the prognosis is fair to good.

▼ ***Key Point*** Accurately assess for deep pain sensation prior to recommending surgery on paralyzed animals. The animal must exhibit conscious perception of pain, not just a withdrawal reflex.

Based on Clinical Signs

- The presence of conscious proprioceptive deficits and sensory ataxia only in animals with non-neoplastic extramedullary compression is a favorable prognostic sign because it indicates compression affecting only the proprioceptive fibers.
- In general, the longer the duration of spinal cord injury, the more guarded the prognosis. The spinal cord undergoes irreversible degenerative changes if compressed or inflamed for a long period of time.

Based on Etiology

Anomalies

- Anomalous conditions usually have a nonprogressive course and thus their prognosis depends on the extent of spinal cord injury.
- Anomalous conditions that either decompensate after minor trauma (atlantoaxial subluxation) or gradually worsen over time (COMS) may benefit from surgical decompressive procedures.

Degenerative Disorders

- Neurodegenerative conditions often progress to severe disability and have a guarded to poor prognosis.

Trauma

Intervertebral Disc Disease

- The prognosis for intervertebral disc disease and trauma will depend on the conditions outlined above for compressive lesions.
- In general, extramedullary compressive lesions have a better prognosis than intramedullary destructive lesions.

Spinal Fractures

- In an animal with spinal fractures, if radiographs indicate severe vertebral displacement, it is likely that the neurologic deficit is irreversible; therefore, advise the owner that surgical intervention probably will not be beneficial. However, in cases in which MRI, or other imaging modalities, indicates that the spinal cord

may be intact, a significant percentage will improve if surgery, combined with aggressive medical therapy, is performed within a few hours of injury.

Infection

- Infectious myelitis has a guarded prognosis unless a specific causative agent can be identified and/or response to antimicrobial therapy occurs. Spinal cord infections for which no treatments are available (canine distemper, rabies, and feline infectious peritonitis) have a poor prognosis.
- Discospondylitis has a fair to good prognosis if antimicrobial therapy is instituted before the onset of paresis or more severe neurologic deficits. If plegia is present, the prognosis is poor.

Meningitis and Myelitis

- Immune-mediated meningitis generally has a good prognosis with appropriate immunosuppressive therapy.
- Myelitis due to GME has a guarded prognosis, especially if immunosuppressive therapy is not started promptly. GME can progress rapidly resulting in irreversible cord damage. GME is treatable but is rarely curable. Remission times will vary depending on the severity of the CNS involvement (see Chapter 126).

Vascular Disorder

- The prognosis for fibrocartilagenous embolic myelopathy will depend on the severity of the neurologic deficit (see preceding page). For any vascular disorder of the spinal cord, it is advisable to monitor affected animals for at least 48 hours for signs of improvement. Early signs of recovery may change the long-term prognosis.

Neoplasia

- The prognosis for intramedullary tumors is usually poor because surgical removal is not possible and radiation therapy is often not effective. Glucocorticosteroids may slow progression but do not effect a cure.
- The prognosis for extramedullary nerve sheath tumors is variable depending on their location and extent of involvement. The prognosis is poor when multiple nerve roots are involved, but can be good if only one nerve root is involved and surgical removal can be performed. Radiation therapy can increase remission times for nerve sheath tumors. Even in these cases, however, the tumor will eventually regrow and invade the spinal cord.
- *Extramedullary meningiomas* can often be surgically debulked. They are also radiation sensitive. Survival times with combined therapy may be as long as 2 years.
- *Extradural lymphoma* can be treated with chemotherapy and/or radiation therapy but recurrence usually occurs within 1 year.
- *Vertebral osteosarcomas* are difficult to resect and often result in pathologic fractures (see Chapter 101). Multiple myeloma is chemotherapy responsive and has a fair to good prognosis if therapy is instituted before bony destruction has become severe.

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Chapter

129 Peripheral Nerve Disorders

Linda G. Shell*

ANATOMY AND PHYSIOLOGY

The peripheral nervous system (PNS) is composed of 12 pairs of cranial nerves (see Chapters 125 and 126) and 36 pairs of spinal nerves that arise from the spinal cord. Spinal nerve fibers give rise to the peripheral nerves, which usually are composed of both sensory and motor fibers. Sensory nerve fibers are activated by peripheral receptors (Fig. 129-1). Impulses are transmitted up the peripheral nerve to the spinal cord. Some disorders affect only the sensory nerve fibers or ganglia, causing clinical signs such as hyperesthesia and analgesia, proprioceptive deficits, and self-mutilation (Table 129-1). In many cases sensory losses may be difficult to detect.

Motor or efferent nerve fibers arise from nerve cell bodies in the gray matter of the spinal cord. They carry information from the central nervous system (CNS) to the striated muscles (see Fig. 129-1). Motor deficits, characterized by limb weakness, muscle atrophy, and reduced spinal reflexes, occur with injury to any of the following: lower motor neuron in the gray matter of the spinal cord, ventral nerve root, spinal nerve, peripheral motor nerves, neuromuscular junction, and muscle (see Fig. 129-1). Disorders of the neuromuscular junction and muscle are discussed in Chapter 130.

Neuropathy is a general term denoting pathologic changes and/or functional disturbances in the PNS. *Polyneuropathy* refers to involvement of several nerves, usually resulting in bilaterally symmetrical signs.

CLINICAL SIGNS

Motor nerve disorders generally cause weakness and muscle atrophy. Sensory nerve disorders cause hyperesthesia or anesthesia, self-mutilation, and other abnormalities (see Table 129-1). The clinical signs of motor nerve disorders are similar to those of muscle disorders and can be distinguished using muscle enzyme determinations and muscle and nerve biopsies (see Chapter 130).

▼ ***Key Point*** Many common peripheral nerve disorders are manifested as one of the following clinical problems: acute flaccid tetraplegia, chronic progressive tetraparesis, monoparesis or monoplegia, and sensory disturbances (Table 129-2).

PRINCIPLES OF DIAGNOSIS

History and Physical Examination

- The *history* allows classification of the disease process as acute or chronic and progressive or nonprogressive.
- Perform a careful *physical examination* to detect signs of involvement of other systems (e.g., endocrine disorders) that may influence the peripheral nerves.
- Perform a *neurologic examination* (see Chapter 125) to localize the process to the PNS if reduced muscle mass and tone and reduced spinal reflexes are found on the physical examination.

Laboratory Evaluation

- Initial studies usually consist of a hemogram, blood chemistry profile, and urinalysis to evaluate for metabolic, endocrine, and neoplastic disorders.
- Elevated serum concentrations of muscle enzymes (creatine kinase, aldolase, lactate dehydrogenase [LDH], and aspartate aminotransferase [AST]) suggest a muscle disorder.
- Low cholinesterase levels in whole blood or serum may indicate exposure to organophosphates.
- Blood and tissue samples can be analyzed for heavy metal levels.
- Thoracic radiographs are often indicated in neuropathic disorders to evaluate for evidence of megaesophagus. If a paraneoplastic neuropathy is suspected, thoracic radiographs and abdominal ultrasound are indicated to screen for neoplastic disease.

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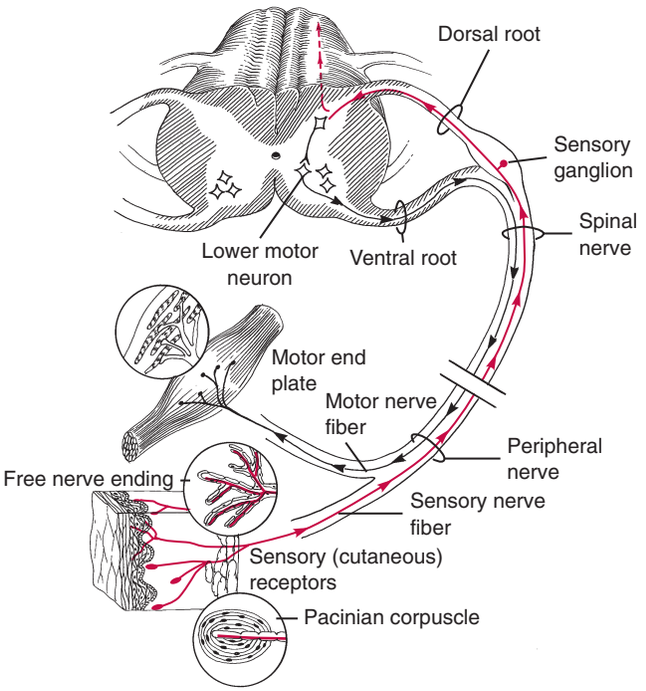

Figure 129-1 Impulse pathways in peripheral and spinal nerves.

Table 129-1. CLINICAL SIGNS OF MOTOR AND SENSORY NERVE DEFICITS

Motor Nerve Deficits	*Sensory Nerve Deficits*
Weakness/paralysis	Hyperesthesia/anesthesia
Muscle atrophy	Self-mutilation
Reduced reflexes	Loss of proprioception
Reduced muscle tone	Dysmetria
	Reduced reflexes

Table 129-2. DIFFERENTIAL DIAGNOSIS BASED ON CLINICAL SIGNS OF NEUROPATHY

Problem	Differential Diagnosis
Monoparesis or Monoplegia	
Acute onset	Trauma to nerve root or peripheral nerve
	Fibrocartilaginous infarct
	Intervertebral disc herniation to lateral side
Chronic onset	Tumor of nerve root or peripheral nerve
	Intervertebral disc herniation to lateral side
	Joint disease
Acute Flaccid Tetraplegia	
	Acute polyradiculoneuritis (coonhound paralysis)
	Tick paralysis (see Chapter 130)
	Botulism (see Chapter 130)
	Myasthenia gravis crisis (see Chapter 130)
	Post-vaccinal polyneuropathy
	Acute idiopathic polyneuropathy
	Protozoal neuritis/myositis
Chronic Progressive Tetraparesis	
Immature	Globoid cell leukodystrophy
	Giant axonal neuropathy (German shepherds)
	Progressive axonopathy (boxers)
	Hypertrophic neuropathy (Tibetan mastiffs)
	Motor neuron diseases (Brittany spaniels, pointers, rottweilers)
Mature	Chronic relapsing polyradiculoneuritis
	Distal denervating disease
	Distal polyneuropathy (Doberman pinschers)
	Distal symmetrical polyneuropathy
	Metabolic neuropathy
	Neoplastic and paraneoplastic neuropathy
	Toxic neuropathy
	Nutritional neuropathy
	Various myopathies
Sensory Disturbances	
Immature	Acral mutilation in pointers
	Sensory neuropathy (longhaired dachshunds)
Mature	Sensory neuropathy (ganglioradiculoneuritis)

Electrodiagnostics

- Use *needle electromyography (EMG) studies* to record electrical activity in skeletal muscle (see Chapter 125).
  - Needle EMG studies are used to confirm the presence and distribution of peripheral nerve and muscle disorders and can be performed on a cooperative awake patient or an anesthetized patient.
  - Spontaneous abnormal activity, such as fibrillations and positive sharp waves (denervation potentials), are found in many neuropathies.
- Use *nerve stimulation studies* to determine the location and nature of peripheral nerve abnormalities (see Chapter 125).
  - Reduction of the conduction velocity or a change in amplitude, duration, or waveform of the evoked action potential suggests pathologic conditions.
  - Nerve conduction studies are recorded using specialized electrodiagnostic equipment (usually by a specialist at a referral center) under general anesthesia. Both motor and sensory nerves can be evaluated.

Muscle and Nerve Biopsy

- *Muscle biopsy* specimens not only distinguish different muscle disorders but can also differentiate nerve from muscle disorders if histochemical staining is used (see Chapter 130).
- Sensory and motor nerve biopsies involve removing a fascicle of the nerve several centimeters in length, leaving the rest of the nerve intact. Because special handling and processing are required, these biopsies are probably best performed by a specialist at a referral center.

Cerebrospinal Fluid Analysis

- Spinal fluid analysis occasionally is beneficial in diagnosis of disorders of the nerve roots such as acute polyradiculoneuritis and protozoal diseases.

PRINCIPLES OF TREATMENT

▼ ***Key Point*** The key to treatment is to find the cause. Unfortunately, a specific cause of many of the acquired peripheral neuropathies may not be obvious even after extensive diagnostic evaluation.

Treatment often must rely on supportive care. In all peripheral nerve disorders that cause decreased mobility and muscle wasting, the following measures are important:

- Use waterbeds or heavily padded surfaces for bedding, to prevent decubital ulcer formation.
- Flex and extend the joints several times a day to prevent tendon and muscle contraction (see Chapter 95 on physical therapy).
- Maintain proper nutritional intake.
- Ensure frequent and complete urinary bladder evacuation.
- Use corticosteroids only for those neuropathies associated with immune-mediated diseases such as systemic lupus erythematosus.

SPECIFIC PERIPHERAL NERVE DISORDERS

A wide range of disease processes, varying from simple trauma to more complex inherited disorders, can affect the peripheral nerves. For the purpose of this discussion, peripheral nerve disorders are categorized according to their etiology, as anomalous/inherited/congenital, metabolic, nutritional, neoplastic, inflammatory/immunologic, idiopathic, traumatic, and toxic.

Anomalous, Inherited, and Congenital Disorders

Anomalous causes of peripheral nerve disease usually are noticed before 1 year of age. For each of the following anomalies, signalment and clinical signs are keys to a presumptive diagnosis, and thus only additional procedures are described under Diagnosis.

▼ ***Key Point*** Many anomalous causes of neuropathies are breed-specific and are not treatable.

Globoid Cell Leukodystrophy

This storage disease is caused by an inherited (autosomal recessive) deficiency of the enzyme beta-galactocerebrosidase that results in damaged oligodendrocytes and Schwann cells in the CNS and PNS, respectively.

- *Signalment:* West Highland white and Cairn terriers, beagles, poodles, Pomeranians, basset hounds, and cats <1 year of age.
- *Clinical signs:* Pelvic limb ataxia progressing to tetraparesis, hyporeflexia, hypermetria, and head tremors. Nystagmus, blindness, and anorexia may develop prior to death.
- *Diagnosis:* Nerve biopsy demonstrating segmental demyelination, axonal degeneration, and endoneural globoid cell accumulation; biochemical evaluation of beta-galactocerebrosidase enzyme activity in leukocytes, brain, and spinal cord.

Glycogen Storage Disease in Norwegian Forest Cats

This metabolic defect is a deficiency of a glycogen branching enzyme and is believed to be inherited as an autosomal recessive trait.

- *Signalment:* Norwegian Forest cats 5 months of age.
- *Clinical signs:* Hyperthermia, movement associated whole body tremors, muscle atrophy, and ataxia that progresses to tetraparesis with decreased spinal reflexes, cranial nerve signs, seizures, and death.
- *Diagnosis:* Transient elevations in creatine kinase; spontaneous needle EMG activity; decreased amplitude of evoked action potential and normal to slightly reduced motor nerve conduction velocities on nerve stimulation; PAS-positive material in central and peripheral nervous system (as well as multiple organs) that results in neuronal loss and axonal degeneration.

Other Storage Diseases Affecting Peripheral Nerves

- *Niemann-Pick disease* usually presents with cerebral or cerebellar signs in 2- to 5-month-old Siamese cats, but some cats have signs of tetraparesis, reduced spinal reflexes, and hypotonia. Spontaneous needle EMG activity and reduced motor and sensory nerve conduction velocities are present. Peripheral nerves show demyelination and remyelination with vacuolated macrophages surrounding affected nerve fibers.
- *GM_2 gangliosidosis* in dogs and cats usually presents as cerebellar signs, but isolated cases of peripheral nerve signs have been described. Peripheral nerve histopathology shows Wallerian degeneration of peripheral axons and accumulation of lamellar inclusions in Schwann cells.
- *Alpha-L-fucosidosis* is an autosomal recessive storage disease in English springer spaniels that produces behavioral changes and ataxia beginning at 12 to 14 months of age. Signs progress until dogs become incapacitated at around 4 years of age. Spinal reflexes become depressed and peripheral nerves may be palpably thickened. Nerve enlargement is caused by infiltration of foamy macrophages and loose fibroedematous endoneurial tissue.

- *Hyperchylomicronemia* is an inherited disorder of lipoprotein metabolism resulting in fasting hypertriglyceridemia and hyperchylomicronemia and subsequent deposition of excessive lipids around peripheral nerves. Clinical signs are due to compression of nerves from the lipid accumulations and are reversible if plasma triglyceride concentrations can be controlled with diet and drugs. The radial and tibial nerves appear to be most commonly affected.

See Chapter 126 for a discussion of other lysosomal storage diseases affecting the nervous system.

Hyperoxaluria Type 2 in Domestic Shorthaired Cats

This metabolic defect is believed to be inherited as an autosomal recessive trait. While the predominant feature is acute renal failure due to deposition of calcium oxalate in the kidneys, some cats have lower motor neuron weakness due to Wallerian degeneration of peripheral nerves.

- *Signalment:* Domestic shorthaired cats <1 year of age.
- *Clinical signs:* Crouching, cow-hocked stance with weakness, hyporeflexia, and diminished pain perception.
- *Diagnosis:* Chemistry changes compatible with acute renal failure; increased concentrations of oxalate and L-glycerate in urine; axonal swellings with neurofilament accumulations in proximal axons in spinal ventral horn cells, ventral roots, and intramuscular nerves.

Giant Axonal Neuropathy in German Shepherds (Alsatians)

This is an inherited (probably autosomal recessive) neuropathy characterized primarily by distal axonal swellings filled with tightly packed, whorled neurofilaments in the PNS and CNS. Based on the spatial-temporal spread of lesions, it is considered a central peripheral distal dying back neuropathy.

- *Signalment:* German shepherds 1 to 2 years of age.
- *Clinical signs:* Progressive symmetrical paraparesis followed by loss of patellar reflexes, distal muscle atrophy, hypalgesia in the pelvic limbs, fecal incontinence, weak bark, vomiting, regurgitation from megaesophagus, and aspiration pneumonia. Some dogs have a curly coat.
- *Diagnosis:* Spontaneous needle EMG activity in distal muscle groups; decreased amplitude of evoked action potential and reduced motor and sensory nerve conduction velocities on nerve stimulation; giant axonal swellings found on nerve histopathology.

Hypertrophic Neuropathy in Tibetan Mastiffs

This inherited (autosomal recessive trait) chronic demyelinating disease of the PNS is most likely due to an inability of the Schwann cells to form and maintain a myelin sheath during rapid growth periods. Remyelination can occur and some dogs may regain some strength within 4 to 6 weeks but do not usually have normal strength.

- *Signalment:* Tibetan mastiffs 7 to 12 weeks of age.
- *Clinical signs:* Pelvic limb weakness that rapidly progresses to generalized weakness, hyporeflexia, hypotonia, recumbency, and dysphonia. Some dogs may regain the ability to stand but remain weak.
- *Diagnosis:* Occasional spontaneous needle EMG activity that may diminish as the affected dog ages; slowed motor and sensory nerve conduction velocities; Schwann cell proliferation and relatively little axonal degeneration on nerve histopathology.

Progressive Axonopathy of Boxers

Progressive axonopathy is an inherited (probably autosomal recessive) neuropathy characterized by axonal degeneration and demyelination and remyelination in the PNS and CNS. Impaired transport of neurofilaments may be involved in the pathogenesis.

- *Signalment:* Boxer dogs <1 year of age.
- *Clinical signs:* Slowly progressive pelvic limb ataxia with a swaying hypermetric gait; hypotonia; loss of patellar reflex and conscious proprioception; and mild muscle atrophy. Thoracic limb involvement and mild cerebellar signs may occur late in the disease. Signs may stabilize by 12 to 18 months.
- *Diagnosis:* Normal or slightly reduced motor and sensory nerve conduction velocities; small or absent evoked muscle action potential; axonal swellings and degeneration on nerve biopsy and spinal cord histopathology; axonal spheroids with disorganized neurofilaments on brain histopathology.

Acral Mutilation and Nociceptive Loss in Pointers

This is a suspected inherited (probably autosomal recessive) nociceptive defect in English and shorthaired pointers resulting in reduced number of primary sensory neurons and a reduction of myelinated and unmyelinated fibers.

- *Signalment:* Pointers 3 to 4 months to 1 year of age.
- *Clinical signs:* Biting and licking at paws progressing to mutilation of paws and possibly autoamputation; normal gait, posture, and spinal reflexes, with loss of pain sensation in digits of the pelvic limbs.
- *Diagnosis:* Normal EMG activity and sensory and motor nerve conduction velocities; pathologic changes of the primary sensory neurons include degeneration of nerve fibers in the dorsal roots and peripheral nerves and reduced number of cell bodies in spinal ganglia, with the remaining cell bodies appearing smaller than normal.

Sensory Neuropathy in Longhaired Dachshunds

This is a familial disorder (possibly autosomal recessive trait) characterized by degeneration of large and small, myelinated and unmyelinated, sensory and autonomic nerve fibers. A similar neuropathy has been reported in a Jack Russell terrier.

- *Signalment:* Young longhaired dachshunds 2 to 3 months of age.
- *Clinical signs:* Slowly progressive pelvic limb ataxia, urinary and fecal incontinence, loss of conscious proprioception, and decreased pain perception over the entire body; normal patellar reflexes but absent flexor reflexes.
- *Diagnosis:* Reduced sensory nerve conduction and normal motor nerve conduction; normal EMG activity; loss of large myelinated and unmyelinated fibers in sensory nerves on nerve histopathology.

Motor Neuron Diseases in Brittany Spaniels, English Pointers, and Rottweilers

These disorders are characterized by progressive degeneration and eventual loss of the motor neurons in the gray matter of the spinal cord and the motor nuclei of the brain stem. An autosomal dominant mode of inheritance with variable penetrance occurs in Brittany spaniels while an autosomal recessive mode of inheritance is suspected in English pointers.

- *Signalment:* Young Brittany spaniels, pointers, and rottweilers.
- *Clinical signs:* Progressive weakness, muscle atrophy, and hyporeflexia.
  - Megaesophagus and head tremors have been observed in some affected rottweilers while some Brittany spaniels will have respiratory muscle weakness and difficulty prehending and swallowing food.
  - Three variants exist in Brittany spaniels: the accelerated form, with signs at 6 to 8 weeks of age; the intermediate form, with signs at 6 to 12 months of age; and the chronic form, with milder signs at >1 year of age.
- *Diagnosis:* Neuronal chromatolysis and axonal swellings with neurofilament accumulations on histopathology of the spinal cord and brain.

Inherited Axonal Polyneuropathy in Leonberger Dogs

This distal symmetrical polyneuropathy has been documented in a large multigenerational family of Leonberger dogs and is suspected to involve an X-linked inheritance.

- *Signalment:* Leonbergers 1 to 9 years of age.
- *Clinical signs:* Exercise intolerance, weakness, atrophy of distal limb muscles, change in or loss of bark, dyspnea, and hyporeflexia of both spinal and cranial nerves.
- *Diagnosis:* Spontaneous needle EMG activity; slowed motor nerve conduction velocities, loss or marked attenuation of compound muscle action potentials; neurogenic muscle atrophy on muscle biopsy; axonal loss, decreased myelinated fiber density, and smaller-sized axons on nerve histopathology.

Hereditary Polyneuropathy in Alaskan Malamutes

This autosomal recessive disorder was last reported in Norway in 1982 and was characterized by degeneration of myelinated axons in peripheral nerves and nerve roots.

- *Signalment:* Alaskan malamutes 7 to 18 months of age.
- *Clinical signs:* Progressive posterior ataxia, exercise intolerance, megaesophagus, atrophy of shoulder and thigh muscles, and hyporeflexia. The disease is progressive but can be remitting and relapsing.
- *Diagnosis:* Spontaneous EMG activity; slowed motor nerve conduction velocities; axonal degeneration and demyelination on peripheral nerve and nerve root histopathology.

Idiopathic Polyneuropathy in Alaskan Malamutes

This appears to be a familial disorder different than the hereditary polyneuropathy (described above) based on the course and the neuropathology. The disease is progressive and not remitting or relapsing. It may be a type of distal axonopathy.

- *Signalment:* Alaskan malamutes 10 to 18 months of age.
- *Clinical signs:* Progressive paraparesis, exercise intolerance, generalized hyperesthesia, and hyporeflexia. No megaesophagus has been reported.
- *Diagnosis:* Spontaneous EMG activity; slowed motor nerve conduction velocities; reduced amplitude of evoked muscle action potential; axonal degeneration of myelinated and unmyelinated fibers on peripheral nerve histopathology.

Polyneuropathy in Rottweilers

This distal sensorimotor polyneuropathy is suspected to have a genetic etiology.

- *Signalment:* Rottweilers 1 to 4 years of age.
- *Clinical signs:* Paraparesis that progresses to tetraparesis within a year, hyporeflexia, hypotonia, and muscle atrophy most prominent in the distal limb muscles. The disease may be remitting and relapsing and may relapse with corticosteroid treatment.
- *Diagnosis:* Spontaneous EMG activity in distal limb muscles; slowed motor and sensory nerve conduction velocities; axonal degeneration of myelinated and unmyelinated fibers in distal nerve segments on nerve histopathology; demyelination secondary to axonal loss.

Laryngeal Paralysis-Polyneuropathy Complex in Dalmatians

This generalized polyneuropathy is suspected to be inherited in an autosomal recessive manner. The disease is progressive, and affected dogs usually die from aspiration pneumonia within months of beginning clinical signs.

- *Signalment:* Dalmatians 2 to 6 months of age.
- *Clinical signs:* Megaesophagus, generalized weakness, hyporeflexia, hypotonia, muscle atrophy, and weak facial and lingual muscles. Acute respiratory distress due to laryngeal paralysis is a prominent presenting sign.
- *Diagnosis:* Spontaneous EMG activity in distal limb muscles; normal to slowed motor and sensory nerve conduction velocities; axonal degeneration and loss of large- and medium-diameter myelinated fibers in distal nerve segments on nerve histopathology.

Neuropathy in Birman Cats

This is a central peripheral distal axonopathy that is likely of genetic origin.

- *Signalment:* Birman cats 8 to 10 weeks of age.
- *Clinical signs:* Progressive plantigrade gait, pelvic limb ataxia, and hypermetria of limbs.
- *Diagnosis:* Distal loss of myelinated fibers in sciatic nerves and cerebral and cerebellar white matter.

Peripheral Neuropathy in Aged German Shepherds

Three 9-year-old German shepherd littermates raised in different households developed progressive lower motor neuron signs. The pathogenesis is unknown but a genetic basis is suspected.

- *Signalment:* Older German shepherds.
- *Clinical signs:* Paraparesis that progresses to tetraparesis, reduced spinal reflexes, and muscle atrophy.
- *Diagnosis:* Endoneurial fibrosis of peripheral nerves, Wallerian degeneration, secondary demyelination, and regenerating axons on peripheral nerve histopathology.

Hypomyelinating Neuropathy in Golden Retrievers

Two littermates had a marked absence of peripheral nerve myelin resulting in mild weakness of the pelvic limbs. Clinical signs were not progressive and stabilized. The pathogenesis is unknown but an autosomal recessive condition is suspected.

- *Signalment:* Golden retrievers 5 to 7 weeks of age.
- *Clinical signs:* Mild paraparesis, reduced spinal reflexes, and muscle atrophy.
- *Diagnosis*: Rare EMG changes; marked slowing of motor nerve conduction velocities; hypomyelination of peripheral nerves without evidence of demyelination or remyelination or inflammation or degeneration.

Metabolic/Endocrine Disorders

Most metabolic and endocrine disorders do not produce a clinically evident peripheral neuropathy. Diabetes mellitus and hypothyroidism are the most commonly recognized endocrine diseases that may affect peripheral nerves and/or muscles (see Chapter 130 on hyperadrenocorticism-induced myopathy).

▼ ***Key Point*** Evaluate all animals with signs of a chronic neuropathy for an underlying endocrine or metabolic abnormality.

Diabetes Mellitus

Diabetes mellitus can cause both a sensory and motor neuropathy in pelvic and thoracic limbs in cats. Although the exact pathophysiology is not fully understood, an increase of fructose in peripheral nerves without sorbitol accumulation suggests an increase in sorbitol dehydrogenase, which may mean that the pathogenesis involves the flux in the polyol pathway rather than an accumulation of sorbitol.

- *Clinical signs:* The pelvic limbs are more affected than thoracic limbs. Weakness (especially of the pelvic limbs), muscle atrophy, and a plantigrade stance are commonly found.
- *Diagnosis:* Laboratory evidence of diabetes mellitus (see Chapter 34), needle EMG, denervation potentials, decreased motor and sensory nerve conduction velocities, and finding demyelination, Schwann cell injury, and distal axonal loss on nerve histopathology.
- *Treatment:* Weakness usually improves over weeks to months with proper control of the diabetes mellitus (see Chapter 34).

Hypothyroidism

Hypothyroidism (see Chapter 31 for detailed description) occasionally is associated with polyneuropathies, but the pathophysiology is not understood. Most likely there is a relationship between thyroid hormone activities and neuronal metabolism.

- *Clinical signs:* Variable onset and progression of weakness, muscle wasting, normal or reduced spinal reflexes, and cranial nerve disturbances. Facial, vestibulocochlear, and trigeminal nerves are most commonly affected although megaesophagus and laryngeal paralysis have also been reported. Other clinical signs of hypothyroidism, such as obesity, mental depression, and dermatologic lesions, are not always present.
- *Diagnosis:* Needle EMG changes and decreased motor nerve conduction velocities; thyroid function testing (as described in Chapter 31).

- *Treatment*: Replacement hormone therapy can result in gradual improvement in neurologic signs over 1 to 3 months (see Chapter 31).

Nutritional Disorders

Nutritionally induced neuropathies are uncommon in veterinary medicine; however, consider vitamin B deficiency, because of an inadequate diet or impaired intestinal absorption (e.g., malabsorption or small intestinal bacterial overgrowth), especially in idiopathic cases.

Neoplastic Disorders

Neoplasia can affect the peripheral nerves directly via the development of nerve sheath tumors, indirectly by metastasis or compression of nerves from adjacent tumors, and indirectly by having remote or paraneoplastic effects.

Nerve Sheath Tumors

These are the most common primary tumors affecting the PNS. Schwannomas (malignant transformation of Schwann cells) are the most common type; tumors arising from endoneural and epineural fibroblasts (neurofibromas, neurofibrosarcomas) also occur.

- *Signalment:* Mature dogs and cats.
- *Clinical signs:* Signs vary with tumor location. Spinal nerve roots of the brachial plexus are most susceptible. Nerve root tumors at C8 to T2 often cause ipsilateral Horner's syndrome and ipsilateral loss of the cutaneous trunci reflex. Neoplastic cells invade adjacent spinal nerve roots, causing dysfunction of multiple peripheral nerves. Proliferation of neoplastic cells within the spinal canal can result in a compressive myelopathy.

▼ ***Key Point*** Vague lameness progressing to weakness and muscle atrophy of the affected limb is the most common sign of a nerve sheath tumor.

- *Diagnosis:* Needle EMG denervation potentials; histopathology. If spinal nerve roots are involved, survey spinal radiographs may show an enlarged intervertebral foramen or myelography may show an intradural-extramedullary mass. Computed tomography (CT) or magnetic resonance imaging (MRI) scans may identify enlarged or thickened nerve roots or peripheral nerves.
- *Treatment:* Surgical excision of the tumor and/or amputation of the affected limb (see Chapter 116). Recurrence is common. Radiation therapy may delay recurrence by 1 to 2 years.

Lymphoma

Lymphoma is the most common tumor of non-neural origin affecting the PNS. Neoplastic cells can infiltrate nerve and nerve roots and produce signs of a mono- or polyneuropathy.

- *Signalment:* Mature dogs and cats.
- *Clinical signs:* Signs may be very similar to peripheral nerve sheath tumors but there may be more than one limb affected. Signs of multicentric lymphoma are usually present.
- *Diagnosis:* Electrodiagnostic testing and imaging as for peripheral nerve sheath tumors above. Cerebrospinal fluid analysis will often reveal neoplastic lymphocytes due to concurrent involvement of the CNS meningeal layers.
- *Treatment* consists of chemotherapy (see Chapters 27 and 126). Peripheral nerve damage may be permanent.

Paraneoplastic Neuropathies

Cancer patients may have clinical or subclinical neuropathies for which the pathogenesis is poorly understood. An immune-mediated mechanism for the neuropathy is suspected; autoantibodies may be produced against antigens shared by the tumor and the nervous system. Most cases with clinically significant neuropathies have been associated with pancreatic islet cell tumors and hyperinsulinism (see Chapter 35). However, signs of a neuropathy in any middle-aged to older patient could potentially be associated with any neoplasia.

- *Clinical signs:* Weakness (especially in the pelvic limbs), decreased muscle tone, and reduced spinal reflexes.
- *Diagnosis:* Identification of a primary neoplasm and the elimination of other causes. Decreased sensory and motor nerve conduction velocities also may be seen. Demyelination, remyelination, and axonal necrosis and atrophy may be observed on nerve histopathology.
- *Treatment:* Remove the underlying neoplasm if possible. (See Chapter 35 for removal of pancreatic islet cell tumors.)

Inflammatory and Immune-Mediated Disorders

These disorders can affect the neuromuscular junction, peripheral nerves, spinal nerves and roots, and ventral horn cells in the gray matter of the spinal cord.

Protozoal Neuritis/Myositis

Organisms such as *Toxoplasma gondii* and *Neospora caninum* can cause inflammatory and degenerative changes in peripheral nerves and dorsal and ventral nerve roots, as well as muscle. Dogs less than 4 months of age are frequently presented for hindlimb hyperextension, but others may be presented for acute or progressive flaccid weakness. (See Chapter 21 for diagnosis and treatment of protozoal infections.)

Acute Polyradiculoneuritis (Coonhound Paralysis)

This is one of the most common peripheral nerve disorders in dogs. It is characterized by a mild lymphocytic radiculitis with demyelination of the ventral (and occasionally the dorsal) spinal roots and axonal degeneration. Immune-mediated destruction of the myelin is suspected.

- *Signalment:* Adult dogs of any age, breed, or sex; frequently observed in hunting dogs 7 to 14 days after contact with a raccoon; occasionally reported in cats.
- *Clinical signs:* Pelvic limb weakness progressing to hyporeflexic or areflexic tetraparesis or tetraplegia within 1 to 2 days; and rapid muscle atrophy. Voluntary tail movement is often unaffected. Thoracic limb weakness occasionally develops first. Responses to mild pain stimuli often are exaggerated. Some dogs develop facial paralysis, change in bark, and dysphagia. Respiratory muscle paralysis occurs occasionally, requiring the use of mechanical ventilation. Many affected dogs retain voluntary control of urination/defecation.
- *Diagnosis:* Needle EMG denervation potentials; normal or slowed motor nerve conduction velocities; dispersed and low amplitude action potential suggesting demyelination and axonal injury; delayed or absent F waves reflecting ventral nerve root injury; increased spinal fluid protein from lumbar subarachnoid space but not from cisterna magna.

▼ ***Key Point*** Differential diagnoses for coonhound paralysis include botulism, tick paralysis, fulminant myasthenia gravis, and protozoal infection of nerve and muscle.

- *Treatment:* Supportive care: physical therapy (see Chapter 95) and urinary bladder evacuation. Spontaneous remission usually occurs but may take weeks or months and recovery may not be complete. Complications include cystitis, aspiration pneumonia, tendon contracture, decubital ulcers, respiratory paralysis, and death.

Brachial Plexus Neuritis

This is a rare weakness of the thoracic limbs that has been compared to serum neuritis in humans. In one case, a newly instituted horse meat diet was incriminated as the cause of the allergic neuritis. Flexor reflexes in the thoracic limbs are reduced or absent and muscle atrophy is present. Pelvic limb function is normal. Spontaneous recovery may take weeks to 4 months.

Post-vaccinal Polyneuropathy

This disorder is rare and occurs 7 to 10 days after rabies vaccination. Clinical signs are similar in appearance to those of acute polyradiculoneuritis. Spontaneous recovery usually occurs over a period of weeks to months.

Idiopathic Disorders

The causes of many acquired peripheral nerve disorders often are unknown. There are many single case reports but very few series of cases for the majority of these disorders. To consolidate these disorders, they are grouped here according to the predominant site of pathology. Many of the cases described under a single heading actually may have multiple, but as yet unknown, causes.

Idiopathic Neuropathies Affecting the Neuronal Cell Body

Lower Motor Neuron Disease

This progressive disorder is characterized by an acute loss of ventral horn cells within the spinal cord and has been reported in nine dogs in New Zealand.

- *Clinical signs:* Acute onset of paraparesis or tetraparesis progresses over 2 to 4 weeks until euthanasia is performed. Sensory and autonomic functions are preserved.
- *Diagnosis:* The diagnosis is based on spinal cord histopathology.

Sensory Neuropathy Ganglioradiculitis

This has been reported in several adult dogs with progressive ataxia, decreased patellar reflexes, and normal muscle tone and limb strength.

- *Clinical signs:* Variable degrees of facial hypalgesia, dysphagia, and prehension difficulty may occur.
- *Diagnosis:* Few to no needle EMG changes, normal to slightly reduced motor nerve evoked action potentials, and reduced sensory nerve evoked action potentials and conduction velocity are found in affected dogs. Histopathology shows degeneration of sensory neurons within dorsal root and cranial nerve ganglia.

Dysautonomia

Dysautonomia is characterized histopathologically by a loss of neurons in all autonomic ganglia, some cranial nerve ganglia, and occasionally ventral horn cells. It was common in cats in the United Kingdom in the 1980s, but incidence has since declined. Isolated cases have been observed in other countries. A disorder with similar features has been reported in dogs in the United Kingdom and midwestern United States.

- *Clinical signs:* Signs develop over 2 to 3 days and consist of lethargy, anorexia, regurgitation or vomiting, constipation or diarrhea, dysuria, and dysphagia. Mydriasis, megaesophagus, dry mucous membranes, bradycardia, and protrusion of the nictitating membrane are often found on physical examination.

- *Diagnosis:* Electrodiagnostic testing is usually normal except for occasional spontaneous EMG activity. Pupillary pharmacologic testing shows increased sensitivity to direct-acting parasympathomimetics or sympathomimetics.
- *Treatment:* The survival rate in cats is around 25% with prolonged (months to years) and dedicated nursing care. Survival rate in dogs is 10% to 30% after months to a year of very slow recovery.

Idiopathic Neuropathies Affecting the Proximal Axon

Acute Idiopathic Polyneuropathy

- *Clinical signs:* This has been reported in 14 dogs that had an acute onset of generalized flaccid paralysis, similar to that described for acute polyradiculoneuritis (coonhound paralysis) except that there was no known exposure to raccoons or other neurotoxins.
- *Treatment:* Most dogs recovered spontaneously. Those that died had mononuclear inflammation of the nerve roots and extensive peripheral nerve demyelination.

Chronic Relapsing Neuropathy

This generalized neuropathy in both dogs and cats has a remitting and relapsing clinical course.

- *Clinical signs:* Signs consist of an insidious or acute onset of weakness in one or more limbs, muscle atrophy, and hyporeflexia.
- *Diagnosis:* The diagnosis is based on needle EMG changes, reduced motor and sensory nerve conduction velocities, and nerve histopathology showing demyelination and remyelination and variable degrees of mononuclear cell infiltrates in peripheral nerves and nerve roots.
- *Treatment:* Immune-suppressive doses of prednisone may reverse clinical signs and may be necessary for many months.

Idiopathic Neuropathies Affecting the Distal Axon

Distal Denervating Disease

This disorder has been reported in dogs in the United Kingdom.

- *Clinical signs:* Dogs present with variable onset of tetraparesis, loss of bark, diffuse muscle atrophy, and areflexia.
- *Diagnosis:* Spontaneous needle EMG changes, normal to reduced motor nerve velocity, and a small dispersed action potential are compatible with primary axonal loss. Histologically, pathological changes are restricted to the distal motor axon.
- *Treatment:* A majority of dogs recover spontaneously in 1 to 5 months.

Distal Polyneuropathy in Doberman Pinschers (Dancing Doberman Disease)

This is a chronic, progressive distal axonopathy.

- *Clinical signs:* Signs begin with persistent rear limb flexion when the dog is standing. When both rear limbs are affected, the dog may appear to have bicycling motions in the rear legs or a shifting leg lameness. The pelvic limb reflexes may be exaggerated and the gastrocnemius muscles are often atrophied. Age of onset varies between 6 months and 7 years of age. Progression over months to years may produce generalized weakness, muscle atrophy, and proprioceptive deficits.
- *Diagnosis:* Needle EMG may show spontaneous activity; motor and sensory nerve conduction velocities are usually normal. Some dogs have histopathology changes compatible with a primary axonopathy, while others have muscle changes suggesting a form of myotonic myopathy.

Distal Symmetrical Polyneuropathy

This disorder has been reported in adult large-breed dogs.

- *Clinical signs:* Dogs have pelvic limb weakness that progresses to tetraparesis, and atrophy of distal limb and masticatory muscles.
- *Diagnosis:* Spontaneous EMG changes are present. Motor nerve conduction velocities are normal or slightly reduced, while evoked muscle action potentials are small and prolonged, suggesting axonal injury. Muscle and nerve histopathology confirm denervation and distal axonopathy, respectively. No effective treatment has been reported.

Traumatic Injury

Traumatic injuries to peripheral nerves are common causes of monoparesis or monoplegia.

Nerve Injuries

Nerve injury can occur from automobile trauma, intramuscular injections, fractures and repair of fractures, lacerations, and bite wounds. Tables 129-3 and 129-4 list the nerves that can be injured, their site of origin, and the clinical signs associated with each injury. Injuries are commonly classified as neurapraxia, axonotmesis, and neurotmesis.

Neurapraxia

Neurapraxia is a temporary loss of physiologic function without physical disruption of the nerve fibers. It results in weakness with intact pain perception. Motor function usually returns to normal within days to weeks.

Table 129-3. SIGNS OF NERVE INJURY IN THE THORACIC LIMB

Nerve	Origin	Clinical Signs of Dysfunction	Reflexes Affected
Suprascapular	C6–7	No gait changes; pronounced atrophy of supraspinatus and infraspinatus muscles	None
Radial	C6–T1	*Injury proximal to branches that supply triceps muscle:* Unable to support weight; limb collapses; may carry the limb if musculocutaneous nerve is functional; atrophy of triceps muscle *Injury distal to branches that supply triceps muscle:* Can support some weight, but knuckles on dorsum of paw	Reduced to absent triceps and extensor carpi radialis reflexes
Musculocutaneous	C6–C8	Gait may appear stiff and choppy; slight withdrawal and straightening of angle-to-elbow joint	Reduced biceps reflexes
Median and ulnar	C8–T2	Slight carpal extension ("dropped carpus")	Reduced carpal flexion on withdrawal reflex
Axillary	C6–C8	None	Reduced shoulder flexion on withdrawal reflex

Table 129-4. SIGNS OF NERVE INJURY IN THE PELVIC LIMB

Nerve	Origin	Clinical Signs of Dysfunction	Reflexes Affected
Femoral	L4–L6	Unable to support weight; limb collapses or may be carried; short stride; lack of pain perception on medial surface of thigh, stifle, leg, and paw; atrophy of quadriceps muscle	Reduced to absent patellar reflex
Sciatic	L6 to S1–S2	Supports weight on limb but knuckles on dorsum of paw; unable to flex or extend hock; atrophy of biceps femoris, semimembranosus, semitendinosus, cranial tibial, gastrocnemius, and other muscles; lack of pain perception on caudal and lateral sides of leg	Reduced to absent withdrawal reflex
Peroneal	L6–S1	Straightening of hock; knuckles on dorsum of paw and fetlock	Reduced to absent hock flexion on withdrawal reflex
Tibial	L6–S2	Increased flexion to hock ("dropped" hock)	None
Obturator	L4–L6	Abduction of limb on slippery surface	None

Axonotmesis

Axonotmesis is the interruption or severance of axons within a nerve but the supporting connective tissue sheath remains intact. Both motor and sensory deficits can be present. Following disruption of the axons, the distal axonal fragments degenerate. The proximal axonal segment must regrow along the intact connective tissue sheath at the rate of 1 to 3 mm/day or about 1 inch per month. Because the connective tissue sheath is intact, axonal regeneration may result in functional recovery, but this may take weeks to months, depending on the extent and the location of the injury. If the proximal axon segment is more than 12 inches from the muscle it innervates, it is unlikely that it will be able to make anatomic contact with the muscles because the connective tissue sheath shrinks and muscle fibers become fibrotic with time.

Neurotmesis

Neurotmesis is severance of both axons and their connective tissue sheath. Axonal regeneration is hampered because there is no scaffold of connective tissue to guide the direction of growth of the axons. Without surgical intervention to appose the two severed ends of the nerve, it is unlikely that any function will return.

▼ ***Key Point*** The closer the injured nerve is to the muscle it innervates, the better the prognosis.

Nerve Root or Brachial Plexus Avulsions

These avulsions are common sequelae of road traffic accidents or jumping from moving vehicles. It is more common for the nerve roots to be torn or avulsed from the spinal cord than for the brachial plexus to be severed (injured). Occasionally motor nerve roots (ventral nerve roots) are affected and sensory nerve roots (dorsal nerve roots) are spared.

- *Clinical signs:* Sudden onset of a combination of the nerve injuries to the forelimb as described in Table 129-3. Signs of radial nerve injury are almost always present.

Table 129-5. POSSIBLE CAUSES OF TOXIC NEUROPATHY IN HUMANS AND ANIMALS

Chemical Agents	*Heavy Metals*
Organophosphorus compounds	Arsenic
Parathion	Lead
Malathion	Gold
Tri-ortho-cresyl phosphate	Thallium
Di-isopropyl fluorophosphate	Mercury
Acrylamide	*Drugs*
Lindane	Vincristine
Polychlorinated biphenyls	Vinblastine
Carbon tetrachloride	Doxorubicin
Methylbutyl ketone	Chloramphenicol
Zinc pyridinethione	Ampicillin
Carbon disulfide	Erythromycin
N-hexane	Tetracycline
Chlorophenothane	Nitrofurantoin
	Diphenylhydantoin

- Damage to the T1–T3 ventral nerve roots may cause an ipsilateral Horner's syndrome.
- Damage to C8 and T1 nerve roots may result in loss of ipsilateral cutaneous trunci (panniculus) reflex.
- Damage to C5, C6, and C7 nerve roots may cause ipsilateral paralysis of the diaphragm.

- *Diagnosis:* History of trauma and clinical signs of monoparesis, needle EMG denervation potentials 5 days after injury; decreased motor nerve conduction velocity within 3 days of injury.
- *Treatment:*
  - Perform daily physical therapy to prevent tendon and muscle contraction (see Chapter 95).
  - Use a sock, boot, or bandage to prevent abrasions.
  - Regrowth of injured nerves (axonotmesis or neurotmesis) is slow and may take months. Perform monthly examinations.
  - Consider amputation if there is self-mutilation or unacceptable improvement in motor abilities after 6 to 8 months.

Toxic Neuropathies

Toxic neuropathies are diagnosed infrequently; however, the list of agents with the potential to cause neuropathies is quite extensive (Table 129-5). Nitrofurantoin, vincristine, vinblastine, and doxorubicin can have adverse effects on peripheral nerves; however, reports in veterinary literature are scant. Arsenic, lead, and mercury appear to be uncommon causes of neuropathies in animals. Certain organophosphorus compounds can cause a delayed neuropathy in sensitive species usually within 2 to 3 weeks of exposure. With chronic organophosphate toxicity, long, large-diameter axons in the peripheral nerves and the spinal cord undergo distal degeneration ("dying-back"), causing a mixture of lower motor neuron clinical signs (muscle atrophy, weakness, reduced spinal reflexes) and upper motor neuron signs (weakness, exaggerated spinal reflexes).

- *Treatment:* There is no specific treatment for the toxic neuropathies other than stopping or reducing the exposure potential.

▼ ***Key Point*** Suspect toxic causes when there is history of exposure or when there is no other reason for the clinical signs.

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Chapter

130 Disorders of Muscle and Neuromuscular Junction

G. Diane Shelton

Neuromuscular disorders of dogs and cats are disorders of the motor unit. The motor unit is the morphologic and functional unit of skeletal muscle and includes the following:

- Motor neuron, consisting of the cell body and axon extending along a peripheral nerve
- Neuromuscular junction
- Myofibers innervated by the motor neuron

This chapter focuses on disorders of muscle and the neuromuscular junction. Disorders of peripheral nerves are discussed in Chapter 129.

ETIOLOGY

Underlying causes of disorders of muscle and neuromuscular transmission are listed in Table 130-1 and include hereditary or suspected hereditary disorders and acquired disorders with autoimmune, metabolic, endocrine, neoplastic or paraneoplastic, infectious, toxic or drug-induced, and ischemic etiologies.

Hereditary Disorders

Several neuromuscular diseases have a known or suspected genetic basis.

Canine Dystrophin-Deficient Muscular Dystrophy

- Canine X-linked muscular dystrophy has striking phenotypic and genotypic similarities to Duchenne muscular dystrophy (DMD) in humans. While this disorder occurs most commonly in males, females may be affected if a carrier female is bred to an affected male. Although this form of muscular dystrophy has been most extensively studied in the golden retriever, several breeds may be affected, including Irish terriers, Samoyeds, rottweilers, Japanese spitz, and Labrador retrievers. Onset is about 10 to 12 weeks of age. As in humans with DMD, affected dogs lack the Duchenne gene transcript and its protein product, dystrophin.
- Clinical signs include stunted growth, weakness, gait abnormalities, and muscle atrophy, with hypertrophy of selected muscles in some cases.
- Serum creatine kinase (CK) levels are dramatically elevated (>10,000 U/dL compared with normal levels of <100 U/dL).

Feline Dystrophin-Deficient Muscular Dystrophy

- A lethal muscle hypertrophy has been described in young male cats associated with dystrophin deficiency.
- Clinically the cats have generalized skeletal muscle hypertrophy, glossal hypertrophy and dysfunction, and excessive salivation. Progressive hypertrophy of the diaphragmatic muscles may result in occlusion of the esophagus.
- Serum CK levels are dramatically elevated and dystrophin is lacking in skeletal muscle.

Muscular Dystrophy with Merosin (Laminin Alpha-2) Deficiency in Dogs and Cats

- Congenital muscular dystrophies (CMDs) with deficiency of laminin alpha-2 make up a large group of autosomal recessive muscle diseases in humans. Recently, muscular dystrophy associated with absence of laminin alpha-2 was described in a young female Brittany-springer spaniel mixed-breed dog, and in domestic shorthaired, flame point Siamese, and Maine coon cats. Onset is less than 6 months of age.
- Clinical signs may vary from muscle weakness and atrophy to progressive spasticity and contractions.
- The serum CK levels are moderately elevated. Laminin alpha-2 is lacking in skeletal muscle.

Muscular Dystrophy with Sarcoglycan Deficiency

- The limb-girdle muscular dystrophies (LGMDs) make up a diverse group of myopathies in humans. Mutations of sarcoglycans (SGs), which span the muscle membrane, typically cause the most severe forms of LGMD. Recently, SG deficiencies have been

Table 130-1. CAUSES OF NEUROMUSCULAR DISEASES AND BREED PREDISPOSITION

Hereditary Disorders

Canine X-linked Muscular Dystrophy
Golden retriever
Irish terrier
Rottweiler
Several other breeds

Laminin Alpha-2 Deficiency
Domestic shorthaired cat
Flame point Siamese
Maine coon
Brittany spaniel/springer spaniel

Sarcoglycan Deficiency
Chihuahua
Boston terrier
Cocker spaniel

"Central Corelike" Myopathy
Great Dane

Nemaline Rod Myopathy
Domestic shorthaired cat
Border collie

Congenital Myasthenia Gravis
Jack Russell terrier
Springer spaniel
Smooth fox terrier

Familial Canine Dermatomyositis
Collie
Shetland sheepdog

Glycogen Storage Disorders (Glycogenoses)

Acid Maltase Deficiency (Glycogenosis Type II)
Lapland dogs

Branching Enzyme Deficiency (Glycogenosis Type IV)
Norwegian forest cat

Debranching Enzyme Deficiency (Glycogenosis Type III)
German shepherd

Phosphofructokinase Deficiency (Glycogenosis Type VII)
English springer spaniel

Hereditary Myopathy of Labrador Retrievers

Hereditary Myotonia
Chow Chow
Miniature schnauzer

Mitochondrial Myopathy
Clumber spaniel
Sussex spaniel
Old English sheepdog

Hypertonicity Syndromes
Cavalier King Charles spaniel
Springer spaniel
Wheaton terrier
Border terrier

Acquired Disorders

Autoimmune Disorders
Generalized myasthenia gravis
Focal myasthenia gravis
Masticatory muscle myositis
Polymyositis
Extraocular myositis

Metabolic Disorders
Abnormalities of glycogen metabolism
Abnormalities of lipid metabolism and oxidative phosphorylation
Electrolyte alterations
Hyperthermia (malignant and exercise-related)

Endocrine Disorders
Hypothyroidism
Hypoadrenocorticism and hyperadrenocorticism

Neoplastic and Paraneoplastic Infectious Disorders
Toxoplasma gondii
Neospora caninum
Hepatozoon canis
Ehrlichia canis
Feline immunodeficiency virus

Toxic or Drug-Induced Disorders
Tick paralysis
Botulism
Organophosphate toxicity
Drugs affecting neuromuscular transmission

Ischemia

identified in Chihuahua, Boston terrier, and Cocker Spaniel breeds.
- Serum CK levels are markedly elevated, and an absence of SG subunits can be demonstrated within skeletal muscle.

Hereditary Myopathy of Labrador Retrievers

- Although hereditary myopathy of Labrador retrievers (HMLR) is commonly referred to as "type II fiber deficiency" or "muscular dystrophy," the precise underlying abnormality is still unknown. A disorder in young Labrador dogs, clinically indistinguishable from HMLR and termed *centronuclear myopathy*, has recently been described in a French pedigree. Linkage analysis has shown that the gene for the disorder in the French pedigree is localized on canine chromosome 2.
- The mode of inheritance is autosomal recessive.
- Both disorders present clinically with progressive muscle weakness, exercise intolerance, and abnormalities of gait and posture. There is, however, a wide variation in clinical presentations and pathologic findings in HMLR.
- Within muscle biopsy specimens, variable morphologic features have been reported; some biopsies show changes typical of neuropathic disease, whereas others show myopathic changes. The fiber type proportions are also variable. To date, pathologic changes in the spinal cord and peripheral nerves

have not been found, even in cases in which histologic changes within the muscle biopsy suggest an underlying neuropathic disorder.

"Central Core-Like" Myopathy

- Myopathy with pathologic changes in the central region of muscle fibers has been reported in several young Great Danes from the United Kingdom showing clinical signs of progressive exercise intolerance, muscle atrophy, and tremors. Recently, an affected dog was confirmed from North America (Shelton, unpublished), suggesting that this myopathy may be more widespread. Excitement associated with feeding or exercise precipitates episodes of general body tremors and collapse. This condition is not pathologically analogous to the human disorder with this name.
- The precise biochemical defect requires further investigation.

Nemaline Rod Myopathy

- Five related cats were described with an early onset of mild weakness with progression to tremors, reluctance to move, and a crouched, hypermetric gait. Muscle atrophy was progressive. A similar myopathy has been seen in a young Border collie.
- Numerous nemaline rods were present within myofibers.

Familial Canine Dermatomyositis

- Familial canine dermatomyositis is well documented in young collies and less well characterized in Shetland sheepdogs. In collies, the inheritance pattern appears to be autosomal dominant with variable expression.
- Initially there is a variably severe dermatitis on the skin of the face, ears, distal extremities over bony prominences, and tail tip that may be followed by an inflammatory myopathy of the masticatory muscles and muscles distal to the elbow and stifle.
- There is evidence of an immunologic pathogenesis in dermatomyositis, but exact mechanisms are uncertain.

Glycogen Storage Disorders (Glycogenoses)

- Although rare in companion animals, disorders of lysosomal glycogenosis (acid maltase deficiency, an alpha-glucosidase that releases glucose from maltose, oligosaccharides, and glycogen) and non-lysosomal glycogenosis (branching enzyme deficiency, debranching enzyme deficiency, and phosphofructokinase (PFK) deficiency affecting glycogenolysis, glycolysis, or glycogen synthesis) have been described.
- In dogs, clinical presentations for the non-lysosomal glycogenoses are not usually specific to the neuromuscular system since glycolysis plays a relatively minor role in canine muscle energetics.
- In branching and debranching enzyme deficiencies, muscle involvement may be overshadowed by liver dysfunction, hypoglycemia, or cardiomyopathy. In PFK deficiency, chronic hemolytic anemia and episodic stress-related hemolytic crises without overt muscle weakness may predominate.

Myotonia Congenita

- An inherited myotonic myopathy has been described in the chow chow and miniature schnauzer breeds in which clinical signs of difficulty rising after a period of rest, muscle stiffness, and a stilted or bunny-hopping gait are visible when puppies are first able to walk. An autosomal recessive mode of inheritance is suspected in the chow chow and has been confirmed in the miniature schnauzer. A missense mutation in both alleles of the gene encoding the skeletal muscle voltage-dependent chloride channel C1C-1 has been identified in the miniature schnauzer.
- A DNA-based test capable of detecting the mutant allele in affected and carrier miniature schnauzers has been developed and is available at the Josephine Deubler Genetic Disease Testing Laboratory at the University of Pennsylvania (www.vet.upenn.edu/penngen).
- Myotonia congenita has also been described in domestic cats, although the mode of inheritance and the molecular defect have not been determined.

Mitochondrial Myopathy

- Although there has been an explosion of information related to mitochondrial-associated diseases in humans in the past 10 years, only a few case reports are in the veterinary literature regarding this potentially important group of disorders.
- Marked exercise intolerance associated with metabolic acidosis and excessive elevations in lactate and pyruvate support a mitochondrial myopathy. In Clumber and Sussex spaniels, a deficiency of pyruvate dehydrogenase has been described. A similar exertional lactic acidosis has been reported in Old English sheepdog littermates associated with altered cytochrome-*c* oxidase activity and reduced mitochondrial mRNA.
- Given the importance of oxidative metabolism in canine muscle energetics, additional reports of these disorders should be forthcoming.

Hypertonicity Syndromes

- Hypertonicity syndromes (paroxysmal movement disorders) are being identified in several breeds of dogs, including the cavalier King Charles spaniel (CKCS), springer spaniel, Wheaton terrier, and Border terrier. With the exception of the CKCS, these disorders are poorly characterized.

- In the CKCS, clinical signs are apparent between 3 and 7 months of age. Variable periods of exercise or excitement precipitate pelvic and thoracic limb hypertonicity that may result in complete incapacitation.
- Treatment with the benzodiazepine drug clonazepam can result in almost complete remission. Although not completely evaluated, resolution of clinical signs has been anecdotally reported, with the dogs asymptomatic and no longer requiring medication.

Congenital Myasthenia Gravis

A congenital familial form of myasthenia gravis (MG), inherited as an autosomal recessive trait, is described in Jack Russell terriers, springer spaniels, and smooth fox terriers. Failure of neuromuscular transmission results from a deficiency in muscle acetylcholine receptor (AChR) content, but unlike the acquired form of MG, it is not related to autoantibodies to AChR.

Acquired Neuromuscular Disorders

Autoimmune Disorders

Some of the most commonly occurring neuromuscular disorders of dogs are in this group. Included are acquired MG, masticatory muscle myositis (MMM), and polymyositis (PM). Although considered in the hereditary group, dermatomyositis in collies and shelties is also postulated to have an autoimmune basis.

Acquired Myasthenia Gravis

- Acquired MG is common in dogs and occasionally found in cats. Feline MG is associated with an increased incidence of thymoma. Acquired MG probably is the best defined of all the neuromuscular disorders with respect to mechanisms of injury and pathogenesis. It is now well documented that acquired MG is associated with autoantibodies directed against the nicotinic AChRs on the postsynaptic membrane of the neuromuscular junction. As a consequence of autoantibody binding, there is loss of AChRs resulting in impaired neuromuscular transmission and marked muscle weakness. AChR loss is a result of the following:
  - Increased endocytosis due to cross-linking of AChRs by antibody
  - Complement activation leading to focal lysis of the postsynaptic membrane
  - Direct inhibition of AChR function by bound antibodies

Masticatory Muscle Myositis

- MMM is a focal inflammatory myopathy that selectively affects the muscles of mastication. This selective distribution may be attributed to histochemical and biochemical differences between canine masticatory and limb muscles that provide the basis for a selective immune-mediated response.
- Although the role of autoantibodies is not yet determined, autoantibodies against cytoplasmic and sarcolemmal proteins of masticatory muscle type 2M proteins have been demonstrated by immunocytochemical methods both within muscle biopsy sections and indirectly in the serum in cases of MMM. Demonstration of these antibodies is a diagnostic marker for the disease.

Extraocular Muscle Myositis

- Another focal inflammatory myopathy is described in which the cellular infiltration is localized to canine extraocular muscles with lack of involvement of the masticatory and limb muscles.
- An immune-mediated condition is suggested by a marked lymphocytic cellular infiltrate within extraocular muscles and a rapid response to corticosteroid therapy alone. Although the specific immune mechanism is not known for this disorder, myofiber-specific antigens may play a role in the selective involvement of the extraocular muscles.

Polymyositis

- Not as common as MMM, PM is a generalized inflammatory myopathy in which muscle damage is the result of cell-mediated immunity. An association has been reported with systemic lupus erythematosus and with an immune-mediated arthritis/PM complex (see Chapter 24).
- PM also may be associated with malignancies; it has been reported as a paraneoplastic disorder associated with thymoma. Boxer dogs may have an increased incidence of preneoplastic myositis.

Metabolic Disorders

Enzyme Deficiencies

- Although neuromuscular disorders associated with defined enzyme deficiencies have an early onset and are associated with specific breeds, some abnormalities, in particular those associated with oxidative metabolism, may occur later in life. With further understanding, some of these disorders may need to be reclassified as heritable, while others may be the result of environmental influences, toxins, or drugs that affect oxidative pathways.
- Reversible mitochondrial myopathies are well described in the human literature secondary to azidothymidine therapy.
- I have evaluated several cases of lipid storage myopathy in various breeds of dogs having an older age of onset. Canine lipid storage myopathy has been associated with intramyofiber lipid droplets in muscle biopsy samples, elevated lactate and pyruvate, and secondary carnitine deficiency.

Malignant Hyperthermia Syndrome

- Malignant hyperthermia is a clinical syndrome classically characterized by skeletal muscle rigidity, tachypnea, rapid elevation of core body temperature, severe metabolic acidosis, hypercarbia, and cardiac arrhythmias, which invariably leads to death if left untreated.
- Administration of certain anesthetic agents, particularly halothane and quaternary amide muscle-relaxant drugs may induce hyperthermic episodes. Information on this syndrome can be obtained in a review by Brunson and Hogan (2004).

Electrolyte Imbalances

- Alterations in the levels of serum K^+ and Ca^{2+} due to underlying metabolic disorders can affect the excitability of neurons and muscle fibers, resulting in an increase or decrease in membrane excitability and resultant episodes of muscle weakness.
- A condition analogous to hyperkalemic periodic paralysis in humans has been described in a young American Staffordshire terrier.
- Studies in cats have shown that certain diet types (e.g., acidifying diets containing insufficient potassium) and diseases (especially renal disease) are associated with an increased occurrence of hypokalemia and clinically evident weakness that resolves following potassium administration.
- Alterations in the levels of serum phosphate and magnesium may also result in neuromuscular dysfunction, although they are poorly characterized.
- Electrolyte disorders and their therapy are discussed in Chapter 5.

Endocrine Disorders

Myopathies can be associated with endocrine disorders, especially hypothyroidism and glucocorticoid excess. In hypothyroidism (see Chapter 31), peripheral neuropathies and myopathies are reported to occur, whereas myopathy, myotonia, and rarely peripheral neuropathy are associated with hyperadrenocorticism (see Chapter 33). Muscle weakness, probably as a consequence of hyperkalemia, is frequently associated with hypoadrenocorticism (see Chapter 33).

Neoplastic and Paraneoplastic Disorders

- An association between neoplasia and neuromuscular disorders is suspected but not proven.
- Thymoma is sometimes associated with MG and PM. Thymoma may also be diagnosed after the diagnosis of MG is established, and it should be considered if AChR antibody titers remain elevated for long periods. Consider evaluating AChR antibody titers before surgery in all dogs with a suspected thymoma.
- Positive AChR antibody titers and clinical signs of MG have been reported in two cases of canine osteosarcoma and in single cases of cholangiocellular carcinoma and anal sac adenocarcinoma.
- Postulated mechanisms of paraneoplastic-associated muscle damage include the following:
  - Autoantibodies produced against tumor antigens that crossreact with muscle components
  - The release of myotoxic substances by the neoplasm
  - The possibility that the neoplasm and the underlying muscle disorder have a common pathogenesis

Parasitic Disorders

- A study by Evans and colleagues (2004) suggests that parasitic myositis, particularly that associated with the protozoan *Neospora caninum,* may be more common than once thought.
- While infectious agents may occasionally be identified within muscle biopsy specimens, an inflammatory myopathy secondary to an infectious agent should not be ruled out if organisms are not identified (further discussion of protozoa is found in Chapter 21).
- An association between PM and *Ehrlichia canis* infection in dogs has been reported.
- Other parasites, such as *Trichinella spiralis, Sarcocystis,* and *Hammondia,* elicit minimal inflammation and may be found incidentally in muscle biopsies.

Viral Disorders

- Some strains of feline calicivirus are associated with transient myalgia.
- A generalized lymphocytic myositis has been reported in adult cats infected with feline immunodeficiency virus.

Toxic or Drug-Induced Disorders

Neuromuscular blockade may be the result of various neurotoxins.

- Neurotoxins that inhibit the evoked release of acetylcholine (ACh) at the neuromuscular junction are secreted by ticks such as *Dermacentor* and *Ixodes* species, resulting in tick paralysis.
- Ingestion of the exotoxin of *Clostridium botulinum* results in clinical signs of botulism by a similar mechanism.
- Organophosphate insecticides containing long-acting anticholinesterases reversibly or irreversibly bind acetylcholinesterase, permitting continuous cholinergic stimulation with accumulation of ACh at central, muscarinic, and nicotinic cholinergic synapses. Myasthenia-like syndromes are reported with organophosphate intoxication.
- Several drugs have been shown to reduce the safety margin of neuromuscular transmission, including aminoglycoside antibiotics, antiarrhythmic agents, phenothiazines, methoxyflurane, and magnesium

given parenterally or in cathartics. These agents can potentiate neuromuscular blocking agents used during surgical procedures and may worsen or unmask preexisting disorders of neuromuscular transmission.
- PM may occur rarely in association with certain drug therapies. In human medicine, the drug most often implicated has been D-penicillamine. PM can occur as part of a generalized allergic drug reaction in Doberman pinschers following trimethoprim-sulfadiazine administration; however, this has not been confirmed by muscle biopsies or electromyographic studies.
- MG has been documented to occur in hyperthyroid cats on methimazole therapy. The mechanism may be similar to D-penicillamine–induced MG described in humans.

Ischemic Disorders

Ischemia as a result of thromboembolic disease and vascular occlusion is the most common cause of ischemic myopathy and neuromyopathy in dogs and cats. Circulation may be partly or completely compromised; the severity of clinical signs varies with the degree of occlusion.

CLINICAL SIGNS

▼ ***Key Point*** Muscular weakness is the clinical sign common to all neuromuscular disorders. Expression of muscular weakness may be limited to certain muscle groups or may be generalized. The clinical expression of muscular weakness may also vary in severity.

Generalized signs of motor system involvement include the following:

- Gait abnormalities
- Paresis or paralysis
- Exercise-related weakness

Other clinical signs that may occur concurrently with generalized weakness or in the absence of detectable weakness include the following:

- Masticatory dysfunction
- Dysphagia (pharyngeal dysfunction)
- Regurgitation (esophageal dysfunction)
- Dysphonia and dyspnea (laryngeal dysfunction) indicating involvement of selected motor units serving visceral functions

DIAGNOSIS

A thorough history and careful general physical and neurologic examinations are critical to the evaluation of neuromuscular disorders. Perform routine and special diagnostic testing procedures based on the differential diagnosis. Following the examination, it should be possible to tentatively localize the disorder to the motor unit.

History

Evaluate for the following:

- Time course of onset and progression of signs
- Exposure to an outdoor environment, ticks, and other animals
- Exposure to chemical agents
- Recent illnesses and recent medications
- Exposure to different geographic locations

Physical and Neurologic Examinations

Following a careful general physical examination, including a thorough evaluation of the cardiovascular system, perform a complete neurologic evaluation, as described in Chapter 125.

- Weakness (motor sign) is common to all motor unit abnormalities.
- Evaluate muscle strength by observing the animal's gait as it walks and, if necessary, after more strenuous exercise.
- Examine for stiffness of movement, seen in inflammatory myopathies, myotonias, and MG.
- General proprioception and pain sensation are usually intact in the majority of motor unit disorders. Rarely, the presence of ataxia (sensory sign) suggests an underlying neuropathic disorder with involvement of large, myelinated proprioceptive fibers or their cell bodies in sensory ganglia.
- Assess muscle tone and spinal reflexes.
- Note muscle atrophy or swelling.

Because the clinical expression of weakness varies considerably in severity and distribution, perform other tests such as wheelbarrowing, hopping, or hemiwalking.

Clinical signs such as dysphagia, regurgitation, dysphonia, and dyspnea may indicate selective involvement of motor units. These clinical signs may occur in the absence of generalized weakness and may indicate disorders of motor units originating in cranial nerves.

▼ ***Key Point*** Differentiate vomiting from regurgitation because a wrong assessment may lead to an inappropriate diagnosis.

Laboratory Tests

Perform a complete blood count (CBC), serum chemistry profile (including electrolytes and CK), and urinalysis in all cases to evaluate possible underlying metabolic abnormalities. Although not indicated in all instances, other laboratory assays may assist in obtaining a diagnosis.

Serum Creatine Kinase Assay

Serum CK levels are elevated in muscle disorders associated with damage to myofibers and membranes. Although CK is a sensitive indicator of the presence and severity of myonecrosis, it has not been reliable in the diagnosis of inflammation. Modest elevations in CK can occur in neuropathies.

▼ ***Key Point*** An elevation of serum CK is not diagnostic of myositis. Perform a muscle biopsy to confirm the diagnosis.

Resting and Postexercise Plasma Lactate and Pyruvate Assays

Evaluate plasma lactate and pyruvate levels at rest and following 10 minutes of strenuous exercise to diagnose disorders of oxidative metabolism. Perform these evaluations in any animal with exercise intolerance. Collect blood for lactate analysis in sodium fluoride-potassium oxalate tubes (gray top), centrifuge immediately, then separate the plasma. Special handling is required for pyruvate analysis.*

Thyroid and Adrenal Function Tests

Myopathies can occur secondary to disorders of both the thyroid and adrenal gland. Hypothyroidism can occur concurrently with autoimmune neuromuscular disorders such as acquired MG, and an optimal clinical response may rely on the treatment of both disorders.

Antinuclear Antibody Assay

A positive antinuclear antibody (ANA) titer in association with an inflammatory myopathy suggests an underlying systemic autoimmune disorder. A subset of canine patients with MG also has positive ANA titers.

Serologic Tests

- Serum *Toxoplasma gondii* and *Neospora caninum* titers, as described in Chapter 21, may be useful in the evaluation of inflammatory myopathies and peripheral neuropathies caused by protozoa. If found, demonstration of the organism in a muscle biopsy specimen is diagnostic.
- Serum *Ehrlichia* titers may be indicated in dogs, as described in Chapter 17.
- Evaluate cats suspected of feline immunodeficiency virus-associated myopathy with feline immunodeficiency virus serology, as described in Chapter 9.

*Assays are available from the Comparative Neuromuscular Laboratory, Basic Science Building, Room 2095, University of California–San Diego, La Jolla, CA 92093-0709 (telephone: 858-534-1537).

Plasma Cholinesterase Levels

Myasthenia-like syndromes and delayed neuropathies are associated with organophosphate toxicity.

Serum Antibodies against Masticatory Muscle Type 2M Fibers

The demonstration of autoantibodies against masticatory muscle type 2M fibers in fresh-frozen muscle sections by immunocytochemical and enzyme-linked immunosorbent assay methods is useful in the diagnosis of MMM. Direct methods for demonstrating the antibodies bound to myofibers within a muscle biopsy and indirect methods for demonstrating antibodies circulating within the patient's serum are available.*

Serum Antibodies against Nicotinic Acetylcholine Receptors

Demonstration of autoantibodies against muscle AChRs by immunoprecipitation radioimmunoassay is the diagnostic test of choice for acquired MG. This assay is sensitive and specific and demonstrates an immune response specifically against muscle AChRs. It is particularly valuable in cases of focal myasthenia in which muscle weakness is localized to pharyngeal or esophageal musculature in the absence of detectable generalized weakness. Serial serum antibody titers also are important in following clinical response to treatment because there is good correlation between serum titers and response to treatment.*

▼ ***Key Point*** Previous corticosteroid administration can lower serum antibody levels in assays for MMM and MG. Collect serum before corticosteroid therapy.

Edrophonium Chloride Challenge Test

A presumptive diagnosis of generalized MG in dogs and cats may be based on an increase in muscle strength following intravenous (IV) administration of edrophonium chloride (Tensilon, Roche) at a recommended dose of 0.1 to 0.2 mg/kg. The most dramatic response to edrophonium chloride is in MG; however, responses are variable: some patients with MG fail to respond, whereas some patients with other neuromuscular disorders may show a partial improvement in muscle strength.

▼ ***Key Point*** Do not eliminate a diagnosis of MG based on a negative response to edrophonium. Submit serum for AChR antibody titers to confirm the diagnosis.

- Perform an edrophonium challenge test in all cases of confirmed MG for determination of the correct treatment protocol. If there is a good response to edrophonium, there should be a good response to

anticholinesterase therapy. If the response to edrophonium is negative, then corticosteroids may be the treatment of choice.
- In cases of focal MG, if the palpebral reflex is absent or decreased, administration of the edrophonium chloride may result in an improved blink.
- During treatment of generalized MG with anticholinesterase drugs, edrophonium chloride may be useful in differentiating a myasthenic crisis (underdosing) from a cholinergic crisis (overdosing).
- In a myasthenic crisis, rapid improvement usually follows IV administration of edrophonium chloride. In cases of anticholinesterase drug overdose, IV administration of edrophonium chloride either will not improve or will worsen the clinical signs.

Electrodiagnostic Evaluation

- Electrodiagnostic testing is a valuable adjunct to the neurologic examination. It provides the following:
  - Information about the location of a lesion within the motor unit (e.g., axon, neuromuscular junction, or muscle)
  - Information about the distribution and severity of the disease process
  - Guidance to appropriate muscle groups and peripheral nerves for subsequent biopsy

  Electrodiagnostic testing includes the following:

  - Evaluation of muscles by electromyography
  - Evaluation of peripheral nerves by measurement of motor and sensory nerve conduction velocities and compound muscle and nerve action potentials (see Chapters 125 and 129)
- Measurement of evoked potentials following repetitive nerve stimulation is useful in the diagnosis of disorders of neuromuscular transmission if performed appropriately. In normal dogs, stimulus rates greater than 5 stimuli/second may result in decremental responses. Use of stimulus rates greater than 5 stimuli/second is not recommended because it can result in an inaccurate diagnosis of MG.
- Single-fiber electromyography studies may be of value in cases of seronegative MG or other disorders of neuromuscular transmission. The technique requires expertise and is only available at a few centers.

Muscle Biopsy

Muscle biopsy allows direct examination of portions of most motor unit components (e.g., intramuscular nerve branches, neuromuscular junction, and myofibers) and of supportive, connective, and vascular tissues. Using fresh-frozen sections, histologic and cytologic detail is preserved and many biochemical and immunochemical reactions within cells and tissues can be localized. Frozen sections also may be used in specific biochemical assays for enzymes and substrates.

▼ ***Key Point*** For maximum information from a muscle biopsy, specimens should be fresh-frozen in isopentane precooled in liquid nitrogen. Biopsy samples must be received cold for subsequent freezing at a laboratory specialized in processing muscle biopsies. Consult with the laboratory before taking a muscle biopsy. Place a second muscle biopsy in fixative for subsequent ultrastructural examination if required.

Appropriate sampling and transport methods are essential to the diagnostic value of the muscle specimen. Selection of the muscle(s) for biopsy is also important.

- Sample an involved muscle; however, avoid end-stage muscle because essential diagnostic features may no longer be present.
- The site of a localized disorder determines which muscle(s) should be sampled; however, in generalized disorders (e.g., polyneuropathy and PM), obtain samples from standard muscles (e.g., vastus lateralis in dogs and cats).
- Following collection, dip the muscle in saline, place it in a watertight container, and transport it on cold packs by a courier service to the laboratory.
- Delivery to the laboratory for processing within 24 hours is critical for optimal results.

Carnitine Quantification in Plasma, Urine, and Muscle

Lipid storage myopathies may result from primary or secondary abnormalities of carnitine. If excessive lipid droplets are present within a muscle biopsy section, carnitine should be quantified in plasma, urine, and muscle for formulation of a treatment plan.

Non-contrast and Contrast Radiographic Studies

Three-view, plain thoracic radiographs are indicated in neuromuscular disorders to rule out concurrent megaesophagus, aspiration pneumonia, thymoma, and other intrathoracic neoplastic processes. Because dysphagia as a result of oropharyngeal dysfunction and megaesophagus is a major problem in certain neuromuscular disorders, contrast studies that evaluate the dynamic swallowing process and motility throughout the esophagus may be indicated (see Chapter 4). Attempt contrast studies only if appropriate fluoroscopy and video recording equipment is available. (See Chapter 65 for discussion of diagnosis and management of esophageal disease.)

▼ ***Key Point*** If a large, air-filled pharynx or a megaesophagus is seen on plain radiographs, do not perform a barium swallow. If a contrast agent is absolutely necessary, use a small amount of dilute barium solution to minimize chances of barium aspiration (see Chapter 4).

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) provides excellent soft tissue resolution and can distinguish among muscle, fat, and connective tissue. This technique may be of value in cases in which specific lesion localization is difficult, such as inflammatory myopathies involving the pharynx and larynx (see Chapter 4).

TREATMENT

Selective breeding and prevention comprise the treatment of choice for the hereditary neuromuscular disorders. New techniques in molecular genetics, available at selected research centers, allow the identification of some underlying genetic defects and carrier animals. Gene replacement therapies are currently in experimental testing stages and may be available in the future for treatment of some of these disorders. Acquired neuromuscular disorders in many instances are secondary to diverse underlying medical problems such as hypothyroidism (see Chapter 31), adrenal gland dysfunction (see Chapter 33), electrolyte disorders (see Chapter 5), and protozoal infection (see Chapter 21). Whenever possible, treat the primary problem. Specific treatment is available for some neuromuscular disorders. These are described below.

Generalized Myasthenia Gravis

Anticholinesterase Drugs

These drugs are the cornerstone of treatment for MG. They inhibit enzymatic hydrolysis of ACh at the neuromuscular junction, thereby increasing the effective concentration of ACh and the duration of its effect in the synaptic cleft and prolonging the interaction of released ACh with remaining AChRs.

- If there is a positive response to edrophonium chloride testing and the animal can tolerate oral medication, administer pyridostigmine bromide syrup (Mestinon, Roche) diluted 1:1 in water at a dosage of 0.5 to 3.0 mg/kg q8–12h PO beginning at the low end of the dosage scale and gradually increasing.
- In cases of focal MG without generalized weakness or a fatigable palpebral response, begin pyridostigmine bromide syrup at a dosage of 0.5 to 1.0 mg/kg q8–12h PO.
- If oral delivery of drugs is a problem owing to megaesophagus or pharyngeal dysfunction, give injectable neostigmine (Prostigmin, Roche) at a dosage of 0.04 mg/kg q6h IM until the animal is able to handle oral medication.
- In critical animals, constant rate infusion of pyridostigmine bromide (0.01–0.03 mg/kg/hour) may be used until oral feedings are resumed or a feeding tube is placed.
- Initiate concurrent treatment for aspiration pneumonia (see Chapter 163) as needed.

▼ ***Key Point*** In the treatment of MG, titrate dosages to fit each animal's needs; requirements may vary from day to day in response to activity levels and stress.

Corticosteroids

Do not use corticosteroids as initial therapy in MG unless there was a negative response to edrophonium chloride testing. Although it is true that MG is an autoimmune disease, clinical signs of weakness can be controlled in most cases with anticholinesterase drugs.

Contraindications

- Some dogs become weaker with immunosuppressive dosages of corticosteroids, possibly precipitating a myasthenic crisis.
- In many dogs with MG, there is spontaneous remission within variable periods of time; therefore, generalized immunosuppression may not be warranted, particularly in light of the side effects of these drugs in dogs.

Indications

- If muscle strength is not greatly improved following anticholinesterase treatment and aspiration pneumonia is not present, administer prednisone at 0.5 mg/kg q12h, gradually tapering to an alternate-day dosage.
- High-dose IV methylprednisolone therapy may be of benefit in severe cases of MG. One gram of methylprednisolone is suggested every 5 days.
- Other autoimmune disorders, for which a specific treatment for the underlying clinical signs is not available, may occur concurrently with MG. In these cases, immunosuppression with corticosteroids is warranted.

Other Immunosuppressive Treatments

Reserve agents such as azathioprine and cyclophosphamide for the rare refractory cases that do not respond to conventional therapy.

▼ ***Key Point*** Rare cases may present in myasthenic crisis with peracute onset of collapse and respiratory insufficiency. Anticholinesterase drugs may be of no benefit in these cases; thus, respiratory support and plasmapheresis may be necessary.

Management of Pharyngeal Dysphagia and Megaesophagus

▼ ***Key Point*** Early recognition of regurgitation due to megaesophagus is important in the successful management of MG; management includes alteration in methods of delivery of food and water.

- Administer anticholinesterase drugs 1 hour before feeding.
- Deliver food and water with the animal in an upright position (see Chapter 65).
- Ensure that the animal remains upright for at least 10 minutes following feeding.
- If upright feeding fails to control regurgitation, place a gastrostomy feeding tube, as described in Chapter 3, to bypass the dysfunctional pharynx and esophagus.

▼ ***Key Point*** In the absence of severe aspiration pneumonia and with appropriate management, the prognosis for complete remission of MG is fair to good. In many animals, the megaesophagus resolves and regurgitation is eliminated. Continue treatment until serum AChR antibody titers are normal.

Focal Myasthenia Gravis

Megaesophagus and pharyngeal dysfunction in the absence of detectable generalized weakness may occur in MG. The diagnosis in these cases is made by demonstration of positive serum AChR antibody titers.

- The single most important part of treatment is elevation of food and water (see Chapter 65).
- The value of anticholinesterase drugs in focal MG is not known; however, lower doses may be of some benefit in controlling regurgitation. In the absence of generalized weakness, monitoring drug response is difficult and overdosages may occur.
- In the absence of aspiration pneumonia and pharyngeal weakness, a large percentage of dogs with the focal form of MG go into spontaneous remission. Although it is not known whether the benefits of corticosteroids outweigh the risks, in focal MG as in generalized MG the presence of concurrent autoimmune disorders without a specific therapy warrants the use of corticosteroids.

Immune-Mediated Inflammatory Myopathies

Masticatory Muscle Myositis

- During the acute stages of MMM, masticatory muscle swelling and trismus (inability to open the jaw) usually resolve rapidly subsequent to immunosuppressive dosages of glucocorticoids (prednisone, 2–3 mg/kg q12h PO).
- Determine response to therapy by the ability to open the jaw and by serial determinations of serum CK levels.
- If the response is favorable, decrease the dosage after 1 to 2 weeks to 1.0 mg/kg q12h PO; then gradually decrease to the lowest effective alternate-day dosage. Maintain this alternate-day dosage for 4 to 6 months. In refractory cases, azathioprine can be used concurrently with prednisone to maintain complete clinical remission.
- If MMM is not treated appropriately, relapses are common.

▼ ***Key Point*** In acute MMM, glucocorticoids usually produce rapid resolution. In chronic MMM, glucocorticoid therapy may improve jaw mobility even though a significant proportion of muscle is replaced by fibrous connective tissue.

Polymyositis

- In the absence of aspiration pneumonia or an underlying infectious agent, treat dogs with PM with immunosuppressive doses of corticosteroids. Initiate a treatment regimen similar to that for MMM.
- In refractory cases, use corticosteroids and other immunosuppressive agents such as azathioprine or cyclophosphamide concurrently.

Lipid Storage Myopathy

- Large intramyofiber lipid droplets within a fresh-frozen muscle biopsy sample are an indication of an underlying metabolic abnormality. Evaluate lactate, pyruvate, and carnitine status.
- Treat orally with L-carnitine (50 mg/kg q12h), coenzyme Q10 (100 mg q24h) and a good-quality B vitamin for a minimum of 2 months for determination of response. The treatment may need to be continued indefinitely.

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Section

10 Ophthalmology

David A. Wilkie

Chapter

131 Ophthalmic Equipment and Techniques

David A. Wilkie

OPHTHALMIC EQUIPMENT

The instruments and other equipment necessary for ophthalmic examination and surgery can be generally categorized as basic and advanced.

Diagnostic Equipment

Basic

- Penlight
- Direct ophthalmoscope with Finnoff transilluminator
- Indirect lens (20 diopter)
- Monocular biomicroscope
- Tonometer (Schiøtz) or Tonopen Vet (Mentor O&O)
- Miscellaneous
  - Schirmer tear test strips
  - Fluorescein stain
  - Nasolacrimal cannula (23 gauge)
  - Dilating agent (e.g., tropicamide)
  - Topical anesthetic (e.g., proparacaine)
  - Graefe forceps for third eyelid manipulation
  - Kimura spatula for cytology

Advanced

- Biomicroscope (slit lamp)
  - Monocular or binocular
- Indirect ophthalmoscope
- PanOptic ophthalmoscope
- Indirect lenses (15, 20, and 30 diopter)
- Applanation tonometer
- Gonioscopy lens
- Streak retinoscope
- Ultrasound (7.5, 10.0, and 20.0–50.0 MHz)
- Fundus camera
- Electroretinography

Surgical Equipment

Basic

- Magnifying loupes (4–6×)
- Colibri corneal forceps (0.3-mm teeth with tying platform)
- Bishop Harmon forceps (0.3- or 0.8-mm teeth)
- Barraquer needle holder (curved, without lock device; 9 mm × 0.85 mm jaws)
- Westcott tenotomy scissors
- Stevens tenotomy curved scissors
- Barraquer eyelid speculum
- Beaver blade handle
- Bard-Parker blade handle
- Desmarres chalazion clamp
- Strabismus hooks (two)
- Jamieson calipers
- Jaeger eyelid plate
- Irrigating cannula (23 gauge)

Advanced

- Operating microscope
- Right and left corneal section scissors

- Lens loop
- Angled tying forceps
- Carter sphere introducer
- Castroviejo cyclodialysis spatula
- Various intraocular forceps
- Diode or Nd : YAG laser
- Corneal trephines
- Phacoemulsification/irrigation-aspiration device
- Vitrector

Other

- Suture material
- 7-0 to 10-0 Vicryl or Dexon—ophthalmic spatula needle
- 9-0 nylon
- 6-0 monofilament—ophthalmic cutting needle (nylon, Surgilene, prolene)
- Blades
  - #64, #63, and #65 Beaver blades
  - #11 and #15 Bard-Parker blades
  - Diamond or sapphire knives
- Irrigating solutions
  - Ophthalmic balanced salt solution (BSS)
  - Lactated Ringer's
- Weck-cel surgical spears
- Prosthesis implants (18–19 mm)

OPHTHALMOLOGY TECHNIQUES

The general veterinarian in private practice should be able to perform the following routine ophthalmic procedures:

- Culture of the eye
- Schirmer tear test
- Tear breakup time
- Examination of the nictitating membrane (third eyelid)
- Direct ophthalmoscopy
- Indirect ophthalmoscopy
- Monocular biomicroscopy
- Fluorescein stain of the cornea
- Nasolacrimal irrigation
- Tonometry (Schiøtz, Tonopen)
- Conjunctival/corneal cytology

To properly evaluate and treat the patient with ocular disease, the clinician must have an accurate understanding of ophthalmic anatomy (Fig. 131-1).

In addition, based on the information obtained by these diagnostic tests, the clinician should be able to arrive at a diagnosis and formulate a plan for further diagnostic tests or treatment or, if indicated, referral.

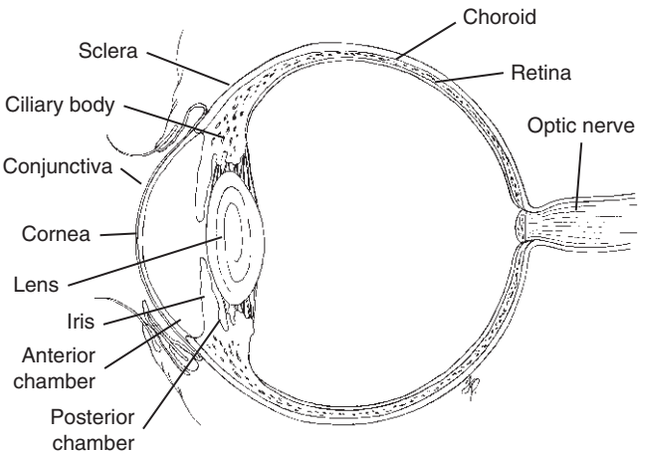

Figure 131-1 Normal ophthalmic anatomy.

Culture

Indications

- Chronic, nonresponsive corneal ulcer
- Acute, severe melting corneal ulcer
- Purulent ocular discharge
- Infectious blepharitis

Equipment

- A sterile, moist, synthetic culture swab is preferable, but a sterile cotton swab can be used.

Technique

The general principles and techniques for obtaining a culture from the eye are the same as for other organs.

1. Using a sterile swab moistened in transport media, obtain the sample in an aseptic manner from the area of concern; for example:
   a. If the lesion is a corneal ulcer, touch the swab to the ulcer (do not place in the conjunctival fornix).
2. Do not use a topical anesthetic for this procedure because it may interfere with the growth of organisms.
3. Label the sample and submit for aerobic and possibly fungal culture and sensitivity testing. It should be streaked onto nutrient agar as soon as possible.
4. Perform culture in combination with cytology or, if applicable, polymerase chain reaction (PCR) testing, when an infectious agent is suspected.

Schirmer Tear Test

Indications

- Assessment of normal aqueous tear production
- Chronic pigmentary keratitis
- Epiphora, including chronic mucoid epiphora

Equipment

- Commercially available Schirmer tear test (STT) strips

Technique

1. Place the notched end of the test strip in the lower conjunctival fornix. Do not touch this end.
2. Hold the eye closed and allow the strip to remain in place for exactly 1 minute. If convenient, both eyes may be tested at the same time.
3. Remove the strip and, using the standard measurement on the package, measure and record tear production. Normal dogs secrete 15 mm or more in 1 minute. While the normal value in the cat is reported to be similar to the dog, cats can have very low STT values without clinical signs. It is thought that stress may decrease the STT value in cats, and results must be interpreted along with clinical signs.
4. Do not use topical anesthetic for this test because the objective is to measure the response of the eye to an irritant. This requires the response of the ophthalmic branch of cranial nerve (CN) V as the afferent arm and the parasympathetic fibers in CN VII as the efferent arm.
5. In addition to the Schirmer tear test, evaluation of the tear breakup time to assess the mucin portion of the precorneal tear film and corneal staining with rose Bengal are also tools used in the assessment of the precorneal tear film and corneal surface health.

Tear Breakup Time (TBUT)

Indications

- Assessment of qualitative aqueous tear production
- Chronic pigmentary keratitis
- Epiphora, including chronic mucoid epiphora

Equipment

- Fluorescein stain
- Blue light and magnification (a slitlamp works best)
- Watch with a second hand

Technique

1. Place a drop of fluorescein stain on the cornea. Do not rinse it off.
2. Hold the eyelids closed and place the slitlamp to your eyes and the blue light on the eyelids.
3. Open the eyelids and, holding them open, begin timing while examining the green precorneal tear film. Continue to hold the eyelids open. The precorneal tear film should appear as a uniform, continuous film across the cornea. When the tears begin to separate into an oil and water pattern, stop timing.
4. Normal tears will remain stable for approximately 21 seconds. Failure to form a normal tear film or early breakup indicates a qualitative tear film abnormality. This is a result of a loss of goblet cells and tear film mucin.

Examination of the Nictitating Membrane

Indications

- Chronic conjunctivitis
- Suspicion of a foreign body
- Abnormalities of the gland or cartilage
- Mass lesion of the nictitating membrane (third eyelid)

Equipment

- Topical anesthetic
- Atraumatic forceps

Technique

1. Examine the palpebral surface of the third eyelid by gently retropulsing the globe and allowing the nictitating membrane to prolapse passively while the lower eyelid is retracted. This is useful for assessing the mobility of the third eyelid and for protecting the eye when obtaining a conjunctival scraping.
2. Examine the bulbar surface of the third eyelid. This requires topical anesthesia.
   a. The topical anesthetic of choice is proparacaine (Alcaine), which provides 10 to 15 minutes of anesthesia. Apply 2 drops of anesthetic and wait 2 to 3 minutes for the full effect.
   b. After anesthetizing the surface, gently grasp the leading edge of the third eyelid with small nontoothed forceps. Take care to avoid damaging the cornea.
   c. Gently pull the third eyelid up and out to allow examination of the posterior surface.
3. Examine all surfaces and the inner and outer fornices of the third eyelid for a foreign body and for lymphoid follicles, which indicate a chronic inflammatory process.

Biomicroscopy

This technique provides a magnified and 3-dimensional method to examine the globe from the eyelid surface back to the anterior third of the vitreous.

Indications

- Detailed examination of the anterior segment of the eye to examine the following:
  - Eyelids
  - Conjunctiva
  - Third eyelid
  - Cornea
  - Aqueous
  - Iris
  - Lens
  - Anterior vitreous

- Ability to examine for depth of lesion by providing an optical section (3-dimensional perspective)
- Detailed examination with higher magnification (5–20×) of specific areas such as the cornea, iris, and lens

Equipment

- Inexpensive monocular biomicroscope
  - Heine HSL-150
  - Eidolon 510L
- Expensive binocular biomicroscope
  - Kowa SL-14
  - Zeiss HSO-10

Technique

1. Turn on the slitlamp and use the rheostat to adjust the light intensity. If applicable, adjust the width of the slit beam.
2. A dilated pupil will facilitate examination of the structures posterior to the iris.
3. Darken the examination room.
4. Place the slitlamp to your eye and position the slitlamp 1 to 2 inches from the patient's cornea. Achieve focus by fine movements toward or away from the patient. The depth of focus is such that the cornea and the lens are not in focus simultaneously. Slowly sweep the beam of light from left to right and back to examine the entire eye from eyelids to anterior third of the vitreous. Work systematically from eyelids to vitreous focusing deeper with each pass of the light beam.
5. With a narrow slit beam it is possible to locate the depth of a lesion such as a corneal ulcer or cataract. In addition, the magnification provided aids in visualization of foreign bodies, aqueous flare, iris detail, and eyelid abnormalities such as distichia and ectopic cilia.

Direct Ophthalmoscopy

This technique provides an upright image of the fundus and associated structures and magnifies the image 15 to 18 times. In small animals, the field of view is narrow and therefore difficult to use for general screening of the eye.

Indications

- Examination of the ocular fundus
- Detailed examination with higher magnification of specific areas such as the optic nerve and blood vessels

Equipment

- Dilating agent (e.g., tropicamide)
- Charged, direct ophthalmoscope

Technique

1. Turn on the ophthalmoscope and use the rheostat to adjust the light intensity.
2. Turn the diopter wheel to the zero (0) setting. This usually is the proper setting to view the fundus.
3. Darken the examination room.
4. Place the ophthalmoscope to your eye, and from a distance of 12 to 24 inches obtain the tapetal reflection. While looking through the ophthalmoscope move toward the animal's eye, observing for any interference with the tapetal reflection, which may indicate opacity of the transmitting media, cornea, aqueous humor, lens, or vitreous. When you are 1 to 2 inches from the patient's cornea, the retina, optic nerve, retinal vessels, and tapetum will be clearly in focus.
5. Locate a blood vessel and follow it to the optic nerve. Evaluate the optic nerve and blood vessels and scan the fundus for abnormalities of color, clarity, size, and shape. Use the diopter wheel to adjust the focus, and to evaluate raised and depressed lesions (numbers in red indicate negative or deeper; those in black are positive or more superficial).
6. While higher magnification is achieved with direct as compared to indirect examination, opacities of the transmitting media will interfere with direct examination preventing visualization of the posterior segment with this technique.

Indirect Ophthalmoscopy

Although practice is required to become proficient in this technique, once it is mastered it is more useful than direct ophthalmoscopy for screening the fundus in small animals. Also, the equipment needed is less expensive unless a headset is used. Indirect ophthalmoscopy provides an inverted, reversed image magnified 3 to 5 times. This image, although of a lower magnification than with direct ophthalmoscopy, has a much larger field of view and is better for routine screening of the eye. In addition, indirect examination will allow identification of the posterior segment through mild opacities of the cornea, aqueous, lens, and vitreous.

Indications

- Examination of the ocular fundus

Equipment

- Dilating agent (e.g., tropicamide)
- Light source (e.g., penlight)
- Indirect, handheld 20-diopter lens
- Binocular headset for clinicians with advanced interest in ophthalmology

Technique

1. Dilate the patient's pupil with 1 or 2 drops of tropicamide (Mydriacyl). Allow 10 to 15 minutes for complete dilation (the effect will last 8 to 12 hours in dogs).
2. Begin the examination at arm's length from the patient, having an assistant restrain the patient and hold the eyelids open.
3. Darken the examination room.
4. With a focal light source (e.g., a penlight or direct ophthalmoscope with Finoff transilluminator) held at arm's length from the patient, obtain the tapetal reflection.
5. Holding the lens in the other hand, place the lens 1 to 2 inches in front of the patient's eye, in the path of the light. The fundus should appear as an upside down and reversed virtual image in front of the lens.
   a. Be sure to look at the image that is in front of the lens and not at the lens or the eye.
6. To view other areas of the fundus, you must move yourself, the light source, and the lens while keeping all of these in alignment. Remember that because the image is inverted you must move in the opposite direction to the image.
7. If the image is lost, move the lens out of the light beam and start again.
8. An indirect headset, while expensive, will greatly facilitate examination.
9. A alternative to an indirect headset is a monocular indirect ophthalmoscope, the Welch Allyn PanOptic ophthalmoscope.

Fluorescein Stain of the Cornea

Fluorescein is a hydrophilic drug that binds to the corneal stroma, but not to the epithelium or to Descemet's membrane.

Indications

- Red or painful eye
- An obvious corneal irregularity
- Ocular trauma or a foreign body
- Tear breakup assessment
- Suspected feline herpes keratitis
- Assessment of nasolacrimal duct function

Equipment

- Prepackaged fluorescein strips (commercially available)
- Sterile ocular collyria (eyewash solution)
- Cotton balls

Technique

1. Remove the fluorescein strip from the package, holding it by the green end. Fold the strip lengthwise to create a trough.
2. Place 2 or 3 drops of sterile eyewash solution on the strip and tilt it to allow the stain to drip onto the eye. Do not touch the eye with the strip because this may result in an iatrogenic area of stain retention.
3. With the eyewash solution, gently irrigate excess stain from the eye onto a cotton ball; examine the eye for stain uptake, using a penlight. Identification of the fluorescein uptake is improved by using a blue or Woods light, which excites the fluorescein molecules, making them fluoresce green. To assess TBUT, do not irrigate the flourescein from the cornea (see TBUT).

Assessment of Nasolacrimal Duct Function

1. To evaluate the patency of the nasolacrimal duct, perform the previously described steps, but do not rinse the fluorescein from the eye. The stain should appear at the nares within 5 minutes.
2. A positive test is definitive for a patent nasolacrimal duct but does not prove that both puncta are patent. A negative test suggests a problem, and irrigation of the duct is indicated.

Nasolacrimal Duct Irrigation

- This procedure can be performed on a minimally restrained dog, using only topical anesthesia.
- Sedation or general anesthesia usually is required for cats.

Indications

- Epiphora without an obvious etiology
- Failure of passage of fluorescein stain
- Mucopurulent ocular discharge

Equipment

- Topical anesthetic
- Syringe (3 or 6 ml)
- Nasolacrimal duct cannula (23 or 25 gauge)

Technique

1. Apply a topical anesthetic and connect a nasolacrimal duct cannula to a syringe filled with eyewash solution.
2. While an assistant restrains the animal's head, elevate and roll the upper eyelid in the medial canthus to expose the superior punctum.
3. Place the thumb or index finger on the plunger of the syringe, in preparation for injection. Hold the syringe loosely so that no injury will result if the patient should jerk its head. If possible, rest your hand on the patient's head in case the patient moves.
4. Gently insert the cannula in the punctum and, without forcing, allow it to seat itself in the duct. Apply gentle pressure to the plunger and observe fluid emerging from the inferior punctum.
5. Occlude the lower punctum, tip the nose down, and continue flushing. Fluid should now appear at the nostril.

▼ ***Key Point*** Do not use excessive force when placing the catheter or when irrigating.

6. If a patent duct cannot be established and the epiphora is severe, consider medical therapy such as topical antibiotics or anti-inflammatories and repeated irrigation, or examine under general anesthesia to further pursue the problem. Ultimately, skull radiographs and a contrast dacryocystorhinography can be used to further evaluate the nasolacrimal canaliculi, sac, and duct.

Tonometry

Be sure to have a functioning tonometer and be familiar with its use. There are two specific ways to determine intraocular pressure (IOP): indentation tonometry and applanation tonometry.

Indications

- Diffuse corneal edema
- Anisocoria
- Fixed and dilated pupils
- Episcleral congestion
- Blindness
- Buphthalmos
- Anterior uveitis
- Breeds predisposed to primary glaucoma—annual IOP determination
- Monitoring of medically or surgically controlled glaucoma
- Evaluation of the contralateral eye in animals with unilateral primary glaucoma

Schiøtz Indentation Tonometry

The Schiøtz tonometer is an indentation tonometer and measures the amount of corneal indentation that occurs when a given weight is placed on the cornea. The result is inversely proportional to the intraocular pressure. Obtain the actual pressure from a table of values. The Schiøtz tonometer requires assembly, disassembly, and cleaning in order to ensure its accuracy. The foot plate is large and the patient must be cooperative in order to place the foot plate on the cornea in a vertical position. If the animal is fractious or the eye painful, it is unlikely that accurate placement will be obtained and erroneous values will result. The result is that glaucoma is not diagnosed or monitored accurately and IOP determination is not performed at the frequency indicated by the breed or clinical signs.

Equipment

- Topical anesthetic
- Clean and calibrated Schiøtz tonometer
- Conversion chart

Technique

1. Anesthetize the cornea with topical proparacaine.
2. To assemble the tonometer, place the shaft in the housing and attach the 5.5-g weight. Hold the instrument vertically and check that the plunger slides freely within the hollow sleeve.
3. Use the metal calibration standard to test the accuracy of the tonometer. When the instrument is placed on the standard it should read zero (0) on the scale (i.e., the 5.5-g weight does not indent the metal standard).
4. While an assistant gently elevates the patient's nose, elevate the upper eyelid and place the tonometer foot plate on the cornea. Keep the tonometer vertical and on the center of the cornea. The tonometer should rest on the eye and does not need to be pushed down.
5. Take three readings and average them. Using the conversion chart, convert the averaged value to an approximation of the intraocular pressure, matching the weight used with the reading obtained.
6. Normal values for dogs are 15 to 25 mm Hg; the variation in both eyes should be no greater than 5 mm Hg.

Applanation Tonometry—Tonopen

Applanation tonometry determines IOP by evaluating the force required to applanate or flatten a given surface area of cornea. In recent years the Tonopen (Mentor O&O) has been evaluated and shown to be similar to other applanation tonometers in accuracy. It is lightweight, portable, accurate, and self-calibrating, and it averages several readings and gives a percentage error to ensure accuracy. In addition, the small foot plate allows this tonometer to be used on painful eyes in less cooperative patients because only a small area of cornea is required to obtain a reading, and the position of the patient's head is not related to obtaining the reading. This is the current accepted gold standard in veterinary ophthalmology. All small animal practices should have access to a functional Tonopen.

Equipment

- Topical anesthetic
- Calibrated Tonopen

Technique

1. Anesthetize the cornea with topical proparacaine.
2. Activate the Tonopen and gently tap the transducer tip, which is protected by a sleeve, against the cornea. A gentle bouncing motion of the transducer tip against the cornea works best. The device will give an audible tone as each reading is accepted and a longer tone when enough readings have been averaged.

3. Obtain the patient's IOP from the digital reading at the Tonopen display window. The standard error bar should be over the <5% error. If there is a greater percent error, repeat the procedure until a reliable measurement is obtained.

Cytology

Cytology is a simple, fast, and inexpensive method for characterizing the type of inflammatory process, and in many cases it is used to obtain a diagnosis.

Indications

- Obtain a sample for Gram stain
- Characterize the type of inflammation (i.e., neutrophilic, lymphocytic, eosinophilic)
- Aid in the diagnosis of feline conjunctivitis (e.g., for *Chlamydophila, Mycoplasma*)
- Obtain samples for PCR testing

Equipment

- Topical anesthetic
- Platinum spatula, cytology brush, or other instrument suitable for sample collection
- Microscope
- Microscope slides
- Stain

Technique

1. Place a topical anesthetic in the animal's conjunctival sac.
2. Gently retropulse the globe and retract the lower eyelid, thus exposing the third eyelid.
3. Using a spatula or other suitable instrument, scrape the palpebral surface of the third eyelid and the adjacent palpebral conjunctiva. Avoid damaging the surface, but use sufficient force to exfoliate cells. For ulcerative keratitis the sample must be obtained from

Table 131-1. OPHTHALMIC CLINICAL SIGNS ASSOCIATED WITH SYSTEMIC DISEASES

Ophthalmic Clinical Sign	Associated Systemic Disease
Keratitis sicca	Hypothyroidism Autoimmune Drug-induced (sulfonamides, edotodolac) Facial nerve paralysis Otitis media/interna Distemper
Anterior uveitis/chorioretinitis	Infectious (bacteria, rickettsia, mycoses, viruses) Traumatic Neoplastic Autoimmune
Glaucoma	Anterior uveitis Neoplasia Trauma Hyphema
Retinal detachment	Trauma Infectious (bacteria, rickettsia, mycoses, viruses) Neoplasia Autoimmune Systemic hypertension (renal disease, diabetes mellitus, pheochromocytoma, hyperthyroidism, idiopathic) Hyperviscosity
Blindness	Trauma Neoplasia Reticulosis Infectious (bacteria, rickettsia, mycoses, viruses) Autoimmune Other central nervous system diseases
Horner's syndrome	Thoracic mass Spinal cord trauma C1-T2 Neck trauma Otitis media/interna Orbital mass lesion
Hyphema	Coagulopathy Trauma Systemic hypertension (renal disease, diabetes mellitus, pheochromocytoma, hyperthyroidism, idiopathic) Infectious Neoplasia

the ulcer margin to accurately evaluate for potential pathogens.
4. Place the cells on a glass slide and streak them to form a monolayer.
5. Submit the slide for Gram staining (to characterize the type of bacteria); for Giemsa, Wright, or Diff-Quik staining (to examine for cell type, inclusion bodies, etc.); for fluorescent antibody testing (*Chlamydia,* herpesvirus); or for PCR testing (herpesvirus, mycotic keratitis).

Ocular Ultrasound

Ultrasound is a simple, fast, and inexpensive method for examination of the lens and posterior segment in eyes with opacities of the transmitting media. In addition, ultrasound can be used to evaluate the orbit, although computed tomography and magnetic resonance imaging are superior for orbital examination.

Indications

- All opacities of the transmitting media
  - Corneal edema
  - Hyphema
  - Cataract
- Evaluation of intraocular mass lesions
- Orbital disease indicated by exophthalmos

Equipment

- Topical anesthetic
- Sterile K-Y jelly as a coupling jel
- Ultrasound with a 5.0- to 10.0-MHz transducer probe
- Ultrasound biomicroscopy can be performed with dedicated 20.0- to 50.0-MHz ophthalmic ultrasound

Technique

1. Place a drop of topical anesthetic in the animal's conjunctival sac.
2. Place sterile ultrasound coupling gel or K-Y jelly on the transducer tip or on the corneal surface.
3. Place the transducer directly on the cornea, or the scan may be performed through closed eyelids or an offset device.
4. Image the globe in both the horizontal and vertical planes through the visual axis.
5. In general, ultrasonographic images are described as hyperechoic, hypoechoic, and anechoic. There are four major ocular acoustic echoes within a normal eye: anterior cornea, anterior lens capsule, posterior lens capsule, and retina/choroid/sclera. Additional echodensities may be generated by the iris, ciliary body, optic nerve, orbital fat, muscles, and other orbital structures.

OCULAR MANIFESTATIONS OF SYSTEMIC DISEASE

Ophthalmic clinical signs frequently are manifestations of systemic disease (Table 131-1). For many of these ophthalmic signs, specific ocular causes must be differentiated from the systemic ones provided in Table 131-1. For a more complete discussion of these diseases and their treatment, refer to appropriate chapters in this book.

Chapter

132 Diseases of the Eyelid

Susan E. Kirschner

Diseases of the eyelid result in a variety of clinical signs. Initially, the eyelids alone may be affected, but because of their close proximity to the cornea and conjunctiva, disease of these structures frequently results. Because corneal and conjunctival involvement is often more severe and more obvious, eyelid disease may be overlooked. Manage concurrent conjunctival and corneal disease as described in Chapters 133 and 134, respectively, in this section.

Diseases of the eyelid can be broadly categorized by their appropriate treatment (i.e., surgery or medical therapy), as listed in Table 132-1.

ANATOMY

- The eyelid functions to protect and moisten the cornea and to remove debris. The eyelid is covered by skin and lined internally by palpebral conjunctiva.
- The eyelid is closed by the orbicularis oculi muscle, which is innervated by the palpebral branch of the facial nerve. Paralysis of this nerve results in inability to close the eyelids. Spasm of the orbicularis oculi muscle results in spastic entropion.
- The eyelids are opened by the levator palpebrae and Mueller's muscle, which are innervated by the oculomotor nerve and by post-ganglionic sympathetic fibers, respectively. Paralysis of either of these nerves results in ptosis, or drooping of the eyelid.
- The meibomian glands line the conjunctival surface of the eyelid margin. They open onto the eyelid margin, where they secrete an oily fluid that helps prevent evaporation of the precorneal tear film. Distichia, ectopic cilia, and some tumors originate from the meibomian glands.

PRINCIPLES OF EYELID SURGERY

- The skin covering the eyelids is thin and easily traumatized. Perform clipping and aseptic preparation gently. A povidone-iodine solution diluted with saline solution to a 1:10 concentration is appropriate for preparing the eyelids for surgery.
- The eyelids have an extensive blood supply, and injured tissue heals well. Therefore, remove only clearly necrotic tissue. Removal of excess tissue can result in abnormal lid function.
- Close eyelid skin incisions with 4-0 to 6-0 monofilament nonabsorbable suture in a simple interrupted pattern. Close conjunctival wounds with 6-0 to 8-0 absorbable suture material. Remove nonabsorbable sutures 2 weeks following surgery.
- An Elizabethan-type collar may be necessary to prevent self-trauma.

▼ ***Key Point*** Accurate closure of the eyelid margin is the most important component of eyelid defect repair.

ANKYLOBLEPHARON

Ankyloblepharon is a condition seen in neonatal puppies in which the eyelids do not open properly.

- This condition may result in a subpalpebral infection called *ophthalmia neonatorum*.
  - If infection occurs, gently massage the eyelids to open a portion of the palpebral fissure. Occasionally, scissors or a scalpel blade is required to partially open the eyelids.
  - Lavage the subpalpebral area with a 1% povidone-iodine solution and apply a topical antibiotic solution or ointment (e.g., triple antibiotic, erythromycin, gentamicin) three to four times daily.
- If the infection is left unattended, the cornea may ulcerate or perforate.
- If the entire palpebral fissure is opened prematurely, corneal damage may result from exposure and desiccation.
  - To protect against corneal desiccation, use an artificial tear ointment four to six times daily.

Table 132-1. CLASSIFICATION OF EYELID DISEASES ACCORDING TO TYPE OF THERAPY

Surgery	*Medical Treatment*
Ankyloblepharon	Bacterial blepharitis
Coloboma	Chalazion/hordeolum
Entropion	Allergic blepharitis
Ectropion	Parasitic and fungal blepharitis
Distichiasis/ectopic cilia	
Lagophthalmos	
Neoplasia	

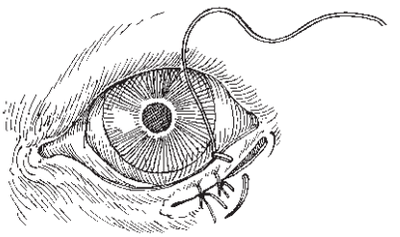

Figure 132-1. Correction of ventral entropion.

COLOBOMA

In this disorder, which affects kittens and occasionally puppies, a portion of the lid margin does not form.

- The major clinical signs are epiphora and blepharospasm.
- Coloboma may be confused with entropion because eyelid hairs often contact the cornea.
- Many cases can be corrected by everting the lid with entropion correction surgery, thus preventing corneal trauma by facial hairs.
- Extensive colobomas require reconstructive surgery performed by a veterinary ophthalmologist.

ENTROPION

Entropion often is observed in young dogs and is common in the chow, Shar-Pei, and hunting breeds. It can also occur in cats.

- Clinical signs vary from conjunctivitis with mild serous discharge to severe blepharospasm with corneal ulceration and purulent discharge.
- Diagnosis is made by examination of the eyelids. When the eyelid is rolled inward, facial hairs often directly contact the cornea.
- Correct neonatal entropion in the Shar-Pei with temporary everting sutures at 3 to 5 weeks of age. If this technique fails, perform permanent surgical correction.

Classification

▼ ***Key Point*** Entropion may be anatomic, anatomic with secondary eyelid spasm, or primarily spastic.

- Classification of entropion is made when the eyelids are relaxed. This may require topical anesthesia, palpebral nerve blocks, or general anesthesia.

Anatomic Entropion

- The eyelid rolls inward even when the eyelids are relaxed.
- This may be from a defect in the eyelids themselves, or in the case of certain breeds such as the Shar-Pei and the bloodhound, from forehead or brow folds, which force the eyelids inward.
- Surgical correction is indicated.

Anatomic Entropion with Secondary Spasm

- Blepharospasm exaggerates entropion such that a portion of the rolling is from an anatomic abnormality, with the remainder due to squinting.
- Surgically correct the anatomic portion of the entropion; additional temporary everting sutures may be required until the spasm cycle is broken.

Spastic Entropion

- Blepharospasm results in rolling inward of the eyelid margin. Under anesthesia or when the eyelids are relaxed, the entropion resolves.
- Correct with temporary everting sutures and treatment of the underlying cause of the spasm.

Surgical Techniques

Ventral or Dorsal Eyelid Entropion

1. Remove an ellipse of skin parallel to and 2 to 3 mm from the lid margin (Fig. 132-1). The amount of skin removed depends on the severity of the entropion. Remove more tissue for upper lid entropion than for lower lid entropion.
2. Remove the tissue with a scalpel or by crushing the selected tissue with a hemostat and then removing the crimped tissue with scissors.
3. Close the skin routinely with monofilament nylon sutures (e.g., 4-0) in a simple interrupted pattern.

Lateral Entropion

1. Remove a V-shaped area of skin (Fig. 132-2*A*) at the lateral canthus.
2. If the lateral canthus is extremely lax, dissect the underlying orbicularis oculi muscle free (Fig. 132-2*B*) and suture it to the lateral orbital rim with 4-0 or 5-0 nonabsorbable monofilament suture material (Fig. 132-2*C*).

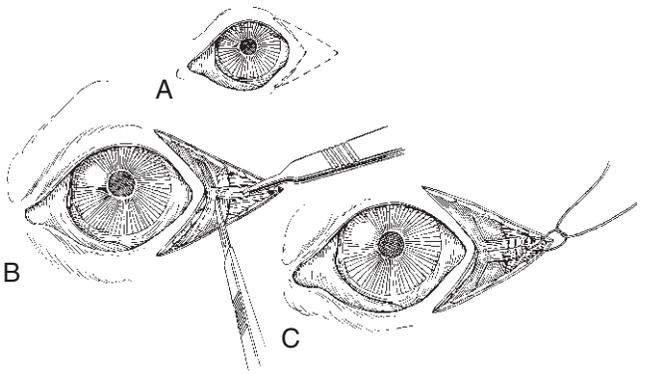

Figure 132-2. Correction of lateral entropion. *A,* Area of skin to be removed; *B,* orbicularis oculi dissected free; and *C,* orbicularis oculi sutured to the lateral orbital rim.

3. Close the skin with 4-0 or 5-0 nonabsorbable sutures in a simple interrupted pattern.

Medial Entropion

1. Evert the skin with an elliptical incision, as for ventral entropion.
2. Alternatively, perform a medial canthoplasty. Make a V-shaped incision along the eyelid margin that encompasses the caruncle (Fig. 132-3*A*). Take care not to injure the underlying lacrimal canaliculi. Transect the medial canthal ligament to release the medial canthus.
3. Close the incision by suturing the upper lid to the lower lid to create a horizontal closure (Fig. 132-3*B* and *C*). This has the effect of correcting the entropion and slightly shortening the palpebral fissure.

Temporary Everting Sutures for Spastic Entropion and for Neonatal Entropion in Shar-Peis

1. Use minimal anesthesia for very young puppies. Occasionally, light inhalation anesthesia via a mask is required (see Chapter 2).
2. In older dogs, inject a short-acting anesthetic (see Chapter 2).
3. Place one to two 4-0 to 5-0 nylon sutures in a mattress pattern in each eyelid. Sutures should be partial thickness only. Make the first bite 1 to 2 mm from the eyelid margin. Place the second bite at a sufficient distance to cause eversion of the eyelid margin when the suture is tied (Fig. 132-4).
4. Leave the sutures in place for 3 to 4 weeks. Premature suture removal may result in recurrence of the entropion.

Entropion Caused by Heavy Brow Folds

1. The skin of the forehead may be removed en bloc, or the folds may be elevated.

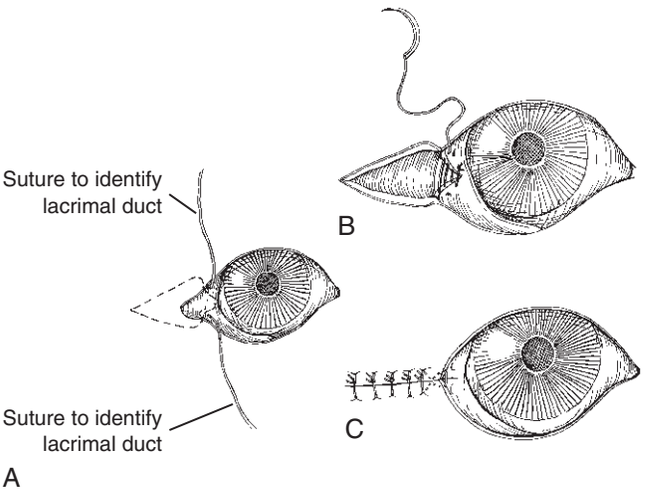

Figure 132-3. Correction of medial entropion by medial canthoplasty. *A,* Mark the lacrimal canaliculus with a suture—then make a V-shaped incision along the eyelid margin, encompassing the caruncle. *B and C,* Close the incision in two layers, creating horizontal closure.

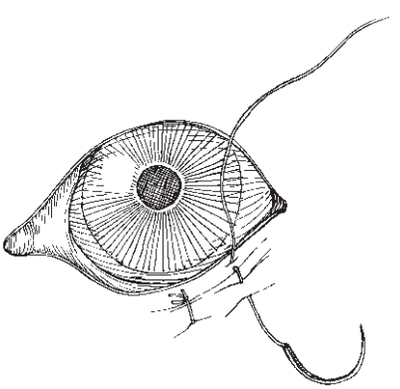

Figure 132-4. Temporary lid-everting sutures.

2. To elevate the folds, use surgical mesh, such as mersilene, cut into strips 3 to 4 mm wide and 10 to 15 cm long, and a straight surgical needle with an eye capable of receiving the end of the mesh strip.
3. Make a horizontal skin incision 1 to 2 cm above the lid margin, and a second one 8 to 12 cm higher on the brow.
4. Pass the mesh suture from the upper incision, beneath the skin to the lower incision, then horizontally through subcutaneous muscle, then beneath the skin back to the upper incision. Tighten to achieve the desired effect. Tie as one would with a typical suture.
5. Place two to six of these lifting sutures, as needed. Close the skin incisions with 3-0 to 4-0 nylon suture.

ECTROPION

- Ectropion may be caused by excessive eyelid length or by decreased tone of the eyelid muscles. This results in sagging of the lower eyelid, with exposure of conjunctiva. In addition, ectropion can result iatrogenically from overcorrection of entropion.
- Increased conjunctival exposure often results in chronic conjunctivitis or exposure keratitis. Poor lid-to-cornea fit may exacerbate keratoconjunctivitis sicca (KCS) because of abnormal tear distribution.
- Most cases of ectropion can be corrected by a full-thickness wedge resection of the affected portion of the eyelid (see under Neoplasia for procedure).
- Shortening of the palpebral fissure via a permanent lateral tarsorrhaphy is beneficial in many dogs (see description under Treatment of Lagophthalmos).

DISTICHIASIS

Distichiasis is a condition in which hairs that originate from the meibomian glands and emerge from their ducts contact the cornea and cause irritation. It is common in cocker spaniel, golden retriever, and Shih Tzu breeds and occasionally is seen in other breeds.

▼ ***Key Point*** Reserve surgical removal for animals in which epiphora, blepharospasm, or corneal disease is a significant clinical sign and when other ocular disease has been ruled out.

- The most common complication of distichiasis surgery is recurrence 3 to 5 months postoperatively.

Surgical Technique

Cryoepilation

1. Evert and stabilize the lid with a chalazion clamp and freeze a 3-mm band along the base of the meibomian glands, on the conjunctival surface of the eyelid, below each abnormal cilium. Freeze time varies, depending on whether nitrous oxide or liquid nitrogen is used. In general, the ice ball should extend to the lid margin, taking care not to freeze the full thickness of the lid.
2. A double freeze-thaw cycle is most effective.

Electroepilation

Reserve this time-consuming technique for cases in which only a few hairs are to be removed.

1. Insert an electrolysis stylet along the hair shaft into the base of the follicle.
2. Apply low amperage (2–4 mA) coagulating current until a small amount of meibomian gland material bubbles out of the duct opening.

CO_2 Laser Epilation

1. This is best used with the high magnification that a surgical microscope provides.
2. Use a focused beam to burn along the hair shaft down to the root.

ECTOPIC CILIA

- Ectopic cilia are hairs originating from the meibomian gland that emerge through the conjunctival surface of the eyelid.
- The most common clinical signs are blepharospasm and corneal ulceration.
- The most common location is the central upper eyelid, 2 to 4 mm from the eyelid margin.

Technique for Removal

1. Stabilize the eyelid during the procedure with a chalazion clamp.
2. Excise the hair and its root en bloc with a #11 scalpel blade, leaving the eyelid margin intact.
3. The conjunctival wound may be left open.

LAGOPHTHALMOS

- Lagophthalmos is a condition in which the eyelids cannot completely close. The most common cause is anatomic exophthalmos, seen in brachycephalic breeds. In these breeds, blink frequency often is decreased, exacerbating the problem.
- It also is associated with buphthalmos (progressive enlargement of the eye), palpebral nerve palsy, and ectropion.
- Corneal disease, including ulceration, pigmentation, neovascularization, and keratinization, may result.
- Treat surgically by permanent closure of a portion of the palpebral fissure.

Technique

1. Excise the eyelid margin of the ventral and dorsal lids at the lateral or medial canthus.
2. Close the eyelids in two layers, as described for wedge resection under Neoplasia.

NEOPLASIA

Etiology

- The most common eyelid tumor in the dog is meibomian gland adenoma. Other tumors seen in the eyelids include papilloma, meibomian gland adenocarcinoma, melanoma, histiocytoma, squamous cell carcinoma, and basal cell tumors.

- Meibomian gland tumors originate in the base of the gland but often emerge from the meibomian gland duct on the eyelid margin.
- Tumors occurring in the eyelids of cats include mast cell tumor, melanoma, fibrosarcoma, neurofibroma, and squamous and basal cell carcinoma.
- Squamous cell carcinomas usually are seen in white cats and appear as non-healing ulcerative lesions. They are locally aggressive and have a high recurrence rate.
- Melanomas of the eyelids have been known to metastasize in cats. Hydrocystomas are black cystic nodules on the lid that mimic melanomas.
- In dogs, most eyelid tumors are benign and are removed to prevent irritation or injury to the cornea or conjunctiva.
- In cats, most eyelid tumors are malignant and carry a guarded prognosis.
- For additional information on skin tumors in dogs and cats, see Chapter 30.

Preoperative Considerations

▼ ***Key Point*** One-fourth of the upper eyelid and one-third of the lower lid can be removed without severe distortion of the palpebral fissure.

- The most common cause of recurrence of meibomian gland adenoma is incomplete removal of the tumor. Keep in mind that even though the bulk of the tumor is at the eyelid margin, the tumor originates from the base of the meibomian gland.

Surgical Technique

- A full-thickness wedge resection of the eyelid is sufficient to remove most tumors.
- Cryosurgery also can be used to treat many eyelid tumors.
  - Although there is a higher recurrence rate with cryosurgery than with excision, it is a relatively safe, simple procedure that may be performed with local anesthesia combined with tranquilization.
- CO_2 lasers can be used for many eyelid tumors.
- Submit all excised tissues for histopathology.

Wedge Resection

1. Using a scalpel blade, incise the skin in a pie-shaped wedge with the base at the eyelid margin. Alternatively, crush along the incision line with hemostats and cut along the crimped line with scissors. Use a tenotomy or Metzenbaum scissors to complete the incision.
2. Close the incision in two layers:
   a. Close the subconjunctival tissue with 6-0 or 7-0 absorbable sutures, with the knots buried within the eyelid.
   b. Close the skin with 4-0 to 6-0 sutures beginning at the lid margin (Fig. 132-5).
3. Close the eyelid margin with a figure-of-eight 4-0 to 6-0 suture, and the remainder of the skin with sutures in a simple interrupted pattern. Alternatively, a horizontal mattress or simple continuous pattern can be used to close eyelid margins.

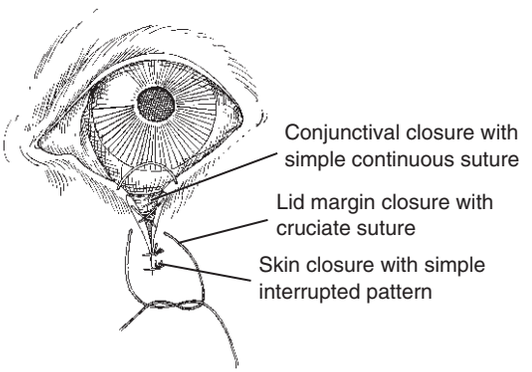

Figure 132-5. Closure for wedge resection of the eyelid. Close the subconjunctiva with 6-0 or 7-0 absorbable suture in a simple continuous pattern; the lid margin with a cruciate suture; and the remainder of the skin with 6-0 nonabsorbable suture, in a simple interrupted pattern.

Cryosurgery

1. Perform a double freeze-thaw cycle. Treat an area extending 3 to 5 mm beyond the tumor.
2. For meibomian gland tumors, place the probe on the conjunctival surface of the eyelid.

CO_2 Laser Surgery

1. For meibomian gland tumors use a focused beam perpendicular to the lid, from the lid margin down into the base of the gland.
2. For tumors on the skin of the eyelid that do not originate from within the lid use an unfocused beam.

INFLAMMATORY EYELID DISEASES

Bacterial Blepharitis

- In blepharitis, the eyelids and lashes are crusted with mucopurulent discharge and are erythematous and swollen. The conjunctiva usually is inflamed, and there may be an associated non-ulcerative keratitis.
- Blepharitis is often a manifestation of other inflammatory skin diseases (see the section on Skin and Ear Diseases), including atopy, food allergy dermatitis, pyoderma, dermatomycosis, demodicosis, and autoimmune diseases.

Treatment

- Apply a topical bactericidal ophthalmic solution or ointment (e.g., neomycin, bacitracin, polymyxin B) three to four times daily.
- Instruct the owner to clean the eyelids daily, using dilute baby shampoo.
- Give systemic antibiotics as described for pyoderma (see Chapter 38).
- If there is associated non-ulcerative keratitis, consider giving topical corticosteroids or cyclosporine ointment once or twice a day.
- If associated with pruritus or other signs of atopy, give systemic antihistamines as needed.
- If a satisfactory response to treatment is not seen within 2 weeks, swab the meibomian gland secretions or upper conjunctival cul-de-sac for culture and sensitivity testing, and perform thyroid function testing.

▼ ***Key Point*** Bacterial blepharitis can be difficult to cure. Inform the owner that some dogs require periodic eyelid scrubs and antibiotic therapy on a long-term basis, along with medications to control concurrent allergies.

Chalazion and Hordeolum

- *Chalazion* is a granuloma of the meibomian gland.
  - Treat with surgical curettage of the granuloma via the conjunctival surface of the eyelid.
- *Hordeolum* is an infection or abscess of a meibomium gland or of an eyelash that results in a focal swelling of the lid.
  - Treat with hot packs and systemic antibiotics.
  - To hasten resolution, apply a topical antibiotic/corticosteroid solution or ointment, such as dexamethasone 0.1%, neomycin, or polymyxin B, q6–8h.

Allergic Blepharitis

- The animal usually presents with erythema and swelling of the eyelids that may be pruritic but is rarely painful. There may be a serous to mucopurulent discharge.
- Chronic or recurrent allergic blepharitis may be a manifestation of atopy.
- Treat with systemic antihistamines such as diphenhydramine (Benadryl, 2 mg/kg q8–12h PO) or corticosteroids (prednisone, 0.5–1.0 mg/kg q12–24h PO) and with topical corticosteroids.
  - Cold compresses help to decrease pruritus.
- For further information on allergy testing and treatment for atopy, see Chapter 46.

Parasitic or Fungal Blepharitis

- The eyelids may be infected by cutaneous parasites such as *Demodex* and *Sarcoptes* or by dermatophytes (ringworm).
- In dogs in which periocular alopecia and skin lesions are present but in which the conjunctiva is relatively spared, perform skin scrapings, dermatophyte cultures, and skin biopsies (see Chapters 43, 42, and 37, respectively).

Granulomatous Blepharitis

- Dogs with this condition present with prominent multifocal firm swellings of the lid margins of both eyes, often associated with the meibomian glands. It is not usually painful. The skin in advanced cases may be ulcerated. Etiology is unknown.
- Mild cases may be treated with topical antibiotic-dexamethasone solution four to eight times a day and oral corticosteroids (e.g., prednisone 0.5–1.0 mg/kg q12–24h). Oral antibiotic therapy is occasionally helpful.
- Some cases are recurrent and require ongoing topical corticosteroids for control.

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Chapter

133 Diseases of the Conjunctiva

Cecil P. Moore

ANATOMY AND PHYSIOLOGY

- Conjunctival mucosa covers the inner aspect of the eyelids, the front and back of the membrana nictitans, and the anterior sclera. Conjunctiva extends from the lacrimal caruncle nasally to the lateral canthus temporally.
- Normal conjunctiva is semitransparent and appears moist and glistening. Numerous small, branching blood vessels are visible within the conjunctiva.
- Sensory innervation to the conjunctiva is via ophthalmic and maxillary branches of the trigeminal nerve.
- The conjunctiva serves as a protective external physical, secretory, and immunologic barrier for the eye.
- Epithelial goblet cells within the conjunctiva produce mucus that contributes to the preocular tear film, harbors immunoglobulin, and traps foreign material and surface debris.

CONJUNCTIVITIS

The term *conjunctivitis* describes nonspecific inflammation of the ocular mucous membrane. Conjunctivitis is the most common cause of "red eye" in animals. To accurately assess the small animal patient presented with conjunctivitis, recognize inherent species differences in susceptibility and establish whether the disorder is primary or secondary. For example, feline conjunctivitis is generally caused by a primary ocular infection. Canine conjunctivitis, by contrast, usually is secondary to ocular surface irritants, tear film deficiencies, or foreign bodies.

Additional pertinent information regarding conjunctival disease is found in other chapters in this book. Conjunctival disease is often associated with viral infections, diseases of the cornea (see Chapter 134), diseases of the lacrimal apparatus (see Chapter 139), and diseases of the eyelids (see Chapter 132).

Etiology

Causes of conjunctivitis are numerous. Frequently, more than one etiologic factor plays a role in the clinical course of the disease.

▼ ***Key Point*** Regardless of the primary cause, bacterial infection is a common complicating factor in conjunctivitis.

Infectious Agents

- Infectious agents cause severe conjunctivitis in cats by infecting epithelial cells. Feline herpesvirus and *Chlamydophila felis* cause the most serious and common ocular infections in cats (see Chapter 11). *Mycoplasma felis, Staphylococci* species, *Streptococci* species, and coliform organisms are bacterial causes of usually less severe forms of feline conjunctivitis.
- Gram-positive aerobic bacteria are most commonly isolated from cases of canine conjunctivitis. Opportunistic bacterial infections are common in dogs following conjunctival irritation from other causes. Canine distemper virus (see Chapter 13) causes conjunctivitis and dacryoadenitis in dogs.

Tear Film Deficiency

- Tear film deficiency results in dehydration of the ocular surface with accompanying inflammation of the conjunctiva and cornea. Aqueous tear deficiency, or keratoconjunctivitis sicca, occurs more frequently in dogs than in cats (see Chapter 139).
- Although less common than aqueous deficiency, inadequacy of the lipid or mucous components may, when present, complicate the surface disease.
- Poor eyelid conformation, as with exophthalmos and/or lagophthalmos, potentiates exposure and drying, which may be further complicating factors.

Foreign Bodies

- Foreign bodies of the conjunctiva can include plant components, synthetic material, or metallic sub-

stances. Plant awns and weed seeds may become embedded in the fornices of the conjunctiva or migrate under the conjunctiva or behind the third eyelid. Embedded plant material is quite reactive and stimulates an intense pyogranulomatous inflammation.
- By contrast, synthetic material, such as glass or plastic, and certain metals, such as lead and stainless steel, are minimally reactive. Depending upon the location and rigidity of the material, conjunctival foreign bodies may cause direct frictional irritation and result in surface ulceration.

Trauma

- Trauma to the conjunctiva may be blunt, resulting in bruising of an intact membrane or penetrating with puncture or laceration.
- Conjunctival lacerations 5 mm in length or larger, or when the nictitans is involved, may require suturing.
- Otherwise, bruises, focal punctures, or smaller lacerations usually resolve uneventfully with symptomatic treatment.

▼ ***Key Point*** In cases of conjunctival trauma, examine the eye thoroughly for the presence of foreign bodies and intraocular lesions.

Chemical Irritants

- Chemical irritants that damage the conjunctiva include noxious gases, alkalis, and acids. Alkaline substances (e.g., lye, fresh lime, or ammonia) cause the most serious injuries.
- When chemical injury has occurred, flush the eye copiously with saline or tap water and evaluate for associated corneal and/or anterior uveal involvement.

Environmental Irritants

- Environmental irritants, such as dust, particles of sand or plant material, wind, and solar irradiation, are additional causes of conjunctivitis in small animals.
- These are particularly common causes in hunting dogs and outdoor working dogs.

Immune-Mediated Conjunctivitis

- Immune-mediated conjunctivitis results from acute allergic chemosis, atopy (see Chapter 46), follicular conjunctivitis, and conjunctivitis resulting from eosinophilic or plasmacytic infiltrates.
- An immune-mediated ulcerative conjunctivitis occurs in Doberman pinschers.

Proliferative Diseases

- Proliferative diseases are categorized as non-neoplastic or neoplastic.

Non-Neoplastic Disease

- Episcleritis and idiopathic granulomatous disease are the main non-neoplastic proliferative conjunctival disorders (see Chapter 134).
- Conjunctival epithelial hyperplasia, granulation tissue, and pigmentary infiltrates are additional examples of non-neoplastic proliferative conditions.

Neoplasia

- Conjunctival neoplasms may be primary or secondary.
- Papillomas, squamous cell carcinomas, and hemangiomas are the most common primary tumors. Less common primary neoplasms are hemangiosarcomas, mastocytomas, and melanomas.
- Adenomas, adenocarcinomas, fibromas, fibrosarcomas, lymphomas, transmissible venereal tumors (TVTs) and melanomas are tumors that may secondarily involve the conjunctiva.

Iatrogenically Induced Conjunctivitis

- Iatrogenically induced conjunctivitis results when topically administered therapeutic agents or surgical manipulations cause conjunctival inflammation.
- A number of drugs may cause conjunctivitis because of irritation from their active ingredients, vehicles, or preservatives. For example, neomycin hypersensitivity may manifest as severe conjunctivitis after topical administration of triple antibiotic combination.
- Surgical procedures result in conjunctivitis from direct insult (e.g., manipulation, dissection, thermal injury, or exposure during or following surgery).

Other Eye Diseases

- Other eye diseases, either ocular surface disorders or intraocular diseases, are frequently associated with conjunctival inflammation.
- Surface diseases in which conjunctivitis is prominent include episcleritis, keratitis, and eyelid disease (e.g., chalazia, entropion, ectropion, and cilia disorders).
- Conjunctival inflammation occurs with uveitis and glaucoma, although deeper episcleral injection is also present and is a hallmark of these intraocular diseases.

Clinical Signs

- ***Hyperemia*** resulting from vasodilation of conjunctival vessels causes the appearance of a red eye. The redness is intensified when conjunctival hemorrhage or episcleral vascular injection is also present.
- ***Ocular discharge*** is characteristic of conjunctivitis and is serous, mucoid (catarrhal), or mucopurulent. The type of discharge may change as conjunctivitis progresses—from serous (mild) to mucopurulent (severe).

- ***Chemosis*** is swelling or "puffiness" of the conjunctiva caused by edema of the mucosa and submucosal tissues.
- ***Pain*** with conjunctivitis varies with the severity of the ocular disease. Squinting and tearing are characteristic of most cases of conjunctivitis. Photophobia and marked blepharospasm generally occur only when other eye disease is present, such as ulcerative keratitis or uveitis.
- ***Tissue proliferation*** is a variable finding of subacute or chronic conjunctival disease. Conjunctival lymphoid follicular hyperplasia may develop in dogs as a nonspecific immune response to persistent antigenic stimulation. In cats, conjunctival follicles are associated with chlamydial conjunctivitis (see Chapter 11). Diffuse thickening of the conjunctiva may occur from epithelial hyperplasia or from chronic inflammatory cell infiltrates. Focal, acquired, proliferative lesions may be either granulomas or neoplastic.

Diagnosis

History

History pertinent to cases of conjunctivitis includes possible systemic illnesses, environment and habits, possible exposure to infectious or chemical agents, possible trauma, and previous ocular diseases, including notation of any medications administered.

Physical Examination

Perform physical examination to rule out multisystemic diseases (see Chapter 1).

Cultures

Culture and sensitivity testing is indicated for the definitive diagnosis and treatment of ocular infection. When culturing for fungi, *Mycoplasma, Chlamydophila,* or viral agents, consult with the diagnostic laboratory in advance regarding special requirements for submitting culture samples.

▼ ***Key Point*** When the need for cultures is anticipated, collect samples prior to applying topical agents or manipulating ocular surface tissues.

Ophthalmic Examination

Ophthalmic examination should be thorough and, in addition to confirming conjunctivitis, is aimed at identifying other forms of eye disease. Perform a complete ophthalmic examination.

- Inspect the external ocular surfaces and the anterior portion of the globe directly using a focal light source with magnification. The focused light is also used to check for pupil symmetry and light responses.
- Perform the intraocular examination with a focused light and an ophthalmoscope. Opacities of the normally clear ocular media (cornea, intraocular chambers, lens) are noted. Perform funduscopy to determine if abnormalities of the retina, choroid, or optic nerve are present.
- Measure aqueous tear production with Schirmer tear test strips as described in Chapters 131 and 139. Rule out aqueous tear deficiency because this is a common disorder in small animals, particularly in dogs, and results in chronic conjunctivitis with a tenacious mucopurulent ocular discharge.

▼ ***Key Point*** The Schirmer tear test strips measure reflex tear production. Evaluate prior to application of any local solutions, including topical anesthetic agents.

- Apply fluorescein stain to determine if surface ulceration is present. Establish nasolacrimal duct patency by allowing fluorescein stain to gravitate into the external nares.
- Following application of a topical anesthetic, examine for foreign bodies. Use blunt-tipped forceps to probe the conjunctiva fornices and to lift the third eyelid, allowing inspection of the posterior surface.
- Use tonometry to rule out other intraocular causes of red eye, for example, glaucoma (elevated pressure) and uveitis (low pressure). Applanation tonometry produces the most accurate intraocular pressure readings in small animal patients (see Chapters 131 and 137).

Cytology

- Cytology of conjunctival scrapings may provide a definitive diagnosis of inflammatory or neoplastic disease.
- Immunofluorescence testing of cytologic specimens can confirm viral or chlamydial infection.
- Fine-needle aspirates of masses can also provide the cytologic material for a definitive diagnosis.

Polymerase Chain Reaction

- Polymerase chain reaction (PCR) utilizes technology that allows detection of the DNA of ocular pathogens when present in very small quantities.
- In cases of feline conjunctivitis, the PCR procedure has been used successfully to diagnose feline herpesvirus-1 (FHV-1) infections. The sensitivity of PCR for FHV-1 diagnosis appears to be superior to other available methods.
- For the PCR test, place conjunctival swabs or scrapings in 1 ml of phosphate-buffered saline (PBS), frozen at −20°C, and submit for analysis.

Biopsy

- Biopsy the conjunctiva when cytology has not allowed the differentiation of inflammatory from neoplastic processes.

- Conjunctival biopsy is also needed to determine goblet cell density in suspected cases of preocular mucin deficiency.

Treatment

Objectives

- Correct or remove the underlying cause.
- Control secondary infection, which often complicates the primary process.
- Remove exudates and clean the eye and periocular area.
- Ensure a moist and well-hydrated ocular surface.
- Reduce inflammation and control discomfort.

Treat the Primary Cause

Because the primary causes of conjunctivitis in small animals are numerous, specific treatments vary considerably. Depending upon the circumstances, the following treatments may apply:

- Treat infection with a specific antimicrobial agent.
- Remove foreign materials.
- Surgically remove or correct for irritants (hairs or masses) that rub the eye.
- Remove offending allergens when possible.
- Treat for allergies (see Chapter 46).
- Treat tear deficiencies medically (see Chapter 139).

See Table 133-1 for more specific treatment recommendations.

▼ ***Key Point*** The following procedures are beneficial as symptomatic treatment and may be used as adjuncts when treating the primary disease, when awaiting results of diagnostic tests, or when treating empirically in nonspecific or undiagnosed cases of conjunctivitis.

Antimicrobial Therapy

- To control or prevent secondary pathogenic or opportunistic bacterial infections, apply broad-spectrum antibiotic ophthalmic drops or ointments topically.
- Avoid prolonged, indiscriminate application of topical antibacterial agents because this may encourage development of antibiotic-resistant bacterial strains or secondary fungal infections. The practice of continuous treatment can also predispose the animal to medication hypersensitivity.

Cleanse Discharges

- Use an eyewash solution (e.g., Dacriose, CooperVision) or physiologic saline solution to irrigate the ocular surface, remove exudates, and clean the eye and periocular area.
- Clip the periocular hairs.
- Use cotton swabs moistened with saline to soak and remove exudates.

Moisten or Hydrate the Eye

- Keep the conjunctival and corneal surfaces moist. If applied 3 to 4 times daily, antibacterial ointments have sufficient lubricating property to ensure continuous moistening of swollen or injured conjunctival tissues.
- When severe chemosis results in prolapse and exposure of swollen conjunctiva, place temporary tarsorrhaphy sutures until the acute swelling subsides (see Chapter 132).
- In cases in which the Schirmer tear test values are subnormal, apply artificial tear solutions topically 4 to 6 times daily. Lacrimostimulants may be indicated (see Chapter 139).

Anti-inflammatory Therapy

- Systemic anti-inflammatory drugs may be used in selected cases to minimize acute swelling, discomfort, and self-trauma. In cases of ocular trauma in dogs, systemic nonsteroidal anti-inflammatory drugs may be beneficial to reduce chemosis, hyperemia, and associated ocular pain.
- In dogs with normal renal function, flunixin meglumine (Banamine, Schering) may be given as a single dose IV of 0.5 to 1.0 mg/kg. This may be followed by oral aspirin at a dosage of 10 mg/kg q12h until signs of inflammation subside. Oral carprofen (2.2 mg/kg q12h) is also effective for controlling ocular inflammation. Monitor the animal closely for the side effects of gastritis and protect the stomach with an H_2 blocker, such as cimetidine (see Chapter 67). Flunixin, aspirin or other nonsteroidal anti-inflammatory drugs are not given to animals in which hemorrhage is the primary manifestation of the conjunctival disease.
- Short-term topical corticosteroids may reduce the swelling and hyperemia of an inflamed conjunctiva.

▼ ***Key Point*** Topical corticosteroids are contraindicated in cases of primary infectious conjunctivitis or corneal ulceration.

- Topical 5% sodium chloride may be applied to reduce chemosis; however, do not apply in eyes producing marginal amounts of aqueous tears because it will further dehydrate the ocular surface.

CONJUNCTIVAL SURGERY

Indications

- Trauma repair
- Diagnostic procedure (e.g., incisional biopsy)
- Focal lesion resection
- Repair of fibrosis/adhesions
- Grafting procedure

Table 133-1. TREATMENT OF SPECIFIC CAUSES OF CONJUNCTIVITIS

Causes	Treatments
Infectious Agents	
Bacterial	
Chlamydophila felis	Tetracycline ointment (q6–8h × 14–28d) (Terramycin, Pfizer; Achromycin, Lederle; Aureomycin, Lederle)
Mycoplasma felis	Tetracycline ointment (q6–8h × 10–14d) *or* Erythromycin ointment (q6–8h × 10–14d) (Erythromycin, Pharmafair) *or* Chloramphenicol ointment (q6–8h × 7d) (Chlorbiotic, Schering-Plough)
Streptococcus spp.	TA ointment (q6–8h × 10–14d) (Neobacimyx, Schering-Plough; TriOptic-P, SmithKline; or equivalent)
Staphylococcus spp.	TA or gentamicin (Gentocin, Schering-Plough) (as per TA above)
Gram-negative aerobes	TA, gentamicin, or ciprofloxacin (Ciloxan, Alcon) (as per TA above)
Viral	
Feline herpesvirus	Trifluridine or tacrolimus (see Chapters 11 and 134) Symptomatic therapy (see text)
Canine distemper virus	Symptomatic therapy (see text)
Keratoconjunctivitis Sicca	
Many causes	Treat cause if determined (see Chapter 139) Topical cyclosporine or tacrolimus (see Chapter 139) Topical antibiotics as needed Artificial tears (see Chapter 139) Lubricant ointments (see Chapter 139)
Foreign Bodies	Remove using magnification Irrigate eye Symptomatic therapy (see text) Complete eye examination
Trauma	
Bruise/focal puncture	Symptomatic therapy (see text)
Laceration	Symptomatic therapy (see text) ± Surgical repair
Chemical Irritants	Copious irrigation Symptomatic therapy (see text)
Environmental Irritants	Flush eyes Topical CS (q6–8h reduced to q12h as response is noted) only if fluorescein stain results are negative Lubricant ointment (q8h reduced to q24h as response is noted, then discontinue) ± Topical antibiotics Avoid reexposure
Immune-Mediated Disorders	
Acute chemosis	Topical and systemic CS
Atopy	Topical ± systemic CS, antihistamines, desensitization (see Chapter 46)
Follicular conjunctivitis	Topical ± intralesional CS, ± abrade follicles
Eosinophilic infiltrate	Topical ± intralesional CS (see Chapter 134)
Plasmacytic infiltrate	Topical ± intralesional CS (see Chapter 134)
Ulcerative conjunctivitis	Topical ± systemic CS, topical cyclosporine A (Optimmune, Schering-Plough)
Proliferative Diseases	
Inflammatory	Topical ± intralesional or systemic CS
Neoplastic	Surgery ± radiation, cryosurgery, or chemotherapy
Other Ocular Diseases	
Surface Diseases	
Eyelid disorders	Medical ± corrective surgery (see Chapter 132)
Keratitis	Medical ± surgery (see Chapter 134)
Episcleritis	Topical ± intralesional or systemic CS (see Chapter 134)
Intraocular Diseases	
Uveitis	Treat cause if determined (see Chapter 136) Topical CS and atropine Systemic anti-inflammatory agents
Glaucoma	Determine if primary or secondary (see Chapter 137) Topical hypotensive agents (see Chapter 137) Systemic hypotensive agents (see Chapter 137) Cycloablative or filtration surgery
Iatrogenic	
Topical agents	Discontinue use of irritating medications
Surgical procedures	Symptomatic treatment until surgical site heals

CS, corticosteroid; TA, Triple antibiotic.

Because the last category applies primarily to the treatment of ulcerative keratitis, refer to Chapter 134 for a discussion of conjunctival flaps and grafts.

Laceration Repair

Preoperative Considerations

- Examine the eye carefully for other damage (e.g., corneal, scleral, and intraocular lesions) and evaluate for retained ocular foreign bodies. Radiograph the head and orbit to check for radiopaque foreign bodies and to assess the extent of head trauma.

▼ ***Key Point*** If the traumatized eye is opaque, consider ultrasound imaging to determine the integrity of the globe and the extent of any intraocular damage.

- Because of the conjunctiva's rapid reparative characteristic, many punctures and small lacerations heal spontaneously without the need for suturing. Suture conjunctival lacerations 5 mm or greater or those associated with eyelid or nictitans lacerations.

Surgical Procedure

Objectives

- Cleanse and disinfect the wound.
- Remove surface foreign material and tissue debris.
- Explore the wound to determine if a foreign body was retained and to determine if deeper structures were damaged.
- Suture the conjunctival wound, if necessary, to restore mucous membrane integrity and function.
- Prevent secondary infection.

Equipment

- Eyelid retractors (e.g., Barraquer wire speculum)
- Small rat-tooth forceps (e.g., Bishop-Harmon forceps)
- Ophthalmic needle holders (Castroviejo)
- Conjunctival or Stevens tenotomy scissors
- Braided 6-0 or 7-0 absorbable suture material (e.g., Dexon, Vicryl) with microcutting needle

Technique

1. Following general anesthesia, insert eyelid retractors and flush the conjunctiva with 1:50 Betadine-to-saline solution; explore the wound for foreign bodies and for damage to deeper structures.
2. After assessing the extent of the conjunctival defect and confirming that surgical repair is needed, minimally debride the margins of the wound and gently undermine adjacent conjunctiva.
3. Close the conjunctival wound in a continuous pattern; space suture bites 1 to 2 mm apart.

Postoperative Care and Complications

- Apply topical antibiotic (e.g., neomycin, bacitracin, or polymyxin B) 3 to 4 times daily for 7 days.
- Administer systemic antibiotics for 1 week.
- If the eye is painful, apply fluorescein stain to identify corneal erosion or ulceration.

Biopsy

Preoperative Considerations

- Conjunctival biopsy and histopathology results should distinguish inflammatory from neoplastic diseases and can be used to determine goblet cell densities in suspected cases of preocular mucin deficiency.
- In tractable animals, conjunctival biopsy procedures can usually be performed following serial applications of topical anesthetic (e.g., 0.5% proparacaine).
- Subconjunctival or intralesional local anesthetic may be injected for deeper biopsies or for lesions of the palpebral, perilimbal, or third eyelid conjunctiva. Sedation and systemic analgesia may also be needed in such cases.

Surgical Procedure

Objectives

- Remove a representative sample of conjunctiva or subconjunctival tissue for histopathology.
- Minimize the resulting defect and avoid distorting the conjunctiva to the extent possible.

Equipment

- Small rat-tooth forceps
- Curved conjunctival or tenotomy scissors (e.g., Stevens, Westcott)
- Vial of 10% buffered formalin

Technique

1. Following local anesthesia, grasp the desired area of conjunctiva with small rat-tooth forceps and tent slightly.
2. Using small, curved scissors, excise a 3 mm × 4 mm specimen.
3. Gently spread the specimen onto a flat surface, such as a small Styrofoam pad or a section of a wooden tongue depressor.
4. Immediately fix the specimen in 10% buffered formalin.

Postoperative Care and Complications

- A small amount of hemorrhage is anticipated but is usually minimal, as fibrin quickly seals the wound.
- Defects resulting from biopsy that are less than 4 mm × 4 mm usually heal uneventfully with topical antibi-

otic treatment. Larger defects should be sutured as described in "Laceration Repair."
- Remove discharges and cleanse the eye as needed. This may be necessary 3 to 4 times the first day but is reduced over the following 5 days to once daily.
- Apply topical antibiotic ointment (e.g., neomycin, bacitracin, or polymyxin B) to the affected eye 3 times daily for 7 days.

Mass Removal

Preoperative Considerations

- Surgical excision alone may be curative for cysts, dermoids, ectopic hairs, focal granulomas, and some tumors involving the conjunctiva (e.g., papillomas and adenomas).
- Surgical excision is an important adjunct in the treatment of inflammatory pseudotumors and more aggressive neoplasms, such as squamous cell carcinomas or adenocarcinomas.
  - Chemotherapy, immunotherapy, cryosurgery, hyperthermia, or beta-irradiation may be needed to treat neoplastic diseases in addition to local excision.
  - Definitive therapy depends upon the specific histopathologic diagnosis.
- General anesthesia is usually required for effective removal of conjunctival masses.

Surgical Procedure

Objectives

- Surgically remove conjunctival masses that interfere with ocular function, threaten preservation of the globe, or pose a threat to survival of the animal.
- Debulk a mass to obtain diagnostic samples and to increase efficacy of adjunctive treatments (e.g., cryosurgery, radiation, immunotherapy, hyperthermia, and chemotherapy).

Equipment

- Same as that listed for "Laceration Repair"
- Vial of 10% buffered formalin

Technique

1. Incise the overlying conjunctiva. Grasp the mass with forceps and elevate. Undermine and excise with small, curved tissue scissors.
2. Small conjunctival wounds (i.e., up to 5 mm in diameter) generally do not require suturing and heal in 2 to 4 days.
3. Suture conjunctival wounds greater than 5 mm in diameter with 7-0 braided absorbable material (Vicryl) in a continuous pattern.
4. To allow primary closure for larger conjunctival wounds, undermining and sliding adjacent conjunctiva may be required.
5. Repair large defects by a pedicle graft of adjacent healthy conjunctiva similar to that of a rotating cutaneous pedicle flap.
6. For conjunctival mass lesions involving the cornea, see Figure 134-1 in Chapter 134.

Postoperative Care and Complications

- Remove discharges and cleanse the eye as needed.
- Apply topical antibiotic ointment (e.g., neomycin, bacitracin, or polymyxin B) to the affected eye 3 times daily for 7 days.
- Prevent self-trauma with a restraint collar.
- Administer systemic analgesic or anti-inflammatory agents as indicated to control discomfort.
- Large defects of the conjunctiva healing by second intention may result in extensive granulation and scarring, with possible symblepharon formation.

Symblepharon Repair

Preoperative Considerations

- Symblepharon results from the fibrosis of two apposing ulcerated epithelial surfaces.
- Neonatal conjunctivitis of kittens, caused by feline herpesvirus, is a common cause in cats (see Chapter 11).
- Postinflammatory adhesions may reduce or obliterate the conjunctival fornices resulting in immobility of the globe.
- Adhesions may result in abnormal tear dynamics and chronic epiphora.
- Corneal involvement results in scarring and opacification, which reduces vision.

Surgical Procedure

Objectives

- Remove scar tissue and free adhesions, thereby restoring normal anatomic relationships and functions of the ocular surface structures.
- Prevent readhesion and minimize postoperative scarring.

Equipment

- Colibri forceps
- Beaver blade (#64) with handle
- Instruments as listed for "Laceration Repair"
- Corneal-scleral conformer

Technique

1. When extensive corneal opacification is present, perform a lamellar keratectomy (see Fig. 134-1, Chapter 134).
2. Incise the perilimbal bulbar conjunctiva with a #64 Beaver blade, undermine and free adhesions with small curved scissors, and elevate the conjunctiva as a mobile circumlimbal flap.

3. Perform sufficient dissection and removal of subconjunctival scar tissue to reestablish the conjunctival fornices.
4. Free the third eyelid by dissecting amid the third eyelid, the globe, and the eyelids, if necessary.
5. Place a bandage soft contact lens over the corneal surface behind the third eyelid.
6. Apply a broad-spectrum antibiotic ophthalmic ointment into the conjunctival cul-de-sac.
7. Place a corneal-scleral conformer over the globe and the front side of the third eyelid.
   a. A conformer may be constructed using a commercially available corneal-scleral protector (Crouch corneal protector, Storz Instrument, St. Louis).
   b. The corneal protector may be reduced to an appropriate size by trimming the perimeter with utility scissors, smoothing the cut margins with a file or fine sandpaper, rinsing the plastic of sanded particles, and sterilizing with gas.
8. Secure the corneal protector with three temporary tarsorrhaphy mattress sutures.

Postoperative Care and Complications

- Place a restraint collar on the animal to prevent self-trauma.
- Immediately postoperatively, administer a mild sedative or analgesic.
- Remove discharges and cleanse the eye as needed.
- Tarsorrhaphy sutures prevent topical treatment of the eye; therefore, administer broad-spectrum systemic antibiotics (e.g., oral amoxicillin).
- Remove tarsorrhaphy sutures, the conformer, and the contact lens in 14 days.
- Following removal, irrigate the eye and initiate topical treatment with an antibiotic ointment 3 times daily for 1 week or until the ocular surface has a negative retention of fluorescein stain.
- Initiate a topical antibiotic or corticosteroid (e.g., neomycin, bacitracin, or dexamethasone) treatment 3 times daily *after* the surface has completely healed (i.e., negative results with fluorescein stain).
- Gradually reduce the frequency of topical treatments, and discontinue after 3 weeks.
- Additional corneal scarring and readhesion of conjunctival surfaces are the main complications with symblepharon surgery; however, the contact lens and corneal conformer minimize these complications and may result in substantial improvement in ocular function.

Conjunctival Grafts

See Chapter 134.

SUPPLEMENTAL READING

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Chapter

134 Diseases of the Cornea and Sclera

Thomas J. Kern

Disorders of the cornea are common in veterinary practice. Acquired corneal disorders such as ulcerative keratitis, melanosis, and pannus are leading causes of preventable blindness in dogs and cats. The high frequency of corneal disorders should not lull practitioners into forgetting the importance of rigorous diagnosis and attentive management. Disorders of the sclera are less common. Their diagnosis may be more difficult than corneal disorders and they may be presented at a more advanced stage.

CONGENITAL DISORDERS

Dermoids

Dermoids are islands of skin embryologically misplaced on the cornea (especially the temporal cornea) and conjunctiva and occasionally malpositioned on the eyelids. They contain epidermis, dermis, fat, sebaceous glands, and hair follicles.

Etiology

- In Burmese cats, dermoids are an inherited condition that frequently involves the eyelids.
- Dermoids are considered a spontaneous nonheritable condition in dogs, although some breeds (e.g., German shepherd) appear to be afflicted at a higher frequency than others; thus a genetic basis cannot be completely ruled out.

Clinical Signs

Dermoids' surface irregularity promotes chronic blepharospasm and epiphora; the hairs cause corneal and conjunctival irritation.

Diagnosis

- On ocular examination, the typical appearance of skin on the cornea or conjunctiva is diagnostic.

Treatment

- Remove by keratectomy (surgical removal of corneal tissue). If removal is complete, corneal scarring is present but minimal.
- If the conjunctiva also must be resected, suture the edges of the conjunctiva to the limbus, using 7-0 Vicryl, to discourage postoperative adhesion of the conjunctiva to the cornea.

Microcornea

Etiology

Microcornea usually is associated with complicated *microphthalmos,* a condition with both genetic and environmental causes.

- Inherited microphthalmos syndromes have been characterized in the Australian shepherd, collie, Shetland sheepdog, Old English sheepdog, Akita, American cocker spaniel, miniature schnauzer, Doberman pinscher, Samoyed, Cavalier King Charles spaniel, and Lancashire heeler.
- Multiple heritable ocular defects associated with partial albinism and deafness occur in the Great Dane and collie. Teratogenic influences on the dam during early pregnancy (e.g., viral or other illnesses, live virus vaccines, drugs) may be responsible.
- Microphthalmos occurs less frequently in cats than in dogs; its causes are poorly characterized.

Clinical Signs

- The cornea appears abnormally small and often is misshapen.

Diagnosis

- Measure the horizontal and vertical diameters of the cornea and compare with those of the normal contralateral eye, if present, or with the eye of a normal animal of similar breed.

Treatment

- Treatment is neither available nor warranted. If the condition is associated with microphthalmos, vision may be impaired.

Corneal Opacities

Persistent Pupillary Membrane–Associated Opacities

Etiology

- An embryologic cleavage defect results in strands of iris attached to the endothelial surface of the cornea. Where attachment occurs, endothelium is absent and Descemet's membrane is abnormal, resulting in permanent nonprogressive opacity.
- The condition is inherited in basenjis and probably in other breeds; the mode of inheritance is uncertain (see Chapter 136).

Axial Geographic Subepithelial Opacities in Puppies

Etiology

- The cause(s) of these variably prominent, well-circumscribed corneal opacities is unknown.
- They are commonly noted during examination of certain breeds (collie, Shetland sheepdog, English springer spaniel) for inherited ocular disorders and thus have an uncertain genetic basis.

Clinical Signs

- Most obvious in the exposure strip of axial cornea, these superficial opacities are usually bilateral, relatively symmetric, painless, and irregular.
- Typical appearance is that of a non-ulcerated geographic axial corneal opacity of variable density.

Diagnosis

- A typical corneal opacity in a dog less than 1 year of age suggests the diagnosis.
- The absence of fluorescein dye retention rules out ulcerative keratitis and lack of corneal vascularization rules out an old corneal scar.

Treatment

- Do not treat. Most opacities substantially disappear by maturity.
- A residual faint opacity may remain near the nasal and temporal limbus.

Colobomatous Defects of the Sclera

Etiology

- Scleral defects occur as part of the spectrum of inherited ocular anomalies in collies, Shetland sheepdogs, and Australian shepherds.
  - The collie/Shetland sheepdog anomaly is said to be due to a simple recessive gene with variable expression; a different mode of inheritance has been postulated for the colobomas.
  - The Australian shepherd defect is inherited as an incompletely penetrant recessive trait.
- Optic disc and peripapillary colobomas occur in basenjis; inheritance may be autosomal dominant.
- Great Danes that are the progeny of two harlequin parents are afflicted with colobomatous microphthalmos similar to that in Australian shepherds.
- Posterior pole colobomas of the optic disc and surrounding sclera of unknown cause are seen occasionally in domestic short- and longhaired cats.

Clinical Signs

- In collies and Shetland sheepdogs, the only commonly visible external sign of the defect is relative or absolute microphthalmos. Choroidal hypoplasia, scleral ectasia, optic nerve coloboma, and retinal detachment may be present in the fundus. Blindness is present with retinal detachment and/or optic nerve coloboma.
- Affected Australian shepherds (and Great Danes) usually have mostly white coat color and unilateral or bilateral microphthalmos. In many microphthalmic eyes there are large equatorial staphylomas (i.e., areas of pitted and thinned sclera posterior to the ciliary body). Iris anomalies (heterochromia, corectopia, persistent pupillary membranes, pseudopolycoria) often are present, as are cataracts, retinal dysplasia, and retinal detachment.
- Basenjis with optic disc colobomas have abnormal vision and may have persistent pupillary membranes, although the two defects may not be related.
- Cats afflicted with posterior segment optic nerve coloboma and scleral ectasia are blind in the affected eye, the external appearance of which is normal except for tonic mydriasis.

Diagnosis

- Indirect ophthalmoscopy provides panoramic views of the ocular fundus and is the most sensitive and practical means of diagnosis.

Treatment

- Therapy for these defects is neither indicated nor available.
- Discourage breeding of affected animals.

CORNEAL DEGENERATIONS AND DYSTROPHIES

▼ ***Key Point*** Corneal dystrophy is a congenital or acquired, usually bilateral, corneal opacity typically

unassociated with neovascularization. Degenerations are often but not invariably unilateral abnormalities, frequently (but not necessarily) associated with neovascularization, which are secondary to other ocular or systemic disorders.

Corneal degenerations and dystrophies may affect epithelium, stroma, or endothelium (epithelial dystrophies are discussed under Corneal Ulceration). In some animals, differentiation between the two disorders is difficult.

Stromal Dystrophy

Etiology

- Stromal corneal dystrophy is a genetic disorder afflicting many breeds of dogs, including the collie, Siberian husky, Cavalier King Charles spaniel, beagle, Airedale terrier, cocker spaniel, Alaskan malamute, bearded collie, bichon frise, German shepherd, Lhasa apso, mastiff, miniature pinscher, Weimaraner, pointer, and Samoyed.
- One line of Manx cats was reported with an inherited bilateral stromal dystrophy.

Clinical Signs

- At least two forms of stromal dystrophy occur in dogs:
  - One form is a bilaterally symmetric oval axial or paraxial subepithelial/anterior stromal crystalline opacity.
  - The second form, in which a deeper stromal opacity involves more peripheral portions of the cornea, occurs in Siberian huskies and occasionally in other breeds.
  - Corneal neovascularization is absent in both forms. Age of onset varies according to breed and individual animals, from 6 months to old age.
- Affected Manx cats developed progressive stromal edema leading to bullous keratopathy and recurrent epithelial erosion.

Diagnosis

- *Dogs:* The typical crystalline, usually bilateral, corneal opacity (fluorescein dye negative) unassociated with corneal neovascularization or other corneal pathologic changes suggests stromal dystrophy.
  - Rule out causes of corneal degeneration, which may appear similar, including keratoconjunctivitis sicca (KCS), lagophthalmos, eyelid defects, and endocrinopathy (e.g., hypothyroidism).
- *Cats:* Progressive corneal edema in Manx cats suggests the diagnosis.

Treatment

- Treatment in dogs is rarely indicated or necessary. Keratectomy may remove superficial opacities, but recurrence is likely. Do not breed affected animals.

Stromal Degenerations

Etiology

Ocular causes of stromal degenerations include

- Ulcerative and non-ulcerative keratitis
- Corneal exposure
- Dryness secondary to KCS or lagophthalmos

▼ ***Key Point*** Systemic diseases suspected to cause degenerations include primary hyperlipidemia, secondary hyperlipidemia (especially associated with hypothyroidism), and hyperadrenocorticism (implicated in calcific degeneration or "band keratopathy").

Clinical Signs

- The central (axial) to paracentral opacities are often bilaterally symmetric and range from crystalline to dense yellow-white; they may be indistinguishable from primary corneal dystrophy.
- In calcific degeneration, the cornea feels "gritty" when touched with a cotton-tipped applicator.
- Neovascularization is often although not invariably present.

Diagnosis

- A typical lesion (with or without neovascularization) and/or a history of a previous condition (e.g., ulcer, other keratitis, lagophthalmos) suggests degeneration rather than dystrophy.

▼ ***Key Point*** Do not assume that concurrent primary or secondary hyperlipidemia or hyperadrenocorticism is the cause unless ocular causes of degeneration have been ruled out. Even then, a causal relationship may be uncertain.

- Clinical differentiation of these two conditions frequently is difficult.

Treatment

- Treatment is rarely indicated or necessary.
- Consider keratectomy for large, dense axial lesions that interfere with vision.
  - Prognosis is guarded, as recurrence is possible; in addition, postoperative corneal opacity may be significant.
- For calcific degeneration, consider keratectomy for superficial lesions. Topical application of 1% EDTA q4h may be helpful.

Endothelial Dystrophy

Etiology

- Endothelial dystrophy is a breed-related, acquired disease resulting in premature loss of corneal

endothelial cells to a level below that required to maintain normal corneal stromal deturgescence.

Clinical Signs

- *Dogs:* Progressive bilateral corneal edema may affect Boston terriers, Chihuahuas, dachshunds, and occasionally other breeds. It can begin focally or in a diffuse pattern and progress from the peripheral to the central cornea or vice versa.
  - Initially painless, the condition frequently results in recurrent corneal erosion when stromal and epithelial edema become extensive. Corneal neovascularization usually is absent.
- *Cats:* Endothelial dystrophy causing progressive bilateral corneal edema has been reported rarely in domestic shorthaired cats.

Diagnosis

- Endothelial dystrophy is presumptively diagnosed when bilateral corneal stromal edema is present unassociated with signs of uveitis or glaucoma.

▼ ***Key Point*** Determine intraocular pressure (IOP) to rule out uveitis (decreased IOP) or glaucoma (elevated IOP) (see Chapters 136 and 137).

- Corneal ulceration, if present, usually is superficial and insufficient to cause the degree of stromal edema observed.

Treatment

- For severe stromal and epithelial edema, consider treatment with topical 5% sodium chloride (Muro-128, Bausch and Lomb) q4–6h to discourage corneal erosion.
- When erosions occur, debride non-adherent epithelium and administer topical broad-spectrum antibiotics and 1% atropine.

Endothelial Degeneration

Etiology

- Intraocular inflammation or hemorrhage, primary and secondary glaucoma, anterior lens luxation, and corneal injury may cause endothelial degeneration.
- Natural infection with canine adenovirus-1 (infectious canine hepatitis) or vaccination with modified live vaccines containing adenovirus-1 or adenovirus-2 may result in immune-mediated anterior uveitis and endothelial destruction 7 to 10 days following exposure (see Chapter 16).
  - The proportion of dogs affected can be high (in natural infection, about 20%), low (adenovirus-1 vaccination), or very low (adenovirus-2 vaccination).

Clinical Signs

- Chronic focal or diffuse corneal edema (giving the cornea a ground-glass appearance) with or without superficial or deep corneal neovascularization characterizes endothelial degeneration. If the edema resolves, only transient endothelial dysfunction occurs.

▼ ***Key Point*** Corneal endothelial cells in many adult domestic animals have little to no regenerative capacity. Repair occurs by hypertrophy and migration of remaining endothelial cells.

- Most dogs with adenovirus-mediated uveitis present with generalized corneal edema after resolution of transient uveitis.
  - A small proportion of affected dogs, especially sight hounds and Arctic breeds, quickly develop intractable secondary glaucoma.

Diagnosis

- Diffuse, moderate to severe generalized corneal edema strongly suggests endothelial dysfunction.
- Perform a careful ocular examination to rule out antecedent causes (e.g., inflammation, glaucoma, hyphema, lens luxation).

Treatment

- Direct treatment toward prevention by effectively controlling the causative or attendant conditions (e.g., glaucoma, uveitis, hyphema) before irreversible endothelial degeneration occurs.

Prognosis

- Most dogs with adenovirus-related endotheliopathy recover endothelial function, and the corneal edema resolves within a few weeks.
- Corneal edema secondary to other causes has a variable prognosis for resolution.

CORNEAL ULCERATION

Loss of one or more corneal epithelial layers commonly is termed *corneal erosion* or *abrasion*. Full-thickness loss of epithelium with at least some stromal loss is termed *ulceration*.

- *Simple corneal ulceration* is that which heals uneventfully in a normal amount of time (3 days).
- *Complicated corneal ulceration* involves delayed healing associated with infection or other pathologic processes.
- *Progressive corneal ulceration* involves a deepening or enlarging area.

Etiology

Traumatic Injury

This is probably the most common cause of ulcerative keratitis in dogs and cats.

- Blunt trauma may cause focal or diffuse damage to any or all corneal layers. Corneal laceration may be partial or full thickness. Aqueous loss, anterior chamber collapse, and iris prolapse may ensue.
- Most traumatic corneal erosions and ulcers heal rapidly; however, some become persistent if epithelial basement membrane damage is severe or if a foreign body persists in the conjunctival fornix.
- Traumatic injury may begin a cascade of pathologic complications resulting in complicated ulceration.

Bacterial Infection

At least minor epithelial injury is required for colonization to occur; bacteria do not adhere to normal epithelial cell membranes.

- Pathogenic and normally nonpathogenic commensal organisms may infect the cornea. Staphylococci and streptococci are the ocular bacterial organisms most frequently isolated from normal eyes of dogs and cats.
- Topical antibiotic or corticosteroid therapy may result in overgrowth of pathogenic fungi, yeasts, and bacteria. However, infection of corneal ulcers by fungi is rare in dogs and cats.

Pseudomonas

- *Pseudomonas* infection commonly results in corneal melting, perforation, and loss of the eye.
- Proteolytic enzymes produced by the bacteria, inflammatory cells, and response to infection by the cornea itself cause stromal proteoglycan and collagen destruction, giving the affected cornea a mucoid appearance as melting occurs.

Feline Herpesvirus (FHV)

- FHV infection is an important cause of corneal ulceration in cats (see Chapter 11). Superficial ulcers may be small, punctate, or linear branching fern-like figures classically described as dendrites. Larger, geographic superficial to deep ulcers form from coalescence of smaller focal ulcers. Stromal ulcers, descemetoceles (i.e., a circular loss of stroma down to Descemet's membrane), and perforations may develop.

Epithelial Dystrophy (Erosion, Indolent Ulcer, Boxer Ulcer)

- An apparently inherited corneal epithelial basement membrane dystrophy has been recognized in boxers and probably occurs in other breeds. A different inherited epithelial dystrophy afflicts Shetland sheepdogs. Affected dogs are usually middle-aged or older.
- Trauma and chronic corneal inflammation may result in acquired epithelial basement membrane abnormalities.
- Endocrinopathies such as diabetes mellitus, hyperadrenocorticism, and hypothyroidism may be associated with fragile corneal epithelium that may be susceptible to injury and prone to delayed healing.

Neurotrophic Keratitis

This condition develops following denervation of the cornea's sensory nerve supply from the ophthalmic branch of the trigeminal nerve. Sensory nerves and the neurotransmitters and other substances involved have a beneficial influence on the maintenance of epithelial integrity.

Corneal Dryness

This condition occurs secondary to

- Aqueous tear deficiency (KCS; see Chapter 139).
- Qualitative tear film abnormalities (mucin deficiency).
- Exposure from lagophthalmos due to conformational abnormalities of eyelid closure or facial nerve palsy (see Chapter 139).

Endocrinopathies

Endocrinopathies such as diabetes mellitus, hypoadrenocorticism, and hypothyroidism have been associated with corneal ulceration in dogs; a causative role in the development of ulcers has not been established.

Idiopathic Corneal Ulceration

An idiopathic form is peculiar to the cat and is associated with corneal sequestrum formation (mummification).

- Following chronic, usually superficial, unilateral or bilateral corneal ulceration a brown or black discoloration of the stroma develops. The discolored plaques of degenerate cornea remain in place or slough away after weeks or months.
- A corneal sequestrum is associated with pain and corneal neovascularization.
- Concurrent herpesvirus infection has been demonstrated in some cats.

Clinical Signs

- *Blepharospasm, photophobia,* and *epiphora* are stimulated by painful sensations from damaged epithelium as well as from secondary ciliary muscle spasm.
- *Corneal opacity* results from stromal and epithelial edema and infiltration by inflammatory cells into the affected area.

- *Corneal surface depression* is present if stromal loss, including descemetoceles, has occurred.
- *Neovascularization* denotes complicated ulceration in which healing has been delayed by ocular factors (e.g., KCS, eyelid defects, infection) or non-ocular factors (e.g., self-trauma, inappropriate medical therapy).
  - Superficial neovascularization usually suggests a corneal or external complicating factor and appears as tree-like individual vessels infiltrating focal sectors of cornea.
  - Deep (ciliary) neovascularization denotes intraocular inflammation and appears as an advancing ring of fine vessels evenly infiltrating the peripheral cornea for its entire circumference.
- In *epithelial dystrophy*, the fluorescein dye–positive stained area is surrounded by a halo of poorly adherent or non-adherent epithelium that stains less brilliantly than the center, where epithelium is absent.
  - Corneal neovascularization is absent unless previous traumatic manipulation (e.g., chemical cauterization) has been performed. This is in contrast to chronic corneal ulceration due to traumatic, infectious, and other causes, which routinely incite neovascularization.
  - Blepharospasm and photophobia, if present, frequently are minimal.
- *Miosis* occurs as an axon reflex from stimulation of corneal, conjunctival, and periocular branches of the ophthalmic nerve (see Chapter 136).
- *Aqueous flare* (i.e., the presence of large amounts of serum proteins in the anterior chamber) indicates iridocyclitis (anterior uveitis) with breakdown of the blood-aqueous barrier (see Chapter 136).
- *Hypotony* (reduced intraocular pressure) usually accompanies moderate to severe anterior uveitis and results from reduced aqueous production and, possibly, increased aqueous outflow.

Diagnosis

History

Important aspects include

- Time and circumstances of onset.
- Presence and duration of discharge and blepharospasm.
- Change in the eye appearance between onset and presentation.
- Current and previously treated ocular disorders.

Ocular Examination and Accessory Diagnostic Tests

- Collect samples for corneal culture before instilling any diagnostic solutions.
- The hallmark of corneal ulceration is retention of fluorescein dye, which stains corneal stroma, tears, and aqueous humor.
  - To rule out KCS, perform a Schirmer tear test (Schering Plough) before fluorescein dye application.

▼ ***Key Point*** Descemetoceles demonstrate an annular pattern of dye retention along their walls, but exposed Descemet's membrane in the center does not stain.

- Before applying topical anesthesia, test corneal sensitivity with a cotton-tipped swab.
- Following topical anesthesia, obtain scrapings for cytology and Gram staining from ulcers showing rapid progression, soft edematous margins, or a yellow inflammatory cell infiltrate.
- Because sequestra have been noted in cats experimentally infected with FHV, submit diagnostic tests (viral isolation, polymerase chain reaction, or immunofluorescence testing of conjunctival scrapings; see Chapter 11) to rule out herpesvirus infection.
- The diagnosis of epithelial dystrophy is suggested by a chronic non-adherent epithelial margin with only mild discomfort.

Medical Treatment

▼ ***Key Point*** Topical corticosteroids and nonsteroidal anti-inflammatory drugs are contraindicated with corneal ulceration.

▼ ***Key Point*** Topical anesthetics for *diagnostic* purposes are safe; however, because they are toxic to corneal epithelium, their use in *treatment* is contraindicated.

Simple Erosions and Superficial Ulcers

- Instill topical broad-spectrum antibiotics (e.g., bacitracin, neomycin, polymyxin). Treat with ointments q6h or with aqueous solutions at least q4h.
- Instill topical 1% atropine ointment or solution, to effect, to maintain mydriasis and, presumably, ciliary muscle paralysis (e.g., q6–8h initially, followed by q12–24h, and then every other day).
- Schedule follow-up examinations every few days until epithelialization is complete.

Deep and/or Progressive Ulceration

Base the choice of topical and subconjunctival antibiotics on corneal cytologic findings (Table 134-1).

- Supplement topical 1% atropine therapy with
  - Topical fortified gentamicin or tobramycin drops (Tables 134-2 and 134-3) applied q1–2h.
  - Subconjunctival antibiotic injection (see Table 134-1).

Table 134-1. ANTIBIOTIC SELECTION BASED ON GRAM STAIN OF CORNEAL SCRAPINGS

Gram Stain Finding	Antibiotics*		
	Topical	Subconjunctival	Systemic
Gram-positive cocci	Bacitracin (Neosporin; Burroughs Wellcome) or cefazolin (Genera)	Methicillin (Staphcillin; Squibb), 100 mg, or gentamicin (Gentocin; Schering), 10–40 mg, or tobramycin (Tobrex; Alcon Labs), 10–30 mg	Ampicillin or gentamicin or cefazolin or tobramycin
Gram-negative rods	Gentamicin or tobramycin	Gentamicin, 10–40 mg, and/or carbenicillin, 250 mg, and/or tobramycin, 10–30 mg	Chloramphenicol or gentamicin or tobramycin
Mixed infections	Bacitracin and gentamicin	Methicillin, 100 mg, and gentamicin, 20 mg	Gentamicin or tobramycin

Modified from Kern TJ: Ulcerative keratitis. Vet Clin North Am (Small Anim Pract) 20(3):653, 1990.
*Product name and manufacturer are given in parentheses following the first mention of the generic drug.

Table 134-2. FORMULAS FOR FORTIFIED ANTIBIOTICS IN ARTIFICIAL TEARS

Drug	Form	Quantity of Antibiotic	Quantity of Artificial Tears (ml)	Final Volume (ml)	Final Concentration (mg/ml)
Gentamicin (Gentocin injectable; Schering)	100 mg/ml	2.5 ml (250 mg)	15	17.5	14
Gentamicin (Gentocin injectable; Schering)	50 mg/ml	5 ml (250 mg)	12.5	17.5	14
Tobramycin (Nebcin; Eli Lilly)	40 mg/ml	5.5 ml (220 mg)	15	20.5	11
Bacitracin (Bacitracin sterile USP; Quad Pharmaceuticals)	50,000 IU/vial	150,000 U (3 vials)	15	15.6	9600 IU/ml
Cefazolin (Genera)	1 g/vial	3 ml (1 vial)	15	18	50

Reprinted with permission from Kern TJ: Ulcerative keratitis. Vet Clin North Am (Small Anim Pract) 20(3):655, 1990.

Table 134-3. FORMULAS FOR FORTIFIED FORMS OF PROPRIETARY TOPICAL OPHTHALMIC ANTIBIOTICS

Drug	Bottle Concentration (mg/ml)	Bottle Volume (ml)	Parenteral Antibiotic Added	Final Concentration (mg/ml)
Gentamicin (Gentocin ophthalmic solution; Schering)	3	5	50 mg (1 ml of 50 mg/ml solution)	11
Tobramycin (Tobrex; Alcon)	3	5	10 mg or 40 mg/ml	4 or 9

Reprinted with permission from Kern TJ: Ulcerative keratitis. Vet Clin North Am (Small Anim Pract) 20(3):655, 1990.

- Consider treatment with acetylcysteine or sodium EDTA (0.15 M) q1–2h if corneal melting is apparent or suspected. Efficacy of these drugs is uncertain.

Surgical Treatment

- Consider surgical options for treatment of corneal ulcers that are deep and progressive.

Objectives

- Prevent ulcer progression.
- Repair perforation.
- Protect the corneal surface.
- Retard melting.

Protective Procedures

▼ ***Key Point*** Protective procedures do not provide blood supply or cells to aid in the healing of corneal ulceration. They do interfere with treatment and further evaluation of corneal ulceration.

- *Nictitans flap*—Indications include post-proptosis corneal coverage and, possibly, conservative treatment

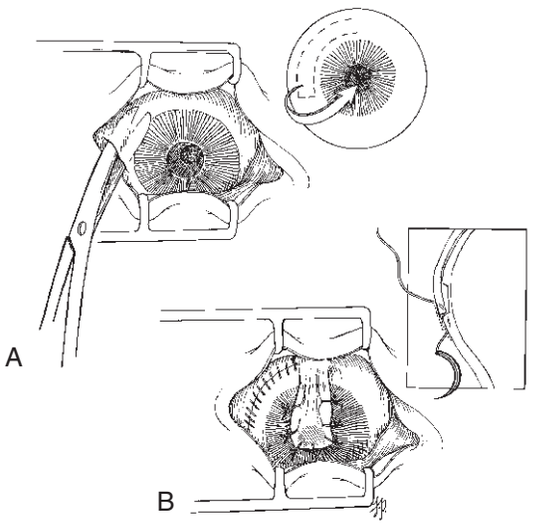

Figure 134-1. Pedicle graft. *A,* Using Stevens tenotomy scissors, elevate the bulbar conjunctiva, incise, and dissect free of the globe. Create and rotate a pedicle of conjunctiva, epithelial surface up, to cover the corneal defect. *B,* Suture the conjunctival pedicle to the cornea, covering the defect, using simple-interrupted sutures. Appose the epithelial margins of the conjunctival graft to the cornea (see inset and Fig. 134-3*B*).

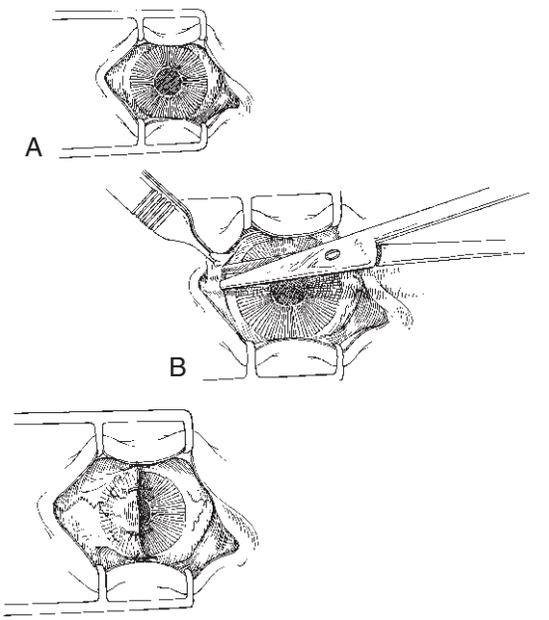

Figure 134-2. Fornix-based hood (180°) flap. *A,* A corneal ulcer is present and is to be repaired with a hood-graft from the adjacent bulbar conjunctiva. *B,* Elevate the bulbar conjunctiva adjacent to the corneal defect and use Stevens tenotomy scissors to incise and dissect free this portion of conjunctiva. *C,* Advance the conjunctiva over the defect and suture in place using simple interrupted sutures. Place sutures in the cornea to stabilize the graft over the corneal defect and in the limbus to relieve tension.

of recurrent superficial erosion following debridement; contraindications include deep or infected ulcers, descemetoceles, and uncorrected perforations.

- *Temporary tarsorrhaphy (closure of the eyelids)*—Indications and contraindications are the same as for nictitans flap.

Supportive Procedures

Supportive procedures include conjunctival flap surgery and cyanoacrylate tissue adhesive application.

Conjunctival Flap

Indications

Deep ulcers, infected ulcers following short-term intensive antibiotic therapy, descemetoceles, sutured corneal wounds that leak, and, rarely, recurrent epithelial erosions.

Type

Depending on the extent and location of the lesion, the flap may be a pedicle graft (Fig. 134-1), fornix-based hood (180 degrees) flap (Fig. 134-2), or circumferential (360 degrees) flap.

Technique

1. Carefully debride any necrotic or melting corneal stroma from the ulcer and its margin, using a #64 Beaver blade.
2. Form flaps by making a conjunctival incision at the limbus. Bluntly dissect the conjunctiva from the underlying connective tissue (episclera) using tenotomy scissors.
3. Free the conjunctival graft by cutting it from its limbal attachment.
4. Suture pedicle and hood grafts to the cornea, using 7-0 polyglactin (Vicryl) or smaller suture material. Attempt to achieve epithelial to epithelial apposition of the conjunctiva and cornea. To relieve tension, the graft can be sutured to the limbus with two sutures.
5. Suture complete 360 degree flaps in a horizontal mattress pattern, top half to the bottom half, along the center of the cornea but not directly to the cornea.
6. Remove sutures in 10 to 14 days.
7. Separate the graft from its blood supply and trim points of adhesion of the flap to the previous corneal defect with tenotomy or iris scissors under topical anesthesia 1 week after suture removal.

Cyanoacrylate Tissue Adhesive Application

Indications

Small partial- or full-thickness perforations, small descemetoceles, and deep stromal ulcers.

Technique

1. Sedate or anesthetize the animal as necessary.
2. Debride the lesion as necessary to remove necrotic tissue, non-adherent epithelium, and adherent mucus.
3. Instill a topical anesthetic (Ophthetic; Allergan Pharmaceuticals).
4. Insert an eyelid speculum.
5. Dry the corneal site of application with a cotton-tipped swab or cellulose sponge.
6. Apply a very thin layer of adhesive (Ophthalmic Nexaband, Abbott Laboratories) through a 30-gauge needle. Application of excessive amounts of adhesive can result in failure of the plug to adhere to the cornea.
7. Wait several minutes for the adhesive to polymerize before removing the speculum. Instill lubricant ointment until blinking returns.
8. Epithelialization occurs underneath the adhesive, which is extruded spontaneously by most animals within a few weeks. Excessive neovascularization may overgrow the plaque, necessitating manual removal under topical anesthesia.

Reconstructive Procedures

Indications

- Reconstructive procedures are indicated for descemetoceles and perforating corneal wounds. Commonly used types include sutures, pedicle flaps, and free conjunctival grafts.

Sutures

Technique

1. Suture perforating wounds and small descemetoceles directly with 7-0 to 9-0 absorbable (e.g., polyglactin 910-Vicryl, Ethicon) or nonabsorbable (monofilament nylon) sutures, using a horizontal mattress or simple interrupted pattern (Fig. 134-3).
2. Remove nonabsorbable sutures in 10 to 14 days.

Pedicle Flap

Technique

1. Raise a pedicle of bulbar conjunctiva, rotate, and then suture it to the edges of the deep corneal wound with absorbable suture material (e.g., polyglactin or polyglycolic acid-Dexon, David and Geck) (see Fig. 134-1).
2. After 2 to 4 weeks, trim the adhered flap connection to the limbus, leaving an island of conjunctiva to be incorporated into the scar.

Free Conjunctival Graft

Technique

1. Dissect an island of conjunctiva slightly larger than the corneal defect from the bulbar or palpebral conjunctiva, and suture it to the cornea directly over the defect.
2. The grafted conjunctiva will become incorporated as a translucent portion of the cornea.

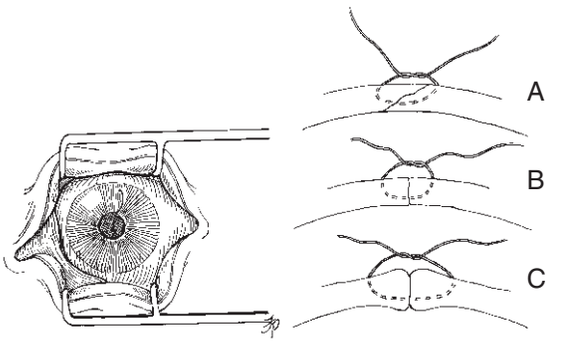

Figure 134-3. Repair of corneal laceration. Note that all sutures are placed to a depth of approximately two thirds of the corneal thickness. *A,* Closure of oblique edges of the laceration. *B,* Closure of vertical wound edges. *C,* Closure of edematous wound margins. Be sure the sutures extend beyond the edematous edge and into healthy cornea.

Referral Reconstructive Procedures

- *Corneoconjunctival transposition* and *autogenous corneal grafting* are forms of lamellar corneal graft requiring special instrumentation and expertise.
- *Penetrating keratoplasty (corneal transplant)* has few indications in veterinary medicine.

Treatment of Chronic Superficial Erosion

- After instilling a topical anesthetic, debride the non-adherent epithelium with a wet or dry cotton-tipped applicator back to the junction with normally adherent epithelium. Frequently, most of the corneal epithelium is removed in the process.

▼ ***Key Point*** Cauterants such as phenol, aqueous and tincture of iodine, trichloroacetic acid, and others are unnecessary and harmful. These agents incite excessive neovascularization that retards rather than accelerates epithelial healing.

- Instill topical broad-spectrum antibiotic drops (q3–4h) or ointments q6h, until healing is complete.
- To maintain mydriasis, administer topical 1% atropine drops or ointment to effect; apply q8h until dilatation occurs, followed by once daily to every other day.
- If the erosion has not healed, or nearly so, within 10 days, consider the following options:
  - Contact lenses.
  - Keratotomy.
  - Drugs.

Contact Lenses

Insertion of a soft contact lens (Hydroblues; Keragenix) following simple debridement frequently is effective.

Indication

- Chronic corneal (indolent) erosion.

Contraindications

- KCS; bacterial keratitis.

Technique

1. Following topical anesthesia, debride non-adherent epithelium with a cotton-tipped swab.
2. Insert soft contact lens (diameter, 15 mm; base curve, 8.4–8.8 mm). A partial temporary tarsorrhaphy is optional.
3. Administer a topical broad-spectrum antibiotic and 1% atropine solutions as described for simple erosions. Apply an Elizabethan collar.
4. Remove the contact lens weekly and stain with fluorescein to monitor ulcer healing. Reinsert the contact lens or insert a new one after cleaning and disinfection; repeat the process until the cornea is healed.

Superficial Punctate or Linear Keratotomy (Anterior Stromal Puncture)

The resultant small, visually insignificant scars are believed to secure the epithelium to the stroma.

Technique

1. Sedate the animal.
2. Instill a topical anesthetic to effect.
3. Debride non-adherent epithelium with a cotton-tipped swab.
4. Under magnification (Optivisor or similar device), make a series of shallow punctures or linear cuts with a sterile 25-gauge needle, spaced approximately 0.5 mm apart throughout the debrided area and extending 1 mm onto the surrounding epithelium.
5. Instill a topical broad-spectrum antibiotic and 1% atropine as described for simple erosions.

Superficial Keratectomy to Remove the Affected Area of Stroma, Epithelium, and Basement Membrane

Disadvantages include

- The need for general anesthesia.
- Proficiency in the surgical technique.
- Possible permanent corneal thinning.

Drugs

Drugs not yet commercially available but showing promise for medical management of chronic corneal erosions include epidermal and nerve growth factors, fibronectin, and substance P.

Surgical Management of Corneal Sequestra

- Perform keratectomy to remove sequestra that lie in the *superficial* half of the cornea; deeper keratectomy encourages iatrogenic corneal perforation.
- Sequestra may recur at the operated site or at other sites.
- For large or deep sequestra, consider performing a conjunctival pedicle graft to support and reconstruct the wound.

NON-ULCERATIVE CORNEAL DISORDERS

Chronic Superficial Keratitis (CSK)

Etiology

- The specific cause of CSK is unknown.
- Its predominance in a small spectrum of dog breeds (German shepherd, greyhound, occasionally others) and in mixed-breed dogs originating from these dog breeds, strongly implicates a genetic predisposition for immune-mediated disease.

Clinical Signs

- Superficial, bilaterally symmetric neovascularization, usually beginning inferotemporally, with or without melanosis, is a hallmark. Pain is not a common sign.
- Rarely, corneal ulceration develops.
- Corneal degeneration, manifested by oval crystalline opacities, may develop with chronicity.

Diagnosis

- Base diagnosis on typical corneal signs in a German shepherd, greyhound, or mixed-breed dog of their extraction, in the absence of other causes of chronic superficial keratitis (e.g., tear deficiency, eyelid abnormalities).

Treatment

- Administer corticosteroids topically (and, intermittently, subconjunctivally) to control this incurable condition.
  - For initial management administer a subconjunctival injection of 5 mg of methylprednisolone acetate (Depo-Medrol; Upjohn).
  - Supplement with a topical corticosteroid ointment or solution on a regimen of reducing frequency (e.g., q3–4h tapering to q8h over 4 weeks).
  - Long-term topical therapy is essential to maintain control; even short periods of owner noncompliance will result in relapse.
  - Only neovascularization responds to this therapy; melanosis and corneal degeneration do not.

- Consider instillation of 0.2% cyclosporine ointment (Optimmune; Schering Plough) or 1 drop of 2% cyclosporine in oil (see Chapter 139) q12h. Over many months, this may reduce corneal melanosis in many conditions, including CSK, by a poorly understood mechanism. CSK is believed to be a T-lymphocyte–mediated disease and has been reported to respond in some instances to cyclosporine therapy.
- Plesiotherapy with strontium-90–generated beta-radiation is an effective adjunctive treatment for neovascularization. However, this is only available through specialty practices and teaching institutions.

▼ ***Key Point*** Do not perform keratectomy for removal of corneal pigmentation. Complications include delayed epithelialization, recurrence of CSK, and corneal perforation.

Feline Eosinophilic Keratitis

Etiology

- The etiology is unknown; feline herpesvirus may play a role.

Clinical Signs

- Corneal neovascularization, which is frequently bilateral and symmetric, leads to formation of a pink-white plaque covered by a granular, crumbled cheese–like material. The superior temporal, inferior temporal, and inferior nasal quadrants are most frequently involved.
- This lesion is unique to the cat.
- Corneal ulceration is present rarely.

Diagnosis

Corneal scrapings contain combinations of eosinophils, mast cells, and mixed inflammatory cells.

▼ ***Key Point*** Identification of numerous eosinophils or mast cells in corneal scrapings is pathognomonic for feline eosinophilic keratitis.

Treatment

Corticosteroids

Intensive topical corticosteroid therapy frequently is successful.

- Give dexamethasone 0.1% (Decadron; Merck) or prednisolone 1% (PredForte; Allergan) as an ointment or solution, q3–4h. Monitor progress closely when epithelial erosion is present.
- If needed, combine topical corticosteroids with subconjunctival methylprednisolone (5 mg per eye). This combination controls the condition in most cats.
- Once the disease is in remission, reduce frequency of topical therapy to minimal levels; discontinue if remission is maintained.
- Some affected cats will have relapses, requiring chronic topical corticosteroid administration at a minimal effective frequency.

Megestrol Acetate

- Administer megestrol acetate (Ovaban; Schering) (0.5 mg/kg q24h until effect, and then 1.25 mg total dose once weekly) *only* to cats that have not responded to topical and subconjunctival corticosteroids.
- Side effects of oral megestrol acetate include weight gain, behavior changes, diabetes mellitus, and mammary gland hypertrophy and neoplasia.

Corneal Melanosis

Etiology

- Among domestic animals, only dogs commonly develop corneal pigmentation, which apparently develops through migration of limbal melanocytes into the basal epithelial layers and anterior stroma.

▼ ***Key Point*** Melanosis develops in dogs in response to chronic irritation from many causes, including KCS, eyelid deformities, lagophthalmos, and chronic superficial keratitis.

Clinical Signs

- Superficial corneal pigmentation develops focally or over large areas. Corneal neovascularization usually precedes or accompanies melanosis.

Diagnosis

- The typical appearance of a variably melanotic cornea is diagnostic.
- Rarely, melanosis must be distinguished from iris prolapse (anterior synechiae are also apparent) or, at the limbus, epibulbar melanoma.

Treatment

- Identify and treat the underlying causes of melanosis if possible (e.g., KCS) or definitively correct them (e.g., entropion, nasal fold trichiasis).
- Rarely, perform superficial keratectomy to improve corneal clarity when vision is reduced, but only after correcting the inciting cause.
- Consider long-term topical therapy for KCS with 2% cyclosporine drops or 0.2% cyclosporine ointment (Optimmune, Schering-Plough) (see Chapter 139), which may retard or reduce corneal melanosis (evidence of benefit is anecdotal).

SCLERAL INFLAMMATION AND TRAUMA

Fibrous Histiocytoma; Proliferative Keratoconjunctivitis of Collies; Nodular Granulomatous Episclerokeratitis

Etiology

- This condition probably is a genetic disorder of collies, but has been noted in other breeds. Clinical and pathologic features of both inflammation and neoplasia are present.

Clinical Signs

- Bilaterally symmetric scleral/episcleral nodules, especially at the temporal limbus, are hallmarks.
- The eyelids, planum nasale, and other mucocutaneous junctions (lips, anogenital areas) may be involved.
- If the cornea is invaded, corneal opacity develops, often with a leading edge of crystalline corneal degeneration.

Diagnosis

- Typical lesions in a collie are presumptive evidence.
- Obtain a biopsy of atypical lesions.
- The histologic appearance is that of fibroplasia with extensive histiocytic proliferation.
- Differential diagnosis includes lymphoma and other neoplasms.

Treatment

- Corticosteroids are the initial treatment of choice. For dogs with ocular lesions only, combine intensive topical corticosteroid therapy (dexamethasone 0.1% or prednisolone 1%) with subconjunctival injection of 3 to 6 mg per eye of triamcinolone, betamethasone, or methylprednisolone acetate.
  - Long-term topical steroid treatment at the minimally effective frequency reduces recurrence.
- For dogs with ocular and oral, nasal, and/or genital lesions, administer oral prednisone (1.1 mg/kg q12h); taper to the effective minimal dose and frequency.
  - Indefinite treatment may be required.
- For dogs with corticosteroid-unresponsive lesions, administer azathioprine (Imuran; Burroughs Wellcome) 2.2 mg/kg q24h PO for 14 days followed by 1 mg/kg every other day for 14 days; then give 1 mg/kg once weekly for 4 weeks and discontinue. Indefinite treatment at a low frequency may be required. Monitor leukocyte and platelet counts in animals on azathioprine therapy. Discontinue treatment if a significant reduction in either is observed.
- Discourage breeding of affected dogs.

Scleritis; Episcleritis; Ocular Nodular Fascitis

Etiology

- The cause is unknown; an immune-mediated etiology is suspected.

Clinical Signs

- Nodular, diffuse infiltrative, and necrotizing forms have been recognized.
  - Nodular lesions resemble fibrous histiocytomas, but often are unilateral and affect dogs other than collies.
  - Diffuse thickening and inflammation of the sclera may be associated with scleral necrosis and moderate to severe uveitis.

Diagnosis

- The diagnosis is based on clinical signs, histopathology, and response to therapy.
- Differential diagnosis includes lymphoma and other neoplasia.

Treatment

Treatment plan is similar to that for fibrous histiocytoma.

Scleral Wounds

Etiology

Blunt or perforating trauma may cause rupture of the globe through the sclera while the cornea is spared.

Clinical Signs

- Chemosis, conjunctival or external ocular hemorrhage, hyphema, and eyelid swelling in a traumatized animal suggest scleral perforation.

Treatment

- Surgical repair of small wounds may result in preservation of the globe as well as vision if the repair is performed promptly.
- Enucleation or evisceration with intraocular prosthesis implantation is indicated if the scleral laceration is large or if other ocular injuries prevent comfortable retention of the globe.

CORNEOSCLERAL NEOPLASIA

Primary Epibulbar Melanoma

Etiology

- These benign neoplasms probably arise from conjunctival or episcleral melanocytes.

- The German shepherd is a predisposed breed, but the disorder has been reported in numerous other breeds.

Clinical Signs

- A nonpainful, pigmented mass near the limbus, involving the sclera (and, later, adjacent cornea), slowly enlarges, expanding horizontally and vertically into the surrounding sclera.

Diagnosis

- The typical appearance suggests the diagnosis.
- Epibulbar melanomas should be distinguished (not always easily) from uveal melanomas, which are intraocular tumors that may expand through the sclera.

Treatment

- Small, superficial lesions may be resectable. Because scleral grafting may be necessary, consider referral to a specialist.
- Observe for a long period to assess the growth rate and characteristics of individual tumors.
  - In dogs, these normally benign neoplasms may be safely observed until/unless deeper extension causes uveitis or glaucoma, prompting enucleation.
  - Recommendations in cats are similar, although based on fewer reported cases.

Secondary Neoplastic Invasion of the Sclera

Etiology

- Primary or secondary intraocular neoplasms may extend through the sclera and into the orbit.
- Rarely, episcleral metastasis of a distant primary or multicentric neoplasm may occur.

Clinical Signs

- Masses may be obvious extensions of intraocular tumors. Episcleral masses may mimic episcleritis or fibrous histiocytoma.

Diagnosis

- Relationship to an intraocular tumor is presumptive evidence. Association of a scleral mass with a visible intraocular tumor suggests that the scleral mass is an extension of it.
- For histopathologic evaluation, completely excise solitary masses.

Treatment

- Consider palliative and diagnostic enucleation of a painful globe.

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Chapter

135 Diseases of the Lens

David A. Wilkie

ANATOMY

The normal canine and feline lens is composed of an outer capsule, epithelial cells beneath the anterior capsule, and lens fibers formed by the migration of epithelial cells to the lens equator, where the cells elongate and create a regular arrangement of fibers. The regular arrangement of these fibers accounts for the transparency of the lens. The lens is posterior to the iris, anterior to the vitreous to which it is attached, and suspended by zonules, which arise from the ciliary body and attach to the lens capsule at the equator (see Fig. 131-1).

CONGENITAL ANOMALIES

Etiology

Lens development takes place early in embryogenesis and is complete in the dog by day 30 of gestation. Any genetic abnormality affecting lens development or any insult to the bitch or queen early in gestation, including infectious, nutritional, chemical, or drug related, can result in congenital lens anomalies. These abnormalities are often associated with other congenital ocular anomalies, including microphthalmia (small globe), persistent pupillary membranes, persistent hyaloid artery, retinal dysplasia, retinal detachment, posterior coloboma or staphyloma, and optic nerve hypoplasia.

Clinical Signs

Examples and features of congenital lens anomalies include the following:

- *Microphakia* (small lens)—With the pupil dilated, the equator of the lens and fine zonules, attaching at the equator and originating from elongated ciliary processes, are visible. The lens may also be luxated.
- *Coloboma* (notch defect)—With the pupil dilated, a notch defect may be visible in any quadrant of the equatorial zone, with or without zonular attachments.
- *Cataract*—See the cataract discussion in this chapter.
- *Lens luxation*—Often associated with microphakia (see discussion in this chapter).

Diagnosis

- Clinical signs (see previous section).
- Present at birth. Microphakia and coloboma are always congenital. Cataract and lens luxation, unless associated with microphakia, may not be congenital. An accurate history and early examination are helpful in differentiating congenital from acquired abnormalities.

Treatment

- Determine concomitant ocular anomalies and their significance to vision.
- Microphakia and coloboma alone require no treatment.
- Cataract, if impairing vision, may be amenable to surgical removal once the integrity of the retina and optic nerve has been ascertained by fundic examination, electroretinogram, ocular ultrasound, and visual-evoked potential.
- Remove a luxated lens if it is inciting uveitis and/or glaucoma, impairing vision, or interfering with corneal endothelial cell function.

Prevention

Congenital anomalies are not necessarily inherited anomalies. Careful inquiry into affected littermates and prevalence of problems in previous matings may raise the suspicion for an inherited defect. If the cause of the abnormality cannot be determined, discourage the use of this and related animals for breeding.

CATARACT

Etiology

Cataract is an opacity of the lens resulting from pathologic changes in lens protein composition or disruption of lens fiber arrangement.

Table 135-1. BREED LIST OF INHERITED OR FAMILIAL CATARACTS IN THE DOG

Afghan hound	French bulldog	Papillon
Alaskan malamute	German shepherd	Pembroke Welsh corgi
Beagle	German shorthaired pointer	Pointer
Bedlington terrier	Giant schnauzer	Pomeranian
Belgian Tervuren	Golden retriever	Poodle (toy, miniature, standard)
Bernese mountain dog	Great Dane	Puli
Bichon frisé	Ibizan hound	Rhodesian ridgeback
Border collie	Irish setter	Rottweiler
Border terrier	Irish water spaniel	Saint Bernard
Borzoi	Irish wolfhound	Samoyed
Boston terrier	Italian greyhound	Schipperke
Bouvier des Flandres	Keeshond	Scottish terrier
Cairn terrier	Kerry blue terrier	Siberian husky
Cavalier King Charles spaniel	Labrador retriever	Silky terrier
Chesapeake Bay retriever	Lakeland terrier	Staffordshire bull terrier
Cocker spaniel	Lhasa apso	Standard schnauzer
Collie	Manchester terrier	Tibetan terrier
Curly-coated retriever	Miniature pinscher	Welsh springer spaniel
Dachshund	Miniature schnauzer	Welsh terrier
English cocker spaniel	Norfolk terrier	West Highland white terrier
English springer spaniel	Norwegian elkhound	Whippet
English toy spaniel	Norwich terrier	Wirehaired fox terrier
Field spaniel	Old English sheepdog	Yorkshire terrier

Data from: Rubin LF: Inherited Eye Diseases in Purebred Dogs. Baltimore: Lippincott Williams & Wilkins, 1989.

▼ ***Key Point*** Cataract must be distinguished from nuclear sclerosis. Nuclear sclerosis is a normal aging change seen in all dogs and cats 6 years of age or older, produced by compression of central lens fibers.

Etiologies of cataract development include the following:

- ***Hereditary***—This is the most common cause of cataract in the dog (Table 135-1). Location, progression, and mode of inheritance of cataracts vary among breeds. The majority of inherited cataracts are bilateral but often asymmetrical in onset and progression.
- ***Inflammatory***—This is a common cause of cataract in the cat. Because the lens needs the aqueous and vitreous humors for nutrition and removal of metabolic wastes, intraocular inflammation can result in capsular and cortical opacities. Posterior synechia from anterior uveitis can result in anterior capsular cataracts.
- ***Metabolic***—Diabetes mellitus in dogs frequently results in rapid (days to weeks) onset of bilateral cataracts because of a shift in metabolic pathways, an accumulation of sorbitol causing an osmotic gradient, and a subsequent disruption of lens fibers. The cataracts are irreversible.
- ***Degenerative***—Cataracts may occur secondary to chronic retinal degeneration or chronic glaucoma.
- ***Traumatic***—Severe blunt trauma to the eye can result in cataract formation from concussive effects or can be secondary to inflammation and/or lens luxation. Penetrating injuries that puncture the anterior lens capsule (e.g., cat claw injuries) result in a focal or diffuse cataract, depending on the severity of the capsular tear. Uveitis may occur secondary to rupture of the lens capsule.
- ***Nutritional***—Puppies and kittens hand fed exclusively milk-replacement formula that is deficient in required amino acids, the most frequently cited being arginine, can develop bilateral cataracts.
- ***Toxic***—Electric shock, radiation therapy involving the ocular region, and certain drugs have been reported to cause cataracts.

Clinical Signs and Diagnosis

▼ ***Key Point*** For a thorough examination of the lens, mydriasis is mandatory because some of the most significant changes occur in the extreme periphery (equatorial zone) or posterior cortex of the lens. Topical tropicamide 1% (Mydriacyl, Alcon) results in mydriasis in 15 to 20 minutes and lasts 6 to 8 hours. An inexpensive, monocular biomicroscope will facilitate examination of the lens and aid determination of location and depth of lesion (see Chapter 131).

- Any *opacity,* anywhere in the lens or its capsule observed after dilation of the pupil, is a cataract.

- The degree of *visual impairment* is dependent on the extent of cataract development in one or both eyes. In addition, the use of the animal must be considered. Incipient and immature cataracts are more significant in hunting and working dogs with respect to vision impairment.
- Differentiate cataracts from nuclear sclerosis. *Nuclear sclerosis* is a bilaterally symmetrical, well-defined, homogeneous haze in the center of the lens observed in animals older than 6 years. Sclerosis is not a true opacity, and it does not obstruct a dilated examination of the fundus or cause clinically significant visual impairment. It may make direct ophthalmoscopy difficult.
- A *focal cataract* can be localized with respect to anterior or posterior by comparing the nasal or temporal direction of movement of the cataract with that of the eye. Anterior cataracts will move in the same direction as the globe; posterior cataracts will appear to move in the opposite direction of the globe. Thus, if the animal looks temporally, an anterior opacity will move temporally and a posterior opacity will move nasally. By localizing cataracts, the surgeon can help determine if they are inherited and predict progression. For example, nuclear cataracts are generally static, whereas equatorial cataracts, where new lens fibers are forming, are generally progressive.

Stages of Development

Incipient

Focal or multifocal opacities of the lens cause no clinical loss of vision and do not impair tapetal reflection or view of the fundus.

Immature

Significant lenticular opacity. Tapetal reflection remains, but an incomplete view of the fundus is present. Vision is affected depending on the extent of lens involvement.

Mature

Dense lenticular opacity with no tapetal reflection or fundus visible results in total vision loss in the affected eye.

Hypermature

As lens protein degenerates and liquefies, the lens can become smaller in the anterior-posterior axis, resulting in a wrinkled anterior capsule and deep anterior chamber.

Resorbing

As lens protein degenerates and liquefies, it can leak through the capsule. This is usually associated with hypermature cataracts but can occur in immature and mature cataracts. The process is faster in young dogs. A resorbing lens has varying amounts of clear, liquefied cortex with the remaining lens material often taking on a sparkling appearance. Although in some animals vision is regained by significant lens resorption, the process generally results in mild to severe lens-induced uveitis (LIU) because of the antigenicity of the leaking lens protein.

Lens-Induced Uveitis

Exposure of excessive amounts of lens protein can overwhelm the normal low-dose T cell tolerance resulting in both a humoral and cell-mediated immune response characterized by lymphocytes and plasma cells. This process is termed *phacolytic* or *lens-induced uveitis*. This may result in hypotony, miosis, flare, keratitic precipitates, synechia, retinal detachment, and glaucoma if allowed to persist (see Chapter 136). In addition, LIU may be associated with intraoperative complications during cataract surgery, a reduction in surgical success, and an increase in postoperative medication.

Phacoclastic uveitis is the result of rupture, spontaneous or traumatic, of the lens capsule. The resulting uveitis is much more severe than seen with lens-induced uveitis and results in secondary glaucoma, pupillary occlusion, and fibroplasia. The most common causes are diabetes mellitus with rapid intumescence or penetrating injury such as a cat claw. The treatment of choice is immediate lens extraction once a lens capsule rupture is observed.

Treatment

▼ ***Key Point*** There is no medical treatment to eliminate cataracts. Surgical removal of cataracts is a referral procedure; consult an ophthalmologist.

- Previously, because of the risks associated with cataract surgery, the cost to the owner, and the ability of a blind dog to acclimatize to their environment, cataract surgery was an elective procedure reserved for those animals with bilateral, mature cataracts. Recently, the improved success rate of phacoemulsification, the availability of intraocular lens implants, and the increased success associated with early surgical intervention have resulted in cataract surgery being offered in cases of unilateral and immature cataracts.
- Regardless, cataract surgery remains an expensive and elective procedure, the exception being a traumatic cataract with secondary lens capsule rupture and impending phacoclastic uveitis. Owners should be aware that not removing a cataract may result in its progression and secondary LIU and associated complications such as retinal detachment, lens luxation, and secondary glaucoma.

- Success rates for cataract surgery vary depending on preexisting uveitis, stage of the cataract, predisposition for glaucoma, surgical procedure used, and surgeon expertise. Success rates with phacoemulsification are reported to be 90% to 95% with little decline over time, while success of the open-sky extracapsular technique is approximately 80% with a steady decline in success over time following surgery to less than 50%.

Preoperative Considerations

- For owners expressing an interest in cataract surgery, refer them to a veterinary ophthalmologist early, while the fundus is still visible and before LIU develops.
- The animal should be healthy. If diabetic, the condition should be well regulated.
- The eyes are examined for concurrent uveitis, glaucoma, abnormal iridocorneal angle, keratitis, and retinal disease.
- If the fundus is not visible through the cataract, an electroretinogram is performed to evaluate for progressive retinal atrophy. An ocular ultrasound is carried out to evaluate for retinal detachment.

Surgical Procedures

Phacoemulsification

- The most common technique for cataract removal in veterinary ophthalmology is phacoemulsification. This uses ultrasonic energy to drive a needle that emulsifies the lens and, through irrigation-aspiration, removes the lens material from the lens capsule. This procedure requires a smaller incision, needs a reduced surgical time, and maintains the anterior chamber compared with the technique of open-sky extracapsular extraction. This results in improved success. The procedure requires a phacoemulsification device, an operating microscope, appropriate surgical equipment, and expertise. Therefore, it is a referral procedure.
- A 3-mm incision is made in the cornea at the limbus, the anterior chamber is inflated using a viscoelastic material, a continuous tear anterior capsulorrhexis is performed, and the lens is removed by phacoemulsification. Care is taken to avoid traumatizing the iris, cornea, and remaining lens capsule. Once the lens is removed and the remaining lens cortex is aspirated, some surgeons will remove a circular portion of the posterior lens capsule to ensure a clear visual axis and minimize postoperative lens capsule fibrosis.
- Currently, the most common lens for replacement in the canine eye is a single-piece lens constructed of polymethylmethacrylate with a 7-mm optical portion, 15- to 17-mm haptic-to-haptic dimension, and a power of 41.5 diopters (53 diopters in cats). If a polymethylmethacrylate lens is to be implanted, the corneal incision is then enlarged to allow insertion of an intraocular lens (IOL). This IOL is placed through the anterior capsule opening and into the remaining lens capsule, allowing the lens capsule to provide support and ensure position. The corneal incision is then closed. Newer-generation acrylic IOLs can be folded and implanted without having to enlarge the corneal incision. If the opposite eye also has a cataract, many surgeons will remove this lens and place an IOL at this time. The animal is then recovered. Failure to replace the cataractous lens with an IOL will leave the animal 14 diopters hyperopic (farsighted) and result in significant visual impairment.
- Certain breeds such as the bichon frisé and Shih Tzu are at increased risk for postoperative retinal detachment. In these and other at-risk eyes, transscleral laser retinopexy may be performed several weeks prior to cataract surgery to create chorioretinal scars and decrease the risk of postoperative retinal detachment.

Postoperative Care and Complications

Complications of cataract surgery can occur immediately to several years postoperatively. Evaluate patients frequently for several months following surgery. Maintain a long-term, 6-month reevaluation schedule for life.

- *Short-term postoperative complications* include anterior uveitis, glaucoma, luxation of the IOL, and retinal detachment.
- *Long-term complications* include chronic low-grade uveitis, glaucoma, corneal endothelial damage with associated corneal edema, fibrous metaplasia across the posterior capsule with opacification of the capsule, posterior synechia, production of new cortical material from remaining epithelial cells, IOL decentration, and retinal detachment.
- Reevaluation includes tonometry to determine intraocular pressure (IOP) and a dilated examination of the posterior capsule and fundus.

Prevention

- Incidence of inherited cataracts can be reduced by discouraging breeding of affected animals and carriers and by encouraging breeders to have yearly Canine Eye Registration Foundation (CERF) examinations.
- Inflammatory cataracts can often be prevented by prompt, appropriate treatment of uveitis (see Chapter 136).

LENS LUXATION

Etiology

- ***Primary zonular degeneration:*** This is an inherited trait in many terrier breeds and has familial tendencies in

Table 135-2. BREED LIST OF INHERITED OR FAMILIAL LENS LUXATION IN THE DOG

Australian cattle dog	Lakeland terrier	Sealyham terrier
Border collie	Manchester terrier	Siberian husky
Cairn terrier	Miniature schnauzer	Skye terrier
Cardigan Welsh corgi	Norfolk terrier	Smooth fox terrier
Chihuahua	Norwegian elkhound	Tibetan terrier
German shepherd	Norwich terrier	Welsh terrier
Greyhound	Pembroke Welsh corgi	West Highland white terrier
Irish setter	Poodle (toy)	Whippet
Jack Russell terrier	Scottish terrier	Wirehaired fox terrier

Data from: Rubin LF: Inherited Eye Diseases in Purebred Dogs. Baltimore: Lippincott Williams & Wilkins, 1989.

other breeds (Table 135-2). Lens luxation usually occurs at middle age with no predisposing ocular disease.

- ***Glaucoma:*** Chronic glaucoma results in a buphthalmic (enlarged) globe that can stretch and break the lenticular zonules, causing the lens to luxate.

▼ ***Key Point*** A primary lens luxation can also cause glaucoma, making it difficult to distinguish which occurred first in some cases.

- ***Uveitis:*** Chronic uveitis may weaken zonules owing to inflammatory cell infiltration.
- ***Cataracts:*** Advanced cataracts may cause degenerative changes in the zonules or zonular attachments.
- ***Trauma:*** Severe ocular trauma may cause lens luxation; however, it is not a common cause unless there is underlying zonule pathology.

Clinical Signs

- The clinical signs of lens luxation vary depending on whether the lens luxates anteriorly or posteriorly. Many times it is the secondary ocular changes that result in the clinical presentation, rather than the lens luxation itself.
- In many eyes with luxated lenses, the vitreous will liquefy and can be found in the anterior chamber. Vitreous appears as filmy white material suspended in the aqueous humor. Its presence, in the absence of lens luxation, may indicate early zonular breakdown and subluxation or an animal's predisposition to lens luxation.

Anterior Lens Luxation

- A penlight beam directed parallel to the iris will reveal the lens positioned in the anterior chamber, anterior to the iris and often blocking the pupil.
- Blue light (Wood's lamp) will cause a clear lens to fluoresce, simplifying the examination.
- A focal area of corneal edema may result from the lens touching the posterior cornea and damaging the corneal endothelium. This may be a permanent change.
- Secondary glaucoma can occur from pupillary occlusion by the lens or attached vitreous or from occlusion of the aqueous outflow through the iridocorneal angle.

Posterior Lens Luxation

- The edge of the lens may be seen through the pupil, resulting in an "aphakic crescent" between the pupil margin and the edge of the lens.
- The lens may fall into the vitreous where it can be seen on the floor of the chamber, trapped in the vitreous, or adhered to the retina.
- Without support of the lens, the iris may tremble with eye movement (iridodonesis). The anterior chamber will be deep.

Diagnosis

- Based on ophthalmic examination
- Tonometry to identify primary or secondary glaucoma
- Ocular ultrasound (if intraocular structures cannot be observed because of corneal or aqueous opacity)

Treatment

- Treatment for lens luxation is surgical. Refer the patient to an ophthalmologist.

▼ ***Key Point*** Anterior lens luxation is a potential emergency; posterior lens luxation is a more elective surgical procedure.

- If immediate referral for an anterior lens luxation is available, do not dilate the pupil. If referral is delayed, some ophthalmologists may prefer the pupil be dilated to minimize corneal endothelial trauma and the risk of pupillary-block glaucoma.
- Determine the intraocular pressure in all eyes with lens luxation.

Surgical Procedures

- Remove a luxated lens through a large limbal corneal incision, removing the lens and lens capsule intact, termed an *intracapsular lens extraction*. Minimize trauma to the vitreous and remove as little of it as possible.
- Removal of an anterior lens luxation is technically easier than removal of a posterior luxation. The latter requires vitrectomy to gain access to the lens, with an increased risk of intraoperative retinal detachment.
- Following intracapsular lens extraction, an IOL can be placed to restore emmetropia. Unlike traditional cataract surgery, in which the IOL can be placed in the lens capsule, the IOL in this instance must be sutured in position. Using two to three 10-0 nylon sutures attached to the IOL haptics, a needle is passed ab interno behind the iris, through the ciliary sulcus, and out the sclera. This is repeated for each suture attached to the haptic. Position the lens posterior to the iris, anterior to the vitreous, and in the ciliary sulcus.
- Close the corneal incision and reinflate the anterior chamber. Using the sutures attached to the haptics, the lens is manipulated into position in the pupillary opening and the 10-0 nylon sutures fixed to the sclera.
- Since the risk of postoperative retinal detachment is high with intracapsular lens extraction, transscleral laser retinopexy may be performed to create chorioretinal scars and decrease the risk of retinal detachment.

Postoperative Care and Complications

- Postoperative complications include retinal detachment, glaucoma, IOL decentration, dyscoria, uveitis, synechia, and vitreous entrapment in the corneal incision.
- If surgical removal is not possible, the lens is best kept in the vitreous chamber. Once there, topical miotics, such as 2% pilocarpine or 0.005% latanoprost, can be used in an effort to trap the lens behind the iris. Follow-up care should include periodic determination of intraocular pressure. Lenses that are luxated and not removed will become cataractous.
- Examine the contralateral eye in instances of primary lens luxation and if unstable, instruct the owner what to watch for as a sign of lens luxation. Alternately, some ophthalmic surgeons will offer to remove a lens due to instability, preferring to replace it with a sulcus-fixated IOL.
- If the lens luxation is secondary to buphthalmia and chronic glaucoma, therapy is directed toward the glaucoma (see Chapter 137).

Prevention

- Examine the contralateral eye carefully for evidence of lens subluxation, such as a deep or shallow anterior chamber, iris tremor, aphakic crescent, or vitreous in the anterior chamber.
- Advise owners to watch the animal's eye at risk for signs of lens luxation and to call immediately if noted.

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Chapter

136 Diseases of the Uvea

David A. Wilkie

ANATOMY AND PHYSIOLOGY

The uvea is the middle or vascular tunic of the eye. It is covered externally by the fibrous tunic and provides much of the blood supply to the inner nervous tunic (retina) (see Chapter 131).

The uvea is composed of *three regions:* the iris, the ciliary body, and the choroid (see Chapter 138).

Iris

- The iris is the anterior most portion of the uvea. It forms an incomplete diaphragm between the anterior and the posterior chambers and regulates the amount of light entering the posterior portions of the eye.
- The color of the iris varies among species, within species, and even within the same animal. Heterochromia is a different color within or between irides.
- The iris contains a sphincter muscle controlled by parasympathetic fibers that travel from the Edinger-Westphal nucleus with the oculomotor nerve (cranial nerve 3) to the ciliary ganglion, where they synapse. The action of the sphincter muscle causes miosis. Intraocular inflammation will also result in contraction of the sphincter muscle. This results in the miosis and pain seen in anterior uveitis. The sphincter muscle can be paralyzed with parasympatholytic agents, causing dilation of the pupil. This is used clinically to better see the posterior portions of the eye and to treat anterior uveitis.

▼ ***Key Point*** The diagnostic parasympatholytic agent of choice is tropicamide (Mydriacyl), whereas the therapeutic parasympatholytic agent of choice is atropine 1%.

- The iris dilator muscle fibers are radially oriented and lie along the base of the posterior epithelium. The dilator muscle is under sympathetic control in mammals. The sympathetic fibers course along the spinal cord to T1 to T3, leave in the ventral roots, course through the anterior mediastinum, and run anteriorly with the internal carotid to the cranial cervical ganglion, where they synapse. They then travel to the eye in association with the ocular vascular supply (see Chapter 141). The action of the dilator muscle is to produce mydriasis.

Ciliary Body

The ciliary body is divided into the pars plicata and pars plana and is located posterior to the iris. The ciliary processes are folds of the ciliary epithelium with a vascular core and are the source of aqueous humor. The ciliary body is also the origin of the lenticular zonules, which serve to anchor the lens. Through these zonules and the ciliary musculature, accommodation occurs.

Choroid

The choroid is continuous anteriorly with the ciliary body and extends posteriorly to the optic nerve. The choroid lies external to the retina and supplies nutrition to the outer portions (rods and cones) of the retina in the dog and cat. The tapetum is located in the dorsal portion of the fundus and lies within the choroid (see Chapter 138).

CONGENITAL ABNORMALITIES

Persistent Pupillary Membranes

Etiology

These are persistent remnants of fetal blood vessels in the anterior chamber that originate from the collarette region of the anterior iris face. They may be seen alone or in association with other congenital abnormalities. Although persistent pupillary membranes (PPMs) are felt to have an inherited component (especially in basenjis), the mode of inheritance is not established in most affected breeds.

Clinical Signs

The clinical signs vary depending on where the PPM strands attach. In general, the color of the PPM will be

similar to that of the iris. PPMs that bridge iris to iris generally result in no clinical signs, whereas those attaching to the anterior lens capsule or corneal endothelium are associated with focal opacities of these structures. Differentiate PPMs from anterior and posterior synechiae when attaching to the cornea or lens, respectively.

Diagnosis

Base the diagnosis on the clinical signs and breed. Perform a complete ophthalmic examination to detect other congenital ocular abnormalities.

Treatment

There is no treatment required and the lesion is nonprogressive. Council breeders about possible inheritance and discourage breeding of affected basenjis and corgis.

Coloboma

Etiology

A coloboma is a developmental anomaly in which a portion of the tissue, in this case the uvea, is absent. Colobomas can affect all three portions of the uvea and are often associated with other congenital anomalies such as PPMs, lens coloboma, or retinal detachment. Colobomas can be inherited or the result of a toxic insult to the developing eye during gestation.

Clinical Signs

Depending on which portion of the uvea is affected, clinical signs will vary. Colobomas of the iris result in dyscoria and may be associated with PPMs or lenticular abnormalities. Colobomas of the ciliary body or choroid are generally not noted by the owner and are seen on a routine ophthalmic examination or are present as a result of other congenital abnormalities or from secondary changes such as retinal detachment. Posterior segment colobomas are seen as part of the collie eye anomaly (CEA) (see Chapter 138).

Diagnosis

Base the diagnosis on the clinical signs and breed. Perform a complete ophthalmic examination to detect other congenital ocular abnormalities.

Treatment

There is no treatment required and the lesion is nonprogressive. Council breeders about possible inheritance and discourage breeding of affected dogs.

Uveal Hypoplasia or Aniridia

A lack of complete development or absence of the affected portion of the uvea, iris hypoplasia, or aniridia is rare and usually associated with other congenital ocular abnormalities. Choroidal coloboma occurs in several breeds of dogs and is seen as part of CEA.

UVEAL CYST

Etiology

Uveal cysts arise from the posterior iris or ciliary body and can remain attached or break free and float in the anterior chamber. They arise as a primary disorder in certain breeds (golden retriever, Boston terrier) or can be secondary to anterior uveitis.

Clinical Signs

Uveal cysts are pigmented, attached to the posterior iris, or free floating in the anterior chamber. They can rupture, depositing on the ventral corneal endothelium or anterior lens capsule. In dogs, iris cysts will transilluminate, facilitating diagnosis. In cats, however, cysts are more densely pigmented, often remain attached, and may not transilluminate, making diagnosis more difficult.

Diagnosis

Base the diagnosis on the clinical signs and breed. A free-floating, pigmented mass that transilluminates is a cyst. If the mass remains attached or fails to transilluminate, it must be distinguished from a uveal melanoma. Use ocular ultrasound to demonstrate the hollow appearance of a cyst and distinguish between a cyst and a melanoma.

Treatment

If the cyst is not interfering with vision, no treatment is required. Large or multiple cysts may require treatment if vision becomes impaired. In addition, in cats, large cysts can be associated with an increase in intraocular pressure (IOP), requiring intervention. Treatment includes mechanical aspiration of the cyst from the anterior chamber or diode or Nd:YAG laser photoablation of the cyst, resulting in the rupture and/or resorption of the cyst.

IRIS ATROPHY

Etiology

Iris atrophy is seen most often in aged animals, especially toy-breed dogs and cats. Iris atrophy has been classified as primary, senile, and secondary. *Primary iris atrophy* is seen in Siamese cats, miniature schnauzers, poodles, and Chihuahuas. This is a slow progressive atrophy of the iris. *Senile iris atrophy* occurs in aged animals of all species and breeds. The distinction between these two forms of atrophy may not be significant. *Secondary iris atrophy* occurs as a sequela to chronic glaucoma, uveitis, or ocular trauma.

Clinical Signs

If the iris musculature is affected, the pupillary light response may be incomplete or absent and anisocoria may be noted. Atrophy of the pupil margin results in dyscoria. Thinning of the iris stroma appears as a focal color change or, if complete, as a hole in the iris.

Diagnosis

The diagnosis is made based on the clinical appearance and signalment. The differential diagnosis includes other internal or external causes of dyscoria, anisocoria, incomplete pupillary light response, or iris color changes. Measurement of IOP, a complete ophthalmic examination, and determination of afferent-versus-efferent pupil response abnormalities are all indicated with iris atrophy (see Chapter 141).

Treatment

No treatment is required. However, differentiate iris atrophy from other pupillary response abnormalities.

ANTERIOR UVEITIS

Uveitis is inflammation of the uvea and is divided into anterior (iris and ciliary body), posterior (choroid), and panuveitis (all three portions of the uvea). Posterior uveitis is often called chorioretinitis because of the intimate association between the choroid and the retina (see Chapter 138). Anterior uveitis is associated with pain and can be the result of both ocular and systemic factors. Because many etiologies of uveitis are systemic, it is essential to ascertain the reason for the inflammation when presented with an animal with anterior or posterior uveitis (Table 136-1).

Table 136-1. SYSTEMIC INFECTIOUS ETIOLOGIES OF ANTERIOR UVEITIS

Mycotic—blastomycosis, cryptococcosis, histoplasmosis, coccidioidomycosis, aspergillosis, other
Rickettsia—ehrlichiosis, Rocky Mountain spotted fever
Toxoplasmosis
Feline immunodeficiency virus, feline leukemia virus, feline infectious peritonitis
Lyme disease
Bacteremia/septicemia
Bartonellosis
Brucellosis
Aberrant parasitic migration—heartworm, roundworm, hookworm, etc.
Canine distemper
Infectious canine hepatitis
Protothecosis
Mycobacteriosis
Leptospirosis
Leishmaniasis

▼ ***Key Point*** If no primary ocular etiology of anterior uveitis can be ascertained, consider systemic disease. This approach applies whether the uveitis is unilateral or bilateral.

Etiology

Corneal Ulceration

Corneal ulceration often results in reflex anterior uveitis. Uveitis occurs due to stimulation of the ophthalmic branch of cranial nerve 5 (CN5) and does not indicate infectious keratitis.

Trauma

Trauma can result in anterior uveitis due to a direct penetration of the globe or a concussive effect. Uveitis may be associated with other ophthalmic abnormalities, such as corneal ulceration, hyphema, lens luxation, retinal detachment, proptosis, and globe rupture. See appropriate chapters for further discussion of these abnormalities.

Infection

Infectious causes of anterior uveitis are numerous and include bacteria, fungi, rickettsia, and protozoal organisms (see Table 136-1). These organisms result in anterior uveitis by direct infections of the eye, immune-mediated responses, or circulating endotoxins. Many of these infectious agents also cause posterior segment (retina, choroid) involvement (see Chapter 138). Direct infection of the eye can occur from penetrating trauma or blood-borne infection. Although anterior uveitis is commonly associated with infectious causes, the organism itself is generally not present within the anterior segment of the eye.

Lens-Induced Anterior Uveitis

Lens-induced anterior uveitis results from traumatic or spontaneous rupture of the lens capsule or from leakage of the lens material through an intact capsule as noted with a hypermature, resorbing cataract. Lens protein is antigenic and, if released, will result in mild to severe anterior uveitis. Cataracts are discussed in Chapter 135.

Autoimmune Anterior Uveitis

Autoimmune anterior uveitis, unassociated with lens protein leakage, is observed in the uveodermatologic syndrome (formerly Vogt-Koyanagi-Harada syndrome). This syndrome is observed in dogs and results in anterior and posterior uveitis, poliosis (depigmentation of the hair), and vitiligo (depigmentation of the skin). See Chapter 48 for discussion of the dermatologic manifestations. In addition, an immune-mediate chorioretinitis is seen in the golden retriever, resulting in bullous retinal detachment.

Table 136-2. CLINICAL SIGNS OF ANTERIOR UVEITIS

Discharge—serous, mucoid	Redness—conjunctiva, iris
Blepharospasm	Photophobia
Miosis	Hypotony
Corneal edema	Aqueous flare/fibrin
Keratitic precipitates	Hyphema
Hypopyon	Blindness

Pigmentary Uveitis

Pigmentary uveitis is seen in the golden retriever and can be unilateral initially but will become bilateral. The iris appears hyperpigmented with pigment deposition on the anterior lens capsule. Aqueous flare with pigment-containing cells in the anterior chamber is seen on biomicroscopy. Posterior synechiae, cataract, and secondary glaucoma are common sequelae. Uveal cysts may also be noted in this disease but should be differentiated from the cysts that are unassociated with uveitis (see under "Uveal Cyst").

Clinical Signs (Table 136-2)

- *Miosis* is a smaller than normal pupil due to contraction of the iris sphincter muscle. Spasm of the iris sphincter muscle, along with the ciliary body musculature, results in pain, noted clinically as photophobia (intolerance of light).
- *Flare* results from a breakdown in the blood-aqueous humor barrier and a subsequent leakage of plasma protein (with or without cells) into the eye. It is observed clinically as a haze in the anterior chamber (Fig. 136-1).
- *Hypotony* is a decrease in the IOP below the normal range of 15 to 25 mm Hg due to decrease in the production of aqueous humor.
- *Cells* are released into the anterior chamber in severe uveitis. The inflammatory cellular response can be neutrophilic or granulomatous. In addition, red blood cells (hyphema) or neoplastic cells can enter the anterior chamber. Cells can appear suspended in the aqueous humor, settled in the ventral anterior chamber (hypopyon), or as keratitic precipitates. Keratitic precipitates appear as focal deposits on the ventral corneal endothelium. They are associated with a granulomatous uveitis and are accumulations of protein, macrophages, and lymphocytes and plasma cells. In the dog they are most often seen in association with lens-induced uveitis or disseminated mycosis, and in cats they are in association with feline infectious peritonitis or toxoplasmosis.
- *Hyperemia* or redness may be seen on examination of the conjunctival, episcleral, and iris blood vessels in eyes with anterior uveitis.
- *Corneal edema,* associated with anterior uveitis, occurs from endothelial cell dysfunction or loss and is diffuse in nature. Diffuse corneal edema indicates intraocular disease and the need for measurement of IOP. If the edema is of a focal nature, the cornea should be stained with fluorescein to rule out a corneal ulcer with secondary anterior uveitis.

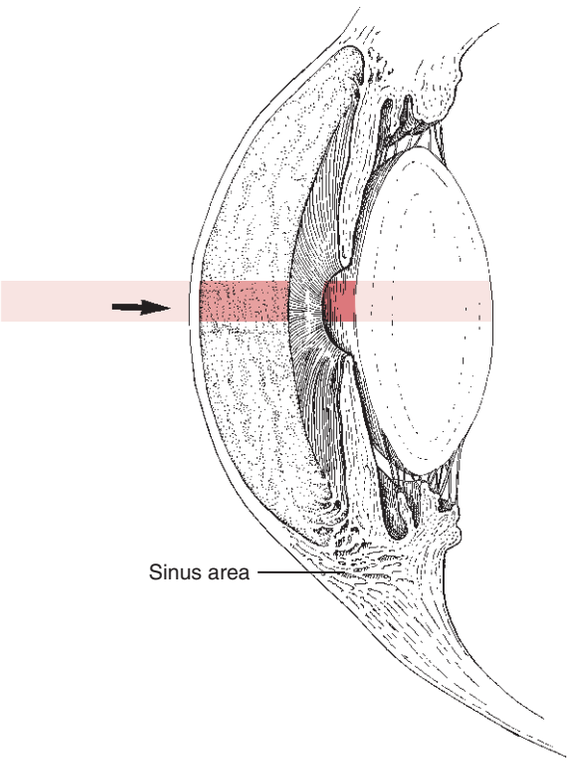

Figure 136-1. Using a bright, focused light source, aqueous flare is seen as a continuation of the light beam through the normally dark-appearing anterior chamber.

Diagnosis

History

A complete history is essential to detect previous or concurrent problems that may be associated with anterior uveitis. The history includes both ophthalmic and systemic problems.

Physical Examination

A complete physical examination is an essential part of the diagnostic evaluation of a patient with anterior uveitis. Palpate all external lymph nodes, auscultate the cardiopulmonary system, palpate the abdomen, and determine the body temperature.

Penlight Examination

A penlight examination is performed to evaluate pupil size, symmetry, and response to light. Assess the severity and character of the uveitis by the degree of aqueous flare and the cellular response. Assess the clarity of the clear media of the eye, cornea, aqueous humor, lens,

and vitreous. Evaluation of flare requires a bright focal light source, and a Finnoff transilluminator works well for this purpose. All abnormalities are described and diagramed in the medical record.

Tonometry

Tonometry is the determination of the IOP. Eyes with anterior uveitis have a decreased IOP (hypotony). A normal or elevated IOP indicates the potential for, or the presence of, glaucoma. While previous recommendations suggested the Schiøtz tonometer was the most cost-effective tonometer for private practice, the Tonopen (Dan Scott and Associates) is a more portable, accurate, and user-friendly tonometer and will result in more frequent and more accurate IOP readings. It is also easier to use on painful eyes (see Chapter 137).

▼ ***Key Point*** The clinical signs of anterior uveitis and glaucoma can be similar. Both diseases can be present together in the same eye. Determination of IOP is therefore essential.

Fundic Examination

Perform fundic examination, either by direct or indirect ophthalmoscopy, to determine the presence or absence of posterior segment involvement. Anterior uveitis in combination with posterior uveitis is termed *panuveitis* and is strongly suggestive of systemic disease, especially those infectious in nature (see Table 136-1). Posterior segment changes indicating active inflammation include retinal hemorrhage, retinal detachment, vasculitis, and infiltration by granulomatous or neoplastic cells. If the posterior lesions are chronic, they will appear as tapetal hyper-reflectivity, pigment clumping and depigmentation of the non-tapetal region, and atrophy of the retinal vasculature (see Chapter 138).

Fluorescein Stain of Cornea

Perform fluorescein stain to examine for a corneal ulcer. Corneal ulcers can result in a secondary anterior uveitis. If detected, the ulcer must be characterized with regards to depth, severity, and infection (see Chapter 134). In addition, determine the etiology and treat appropriately. Anterior uveitis, resulting from a corneal ulcer, resolves once the ulcer is healed.

Routine Laboratory Tests and Radiography

- Perform *biochemical profile, urinalysis,* and *complete blood count* on all patients with anterior uveitis of unknown cause and patients with concomitant systemic abnormalities.
- Perform *serology,* for the specific infectious diseases listed in Table 136-1, as indicated by the findings of the history, physical examination, ophthalmic examination, biochemical profile, urinalysis, and complete blood count.
- *Radiograph* the thorax and abdomen to evaluate for systemic mycosis, disseminated neoplasia, or other organ system involvement.

Cytology

- Cytology of intraocular or extraocular samples may be indicated in selected instances. Intraocular samples include both the aqueous and the vitreous humors. Of these, the vitreous humor sample is the most diagnostic but also the most traumatic to obtain. Anterior chamber samples are frequently not diagnostic. The indication for vitreocentesis is panuveitis in a blind eye for which the diagnosis cannot be obtained by alternate methods.
- Using general anesthesia, insert a 20-gauge needle 4 to 5 mm posterior to the corneal-scleral junction superior temporally.
- Direct the needle toward the center of the eye and aspirate 0.5 to 1.0 ml of fluid for culture and cytology.
- Extraocular cytology includes aspirates of regional lymph nodes or mass lesions.

Treatment

The treatment of anterior uveitis includes nonspecific approaches directed toward decreasing the inflammation and sequelae and specific ones directed toward eliminating the underlying etiology when one has been identified (Table 136-3).

Mydriatic-Cycloplegics

Use mydriatic-cycloplegics to paralyze the iris sphincter and ciliary body musculature. This effect will decrease the pain associated with anterior uveitis and the tendency toward formation of posterior synechia. The mydriatic-cycloplegic of choice is topical 1% atropine (parasympatholytic). Administer atropine to effect (pupil dilation), but do not exceed a treatment frequency of 4 times per day. This results in maximum drug effects with minimal side effects.

▼ ***Key Point*** Atropine is contraindicated in anterior uveitis when accompanied by secondary glaucoma.

Topical Anti-inflammatory Drugs

Topical anti-inflammatory drugs include both corticosteroids and nonsteroidal agents (see Table 136-3). Topical medication does not penetrate beyond the iris and ciliary body. Use only for problems of the anterior segment of the eye.

Corticosteroids

The topical corticosteroid of choice for the treatment of anterior uveitis is 1% prednisolone acetate ophthalmic suspension (Econopred). This agent achieves

Table 136-3. DOSAGES OF COMMONLY USED OCULAR ANTI-INFLAMMATORY AGENTS

Drugs	Trade Names	Dosages
Topical		
Corticosteroids		
1.00% Prednisolone acetate suspension	Econopred Plus	1–6×/d
0.10% Dexamethasone solution	Decadron	1–6×/d
0.05% Dexamethasone ointment	Decadron	1–6×/d
NSAIDs		
0.03% Flurbiprofen	Ocufen	4×/d
1.00% Suprofen	Profenal	4×/d
0.10% Diclofenac	Voltaren	4×/d
Atropine		
1.00% Atropine		1–4×/d
Systemic		
Corticosteroids		
Prednisolone/prednisone		Dog
	Immunosuppressive	1.0 mg/kg PO q12h × 7–14d, then taper
	Anti-inflammatory	0.5 mg/kg PO q12h × 3–5d, then taper
NSAIDs		
Flunixin meglumine	Banamine	Dog: 0.25–0.50 mg/kg IV single dose Cat: Do not use
Carprofen	Rimadyl	Dog: 2.0 mg/kg PO q12h
Etodolac	EtoGesic	Dog: 10–15 mg/kg PO q24h, monitor STT
Immunosuppressive		
Azathioprine	Imuran	Dog: 2.2 mg/kg PO q24h × 5d, then taper
Cyclophosphamide	Cytoxan	Dog: 50 mg/m^2 PO q24h × 4d/wk
Cyclosporine	Atopica, Neoral	Dog: 5–10 mg/kg PO q12–24h

NSAID, nonsteroidal anti-inflammatory drug; STT, Schirmertear test.

the highest intraocular level of the ophthalmic corticosteroids. If unavailable, 0.1% dexamethasone solution or 0.05% dexamethasone ointment can be applied. The frequency of treatment varies according to the severity of the uveitis, ranging from 1 to 6 times a day.

▼ ***Key Point*** Topical corticosteroids delay healing and potentiate infection and collagenase ulceration. Topical corticosteroids are contraindicated for anterior uveitis associated with corneal ulceration.

Topical corticosteroids are also absorbed systemically and alter adrenal and hepatic function.

Nonsteroidal Anti-inflammatory Drugs

The indications for topical nonsteroidal anti-inflammatory ophthalmic drugs are similar to those for topical corticosteroids. They are used as supplements to topical corticosteroids or as substitutes when topical corticosteroids are contraindicated (e.g., in diabetes mellitus). As with topical corticosteroids, nonsteroidal agents may delay the healing of a corneal ulcer. Administer 4 times a day.

Systemic Anti-inflammatory Drugs

Systemic anti-inflammatory drugs include corticosteroids, nonsteroidal agents, and immunosuppressive drugs (see Table 136-3).

Corticosteroids

Systemic corticosteroids are indicated in the management of non-infectious posterior uveitis and in severe anterior uveitis as a supplement to topical corticosteroids. The dosage is dependent on the underlying disease. An immunosuppressive dose is indicated for animals with uveodermatologic syndrome, and an anti-inflammatory dose is indicated for most other cases (see Table 136-3). The side effects of systemic corticosteroids include polyphagia, polyuria, or polydipsia; infection potentiation; altered carbohydrate metabolism; and adrenal suppression. Therapy with systemic corticosteroids begins at a high dose to achieve a response followed by a tapered dose to maintain effect and to decrease adverse side effects.

Nonsteroidal Anti-inflammatory Drugs

Systemic nonsteroidal anti-inflammatory drugs (NSAIDs) include aspirin, flunixin meglumine, carprofen, etodolac,

and others (see Table 136-3). They are indicated to decrease inflammation and facilitate pupil dilation. In small animal ophthalmology, flunixin meglumine is administered as a single dose (0.25–0.5 mg/kg IV) prior to ocular surgery to decrease post-surgical ocular inflammation. Side effects of NSAIDs include gastrointestinal ulceration and hemorrhage and acute renal papillary necrosis. Do not use systemic NSAIDs in combination with systemic corticosteroids. Use with caution in patients with questionable renal function. In addition, etodolac is associated with iatrogenic keratoconjunctivitis sicca.

Immunosuppressive Drugs

Systemic immunosuppressive therapy may be required when animals fail to respond to corticosteroids or NSAIDs or when the required levels of these drugs result in systemic toxicity.

Specific

Specific therapy is dependent on the etiology of the uveitis. See appropriate chapters for treatment of the systemic diseases that cause anterior uveitis.

Sequelae

- ***Secondary glaucoma*** results from the obstruction of the outflow pathway of the aqueous humor. This can occur at the pupil from posterior synechia, at the drainage angle from anterior synechia and preiridal fibrovascular membrane formation, or in the trabecular meshwork from deposits of inflammatory debris and fibrosis. Control of this type of secondary glaucoma through medical therapy is often extremely difficult to achieve (see Chapter 137).
- ***Synechiae*** are adhesions from the iris to adjacent structures, such as the cornea or lens. Synechiae can result in abnormal pupillary light response, misshapen pupil, glaucoma, pigmentation of the cornea or lens, and blindness.
- ***Cataracts*** can occur subsequent to anterior uveitis. The lens is dependent on the aqueous humor for nutrients and waste product removal. Anterior uveitis results in altered lens metabolism and a buildup of inflammatory by-products that may cause opacification of the lens and capsule (cataract) (see Chapter 135).
- ***Corneal edema*** occurs from the failure of the corneal endothelial cell pump or barrier. Corneal endothelial cells are responsible for the maintenance of corneal deturgescence, which is essential to corneal transparency. Endothelial cells need the aqueous humor for nutrients and waste product removal. Anterior uveitis may alter the function of these cells, resulting in diffuse corneal edema. Corneal endothelial cells in the adult dog and cat have little regenerative capabilities; thus damage may be permanent.
- ***Blindness*** secondary to severe anterior uveitis is common and results from secondary glaucoma, cataract formation, synechia, pigment migration, or posterior segment (retina, choroid) changes.
- ***Phthisis bulbi*** occurs as a result of atrophy of the ciliary body and a sustained decrease in aqueous humor production. Chronic hypotony (i.e., low IOP) results, and the eye decreases in size.

Prevention

Although prevention of anterior uveitis is usually not possible, the sequelae of anterior uveitis can be prevented by accurate diagnosis and appropriate and rapid treatment. Therapy directed toward the etiology not only will aid the management of the ocular disease but also may prevent the serious and life-threatening complications of the systemic disease.

UVEAL NEOPLASIA

Uveal neoplasms can be primary or secondary. Primary neoplasms include iris, ciliary body and choroidal melanomas, and ciliary body adenoma or adenocarcinoma. Secondary neoplasms include lymphoma and metastatic carcinomas (most common) or any disseminated neoplasm. Intraocular neoplasms result in damage to the eye through displacement of normal ocular structures, causing lens luxation, dyscoria, and retinal detachment. In addition to an intraocular mass lesion, glaucoma, uveitis, and hyphema are the most common presenting signs of intraocular neoplasia. In general, secondary neoplasms are more inflammatory and destructive as compared with primary neoplasms.

Primary Neoplasia

Of the primary neoplasms, anterior uveal melanoma is most common. Tumor behavior varies depending on the species.

Canine Melanoma

Canine anterior uveal melanomas are generally benign in nature with less than 5% metastatic potential. In addition, it appears that Labrador and golden retrievers and German shepherds may be predisposed to iridal melanomas. In these breeds, the neoplasm may arise in a juvenile dog, and a suggestion of inheritance has been proposed. Breeding of affected Labrador and golden retrievers should be discouraged. The best criterion for predicting malignancy of intraocular melanoma in the dog appears to be the mitotic index.

Feline Melanoma

In contrast to the dog, feline uveal melanoma has been reported to metastasize in 60% of affected cats. Pigmented lesions of the feline iris or ciliary body,

especially those that are raised, displacing adjacent structures or resulting in other intraocular damage, should be removed by enucleation. In addition, perform a complete systemic evaluation including thoracic and abdominal radiographs and palpation of regional lymph nodes. No information exists to suggest that enucleation of these affected eyes affects the rate of metastasis, favorably or unfavorably.

Feline Spindle Cell Sarcoma

Intraocular spindle cell sarcoma can occur in the feline eye as a sequela to ocular trauma or uveitis. The period following ocular trauma or uveitis to the time of diagnosis of intraocular spindle cell sarcoma varies from 5 months to 12 years. These tumors are locally invasive, extending transsclerally or traveling along the optic nerve, and have the potential for metastasis. Enucleation or possibly orbital exenteration is the treatment of choice. Consider enucleation of severely traumatized or chronically inflamed, blind feline eyes to avoid the possible development of an intraocular spindle cell sarcoma.

Other Tumors

In addition to primary intraocular melanoma, ciliary body adenoma and adenocarcinoma, hemangiosarcoma, and astrocytoma have been reported in the dog and cat. These are often slow to metastasize but can cause intraocular damage as they enlarge.

Treatment

The treatment of primary ocular neoplasms varies according to the species, location, and severity of the neoplasm, rate of progression, presence or absence of vision, IOP, and availability of treatment modalities. Enucleation, excisional biopsy with preservation of the globe and/or vision, and laser ablation are all used for primary intraocular neoplasms. Small masses with no associated secondary complications can be documented, followed, and then treated if found to be progressive. In addition, an en bloc excision in the form of a sector iridectomy or iridocyclectomy can be used to excise a mass, preserve vision, and obtain a biopsy. This is a referral procedure. Laser surgery is used most often for pigmented melanomas and uses a diode or Nd:YAG laser to achieve a thermal effect resulting in coagulation necrosis of the tumor mass.

Secondary Neoplasia

Lymphoma is the most common intraocular neoplasm in the dog and cat. In addition, adenocarcinoma, hemangiosarcoma, and several other neoplasms metastasize to the eye. The most common ocular abnormalities seen in association with secondary neoplasms include glaucoma, uveitis, hyphema, retinal detachment, and lens luxation. Treatment should be directed at finding the primary source of the neoplasia followed by systemic therapy, including chemotherapy, surgery, and radiation. Additional therapy might include topical ophthalmic anti-inflammatory drugs and atropine for uveitis or topical and systemic medications aimed at reducing the IOP if secondary glaucoma is present. Topical therapy is often unrewarding. Systemic treatment of the primary problem usually results in a greater ocular response. If the eye is painful, blind, or nonresponsive to systemic treatment, perform enucleation.

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Chapter

137 Glaucoma

David A. Wilkie

Glaucoma is an increase in the intraocular pressure (IOP) beyond that compatible with maintenance of normal ocular physiology and function.

ANATOMY

See Chapter 131.

ETIOLOGY

Primary Glaucoma

Primary glaucoma is not associated with any other event or problem within the eye. It is usually breed related and often hereditary in nature. A partial list of predisposed breeds is given in Table 137-1.

▼ ***Key Point*** When glaucoma is primary, the opposite, unaffected eye may also develop glaucoma. Studies indicate an incidence of 50% involvement of the contralateral eye within 2 years following the diagnosis of glaucoma in the first eye.

Secondary Glaucoma

Secondary glaucoma is the result of an antecedent event within the eye. The etiologies of secondary glaucoma include anterior uveitis, anterior lens luxation, hyphema, intraocular neoplasia, chronic retinal detachment, pre-iridal fibrovascular membrane, and trauma.

- *Anterior uveitis* can cause glaucoma through obstruction of the flow of aqueous humor. This results from peripheral anterior or posterior synechiae, inflammatory debris in the iridocorneal angle, or the formation of a pre-iridal fibrovascular membrane. Anterior uveitis is discussed in Chapter 136.
- *Anterior lens luxation* can obstruct the flow of aqueous humor from the posterior to the anterior chamber or to the iridocorneal angle. The etiologies of anterior lens luxation include hereditary (in terriers), intraocular neoplasia, anterior uveitis, and trauma (see Chapter 135). Anterior lens luxation can also result from chronic glaucoma with enlargement of the globe (buphthalmos) and tearing of the lens zonules.
- *Intraocular* neoplasia, whether primary or secondary, can block the flow of aqueous humor through shedding of neoplastic cells into the iridocorneal angle or displacing of normal intraocular structures (see Chapter 136). In addition, intraocular neoplasia can result in the formation of a pre-iridal fibrovascular membrane.
- *Hyphema* can result from trauma, systemic hypertension, congenital ocular anomalies, vascular disorders, or bleeding disorders (see Chapter 136). Red blood cells can obstruct the trabecular meshwork of the iridocorneal angle resulting in ghost cell glaucoma.
- *Trauma* can result in anterior uveitis, anterior lens luxation, hyphema, or damage to the iridocorneal angle, all of which may lead to secondary glaucoma.
- *Retinal detachment,* when chronic, may be associated with proliferation of a pre-iridal fibrovascular membrane arising from the anterior iris stroma and resulting in anterior and posterior synechiae and iridocorneal angle obstruction. Chronic uveitis and intraocular neoplasia can result in a similar change.

CLINICAL SIGNS

- *Acute glaucoma* is a true medical and ultimately a surgical emergency. The diagnosis is made based on history and clinical signs (Table 137-2). If in doubt, err on the side of a diagnosis of acute rather than chronic glaucoma.
- *Chronic glaucoma* implies ophthalmic changes that cause the irreversible loss of vision (Table 137-3). The clinical changes most indicative of chronic glaucoma are retinal and optic nerve degeneration and buphthalmos.

DIAGNOSIS

▼ ***Key Point*** Although the history, breed, and clinical signs are all important in the diagnosis of glaucoma, definitive diagnosis can be made only through measurement of the IOP.

Table 137-1. BREEDS PREDISPOSED TO PRIMARY GLAUCOMA

American and English cocker spaniel	Malamute
English spinger spaniel	Chow Chow
Welsh springer spaniel	Afghan
Miniature poodle	Akita
Beagle	Cairn terrier
Basset hound	Dalmation
Siberian husky	Bouvier des Flandres
Norwegian elkhound	Shar-Pei
Samoyed	Other

Table 137-2. CLINICAL SIGNS OF ACUTE GLAUCOMA

Episcleral hyperemia
Diffuse corneal edema
Dilated pupil
Slow to absent pupillary light response
Weak to absent menace response
Epiphora
Blepharospasm

Table 137-3. CLINICAL SIGNS OF CHRONIC GLAUCOMA

Episcleral hyperemia	Epiphora
Diffuse corneal edema	Blepharospasm
Corneal striae	Retinal degeneration
Dilated pupil	Optic nerve cupping
Absent pupillary light response	Buphthalmia
Absent menace response	

- IOP measurement requires a tonometer. Digital tonometry is an inaccurate and unreliable method of IOP determination. While previous recommendations suggested that the Schiøtz tonometer was the most cost-effective tonometer for private practice, the Tonopen (Mentor O&O, Inc.) is a more portable, accurate, and user-friendly tonometer and will result in more frequent and more accurate intraocular pressure readings. This in turn will improve the veterinarian's ability to make an early diagnosis and more accurately assess response to treatment (see Chapter 131). The Tonopen is lightweight, portable, accurate, and self-calibrating, and it averages several readings and gives a percentage error to ensure accuracy. In addition, the small foot plate allows this tonometer to be used on painful eyes in less cooperative patients because only a small area of cornea is required to obtain a reading, and the position of the patient's head is not related to obtaining the reading. Normal IOP in the dog and cat is 15 to 25 mm Hg, although most ophthalmologists are concerned with when IOP exceeds 20 mm Hg.
- Once the diagnosis of glaucoma is made based on IOP, establish the etiology (i.e., primary versus secondary) and the degree of ocular damage. Depending on the history and associated ocular changes, the glaucoma can be classified as either acute or chronic.

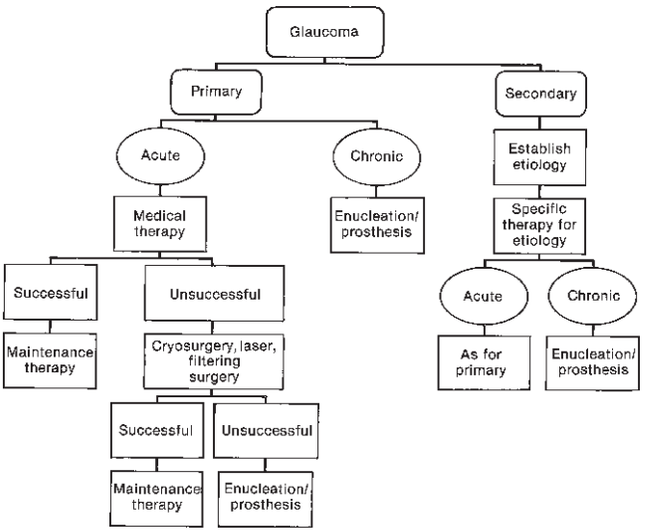

Figure 137-1. Treatment algorithm for glaucoma.

TREATMENT

▼ ***Key Point*** In order to treat glaucoma appropriately, answer two specific questions (Fig. 137-1). Is the glaucoma primary or secondary? Is the glaucoma acute or chronic?

- Treatment can be grouped into medical and surgical approaches. If the glaucoma is acute, a return of a portion of, or all of, the animal's vision is then possible. In acute glaucoma, immediate aggressive medical therapy is required to reduce the IOP to within normal range. Failure of medical therapy to lower and maintain IOP at a normal level indicates the need for surgical intervention and the possible referral to a veterinary ophthalmologist.
- The most appropriate treatment for chronic glaucoma is surgery, the goal of which is to reduce the IOP in order to relieve discomfort. Medical therapy of chronic glaucoma is neither effective nor cost-

Table 137-4. MEDICAL TREATMENT OF ACUTE GLAUCOMA

Drug/Concentration	Trade Name	Dose
Systemic		
Osmotic Drugs		
Mannitol		0.5–1.0 g/kg, IV
Carbonic Anhydrase Inhibitors		
Dichlorphenamide	Daranide	2–4 mg/kg, q8–12h, PO
Methazolamide	Neptazane	2–4 mg/kg, q8–12h, PO
Topical		
Carbonic Anhydrase Inhibitors		
Dorzolamide 2%	Trusopt	q8–12h
Dorzolamide 2% : timolol 0.5%	Cosopt	q8–12h
Parasympathomimetics		
Pilocarpine 2%	Isopto Carpine	q8–12h
Sympathomimetics		
Epinephrine 1%		q8–12h
Dipivefrin HCl 0.1%	Propine	q8–12h
Combination		
Pilocarpine 2% : epinephrine 1%	E-Pilo-2	q8–12h
Sympatholytics		
Timolol maleate 0.5%	Timoptic	q8–12h
Prostaglandins		
Latanoprost 0.005%	Xalatan	q12–24h

effective over time. The surgery of choice is either placement of an intraocular silicone prosthesis or an enucleation.

- Intravitreal injection of gentamicin or lidofovir (Vistide) designed to destroy the intraocular tissues is used by some to reduce intraocular pressure. This results in uveitis, cataract, and often phthisis bulbi and is cosmetically unappealing and unpredictable.

Medical

Medical therapy of acute glaucoma includes some, or possibly all, of the following agents (Table 137-4). The choice of medication varies according to the severity of the glaucoma, the etiology, and the response to the initial therapy.

Osmotic Drugs

- *Osmotic agents* act to dehydrate the vitreous and aqueous humors and thereby decrease the IOP. In order to be effective, they require an intact blood-eye barrier and therefore may not work well in eyes with uveitis or hyphema.

▼ ***Key Point*** One of the initial drugs of choice for rapidly decreasing IOP in the treatment of acute glaucoma is an osmotic agent. The osmotic agent of choice is 20% mannitol, administered intravenously (see Table 137-4).

- Withhold water from the animal for 3 to 4 hours following osmotic administration. The IOP begins decreasing within 20 minutes, with the maximum effect at 2 hours—the duration of effect is approximately 6 hours. An alternative osmotic agent is oral glycerin, but emesis is a frequent side effect.

Carbonic Anhydrase Inhibitors

- *Carbonic anhydrase inhibitors* (CAIs) work to decrease the IOP by blocking the enzyme responsible for the active production of aqueous humor. The systemic CAIs of choice, based on their efficacy and low frequency of side effects, are dichlorphenamide and methazolamide. Administer orally q8–12h (see Table 137-4).
- In addition to the eye, carbonic anhydrase can be found in the kidney, red blood cells, and lungs. Potential side effects of oral CAIs include metabolic acidosis and hypokalemia, manifested as panting, depression, vomiting, diarrhea, and collapse. If any of these side effects are noted, discontinue CAI therapy. Symptoms should resolve within 24 hours, and therapy can be reinstituted at a decreased dosage.
- A topical CAI, dorzolamide 2% (Trusopt, Merck & Co.) and dorzolamide 2%:timolol maleate 0.5% (Cosopt, Merck & Co), are also available. Administer q8–12h; this drug does not cause the systemic side effects seen with oral CAI administration. Topical CAIs are indicated for treatment of glaucoma and

have also become the drug of choice for prophylactic treatment of the contralateral eye.

Autonomic Drugs

- *Autonomic agents* include parasympathomimetics, sympathomimetics, and sympatholytics. Administer topically q8–12h (see Table 137-4). These drugs are synergistic and can, if needed, be applied to the same eye, provided their administration is 5 to 10 minutes apart. In my opinion, none of these is as efficacious in the dog as the newer glaucoma agents such as dorzolamide and latanoprost.

Parasympathomimetics

- *Parasympathomimetics* result in contraction of the iris sphincter and ciliary body musculature. Contraction of the longitudinal ciliary musculature increases the outflow of aqueous humor. In addition, parasympathomimetics result in vasodilation of the conjunctiva and increased aqueous humor protein and may reactivate or exacerbate iritis.
- The parasympathomimetic of choice is 2% pilocarpine (see Table 137-4). Transient topical irritation is often exhibited following administration but resolves 24 to 48 hours following initiation of therapy. An alternative parasympathomimetic is demecarium bromide (Humorsol), a potent and long-acting cholinesterase inhibitor. This has the advantage of once-daily administration.
- Parasympathomimetics are contraindicated in animals with active anterior uveitis that results in secondary glaucoma. Parasympathomimetics exacerbate the pain and symptoms of anterior uveitis.

Sympathomimetics

- *Sympathomimetics* increase the outflow of aqueous humor. Their mechanism of action differs from that of the parasympathomimetics and the two are synergistic.
- The sympathomimetic agent of choice is 0.1% dipivefrin HCl (Propine), a pro-drug of epinephrine (see Table 137-4). Alternatively, 1.0% epinephrine HCl can be administered either alone or in combination with 2% pilocarpine (E-Pilo-2).
- Side effects are minimal and include mild topical irritation, which is avoided with the use of 0.1% dipivefrin HCl. The long-term efficacy of these agents in lowering IOP in canine glaucoma is limited.

Sympatholytics

- *Sympatholytics* decrease the active production of aqueous humor.
- The sympatholytic agent of choice is a non-selective beta-blocking agent, 0.5% timolol maleate (Timoptic). Although disagreement exists over the efficacy of topical timolol maleate in small animal patients, information indicates that it has some IOP-lowering ability. Side effects have not been observed in small animals, but potentially systemic absorption could cause bronchoconstriction and bradycardia, both of which are side effects in humans.
- New topical alpha-2 adrenoreceptor agonists, apraclonidine 0.5% and brimonidine tartrate 0.2%, serve to lower IOP by reducing the formation of aqueous humor and in addition, in the case of brimonidine, increasing uveoscleral outflow. Apraclonidine may also result in mydriasis in the dog and miosis in the cat. Both of these drugs have been associated with side effects such as bradycardia, vomiting, and even death, especially in cats.

Prostaglandins

▼ ***Key Point*** Topical prostaglandins are the first drug of choice in acute, primary glaucoma. They will often lower the IOP to normal within 15 to 30 minutes and may avoid administration of systemic osmotic agents.

- Prostaglandins, administered topically in low concentration, have been found to lower IOP by increasing uveoscleral outflow. They are very species specific and while they have efficacy in dogs, their response is less in the cat. Side effects in humans include iris hyperpigmentation and conjunctival and facial irritation. Side effects are uncommon in the dog.
- Latanoprost 0.005% (Xalatan, Pharmacia) is the most commonly administered topical ophthalmic prostaglandin. In addition, isopropyl unoprostone 0.12% (Rescula, Novartis) is available.
- Administer topical prostaglandins every 12 to 24 hours. Miosis is a common side effect and owners can use this to monitor how frequently to administer the drug. If the pupil is returning to normal after 12 hours, administer the drug every 12 hours.
- These agents are contraindicated with concurrent anterior uveitis.

Plan of Action for Medical Treatment

- When presented with a patient with acute glaucoma, administer latanoprost first.
- If after 30 minutes no response is noted, administer intravenous mannitol.
- These are followed by maintenance therapy with an oral and topical CAI and topical latanoprost if initial response was noted. Topical pilocarpine or timolol can also be administered depending on clinician preference.
- Monitor IOP every 2 to 4 hours for the next 24 hours. If, following the initial reduction in IOP with mannitol, the IOP increases and exceeds 30 mm Hg, repeat mannitol therapy.
- Medical therapy can be increased to include all of the aforementioned topical medications. When adminis-

tering multiple topical medications, space each treatment 5 minutes apart.
- The failure of this aggressive, maximal therapy to lower and maintain IOP within the normal range indicates the need for surgical intervention (see following section). Most acute, primary glaucoma patients will require surgical intervention at initial presentation or shortly thereafter.
- In addition to therapy aimed at lowering IOP, attention is then focused on the resulting reperfusion injury that occurs to the retinal ganglion cells and axons of the optic nerve following rapid reduction of IOP. Newer therapies used in conjunction with pressure reduction are being examined and include calcium channel blocking agents, corticosteroids, and other potentially neuroprotective agents.

Surgical

Cyclocryosurgery

Cyclocryosurgery involves transscleral freezing of a portion of the ciliary body. This procedure selectively destroys an area of the ciliary processes, thereby decreasing the production of aqueous humor. It works best in conjunction with medical therapy and is indicated primarily in cases of acute glaucoma in which IOP is not effectively controlled with medical therapy alone. This is an older technique and has been largely replaced with laser cyclophotoablation.

Objectives

- Reduce the intraocular pressure to a level compatible with maintaining vision.
- Relieve the discomfort associated with glaucoma.

Equipment

- Liquid nitrogen *or* nitrous oxide cryogen unit with an ocular probe, 2.5 mm in diameter.

Technique

1. Place the anesthetized animal in lateral recumbency. Administer a single dose of systemic flunixin meglumine (Banamine) (0.25 mg/kg IV).
2. Use an eyelid speculum to obtain adequate exposure of the globe (Fig. 137-2).
3. Place the cryoprobe on the conjunctiva, 4 to 5 mm posterior to the limbus, in the superior or inferior temporal quadrant of the eye (see Fig. 137-2). Avoid the long posterior ciliary arteries found at the 3- and 9-o'clock positions.
4. Activate the cryoprobe and freeze the site. The actual freezing time varies according to the cryounit. Approximate freeze times and probe tip temperatures are for nitrous oxide, 2 minutes, –60° to –80° C, and for liquid nitrogen, until the ice ball extends 1 mm into the cornea (<30 seconds), –185° C.
5. Freeze multiple sites. The number of freeze sites varies according to the severity of the glaucoma and the cryoprobe. In general, freeze four to eight sites with liquid nitrogen, fewer than are done with nitrous oxide.

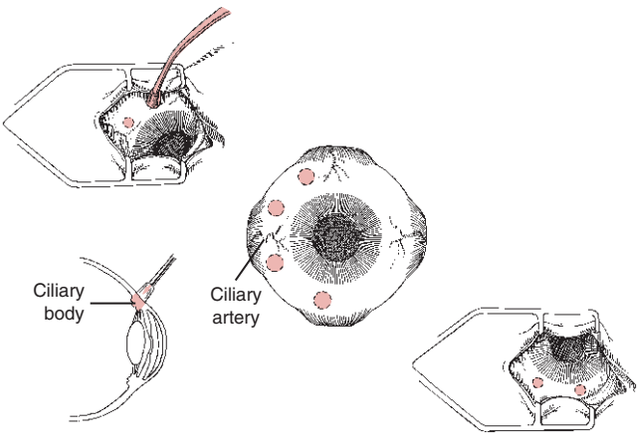

Figure 137-2. Cryosurgery or cyclophotocoagulation selectively destroys portions of the ciliary body (at areas indicated) and effects a decrease in the production of aqueous humor. Avoid damaging the long posterior ciliary arteries.

Following surgery, monitor the IOP. Prescribe medical therapy for glaucoma, based on the response of the IOP to cryosurgery. Treat postoperative discomfort with oral nonsteroidal anti-inflammatory drugs, such as carprofen (2.0 mg/kg PO q12h).

Transscleral Cyclophotocoagulation

▼ ***Key Point*** Diode laser transscleral cyclophotocoagulation is the most common surgical technique for acute, primary glaucoma. It is used in combination with emergency medical therapy.

- This technique uses a contact or non-contact neodymium:yttrium-aluminum-garnet (Nd:YAG) or diode laser to deliver energy that destroys a portion of the ciliary body and reduces aqueous humor formation (see Fig. 137-2).
- While the initial cost of these lasers is high, resulting in their being restricted to a referral-only procedure, the side effects are less than with cyclocryosurgery and the success is greater.
- The key to success appears to be early intervention, thus performing the cyclophotodestructive procedure prior to the development of acute congestive glaucoma. With the introduction of better prophylactic drugs and accurate IOP determination in practice using the Tonopen, early referral has become more common, with laser surgery performed at an

IOP between 20 and 35 mm Hg. The procedure works best in these eyes and has minimal side effects.
- Post-surgical uveitis and a transient ocular hypertension are the most common side effects.
- Treatment of eyes with IOP greater than 50 mm Hg appears to be less effective for achieving long-term control.
- Cyclophotocoagulation should be used in conjunction with, not as a replacement for, medical therapy.

Filtering Procedures

- These are designed to provide an alternate outflow pathway for the aqueous humor. The aqueous is usually redirected to the subconjunctival tissue space through either a filtering hole or an implantation of a filtering device.
- Although the initial success with this procedure may be high, many filtering procedures ultimately fail owing to fibrosis of the new outflow pathway. Filtering procedures work best in conjunction with medical and surgical therapies and for a short time only.
- Refer animals requiring a filtering procedure to an appropriate specialist.

Intraocular Prosthesis

Objectives

- Relieve pain associated with chronic glaucoma.
- Maintain cosmetic appearance of the eye.

▼ ***Key Point*** This procedure is indicated only for chronic glaucomatous eyes that are irreversibly blind. Intraocular prosthetic implants are contraindicated in cases of intraocular neoplasia, infectious panophthalmitis, and midstromal or deeper corneal ulceration.

Equipment

- Routine ocular surgical pack with a cyclodialysis spatula.
- Sterile intraocular silicone implant (Jardon Corp.). The implant is 2 mm larger than the horizontal dimension of the cornea of the normal eye. In the dog, an 18 to 19-mm prosthesis generally is satisfactory.
- Carter sphere introducer.

Technique

1. Place the anesthetized animal in lateral recumbency. Administer systemic flunixin meglumine as discussed in the cryosurgery section.
2. Use an eyelid speculum to obtain adequate exposure of the globe.
3. Make an incision in the superior conjunctiva, 4 to 5 mm posterior to the limbus (Fig. 137-3*A*). Continue the incision 120 degrees around the globe.

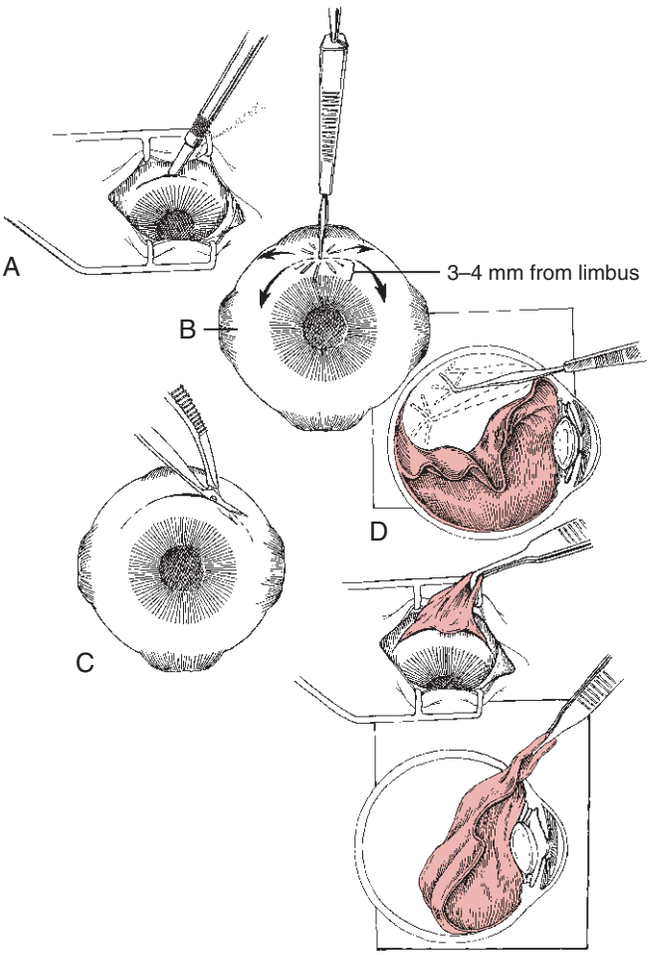

Figure 137-3. Preparation of globe for intraocular prosthesis. See text for details.

4. Dissect the conjunctival and episcleral tissues to the level of the sclera.
5. Make an incision in the superior sclera, 4 to 5 mm posterior to the limbus.
6. Introduce a cyclodialysis spatula into the globe between the fibrous and vascular tunics and gently separate these tunics. Avoid injury to the cornea (Fig. 137-3*B*).
7. Enlarge the scleral incision (Fig. 137-3*C*).
8. Remove the intraocular contents (Fig. 137-3*D*), leaving only the fibrous tunic (cornea and sclera).
9. Place the silicone implant within the globe.
10. Close the sclera and conjunctival tissues with 6-0 absorbable suture (e.g., Vicryl, Ethicon) in simple interrupted or simple continuous pattern.

Postoperative Care

- Administer topical, broad-spectrum antibiotic ointment q6h.
- Apply warm, moist compresses twice daily for 5 to 7 days.

- Administer systemic nonsteroidal anti-inflammatory agents as required (see Chapter 6).
- As the surgical procedure removes the aqueous humor (the primary source of corneal nutrition) the cornea will vascularize over the 2 to 4 weeks following surgery.
- Evaluate the eye 2 weeks after surgery. Note the progression of corneal vascularization and the absence of corneal ulceration. Determine the IOP in the contralateral eye of patients with primary glaucoma at this time.

Enucleation

Objective

- Relieve the pain associated with glaucoma.

▼ ***Key Point*** An enucleation is indicated in animals with chronic glaucoma, causing irreversible blindness, and in which an intraocular prosthetic implant is contraindicated.

Equipment

- Routine ocular surgical pack

Technique

1. Aseptically prepare and suture eyelids closed.
2. Incise the skin 5 to 6 mm away from the eyelid margin 360 degrees around the eyelids. Using sharp dissection, continue the incision to the level of the extraocular muscles.
3. Sever the extraocular muscles at their attachment to the sclera.
4. Clamp and sever the optic nerve and blood vessels. Ligate the pedicle with 3-0 to 4-0 absorbable sutures.
5. If desired, insert an intraorbital silicone prosthesis to minimize the post-surgical "sunken" appearance of the orbit. A 24- to 34-mm prosthesis is used, nearly filling the orbital space.
6. Close the extraocular muscles, periorbita, subcutaneous tissues, and skin in a routine manner. Close the orbital space and subcutaneous tissues utilizing continuous 4-0 absorbable sutures and the skin utilizing 5-0 or 6-0 non-absorbable sutures in an interrupted or continuous pattern.

Postoperative Care

- Administer postoperative analgesics as needed (see Chapter 6).
- Administer postoperative systemic antibiotics for eyes enucleated for infectious panophthalmitis or penetrating keratitis.
- Submit all enucleated eyes to a qualified veterinary pathologist for examination.
- Remove sutures 10 to 14 days following surgery.

Pharmacologic Ablation

In my opinion, this is an unacceptable method for the management of glaucoma. It involves the intravitreal injection of a substance toxic to the eye in the hope that this approach will result in the destruction of the ciliary body, thereby lowering the intraocular pressure. This is an irreversible, inaccurate, and sometimes painful procedure. In addition, the end result is usually a non-cosmetic phthisic globe that may require enucleation.

PREVENTION

- Evaluate IOP in all breeds predisposed to primary glaucoma, as part of the routine yearly physical examination. A sustained, gradual increase in IOP, even if still within normal limits, is sufficient cause to initiate preventive topical therapy.
- In an animal with primary glaucoma in one eye, determine the IOP in the opposite eye, every 2 to 4 months.
- In an animal with primary glaucoma in one eye, use preventive treatment in the opposite eye. This can consist of a systemic CAI administered to control the affected eye, which will also lower the IOP in the opposite eye. Alternatively, treat the unaffected eye topically, if systemic CAIs are not required for the affected eye.
- Measure IOP in all eyes with lens luxation or subluxation, anterior uveitis, or hyphema. If possible, the primary problem is eliminated in an effort to avoid secondary glaucoma.
- It is essential that owners understand that cure is not possible in most instances. Instead, *control, management,* and *prevention* are more appropriate terms to use when discussing glaucoma.

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Chapter

138 Diseases of the Retina, Choroid, and Optic Nerve

Nicholas J. Millichamp / Joan Dziezyc

EVALUATION OF THE POSTERIOR SEGMENT

The posterior segment of the eye includes the vitreous humor; the retina and its vasculature; and the choroid, sclera, and optic nerve. The fundus is the portion of the posterior segment that can be seen with an ophthalmoscope. Considerable variation exists in the appearance of the normal fundus in the dog and cat. To fully appreciate subtle differences in normal fundi, consult available atlases detailing their appearance.

Generally, the fundus is divided into the brightly colored and reflective tapetal region, occupying the upper and more temporal area, and the darkly pigmented non-tapetal region, occupying the lower area and completely surrounding the tapetal area. Apart from these fundic regions, examine the retinal blood vessels and the optic nerve head (optic disc).

Ophthalmoscopy is the technique used to examine the fundus (see Chapter 131). The technique is ideally performed after dilating the pupil (except in an animal with ocular hypertension, glaucoma, or lens luxation) with a short-acting parasympatholytic drug such as tropicamide (Mydriacyl 0.5%, Alcon).

- Direct ophthalmoscopy with a hand-held ophthalmoscope is commonly used in practice. Unfortunately, this technique yields limited information about the fundic appearance even in the hands of experienced ophthalmologists. Small lesions and variations in contrast between normal and abnormal areas of the fundus are often overlooked when utilizing the direct technique.
- Indirect ophthalmoscopy, utilizing a 20D planoconvex lens held 2 to 3 inches from the animal's eye and illuminated with a penlight held at arm's length from the animal, is more useful as a diagnostic technique.

▼ ***Key Point*** Indirect ophthalmoscopy enables the examiner to quickly scan a large area of the fundus and to recognize obvious lesions.

- Ocular ultrasonography and color-flow Doppler ultrasonography are utilized to evaluate the structures of the posterior segment when opacities of the ocular media prevent an ophthalmoscopic examination.
- Electroretinography employs a light stimulus of varying intensity and frequency to elicit a retinal response from rod and/or cone photoreceptors. This test evaluates the functional integrity of the retina and is a procedure that requires referral to a specialist. Neuroophthalmology is discussed in Chapter 141.

DISEASES OF THE VITREOUS HUMOR

The vitreous is a gel composed mostly of water with lesser quantities of mucopolysaccharides and proteins. The normal adult vitreous is transparent and lacks blood vessels. The vitreous cannot itself become inflamed. However, products of inflammation or other abnormalities of adjacent tissues can result in exudate or hemorrhage that enters the vitreous and is seen by ophthalmoscopy.

Etiology

Retention of the Fetal Hyaloid Artery

- Retention of the fetal hyaloid artery or its remnants may be seen in an adult dog as a fine gray strand arising from the optic disc or inserting onto the posterior pole of the lens.

Persistent Hyperplastic Primary Vitreous (PHPV)/Persistent Tunica Vasculosa Lentis

- Persistent hyperplastic primary vitreous (PHPV)/persistent tunica vasculosa lentis is inherited in some breeds, notably the Doberman pinscher. The hyaloid artery is retained and is hyperplastic and associated with vessels that ramify over the posterior lens surface. Blood vessels and associated posterior lens capsular pigmentation and opacities (cataracts) or intralenticular hemorrhage is observed clinically. Color-flow Doppler ultrasonography may enable diagnosis and aid in predicting prognosis in cases of PHPV where the posterior segment cannot easily be seen by ophthalmoscopy. Surgical therapy yields poor results. Do not use these animals for breeding.

Asteroid Hyalosis

- Asteroid hyalosis is a unilateral or bilateral degenerative change associated with aging in dogs. Calcium-lipid complexes are deposited on the vitreous protein matrix. These appear as multiple white sparkles that oscillate slightly with eye movements. Asteroid hyalosis does not significantly impair vision in most dogs although advanced lenticular nuclear sclerosis and severe asteroid hyalosis in old dogs may reduce vision to some extent. No treatment is indicated.

Cholesterosis Bulbi

- Cholesterosis bulbi or synchysis scintillans is a far less common entity in which white cholesterol crystals are deposited in the vitreous secondary to intraocular inflammation. The vitreous often will become liquefied *(syneresis)* as a result of posterior segment inflammation. The cholesterol deposits sink to the bottom of the vitreous cavity. When the eye moves, the deposits swirl in the liquid vitreous before settling again under gravity. The initial cause of ocular inflammation and vitreous liquefaction may often have subsided by the time cholesterosis bulbi is detected. Vision is not affected by the cholesterosis bulbi per se, although it may be compromised by the underlying inflammatory disease.

Vitreous Hemorrhage

- Vitreous hemorrhage most commonly occurs in the dog and cat as a sequel to ocular trauma, intraocular surgery, retinal detachment, or systemic coagulopathy. If the hemorrhage is severe, blindness may result. Spontaneous resorption of vitreous hemorrhage may take several months.

Exudate and Cellular Infiltrate

- Exudate and cellular infiltrate appear as hazy, white, or gray material in the vitreous or on the posterior capsule of the lens. Pigment may also be deposited in the vitreous. Cellular infiltrate may become dense enough to obscure a view of the retina. Investigate for anterior uveitis or chorioretinitis (see later section).

Other

- Other possible vitreous opacities include posterior lens luxation; retinal detachment; foreign bodies; parasites *(Dirofilaria);* and neoplasms arising from the ciliary body, retina, choroid, or optic nerve.

Clinical Signs

▼ ***Key Point*** Opacities of this otherwise clear medium are the most commonly observed clinical findings that indicate disease of the vitreous.

- The effect on the animal's vision depends upon the severity and density of the opacities.

Diagnosis

- *Ophthalmoscopic examination* with a focal light source (penlight) or an ophthalmoscope will reveal the nature of the opacities (asteroid hyalosis, hemorrhage, pigment).
- *Submit blood for a clotting profile* when vitreous hemorrhage occurs unassociated with ocular trauma or intraocular surgery.
- *Perform physical examination, complete blood count, serum biochemistry,* and *serology evaluations* for infectious inflammatory disease (see Chorioretinitis) in cases in which vitreous exudate or cellular infiltrate is seen.
- *Perform ultrasonography* to rule out a diagnosis of coexisting retinal detachment, posterior segment neoplasia, or foreign bodies.

Treatment

- *Vitreous hemorrhage* resorbs slowly over the course of several weeks. Treat the coagulopathy systemically when possible.
- *Exudate and infiltrate* decrease by treating the underlying inflammatory disease with systemic antibacterial, antifungal, and nonsteroidal anti-inflammatory drugs (NSAIDs), as indicated. Corticosteroids can be used in dogs and cats once infectious etiologies are ruled out (prednisone or prednisolone, 1–2 mg/kg, q12–24h PO). NSAIDs (aspirin, 25 mg/kg q12h PO in dogs only) often improve ocular inflammatory disease.

CONGENITAL DISEASES OF CHORIORETINA AND OPTIC NERVE

Etiology

Many of these diseases occur most frequently in dogs and are inherited. Other possible congenital causes include inflammation and necrosis in the developing retina in utero due to infectious diseases, radiation, and teratogens.

Collie Eye Anomaly

- *Collie eye anomaly* (CEA) is a disorder that occurs commonly in rough and smooth collies and less often in Shetland sheepdogs and some other breeds (border collies, Australian shepherds, Lancashire heelers). CEA affects the retinal the choroid and retinal pigment epithelium and, in severe cases, the retina and optic nerve. The disease is usually asymmetric in the two eyes.
- The most characteristic lesion is choroidal hypoplasia (an area of thin, poorly vascularized choroid), which appears as a pale area of fundus temporal to

the optic nerve. The lesion is one of depigmentation of the retinal pigment epithelium and choroid and focal absence of tapetum exposing hypoplastic choroidal blood vessels overlying the sclera. Occasionally, hazy white corneal opacities accompany the chorioretinal lesions.

- In severe cases, colobomas (gaps or holes due to incomplete development) may occur in the optic nerve or choroid. These are often circular or oval lesions which may appear out of focus compared with the surrounding structures when seen by ophthalmoscopy. Retinal detachment or intraocular hemorrhage is found in the most severe cases.
- It has long been believed that the disease has a simple autosomal recessive means of inheritance, although recent studies of large numbers of dogs in Scandinavia have suggested that the inheritance is either polygenic or that choroidal hypoplasia and coloboma are inherited as separate traits. However, a gene for this disease has been located on canine chromosome number 37 and the recessive disease-causing mutation has been identified. Affected dogs are homozygous recessive—that is, both copies of the gene are mutant. All dogs that are homozygous recessive affected will show at least the mild form of the disease (choroidal hypoplasia) and may have more severe manifestations (coloboma, retinal detachment). Genetic linkage testing (from blood sample) can distinguish normal, carrier, and affected dogs (Optigen, LLC, Ithaca, NY; see www.optigen.com).
- Advise breeders to breed together genetically normal dogs (difficult in some breeds due to high incidence of affected animals) or carriers with subsequent testing to identify and eliminate affected dogs from the breeding program.

▼ ***Key Point*** The developmental abnormalities do not worsen after birth. Retinal detachment associated with optic nerve colobomas, however, may occur at any age.

Retinal or Vitreoretinal Dysplasia

- Retinal or vitreoretinal dysplasia occurs in cats and dogs. The disease may be inherited (often recessively) in the dog or may be a sequela to intrauterine infection (canine herpesvirus, feline panleukopenia).
- In the dog, inherited retinal dysplasia may be manifested as bilaterally asymmetric, small focal folds in the outer layers of the retina that do not result in retinal elevation. These folds are observed in the cocker spaniel and the Labrador retriever. The folds may appear as small dark dots, streaks, or circles in the tapetal fundus and gray or dark spots or streaks in the non-tapetal fundus. In some breeds (Sealyham and Bedlington terriers, Labrador retrievers, springer spaniel), the lesion is severe, and the dog is blinded by the retina lying unattached in abnormally formed vitreous.

Multiple Ocular Anomalies

- Multiple ocular anomalies are seen most commonly in Australian sheepdogs. Affected animals may have microphthalmia, iris colobomas, cataracts, retinal dysplasia or detachment, and uvea-lined defects (staphylomas) in the sclera.

Optic Nerve Hypoplasia

- *Optic nerve hypoplasia,* if bilateral, may be noted by breeders or owners in animals a few weeks old. The disease may be inherited in certain breeds, including the miniature poodle and dachshund. Affected eyes lack pupillary light reflexes and are blind. Ophthalmoscopy reveals a small optic nerve head with normal retinal vasculature.

Clinical Signs

Vision may be affected in dogs with severe congenital lesions. The pupillary light reflexes may also be variably affected, depending upon the severity of the lesions.

Diagnosis

Congenital abnormalities of the fundus are most readily diagnosed by the ophthalmoscopic appearance at 4 to 8 weeks of age. Some dogs have been seen to develop circular (or geographic) folds and dysplastic lesions at several months of age. Perform a second examination at 6 to 12 months of age in susceptible breeds. Genetic testing is available for dogs that might be affected with collie eye anomaly and can distinguish normal, carrier, and affected animals (Optigen, LLC, Ithaca, NY; see www.optigen.com).

Treatment and Prevention

The mode of transmission in the inherited diseases is often as an autosomal recessive trait (e.g., CEA and retinal dysplasia in most breeds). Prevent intrauterine infections by vaccination of breeding animals and by avoidance of infection and exposure of pregnant animals to ionizing radiation and teratogenic toxins.

▼ ***Key Point*** There is no treatment for congenital chorioretinal disease. Do not breed affected dogs.

ACQUIRED DISEASE OF THE CHORIORETINA AND OPTIC NERVE

Chorioretinal Degeneration

Etiology

Progressive Retinal Atrophy (PRA)

- Progressive retinal atrophy includes several genetic retinal diseases in which the ultimate outcome is degeneration and loss of retinal structure with

varying degrees of blindness. The different forms of PRA are all progressive and bilaterally symmetric. The disease occurs commonly in many purebred and mixed-breed dogs. The inheritance in most instances in the dog is autosomal recessive. Recessive sex-linked PRA is seen in the Siberian husky and Samoyed. PRA also occurs in various breeds of cat, although it has been best characterized in the Abyssinian.

- PRA may primarily affect the photoreceptors (rods/cones) or the adjacent layer of retinal pigment epithelium. Pigment epithelial dystrophy, or central PRA, is extremely rare in the United States and apparently on the decline in other parts of the world, including Europe. PRA affecting the rods or cones can be distinguished by the age of onset. In early-onset PRA (rod, rod-cone dysplasias), affected dogs show signs of night blindness during the first year of life.
- Affected breeds include the collie, Irish setter, miniature schnauzer, elkhound, and miniature dachshund. In late-onset PRA (progressive rod-cone degeneration), night blindness may be noticed at any age from 1 year on. Breeds affected include the miniature poodle, cocker spaniel, and Labrador retriever.
- The typical ophthalmoscopic appearance of diffuse retinal degeneration is an increased reflectance of light from the tapetal fundus (tapetal hyper-reflectivity). Retinal blood vessels are narrowed or lost, and depigmentation and patchy hyperpigmentation in the non-tapetal fundus may be seen. In advanced cases, atrophy of the optic nerve occurs.
- The various forms of PRA are gradually being identified at the molecular genetic level. In 2005 the DNA markers near the gene for late-onset progressive rod-cone degeneration (prcd-PRA) on chromosome 9 had been identified in a dozen canine breeds. Separate genes for early-onset rod-cone type dysplasia had been identified in a smaller number of breeds. Tests based on these genetic associations may either allow very accurate testing (gene mutation–based tests) or relatively accurate testing (linkage-based tests) of blood samples from dogs that are either normal, carriers, or affected with the disease (Optigen, LLC, Ithaca, NY; see www.optigen.com for details of interpretation of the various tests).

Sudden Acquired Retinal Degeneration (SARD)

- Sudden acquired retinal degeneration (SARD) is a degeneration of the retina that occurs in dogs. The defect that causes the degeneration is unknown.
- Dogs of any age that are otherwise normal may be affected. Obese, middle-aged dogs are most prone to the disorder.
- Some affected dogs may show signs or be clinically diagnosed with hyperadrenocorticism. The most characteristic feature of SARD is the rapid and complete loss of vision, often within a few days or at most weeks. The disease usually affects both eyes equally.

▼ ***Key Point*** In SARD, the photoreceptors are ultrastructurally abnormal at the time when blindness is first noted, although the fundus appears ophthalmoscopically normal.

- Ophthalmoscopic signs of retinal degeneration (tapetal hyper-reflectivity, vascular attenuation) appear over several months. The electroretinogram is extinguished at the time of presentation, which distinguishes the disease from optic neuritis, pituitary neoplasia, and central nervous system blindness.

Nutritional Deficiency

- Nutritional deficiency or taurine deficiency in the cat, especially in cats fed dog food that is deficient in taurine (an essential amino acid in the cat), results in feline central retinal degeneration (FCRD). The typical early lesion is a focal area of tapetal hyper-reflectivity in the temporal fundus. With progression of the lesion, a similar area appears nasally and the two patches join to form a horizontal band above the optic disc. Continued deficiency results in diffuse atrophy throughout the retina. Restoration of a taurine-rich diet halts the degeneration in the early stages, although the fundic lesion remains visible throughout the cat's life.
- Cats with taurine deficiency rarely show any evidence of blindness until the disease is advanced. For discussion of the cardiac effects of taurine deficiency in cats, see Chapter 150. FCRD also occurs in some cats on diets with adequate taurine. The cause in this situation is unknown. Since most cats are now fed diets with adequate taurine the incidence of FCRD appears to have decreased in recent years.

Enrofloxacin and Other Quinolone Antibacterial Drugs

- Enrofloxacin and other quinolone (orbifloxacin) antibacterial drugs have been associated with acute retinal degeneration in cats. Affected animals present with mydriasis and an acute onset of blindness (in older cats an important differential diagnosis would be hypertensive retinopathy). Examination of the fundus reveals tapetal hyper-reflectivity and attenuation of retinal blood vessels. Rust- or gold-colored foci may be seen in the tapetum at low illumination levels. The electroretinogram may be extinguished. The toxic effects on the feline retina appear to be idiosyncratic, varying with dose and length of time the drug is administered. Discontinuing use of the drug may not restore vision or avoid further progression of the degeneration.

▼ ***Key Point*** Never administer enrofloxacin at a total daily dose exceeding 5 mg/kg in cats due to the risk

of causing retinal degeneration. If possible use alternative antibacterial drugs in cats due to the idiosyncratic response of some animals to even low doses of the drug.

Chronic Glaucoma

- Chronic glaucoma results in diffuse retinal atrophy because of ischemia and pressure necrosis of initially the inner and later the outer retina (see Chapter 137).

Inflammation

- Inflammation that subsides or is successfully treated often results in focal lesions of chorioretinal degeneration in the affected areas. These lesions appear as focal hyper-reflective areas in the tapetal fundus or depigmented areas in the non-tapetum. Vision is affected to an extent commensurate with the area and region of the fundus involved (central versus peripheral retina).

Clinical Signs

- *Blindness* is a characteristic feature of retinal degeneration. Night blindness may be noted first in PRA that progresses to complete visual loss. Blindness may be sudden when caused by SARD and slowly progressive when caused by glaucoma.
- *Mydriasis* may be observed. Pupillary light reflexes may be incomplete and sluggish in advanced cases of PRA and can be absent in SARD.

Diagnosis

- *Ophthalmoscopy* identifies retinal degeneration when typical lesions are present.
- *Electroretinography (ERG)* may help one to make a diagnosis of PRA before typical ophthalmoscopic signs are seen and to confirm a diagnosis of SARD. ERG is a test of retinal function. Refer to a specialist.
- Genetic testing of blood samples is now available to diagnose PRA and in selected breeds. Refer to a specialist.

Treatment

No treatment is presently available for PRA or SARD. Chorioretinal degeneration due to glaucoma (see Chapter 137) or inflammation (see Chorioretinitis) can be limited by controlling the primary disease process. A deficiency of taurine in the diet can be corrected to halt progression of the disease (see Chapter 150).

Prevention

Progressive retinal atrophy in either dogs or cats can be prevented by selective breeding of unaffected dogs and of those dogs believed not to be carriers of the PRA gene. Recommend yearly evaluations of all breeding purebred dogs by a board-certified veterinary ophthalmologist, and register these animals through the Canine Eye Registry Foundation (CERF) as phenotypically normal. As genetic testing for PRA and other inherited ocular diseases becomes more available in different breeds this will significantly contribute to the elimination and prevention of the these eye diseases.

Chorioretinitis

Chorioretinitis is inflammation of the retina and choroid. Although inflammation may begin in either of the two layers, their proximity often results in spread and involvement of both. Clinically, the differentiation is of little importance. Choroiditis is also discussed in Chapter 136.

Etiology

Numerous causes of, or diseases associated with, chorioretinitis are recognized in the dog and cat. Chorioretinitis may develop as an extension of anterior uveitis (see Chapter 136) or as an isolated entity. Systemic diseases that can cause unilateral or bilateral chorioretinitis are listed in Tables 138-1 and 138-2. Refer also to the appropriate chapters elsewhere in this book for specifics on these diseases. For some potential etiologic agents (e.g., *Bartonella*) there is currently a suspected association with uveitis or chorioretinitis in dogs and cats, but more clinical data are needed to determine the exact role of these organisms in the disease process.

Table 138-1. DISEASES ASSOCIATED WITH CHORIORETINITIS IN DOGS

Viral	Distemper
Fungal	Blastomycosis
	Coccidioidomycosis
	Cryptococcosis
	Histoplasmosis
	Aspergillosis
	Geotrichosis
Bacterial	*Brucella canis*
	Borrelia burgdorferi
	Leptospirosis
	Bartonella spp. infection
Algal	Protothecosis
Rickettsial	Ehrlichiosis
	Rocky Mountain spotted fever
Parasitic	Toxoplasmosis
	Neosporum caninum
	Leishmaniasis
	Migrating fly larvae
	Toxocara canis larva migrans
Immune-mediated	Autoimmune chorioretinitis
	Uveodermatologic syndrome
Neoplastic	Lymphoma
	Multiple myeloma
	Metastatic neoplasia
Toxic	Miscellaneous toxins (often undiagnosed)

Table 138-2. DISEASES ASSOCIATED WITH CHORIORETINITIS IN CATS

Viral	Feline infectious peritonitis
	Feline leukemia virus
	Feline immunodeficiency virus
Bacterial	Tuberculosis
	Bartonella henselae infection
Fungal	Blastomycosis
	Cryptococcosis
	Histoplasmosis
Parasitic	Toxoplasmosis
	Migrating fly larvae
Immune-mediated	Autoimmune chorioretinitis
Neoplastic	Lymphoma
	Metastatic neoplasia
Toxic	Miscellaneous toxins (often undiagnosed)

Clinical Signs

- *Vision* may be affected in severe cases of chorioretinitis, especially with concurrent optic nerve inflammation. In mild cases of chorioretinitis, visual deficits may not be noticed.
- The *tapetal fundus* areas of chorioretinal exudate or edema appear as hazy gray areas that may have discrete borders and appear elevated. If cellular infiltrate is also present, the areas may appear darker and obscure the underlying tapetum.
- The *non-tapetal fundus* areas of exudate or cellular infiltrate appear gray or white. Perivascular cuffing appears as a hazy white border to retinal vessels.
- *Hemorrhages* may be seen at various depths in the retina.
- *Exudative retinal detachments* may occur.
- *Associated ocular disease* may include anterior uveitis (see Chapter 136) and exudate or hemorrhage in the vitreous.

Diagnosis

▼ ***Key Point*** Unilateral or bilateral chorioretinitis indicates a systemic disease until proven otherwise.

- *Physical examination*—look for any evidence of inflammatory or neoplastic disease elsewhere in the body.
- *Evaluate complete blood count, serum biochemistry profile,* and *urinalysis* for evidence of underlying systemic disease.
- *Evaluate thoracic* and *abdominal radiography* for evidence of systemic mycosis or neoplasia.
- *Evaluate serology* to rule out the various infectious causes of chorioretinitis as described in the chapters on viral diseases, bacterial infections, systemic mycoses, and toxoplasmosis.
- *Evaluate lymph node aspirate* and *skin biopsy samples* in animals with lymphadenopathies or cutaneous lesions.
- *Evaluate vitreous by paracentesis* for cytology and culture, but *only as a last resort* in cases in which all other less invasive systemic diagnostic techniques have been performed and the eye is irreversibly blind.

Treatment

The retina and choroid are inaccessible to most topical medications.

▼ ***Key Point*** To effectively treat chorioretinitis, drugs must be given systemically.

Underlying systemic disease is treated appropriately (as described in the relevant chapters in this book). If all evidence of infectious disease is ruled out, systemic corticosteroids or NSAIDs are given to control the inflammation. Additional therapy with immunosuppressive drugs such as azathioprine (Imuran) may be indicated in immune-mediated chorioretinitis (see Chapter 136).

After achieving an initial improvement in chorioretinitis with a systemic corticosteroid (prednisone) and/or immunosuppressive drug (azathioprine), these drugs may be combined at half of their regular dose for long-term therapy. This may avoid development of side effects from each drug and result in better control of posterior segment inflammation.

Retinovascular Disease

The retinal or choroidal vasculature may be affected in the aforementioned congenital chorioretinal diseases, retinal degenerations, and chorioretinitis. Vascular disease also may occur unrelated to these other entities.

Etiology

- *Coagulopathies,* including canine ehrlichiosis, warfarin and aspirin toxicity, von Willebrand disease, autoimmune hemolytic anemia, and immune-mediated thrombocytopenia in dogs, may cause retinal hemorrhage (see Chapters 22 and 23).
- *Systemic hypertension* in dogs and cats may result in retinal hemorrhage and transudative retinal detachment (see Chapter 153).
- *Congenital cardiac anomalies* may cause engorgement of retinal venules (see Chapter 154).
- *Hyperviscosity syndrome* due to macroglobulinemia in dogs with myeloma and polycythemia causes engorgement of the retinal blood vessels.
- *Anemia* in cats has been associated with retinal hemorrhage.
- *Hyperlipidemia* in cats and dogs results in pink-colored retinal blood vessels.

Clinical Signs

Retinal and vitreous hemorrhage and retinal detachment may result in acute blindness and loss of the pupillary light reflex.

Diagnosis

- *Ophthalmoscopy* reveals retinal hemorrhage, vessel engorgement, increased tortuosity, and color change.
- *Clotting profile* and *complete blood count* assess clotting time, clotting factor deficiencies, thrombocytopenia, and anemia. Coagulopathies are described in Chapter 23.
- *Blood pressure measurement* (see Chapter 153) is indicated in any older dog or cat with retinal hemorrhage or detachment. Rule out renal disease, cardiac disease, and hyperthyroidism in animals with hypertension (see appropriate chapters for each).

Treatment

Direct therapy in all acquired forms of retinovascular disease at the underlying cause. In most cases, retinal hemorrhage resorbs spontaneously, during a few days to weeks, once the disease is under control.

Retinal Detachment

Retinal detachment is separation of the neural retina from the retinal pigment epithelium (RPE). Unilateral detachments may exist undetected.

▼ ***Key Point*** Retinal detachments are often caused by systemic disease in dogs and cats.

Detachments may be partial or complete (infundibular) and arise near the periphery of the retina or adjacent to the optic nerve.

Etiology

- *Congenital developmental disease* includes both CEA and retinal dysplasia.
- *Inflammation* results in accumulations of serous fluid or cellular infiltrate or granulomas between the retina and RPE, causing detachment (non-rhegmatogenous detachments). The same causes of chorioretinitis apply to retinal detachment (see Tables 138-1 and 138-2).
- *Hypertension* (see Chapter 153) causes accumulation of transudate within and beneath the retina.

▼ ***Key Point*** Hypertension secondary to hyperthyroidism or chronic renal failure is the commonest cause of acute retinal detachment, mydriasis, and blindness in older cats. Blood pressure measurements should be measured in any cat with sudden blindness and every 6 months as part of regular geriatric workup in old cats.

- *Tears* in the retina associated with cataract formation, intraocular surgery, or liquefaction of the vitreous may allow vitreous to penetrate between the retina and RPE (rhegmatogenous detachments).
- *Traction* on the retina may result from fibrous tissue that forms in the retina or vitreous secondary to intraocular hemorrhage or chorioretinitis.
- *Neoplasia* or *granuloma* of the choroid or orbit may indent the sclera and detach the retina.
- *Ethylene glycol* toxicity in cats (see Chapter 77) may result in serous retinal folding and detachment.

Clinical Signs

- *Sudden blindness* occurs if bilateral; visual deficits occur if unilateral, depending upon the extent of the detachment.
- *The pupil is often dilated,* and the pupillary light reflexes are weak to absent.
- *A translucent, folded, gray or white sheet of tissue* with retinal blood vessels may be observed behind the lens.

Diagnosis

- *Ophthalmoscopy* reveals focal retinal detachment. Complete retinal detachment can usually be seen clearly with a focal light source.
- *Measure blood pressure* performed to diagnose hypertension (see Chapter 153).
- *Ultrasonography* may support the diagnosis of retinal detachment in cases of intraocular neoplasia or hemorrhage. It is also indicated to detect retinal detachment in eyes with opacities of otherwise clear ocular media (cornea, lens, vitreous).
- *Serology* is indicated if infectious disease is suspected.

Treatment

- *Appropriate therapy for a systemic disease* (hypertension) once diagnosed sometimes results in retinal reattachment, especially if the detachment is not chronic. This response may result in a return of vision and is more likely in dogs than in cats. A cat with bilateral blindness and retinal detachment and hemorrhage should be considered at a late stage of the disease. Serum biochemistries should assess thyroid and renal function. If renal function is reasonably normal treat cats with hypertension with the calcium channel blocker amlodipine besylate (Norvasc), 0.14 mg/kg q12–24h, usually 0.625 mg/cat q24h. Often this will result in rapid resolution of retinal detachment and some restoration of vision. Treatment of the underlying cause of the hypertension (where possible) should be started concurrently (see Chapter 153).
- *Systemic corticosteroids* are used after infectious disease and hypertension have been diagnostically ruled out (see Chapter 136).

- *Systemic NSAIDs* are indicated in retinal detachment, although avoided in cases associated with intraocular hemorrhage (see Chapter 136).
- *Retinal reattachment surgery* is indicated in recent detachments associated with small retinal tears. Laser retinopexy may halt further detachment. Scleral buckling with or without vitrectomy or other retinal tamponade and retinopexy methods may be effective for some detachments and maintain vision. These procedures are performed at some referral centers. In retinal detachments with 360-degree tears, surgery is not indicated.

ACQUIRED DISEASE OF THE OPTIC NERVE

The optic nerve may be involved in several chorioretinal diseases, including chorioretinitis and retinal degeneration.

Optic Neuritis

Optic neuritis is inflammation of the optic nerve. The condition may be recurrent in nature and often results in atrophy of the optic nerve and permanent blindness, regardless of therapy.

Etiology

- *Inflammatory and infectious etiologies* are similar to those causing central nervous system (CNS) disease (see Chapter 126) and chorioretinitis (see Tables 138-1 and 138-2).
- *Neoplasia* (canine granulomatous meningoencephalitis, feline lymphoma) affecting the CNS may cause optic neuritis (see Chapter 126).
- *Ocular trauma* (ocular proptosis) causes optic neuritis.
- *Orbital inflammatory disease* may, in severe cases, result in optic neuritis.
- *Immune-mediated optic neuritis* may be presumed in cases in which no underlying systemic cause can be identified.
- *Miscellaneous toxins* may potentially cause optic neuritis, although diagnosis is rarely possible.

Clinical Signs

- *Acute blindness* is present with bilateral optic nerve involvement, although no visual deficit may be noted if the neuritis is unilateral.
- *Mydriasis* and absence of the pupillary light reflex are evident.

Diagnosis

- *Ophthalmoscopy* allows the diagnosis of intraocular optic neuritis and helps differentiate optic neuritis from retinal detachment as a cause of sudden blindness.
- *The optic disc appears hazy, elevated, and edematous.* The edema often radiates into the peripapillary retina when the inflammation involves the intraocular portion of the nerve. Hemorrhages may be present at the disc or in the adjacent retina or vitreous. Vitreous exudate may obscure the optic disc.
- *Ophthalmoscopic signs may not be present* if the neuritis does not involve the optic disc.
- *Chorioretinitis* can be a concurrent finding.
- *Electroretinography* is indicated to rule out SARD in cases in which the optic nerve appears normal.
- *Ultrasonography* can detect nerve swelling when the retrobulbar nerve is involved.
- *Perform neurologic examination,* cerebrospinal fluid (CSF) analysis, and magnetic resonance imaging (MRI) to diagnose concomitant neurologic disease (see Chapter 125).
- *Evaluate the complete blood count and serology findings* for evidence of infectious etiologies.

Treatment

- Wherever possible, identify infectious etiologies and treat appropriately (see appropriate chapters).
- In cases in which infectious etiologies are ruled out, administer systemic corticosteroids (prednisone, 2 mg/kg q24h PO). Failure to limit the inflammation results in optic atrophy and vision loss. At initial presentation prior to diagnostic workup, it may be reasonable to administer corticosteroids during the first few days to control optic nerve inflammation while carrying out a diagnostic workup for the underlying cause. Continued use of corticosteroids should, however, be based on elimination of infectious causes of the inflammatory disease (especially bacterial and fungal infections).

Papilledema

Papilledema is the bilateral swelling of the optic nerve due to reduced blood and axoplasmic flow from the optic disc. The term is loosely applied in dogs and cats to any form of optic disc edema.

Etiology

- *Pressure applied to the optic nerve* by tumors or granulomas of the nerve or within the orbit can cause stasis of axoplasmic and optic nerve blood flow and can result in papilledema.
- *Neoplasia and inflammation of the CNS* can cause papilledema in dogs and cats by increasing CSF pressure and increasing pressure within and around the optic nerve.

Clinical Signs

- *Vision is usually unaffected.* However, blindness may occur in the absence of optic neuritis when inflam-

matory or neoplastic lesions significantly damage the central optic pathways, including the visual cortex (see Chapters 126 and 141).

Diagnosis

- Attempt to differentiate papilledema from optic neuritis.
- *Ophthalmoscopic appearance of a swollen optic disc, usually with normal vision,* is likely to indicate papilledema. This is unlike optic neuritis in which vision is affected.
- *The optic disc* protrudes into the vitreous. The retinal blood vessels leaving the optic disc appear to cascade over the edge of the disc. The margins of the optic disc appear hazy and indistinct. Hemorrhages may occasionally be observed in the adjacent retina.
- *Perform globe retropulsion* to determine whether a space-occupying lesion is present in the orbit.
- *Neurologic examination* can help localize CNS lesions.
- *Ultrasonography, radiology, and computed tomography (if available)* can be used to locate orbital space-occupying lesions (see Chapter 140).
- *Exploratory orbitotomy* is a difficult technique that can be employed to localize and diagnose any masses detected with the previous methods.

Treatment

- Because papilledema is often associated with CNS tumors, the prognosis is guarded to poor.
- Orbital tumors may occasionally be surgically removed during exploratory orbitotomy.
- *Perform exenteration of the eye and orbital contents* when a mass is localized near the globe.

Optic Nerve Atrophy

Atrophy of the optic nerve may occur as a sequela to other ocular diseases.

Etiology

- Advanced inherited retinal degenerations can occur.
- Glaucoma causes ischemia of the optic nerve at the scleral lamina cribrosa, resulting in atrophy and "cupping."
- Optic neuritis can be either severe or recurrent.
- Optic nerve trauma (traumatic ocular proptosis) can occur.
- Orbital inflammation or neoplasia may be noted.

Clinical Signs and Diagnosis

- Blindness is evident in the affected eye.
- The pupil is mydriatic, and the pupillary light reflexes are absent.
- Ophthalmoscopy confirms the diagnosis. The optic disc appears small and gray, with a loss of retinal blood vessels. The outline of the scleral lamina cribrosa may become visible, particularly in cats. In dogs, the margins of the disc may appear to spread from the disc owing to peripapillary gliosis (hypertrophy of neuronal supporting cells).

Treatment

No treatment is effective once the optic nerve undergoes atrophy.

NEOPLASIA OF THE POSTERIOR SEGMENT

Most tumors of the posterior segment in dogs and cats result from metastasis from other sites. The most common secondary tumor is malignant lymphoma. Primary tumors are rare but include malignant teratoid medulloepitheliomas, melanomas, and optic nerve meningiomas. Therapy entails enucleation (see Chapter 137) or exenteration of the orbit, depending upon the localization of the tumor to the globe.

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Chapter

139 Diseases of the Lacrimal System

Carmen M. H. Colitz

The overall function of tears is to protect and nourish cornea, sweep debris into nasolacrimal canaliculi, and lubricate the eyelids. They also have a refractive function. An understanding of the anatomy and innervation of the lacrimal system, as well as the formation, composition, and function of the precorneal tear film, is important to the understanding of the physiology, pathogenesis, diagnosis, and treatment of its diseases.

ANATOMY AND PHYSIOLOGY OF THE LACRIMAL SYSTEM

- The secretory components of the lacrimal system include the main and accessory lacrimal glands, the gland of the nictitans (third eyelid), the meibomian glands, and the conjunctival goblet cells.
- The main lacrimal gland is a tubuloacinar gland located dorsolateral to the globe between the globe and the orbital ligament and the zygomatic process of the frontal bone. It produces between 50% and 70% of the aqueous tear layer.
- The gland of the nictitans is also a tubuloacinar gland and is located ventromedially at the base of the T-shaped cartilage that supports the nictitans. It produces between 30% and 50% of the aqueous tear layer.
- The accessory lacrimal glands (Krauss and Wolfring) are located in the conjunctival fornices.
- The meibomian (tarsal) glands are modified sebaceous glands located in the distal aspect of the tarsus that open onto the edge of both eyelids in a row of small openings. They number approximately 20 to 40 per eyelid and produce the lipid component of the preocular tear film. The innervation of the meibomian glands is parasympathetic in origin.
- The conjunctival goblet cells are heterogeneously dispersed in the dog; i.e., the highest numbers are located along the lower nasal and middle fornices and the lower tarsal portion of the palpebral conjunctiva. Their function is to produce the mucus component of the tear film.
- The accessory eyelid glands are the glands of Moll and Zeis. The glands of Moll are modified sweat glands, and the glands of Zeis are prominent sebaceous glands. Their function is unknown.
- The excretory components include the superior and inferior lacrimal puncta and their canaliculi, nasolacrimal sac, and ducts.
- The superior and inferior lacrimal puncta allow the exit of the tear film from the lacrimal lake to the canaliculi then to the nasolacrimal duct.

Precorneal Tear Film

- The precorneal tear film has three layers: the lipid layer, the aqueous layer, and the mucus layer.
  - The *lipid layer* is the outer layer that is produced by meibomian glands and functions to prevent evaporation of aqueous layer.
  - The *aqueous layer* is the middle layer that is produced by the main lacrimal gland and gland of the nictitating membrane. It flushes foreign material from the conjunctival sac; lubricates for the passage of the eyelids over the cornea; provides a medium for transferring oxygen, inflammatory cells, immunoglobulins, lysozyme, and lactoferrin to the cornea; and gives a smooth surface to the cornea for optimal optical efficiency.
  - The *mucus layer* is the innermost layer that is produced by goblet cells on the conjunctiva. It functions as a surfactant and stabilizer of the aqueous layer and spreads tears across the cornea, adhering to the microvilli of the corneal and conjunctival epithelium by charged polyanions enhancing the even spread of the tear film over the corneal surface. The mucin also filters trapped and foreign particles, forming mucus strands that are moved to the medial canthus for clearance from the eye.
- Tear drainage from the lacrimal lake is via the superior and inferior lacrimal puncta to the canaliculi, which meet at the lacrimal sac, then subsequently down the nasolacrimal duct and into the nose (or mouth in some).

Innervation of the Lacrimal System

- Both basal and reflex tear production are under the control of the autonomic nervous system.
- The trigeminal nerve plays an important role in the neurogenic control of lacrimation. The ophthalmic division of the trigeminal nerve, as well as the zygomatic nerve, a branch of the maxillary division of the

trigeminal nerve, provides afferent sensory information from the lacrimal gland, periocular structures, and globe. The cornea is directly innervated by free nerve endings of the trigeminal nerve that penetrate the limbus and enter the anterior corneal stroma. Stimulation of these nerve endings results in reflex tear formation.

- The parasympathetic nervous system innervates the efferent arm of lacrimation. The parasympathetic fibers originate in the facial nerve nucleus and are distributed to the lacrimal gland with the zygomatic nerve.

DISEASES OF THE LACRIMAL SYSTEM

Diseases of the lacrimal system can be divided into those that cause a decrease in any component of the preocular tear film or those that cause epiphora. Keratoconjunctivitis sicca is primarily caused by an immune-mediated disease against the lacrimal glands, resulting in a decrease in the aqueous component of the precorneal tear film. The other, less common causes will also be discussed. Diseases that cause epiphora, or excessive tearing, are usually secondary to a problem with tear drainage or irritation from periocular hairs contacting the corneal surface. These and their appropriate therapies will also be discussed.

Keratoconjunctivitis Sicca

- Keratoconjunctivitis sicca (KCS) can be due to qualitative and quantitative deficiencies of precorneal tear film.
- Congenital alacrima or congenital hypoplasia of the lacrimal acini occurs in miniature breeds (pug and Yorkshire terrier), is uncommon, and is characterized by complete lack of precorneal tear film production, resulting in severe dryness.
- Drug-related causes of KCS include systemic sulfonamide therapy, phenazopyridine, topical and general anesthesia, antihistamines, and etodolac.
- Other causes of KCS include supervoltage and megavoltage radiation therapy, excision of the gland of the nictitans, and neurologic abnormalities.

▼ ***Key Point*** The most common cause of KCS is immune-mediated lacrimal adenitis.

Keratoconjunctivitis Sicca Due to Quantitative Tear Deficiencies

Clinical Signs

- Clinical signs of KCS are dependent on the amount of time that the disease is present.
- Acute cases with severe dryness present with acute pain, blepharospasm, and axial corneal ulceration. Ocular discharge in these cases is often mucopurulent to suppurative, and corneal ulceration may progress to perforation if not treated quickly and aggressively.
- The more common presentation is one of chronic conjunctival hyperemia with intermittent mucoid discharge.
- Due to these nonspecific clinical signs, KCS is often misdiagnosed and treated inappropriately.
- With time, the ocular discharge will become mucopurulent due to imbalance of the bacterial flora, allowing abnormal microorganisms such as beta-hemolytic *Streptococcus,* coagulase-positive *Staphylococcus,* gram-negative coliforms, and *Pseudomonas* to grow while normal flora (*Staphylococcus* species) decrease.
- The goblet cells also become hypertrophied and overproduce mucus, adding to the abnormal discharge.
- The cornea becomes lackluster in appearance and irregular, and it can develop edema, pigmentation, vascularization, areas of fibrosis, and possibly ulceration.
- The periocular skin can also become inflamed due to accumulation of ocular discharge, resulting in persistent blepharospasm.

Histologic Changes

- The acute clinical signs of KCS are characterized histologically by epithelial degeneration with vacuolization and epithelial thinning of the cornea and conjunctiva. These changes are due to increased tear osmolarity and dehydration of the corneal and conjunctival surface. Since the cornea is not vascularized normally, these acute changes can result in loss of corneal stroma if an ulcer develops.
- With chronicity, the corneal epithelium thickens and becomes keratinized. Melanin granules are deposited throughout the corneal epithelium and anterior stroma and can become dense. The anterior stroma also becomes infiltrated with vascularization and lymphocytic-plasmacytic inflammation.

Diagnosis

- History, clinical signs, and results of the Schirmer tear test (STT) will establish the diagnosis of KCS in most cases of quantitative tear film deficiencies.
- The STT is a semiquantitative test that assesses aqueous tear production. The usual method is to perform the STT without topical anesthesia. This is the STT 1 and it measures basal and reflex tear production by stimulating the trigeminal nerve endings through local irritation. The STT 2 is less common and is performed following topical anesthesia to eliminate reflex lacrimation. It assesses only basal tear formation. (See Chapter 131 for STT technique.)
- Normal ranges for STT 1 are between 15 and 25 mm/minute. Values in the low-normal range should be reevaluated; if still low and clinical signs are present, then treat for KCS. Values between 10 and 15 mm/min

are considered to indicate early KCS. Initiate therapy and recheck values as described below. Values between 6 and 10 mm/min are diagnosed as mild to moderate KCS, and values below 6 mm/min are considered severe. Topical atropine therapy can influence the STT values, and STT should be reevaluated after therapy has ended.

▼ ***Key Point*** Most cases of KCS are bilateral.

- Unilateral KCS with crusting of the ipsilateral nostril is indicative of neurogenic KCS. The lateral nasal gland is innervated similarly to the lacrimal gland; therefore, aqueous nasal secretions are impaired, resulting in mucopurulent nasal discharge and crusting. STT results will be negligible in cases of neurogenic KCS.

Treatment

- Treatment of KCS due to decreased tear production should (1) stimulate tear production, (2) replace tears until production increases, (3) attempt to reestablish the normal bacterial flora, and (4) decrease inflammation.
- In recent years, two drugs have been used for the stimulation of tear production: cyclosporine and, most recently, tacrolimus. Both medications inhibit T lymphocyte proliferation by blocking interleukin-2 synthesis at the transcriptional level.
  - *Cyclosporine* (0.2%, 1%, or 2%) is a naturally produced immunosuppressant with some antibiotic properties, and it inhibits cytokine production. Under experimental conditions, it is also able to inhibit prostaglandin production. The mechanism by which cyclosporine stimulates tear production is not well understood but may be by its effects on cytokines. Most cases of KCS respond to cyclosporine after 14 to 16 days of therapy, but up to 2 months may be necessary in recalcitrant cases. Therefore, cyclosporine is an excellent drug for the treatment of KCS as it fulfills three of the four requirements of therapy.
  - *Tacrolimus* (0.02–0.03%) has similar immunologic activity as cyclosporine, but it is estimated to be 20 to 50 times more potent than cyclosporine. Difficult cases of KCS may respond to higher concentrations of cyclosporine or to tacrolimus.
- Cyclosporine and tacrolimus are to be used for the life of the animal in cases of immune-mediated KCS.
- *Tear replacement* options are numerous and are often subject to the clinician's preferences. The traditional artificial tear replacers include artificial tear solutions and ointments. The solutions provide moisture but must be applied every 20 to 60 minutes to adequately protect the cornea. Hypo-osmolar tear substitutes are recommended, as tears are hyperosmolar. Examples of artificial tear solutions include Hypotears and Tears Naturale. Artificial tear ointments also protect and sooth the cornea but have longer contact time and blur vision. Examples of artificial tear ointments include Duratears, Lacri-Lube, and AKWA-Tears. Newer viscous, preservative-free tear replacers are more commonly used in veterinary ophthalmology practices and are available over the counter. These are long-lasting preparations that enhance ocular surface moisture and have extended contact time with the ocular surface. Examples of the viscous tear replacers include Genteal gel and Celluvisc.

▼ ***Key Point*** Prolapse of the gland of the nictitans should be addressed surgically by replacing the gland using the imbrication technique. This will preserve the function of the gland.

- Neurogenic KCS is often not responsive to cyclosporine, and oral pilocarpine may be helpful. Pilocarpine is a direct parasympathomimetic that stimulates the lacrimal and lateral nasal glands. A suggested protocol is as follows: Begin at two drops of ophthalmic 2% pilocarpine PO q12h for 3 days, then increase it by one drop per instillation and use for 3 days. Continue this until the dog becomes physically ill (vomiting, diarrhea, hypersalivation) or tear and nasal secretions are produced. This can take many weeks to months, and it is possible that this is the time necessary for the innervation to return.
- Topical antibiotics can be used if bacterial overgrowth is seen on cytology or if there is a corneal ulcer present.
- Oral tetracycline (or doxycycline) in combination with niacinamide can be tried in cases of KCS that do not respond to cyclosporine or tacrolimus as they have immunomodulating effects, not for their antibiotic effects. The tetracycline and niacinamide dosage for smaller dogs (up to 15 kg) is 250 mg PO q8h and for larger dogs (greater than 15 kg) is 500 mg PO q8h. The results are often variable.
- Topical corticosteroids may be used in cases of severe conjunctivitis and blepharitis and if there is no corneal ulceration. Cyclosporine and tacrolimus are innately immunosuppressive and if these are used, corticosteroids are not usually needed.
- Some cases of KCS do not respond to medical therapy, especially the drug-induced (sulfa drugs and etodolac) KCS cases. These may benefit from surgical therapy, i.e., parotid duct transposition. Refer the patient to an ophthalmologist for this procedure.

Keratoconjunctivitis Sicca Due to Qualitative Tear Deficiencies

Etiology

- Abnormalities in the lipid or mucin components of the tear film result in this type of KCS.

- Diseased meibomian glands produce highly polar lipids that disrupt the non-polar lipid surface of the tear fluid, and the normal oily covering of the tear film is lost. This results in premature dispersion of the aqueous layer. In addition, these abnormal lipids may be directly toxic to the epithelial cells. Bacterial (*Staphylococcus* species) or yeast (*Candida* and *Malassezia* species) infections of the meibomian glands result in marginal blepharitis, blepharoconjunctivitis, and meibomianitis. Other causes include generalized seborrhea, lupus erythematosus, bullous pemphigoid, abnormal development of the meibomian glands, and cats with eyelid agenesis.
- Mucin deficiency also causes tear film instability that results in corneal desiccation. Specific causes of mucin deficiency are infectious or immune-mediated diseases resulting in destruction of goblet cells. Other causes include severe scarring, following ulcerative conjunctival disease, and vitamin A deficiency, which causes squamous metaplasia of the conjunctiva and subsequent loss of the goblet cells.

Clinical Signs

- Signs of meibomian gland disease can vary. Acute meibomianitis can cause swollen eyelid margins with obviously plugged meibomian glands. These chalazia can also irritate the corneal surface and cause further damage such as chronic keratitis or corneal ulceration.
- Goblet cell abnormalities and loss of the mucin layer of the tear film result in rapid tear breakup times (BUTs). The corneal surface is lackluster in appearance and obviously irregular or ulcerated.

Diagnosis

- Both mucin and lipid deficiencies will have an adequate aqueous component; therefore, STT will not be affected.
- Magnification is necessary to closely examine the eyelid margins and the meibomian glands.
- Swollen eyelid margins with hyperemia of the mucocutaneous junction and dry crusty exudates are indicative of meibomian gland disease. Chalazia are consistent with chronic meibomianitis with granulomatous infiltrate (see Chapter 132). Abnormal meibomian gland secretions are thick and opaque with a toothpaste-like consistency. Aerobic bacterial or yeast cultures are indicated for this condition.
- Mucin deficiency is best diagnosed with a tear BUT. The BUT evaluates the ability of the corneal surface to retain a homogeneous tear covering. One drop of fluorescein stain is dropped onto the corneal surface and the eyelids are held open. Record the time from the last eyelid blink to the appearance of the first dry spot. A cobalt-blue filter is helpful. Normal BUT is 20 seconds or longer. Shorter BUTs are indicative of a mucin tear deficiency and are often less than 5 seconds.
- A biopsy of the conjunctiva from the lower medial fornix between the third eyelid and the lower eyelid may further support a mucin deficiency by quantitating the number of goblet cells. This is the site of highest goblet cell density.

Treatment

- Treatment of meibomian gland disease is based on culture of microorganisms.
- Use appropriate antimicrobials both topically and systemically. Chronic cases may require intermittent intensive treatment or continuous low-level therapy.
- Expression of the inspissated material may be necessary periodically. Severe cases with granulomatous blepharitis secondary to ruptured meibomian glands may require systemic corticosteroids, warm moist compresses, and/or surgical curettage of the chalazia.
- Lipid substitutes including petrolatum, mineral oil, liquid lanolin, or a combination of these can be used, or an antibiotic or antibiotic-corticosteroid combination in ointment form can be used to replace lost lipid until meibomianitis is resolved.
- Mucin deficiency is more difficult to treat due to concurrent inflammation requiring corticosteroids and corneal ulcers in which corticosteroids are contraindicated. Therefore, treat the corneal ulceration if present, and use topical mucinomimetic tear replacers such as Adsorbobase, 2% methylcellulose (Celluvisc), and Genteal gel.
- Preliminary research has shown cyclosporine to increase mucus production; therefore, it may be useful in cases of mucin deficiency.

Diseases Causing Epiphora

Imperforate Nasolacrimal Duct

- In dogs, this is usually due to failure of the inferior marginal puncta to open. It is often evident beneath a thin layer of conjunctival epithelium, which can be excised. Flushing the nasolacrimal duct will ensure its patency (see Chapter 131 for technique); then treat with an antibiotic-steroid combination ophthalmic eye drop for 2 weeks.
- In cats, it is uncommon but associated with chronic herpesvirus infection causing cicatrisation of the duct opening.

Congenital Nasolacrimal Duct Obstructions

- Most commonly associated with dacryops and nasal cysts. Diagnosis is by dacryocystorhinostomy; treatment is surgical.

Dacryocystitis

- Dacryocystitis is caused by inflammation of the lacrimal sac and nasolacrimal duct.

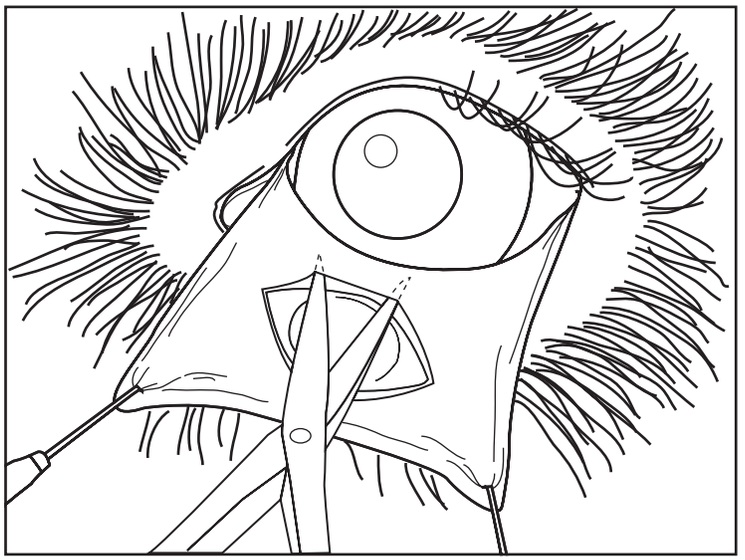

Figure 139-1. Make an elliptical incision in the conjunctiva of the third eyelid around the prolapsed gland, then undermine with ophthalmic scissors.

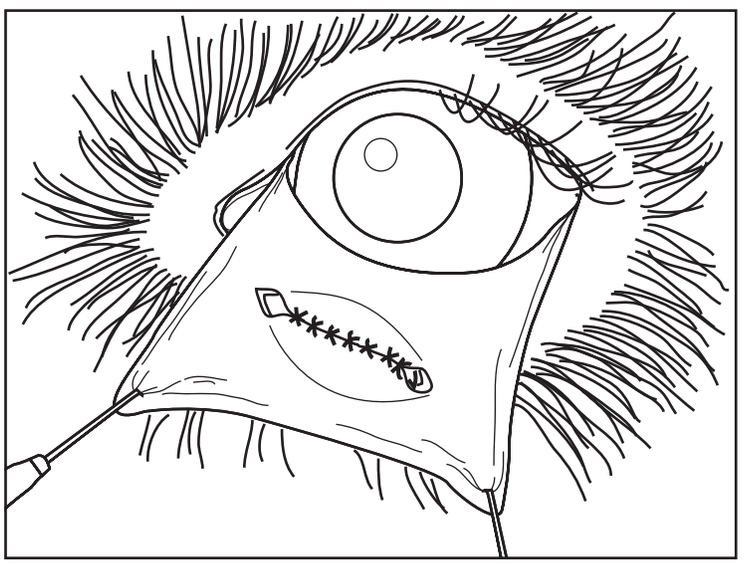

Figure 139-2. Close the conjunctiva over the gland with fine absorbable suture (5-0 or 6-0). Be sure to bury the knots to prevent abrasion of the cornea.

- Causes include foreign bodies that lodge in the nasolacrimal sac, periodontal disease, bacterial or fungal infection, or obstructions such as fractures, trauma, or sinusitis.
- The most common clinical sign is epiphora or mucopurulent ocular discharge.
- Diagnosis is by cytology and culture and sensitivity of the exudate. Dacryocystorhinography may be necessary to localize the lesion.
- Treatment includes removal of the obstruction if possible by irrigation of the nasolacrimal duct. Use appropriate antibiotic and anti-inflammatory therapy. If the disease is chronic and the nasolacrimal apparatus is not patent, dacryocystorhinostomy or dacryocystobuccostomy may be indicated.

Eyelid Abnormalities

- If the nasolacrimal anatomy and tear production are normal, assessment of the animal's periocular conformation should be performed (see Chapter 132).

- Entropion or excessively large nasal folds resulting in trichiasis can rub on the corneal surface, causing epiphora. Surgical correction of these abnormalities will resolve the epiphora (see Chapter 132).
- Distichiasis or ectopic cilia also manifest as epiphora. Cryotherapy (distichiasis) or en bloc excision (ectopic cilia) is indicated for these conditions.

PROLAPSED GLAND OF THE THIRD EYELID (CHERRY EYE)

- The ligament holding the gland of the nictitating membrane or third eyelid fails, allowing the gland to prolapse. This creates a mass like appearance at the ventromedial aspect of the medial canthus.
- With exposure, the gland becomes inflamed and swollen.
- Many breeds of dogs are predisposed to this condition supporting a genetic component. These include American cocker spaniel, Lhasa apso, beagle, and bulldog.
- Diagnosis is made on clinical appearance.
- Since the gland of the nictitating membrane produces up to 50% of the aqueous component of the tear film, it should be surgically repaired using the imbrication technique (Figs. 139-1 and 139-2). In some cases, it may reoccur and a second surgery is indicated.

▼ ***Key Point*** Never remove the gland of the third eyelid for treatment of Cherry Eye as it will predispose to KCS.

Chapter

140 Diseases of the Orbit

Mary B. Glaze

Disorders of the orbit are relatively uncommon in companion animals. Because the area cannot be directly visualized without sophisticated imaging devices or complicated surgical procedures, even the simplest of lesions can pose a diagnostic and therapeutic challenge.

ANATOMY

Orbital Cavity

- The orbit is a cone-shaped cavity that surrounds the eye and its supporting structures.
- Only the medial wall, part of the orbital roof in the dog, and the entire orbital roof in the cat are bony. The medial wall is a thin septum that separates the orbit from the nasal cavity. The floor of the orbit is muscular, with the exception of a small shelf of maxillary bone in the cat. A ligament that bridges the space between the frontal and the zygomatic bones completes the lateral aspect of the canine and feline orbit.
- Three prominent openings at the apex of the orbit permit the passage of its major vessels and nerves.
- The dorsal aspect of the ramus of the mandible moves rostrally when the mouth is opened, compressing the orbital contents.

Orbital Contents

- The contents of the orbit are enclosed by a fibrous membrane, the periorbita, that attaches to the orbital wall at the optic foramen and extends to the orbital rim. The periorbita contains sympathetically innervated smooth muscle fibers.
- The anterior limit of the orbit is formed by a sheet of connective tissue, the orbital septum, that extends from the periorbita at the orbital margin to blend with the tarsus of the lid.
- Of the seven extraocular muscles, six originate at the orbital apex. The inferior oblique arises from the anteromedial orbital wall.
- The orbital fat pad cushions the orbital contents and is found between the periorbita and the surrounding structures. Fat is also located within the periorbita between the extraocular muscles.
- In addition to numerous arteries, veins, and autonomic nerves, the second, third, fourth, and sixth cranial nerves and the ophthalmic branch of the trigeminal nerve traverse the orbit.
- The nictitans occupies the ventronasal portion of the orbit and moves passively in relation to globe movements in the dog. In addition, movement of the feline nictitans is sympathetically controlled.
- The lacrimal gland is contained within the periorbita near the superotemporal aspect of the globe.
- The zygomatic salivary gland occupies the lateral orbital floor, just behind the orbital margin and outside the periorbita.

Neighboring Structures

- Diseases of neighboring structures, including the oral and nasal cavities, teeth, tongue, muscles of mastication, and paranasal sinuses, must always be considered when evaluating orbital disease.
- The nasal cavity and paranasal sinuses are directly adjacent to the medial orbit.
- Tooth roots of the maxillary premolar and the first and second molars abut the orbital floor, separated from the soft tissues of the orbit by only a thin layer of alveolar bone.

ALTERATIONS IN THE GLOBE-ORBIT RELATIONSHIP

The position of the eye within the orbit depends upon the orbital dimensions, the relative globe size, and the volume of the other orbital contents. The normal brachycephalic dog or cat has a shallow orbit and prominent eye. Larger orbits and less prominent eyes are found in mesaticephalic and dolichocephalic breeds. As a general rule, the feline globe nearly fills the orbit and predisposes the animal to alterations in the globe-orbit relationship early in the course of orbital disease.

▼ ***Key Point*** The first clinical sign of orbital disease is often a change in the position or the direction of the globe relative to the orbital rim and to the other eye.

EXOPHTHALMOS

Exophthalmos refers to the abnormal protrusion of a normal-sized eye. Differentiate exophthalmos from buphthalmos, the enlarged eye that accompanies chronic glaucoma, by comparing the horizontal corneal diameter of the animal's affected eye with its normal eye. If the diameters differ, the problem is one of the globe rather than the orbit. Distinguish exophthalmos from (1) the contralateral enophthalmos, (2) the exaggerated palpebral fissures of macroblepharon and facial paralysis, and (3) the characteristically prominent globe of the brachycephalic dog and cat.

Causes of exophthalmos in dogs and cats encompass a spectrum of developmental disorders, inflammatory processes, neoplasias, traumatic lesions, cystic disorders, and skeletal diseases.

Developmental Disorders

Congenital Cysts

- Orbital cysts develop in association with other ocular anomalies, appearing as appendages of microphthalmic eyes or entirely supplanting a recognizable globe.
- These cysts are rare, non-heritable consequences of defective ocular organogenesis.
- If asymptomatic and cosmetically acceptable, no treatment is warranted. Excise large, exposed cysts to prevent secondary drying and irritation.

Craniofacial Deformities

- *Cyclopia* is a rare lethal anomaly in which the orbits and their contents are fused into a single structure. A single midline orbit and a dysplastic eye appearing as either a single or a bilobed sphere characterize the anomaly. The nose and maxilla are rudimentary. The defect has been reported in offspring of cats administered griseofulvin during the first half of gestation. There is no treatment for this anomaly.
- *Orbital malformation* and a subsequent divergence of the ocular axes accompany hydrocephalus.

Arteriovenous Malformations

Etiology

Rarely, fistulas may develop between orbital or periorbital vessels. The cause is unknown.

Clinical Signs

- Exophthalmos is associated with a pulsatile murmur auscultated over the orbit. The bruit diminishes when the carotid artery is compressed.
- The exophthalmos may exacerbate in response to postural changes, as when the animal lowers its head to eat.

Diagnosis

- Confirm the malformation in the anesthetized patient using orbital ultrasonography, color Doppler imaging, or contrast venography.
- For venography, inject 5 to 10 ml of contrast medium into the angularis oculi vein, using a 21-gauge needle or catheter, immediately before and during radiography. Perform a contrast study on the normal side for comparison.

Treatment

- The degree of postural exophthalmos may diminish as the animal and its orbit mature.
- Surgical attempts at ligation and resection are frequently unsatisfactory. One report described severe intraoperative hemorrhage and postoperative recurrence of the lesion in a dog.

Acquired Disorders

Acquired disorders are more common than congenital orbital diseases as causes of exophthalmos in dogs and cats. When clinical signs of orbital disease are present, an attempt should be made to classify the disease as inflammatory, neoplastic, or cystic. As a general rule, acute lesions associated with discomfort and swelling of conjunctiva and eyelids are inflammatory, whereas slowly progressive, nonpainful disorders are secondary to space-occupying masses.

▼ ***Key Point*** In instances of acquired exophthalmos, document the rapidity of onset and the presence or absence of pain, especially upon opening the mouth.

Inflammatory or Infectious Disorders

Orbital Cellulitis or Orbital Abscess

Orbital inflammatory disease is a common cause of *acute, painful,* unilateral exophthalmos.

Etiology

Orbital inflammation is usually the result of trauma, infection, or the extension of a disease from neighboring structures.

- *Trauma:* Trauma produces both septic and nonseptic inflammation. Infections follow breaching of the oral mucosa or eyelids by bite wounds or foreign objects, such as bones. Blunt trauma may damage the osseous and soft tissues of the orbit. Iatrogenic injury may occur as a consequence of aggressive or improper dental extraction techniques. Occasionally, a foreign body will be retained within the orbit, causing recurrent inflammation.
- *Infection:* Aerobic and anaerobic bacteria, fungi, and parasites infect the orbit primarily or extend from the paranasal sinuses and nasal cavity. Orbital fungal pyo-

granulomas can occur with blastomycosis, cryptococcosis, and coccidioidomycosis. In cats, *Aspergillus* and *Penicillium* have been implicated in orbital cellulitis secondary to sinusitis. Larvae of *Dirofilaria immitis* and *Ancylostoma* species, and *Toxocara canis* produce primary orbital cellulitis by invading canine orbital tissues. The nasal mite *Pneumonyssus caninum* is a documented cause of orbital cellulitis and sinusitis in a dog. Even *Cuterebra* larvae occasionally invade the orbit. Granulomatous nodules containing *Onchocerca* species Nematodes have been identified in the canine retrobulbar space.

- *Extension of disease:* Tooth root abscesses (particularly maxillary PM3, PM4, M1, and M2) are the most common cause of orbital cellulitis in dogs and cats. Disorders of the frontal or paranasal sinuses, nasolacrimal system, temporal and pterygoid muscles, or zygomatic salivary and lacrimal glands may also cause secondary orbital inflammation or infection. Inflammation of the posterior sclera may affect adjacent orbital tissues.
- *Rare proliferative inflammatory disorders:* Referred to as pseudotumors, these may mimic orbital neoplasms. Examples include fibrous histiocytoma, undifferentiated inflammatory pseudotumor, and eosinophilic granuloma. In cats, proliferation of spindle cells and fibrovascular tissue within and adjacent to the sclera decreases ocular motility and dictates enucleation for relief of progressive lagophthalmia and keratitis.

Clinical Signs

- Orbital inflammation is characterized by a relatively *acute* unilateral exophthalmos, with conjunctival hyperemia, chemosis, third eyelid protrusion, and pain on opening the mouth.
- The animal may be febrile and exhibit an inflammatory leukogram.
- Abscesses on rare occasion produce swelling or discoloration behind the last upper molar.

Diagnosis

- Diagnosis is based upon history and physical examination. Consider sedation in painful patients objecting to examination.
- Palpate the periocular and periorbital regions.
- Close the eyelids and retropulse (i.e., push) the globe into the orbit to rule out space-occupying masses.
- Thoroughly evaluate the oral cavity. If dental disease is not readily apparent, examine the caudal maxillary teeth with a dental explorer and periodontal probe.
- Hematology, cytology, and culture of orbital aspirates may be of benefit in some cases.
- Radiographically localize orbital foreign bodies with four views: lateral, ventrodorsal, oblique, and frontal. A wire ring positioned over the limbus may serve as a helpful point of reference. Dental radiography should also be performed.
- Orbital ultrasonography of diffuse cellulitis is characterized by a generalized loss of orbital tissue definition. The optic nerve and extraocular muscles are less easily visualized when compared with the normal eye. An abscess may appear as a hypoechoic area within a well-defined hyperechoic wall.

Treatment

- Administer a broad-spectrum systemic antibiotic such as amoxicillin clavulanate for at least 10 days. Response to antibiotic therapy is generally rapid, with resolution within 1 to 2 weeks.
- Protect the corneal surface with an antibiotic ophthalmic ointment in cases of extreme exophthalmos.
- Alleviate the acute swelling and discomfort with warm periocular compresses and a systemic nonsteroidal anti-inflammatory agent (aspirin at a dosage of 10–25 mg/kg q12h PO in dogs). Corticosteroid therapy is controversial because of the potential for sepsis in some patients.
- Establish ventral drainage through the mouth if no response is seen within 48 to 72 hours. Incise the mucous membrane behind the last upper molar with a #15 Bard-Parker scalpel blade. Carefully insert a hemostat through the pterygoid muscle and open gently in the retrobulbar space. Insert a sterile, open-ended tomcat catheter through the mucosal opening to obtain aspirates for cytology and culture.

▼ ***Key Point*** This orbital drainage procedure can damage the optic nerve, globe, or major orbital vasculature; perform carefully.

Masticatory Muscle Myositis (Eosinophilic Myositis)

Inflammation and swelling of the muscles of mastication may compromise the orbital space and push the globe forward.

Etiology

Cellular and humoral destruction of type 2M myofibers and myofibril-specific antibodies in affected dogs suggests an autoimmune disorder.

Clinical Signs

- Temporalis, masseter, and pterygoid muscle swelling is accompanied by fever, pain on opening the mouth, difficulty eating, and trismus (spasm of masticatory muscles).
- Ocular signs include exophthalmos, conjunctival hyperemia, eyelid edema, and third eyelid protrusion.
- The German shepherd appears most susceptible. Shetland sheepdogs, golden retrievers, and Weimaraners are also predisposed, but any canine breed may be affected. The mean age of onset is 3 years.
- The condition is more often bilateral than unilateral.

- Acute episodes may last 10 to 20 days. Recurrences lead to muscle atrophy and decreased prominence of the globe.
- Blindness is a rare complication.

Diagnosis

- Confirm the clinical diagnosis with temporalis muscle biopsy samples to demonstrate mononuclear and eosinophilic infiltrates and type 2M myofiber antigen-antibody complexes (see Chapter 130).
- Peripheral eosinophilia is inconsistent.
- If muscle biopsy is not possible, serum may yield evidence of type 2M myofiber antibodies (see Chapter 130).

Treatment

- Treatment must precede the onset of muscle atrophy to prevent recession of the globe into the orbit.
- Administer oral prednisone, beginning with a daily dosage of 2 mg/kg q12h for 3 weeks to reduce the likelihood of recrudescence. Reduce the dose gradually thereafter, continuing treatment for a total of 6 to 8 weeks.

Bilateral Extraocular Polymyositis

This unusual myositis targets the extrinsic muscles of the eye in primarily young, large-breed, female dogs.

Etiology

A mononuclear infiltrate composed predominantly of T lymphocytes and localized to the extraocular muscle bellies suggests an immune mechanism directed at specific extraocular myofibers. The disorder is reminiscent of euthyroid Graves' ophthalmopathy in humans.

Clinical Signs

- Affected dogs range in age from 5 to 72 months; 80% are between 7 and 10 months of age. Females are affected twice as often as males. Golden retrievers, Doberman pinschers, and springer spaniels are the most commonly affected breeds.
- Chemosis typically precedes the onset of bilateral, sometimes asymmetrical, nonpainful exophthalmos. The globes appear otherwise normal. Vision impairment occurs infrequently as a consequence of retinitis or compressive optic neuropathy. Third eyelid protrusion is rare.

Diagnosis

Document the extraocular muscle swelling with orbital echography, computed tomography, or magnetic resonance imaging. Confirm the clinical diagnosis with extraocular muscle biopsy to demonstrate the mononuclear cell infiltrate of CD3+ T lymphocytes and macrophages directed against fine extraocular myofibers (see Chapter 130). Complete blood counts and serum chemistry values are normal.

Treatment

Administer oral prednisone at 2 mg/kg every 12 hours. Although clinical response is often dramatic in 3 to 5 days, minimize recrudescence by continuing therapy for at least 21 days before tapering the dosage. After the initial 3-week treatment regimen, gradually taper the dosage over a 2-month period. Topical corticosteroid therapy is not effective.

Prognosis

Recurrences are likely and may be triggered by stressors including estrus, surgery, or boarding. Strabismus and enophthalmos are uncommon sequelae.

Neoplasia

▼ ***Key Point*** Most orbital neoplasms are aggressive, malignant tumors that are diagnosed in the advanced stages of development.

Etiology

- Both primary and secondary orbital tumors occur in dogs and cats.
  - Primary neoplasms arise from a variety of tissues within the orbit, including epithelium, bone, nerves, vessels, connective tissue, hemolymphatic tissue, and glandular tissues.
  - Secondary tumors extend from adjacent structures such as the nasal cavity or metastasize from distant sites.
- A retrospective study of 44 dogs identified 18 tumor types; most common were osteosarcoma, fibrosarcoma, and nasal adenocarcinoma. In dogs, 75% of orbital tumors are primary; 70% of feline tumors invade from adjacent tissues. In both species, approximately 90% of orbital tumors are malignant.

Clinical Signs

- *Gradual, painless exophthalmos* is accompanied by periocular swelling, third eyelid protrusion, and globe deviation. Secondary lagophthalmos may cause corneal drying.
- Compression of the globe can cause altered tapetal reflectivity, changes in the course of retinal vessels, or retinal detachment with subsequent abnormalities of the pupillary light response and blindness.
- On occasion, orbital lymphoma and mast cell sarcoma masquerade as inflammatory disease, with rapid onset of painful exophthalmos. Primary orbital neoplasia is typically unilateral. Metastatic disease may affect both orbits. The mean age of dogs with orbital neoplasia is 8 years, ranging from 18 months

to 15 years. Older cats (average 8.9 years) experience a similar risk, yet orbital lymphoma and multicentric fibrosarcoma occur in cats less than 2 years of age.

Diagnosis

- Perform a complete physical examination to evaluate for other neoplastic changes.
- Substantiate the clinical diagnosis and evaluate adjacent structures with radiography, orbital ultrasonography, computed tomography scan, and/or magnetic resonance imaging. Magnetic resonance imaging is recommended for patients in which surgery is proposed.
- Perform thoracic and abdominal radiography and/or ultrasonography to rule out metastatic disease.
- With the animal heavily sedated or anesthetized, obtain orbital aspirates for cytologic evaluation using a 1-inch, 22-gauge needle attached to a syringe.
  - The direction of deviation of the exophthalmic globe suggests the tumor's location and the site for needle entry. For example, lateral strabismus suggests a medial space-occupying mass.
  - To reach the medial mass, insert the needle medial to the third eyelid, penetrate the conjunctiva, and aspirate gently along the medial orbital wall. Other orbital quadrants may be sampled in a similar manner.
  - For masses directly behind the eye, surgically prepare the lateral aspect of the orbit and insert the needle just posterior to the angle formed by the lateral orbital ligament and the zygomatic arch.
  - If available, ultrasound-guided orbital aspiration helps minimize complications and ensure accurate needle placement. One study reported that cytologic examination was diagnostic for orbital neoplasia in 49% of retrobulbar aspirates.

Treatment

- Surgical resection of the neoplasm is the treatment of choice. Orbitotomy and tumor excision may be attempted in cases of circumscribed primary tumors. Surgical approaches to the orbit are described elsewhere. Refer patients requiring exploratory orbitotomy to a veterinary ophthalmologist or surgeon.
- If the extent of involvement precludes total excision of the tumor, orbital exenteration (removal of the globe, adnexa, and orbital contents) is recommended. While some tumors may respond to adjunct chemotherapy or radiation therapy, adverse radiation effects (chronic keratitis, diminished tear production, and cataract formation) should be taken into account before choosing this modality in lieu of exenteration.

Prognosis

Various studies document the poor survival rates associated with orbital neoplasia.

- In an early series of 23 patients, only 3 dogs with orbital neoplasia survived 3 years. The mean survival time after diagnosis in a series of 21 cats was only 1.9 months.
- A more recent study of 25 cases of retrobulbar neoplasia found dogs survived an average of 10 months while affected cats lived only 1 month following diagnosis.
- Of 44 dogs included in Hendrix and Gelatt's study (2000), 56% were euthanized or had died within 6 months of diagnosis.

Orbital Trauma

Traumatic Proptosis

Complete displacement of the globe from the orbit is a true, sight-threatening emergency. Tension on the optic nerve and vascular compromise secondary to tissue compression by the eyelids quickly damage ocular tissues beyond repair. Treatment begins as soon as the patient's systemic condition allows.

Etiology

- The depth of the orbit dictates the force necessary to displace the globe.

▼ ***Key Point*** Proptosis most commonly occurs in the brachycephalic dog because of its shallow orbit and exaggerated palpebral fissure. Excessive restraint alone may be sufficient to dislodge the globe in these breeds.

- In contrast, the eyes of cats and dolichocephalic dogs are rarely displaced from their well-proportioned orbits except in severe head trauma.

Clinical Signs

- The proptosed globe rests in front of the eyelids, its proximity to the orbit determined by the extent of the extraocular muscle damage, the integrity of the optic nerve, and the degree of retrobulbar hemorrhage.
- Chemosis and subconjunctival hemorrhage are often present.
- Prolonged exposure of the cornea leads to ulceration.
- The pupil may be dilated from oculomotor paralysis or constricted from an antidromic axonal reflex of contingent negative variation.
- Lateral strabismus is a common complication of proptosis due to rupture of the medial rectus muscle.

Diagnosis

- Perform a thorough physical examination to assess the other effects of head trauma.
- Examine the eye closely for intraocular damage. Palpate the orbital rim for fractures, and radiograph if indicated. Apply fluorescein dye to the cornea to document ulceration.

Treatment

- Apply a bland ophthalmic ointment to the eye to protect the exposed corneal surface. Since the corneal epithelium is typically compromised due to drying, avoid topical corticosteroids initially.
- Reposition the eye as soon as the animal's general condition stabilizes. If considerable delay is anticipated before surgery, consider a lateral canthotomy to relieve tissue compression and secondary vascular compromise by the eyelid "sphincter."
- Reserve enucleation for ruptured globes, for those with extensive extraocular muscle avulsion, or for those with severed optic nerves.

Surgical Procedure

Objectives

- To reestablish the normal position of the eyelids anterior to the globe
- To protect the cornea from exposure

Equipment

- Two strabismus hooks
- Ophthalmic forceps and needle holder
- 5-0 non-absorbable suture (e.g., nylon)
- Tubing or other material suitable for use as stents

Technique

1. Anesthetize the patient.
2. Irrigate the globe and surrounding tissues with sterile physiologic saline and dilute (1:50) the povidone-iodine solution.
3. Elevate the eyelid margins with either a blunt probe, such as a strabismus hook, or horizontal mattress sutures placed beforehand over stents. Sutures enter the eyelid 5 mm from the margin and exit through the meibomian gland openings along the lid margin to prevent corneal contact. The suture ends can be gathered together in a hemostat and lifted simultaneously as gentle counterpressure is applied against the cornea with a moistened cotton ball or the flat surface of a scalpel handle.
4. Tie the sutures firmly, bringing the eyelid margins into close apposition. Leave a slight separation at the medial canthus to facilitate topical therapy with a broad-spectrum antibiotic ointment 3 to 4 times daily. Miosis secondary to anterior uveitis may be modified by judicious application of topical atropine ointment. Overzealous atropine use can reduce tear production and complicate corneal recovery.
5. Administer an oral broad-spectrum antibiotic, such as ampicillin, for 7 days. Avoid systemic sulfonamides, which may reduce tear production.
6. Administer an initial injection of dexamethasone (0.2 mg/kg) followed by oral prednisone therapy (1 mg/kg) for 5 to 7 days to reduce orbital and optic nerve inflammation.

▼ ***Key Point*** Do not inject medication into the retrobulbar area. Do not aspirate orbital contents or the globe itself.

7. Remove the eyelid sutures when the orbital swelling resolves, usually in 3 weeks. Orbital swelling is evaluated by retropulsing the globe. Use the unaffected eye for comparison. Be patient! Premature suture removal will lead to exposure and secondary corneal ulceration.

Prognosis

- An animal with a minimal amount of extraocular muscle damage, an eye tightly positioned against the eyelids, a positive direct or consensual pupillary light reflex, a miotic pupil, and an absence of hyphema has the best prognosis for salvaging the globe.
- Conversely, unfavorable prognostic indicators include rupture of three or more extraocular muscles, lack of a consensual pupillary reaction, marked intraocular hemorrhage, or a hypotensive globe suggestive of scleral rupture.
- Prognosis for vision is guarded at best. In a study of 84 cases of ocular proptosis, only 27% of canine globes (18 of 66) remained visual after proptosis. All proptosed feline eyes in the study (18 of 18) were blind.
- Potential sequelae include lateral strabismus, chronic keratitis due to lagophthalmia and low tear production, phthisis bulbi, and blindness. Strabismus slowly improves over time in most cases. If exposure and secondary ulceration persist, a medial canthoplasty may be beneficial if the client will not consider enucleation.

Orbital Hemorrhage or Emphysema

Etiology

- Less severe orbital trauma may result in lagophthalmia due to retrobulbar and subconjunctival hemorrhage.
- Fractures of the sinus wall may cause air to collect beneath the conjunctiva.
- Orbital emphysema from entry of air through the nasolacrimal duct is a rare complication of routine enucleation.

Clinical Signs and Diagnosis

- Mild-to-moderate exophthalmos is associated with lagophthalmia, chemosis, subconjunctival hemorrhage, and lid swelling.

- Emphysema-related orbital distention is nonpainful and compressible; needle aspiration reveals only air.
- Perform radiography to rule out a sinus wall fracture in patients with post-traumatic emphysema.

Treatment

- Confine the patient to limit further hemorrhage.
- Use cold compresses to reduce acute swelling.
- Apply topical methylcellulose artificial tear ointments frequently (4–6 times daily) to protect the corneal surface from drying.
- Administer oral or parenteral corticosteroids as described for the proptosed globe (see previous section). Avoid nonsteroidal anti-inflammatory drugs that inhibit platelet function.
- Emphysema usually requires orbital exploration and ligation of the canaliculus.

Arteriovenous Fistula

Orbital vascular fistulas may develop secondary to trauma. Clinical signs and diagnostic procedures are similar to those described for developmental vascular anomalies.

Cystic Diseases

Acquired orbital cysts are uncommon consequences of trauma to orbital glands and incomplete excision of secretory tissues during enucleation.

Zygomatic Mucocele

Leakage of saliva from the zygomatic salivary gland or its duct is an uncommon cause of exophthalmos in the dog and cat.

Etiology

The condition may occur spontaneously or after orbital trauma.

Clinical Signs

A painless swelling beneath the inferior temporal or nasal conjunctival fornix is commonly associated with prominence of the third eyelid. The mucosa behind the last upper molar may protrude.

Diagnosis

- Aspirate fluid from the lesion. The mucocele contains a clear, straw-colored, or blood-tinged tenacious material.
- Perform a zygomatic sialogram to confirm the clinical and cytologic diagnosis.

Treatment

- The treatment is surgical; the location of the swelling dictates the approach for removal of the mucocele.
- Approach mucoceles beneath the inferior conjunctival cul-de-sac transconjunctivally, making an incision between the nictitans and the lower eyelid or through the eyelid surface.
- Lateral mucoceles require a limited orbitotomy, the details of which are described in surgical texts.

Mucocele Following Enucleation

Cystic swelling of the orbit may follow enucleation if mucus or tear-producing tissues are not completely excised.

Etiology

Retained conjunctival goblet cells or glandular tissue from the third eyelid may cause cystic swelling of the orbit.

Clinical Signs

As fluid accumulates within the orbit, the overlying skin distends. A fistula may develop, draining seromucoid fluid.

Diagnosis

- Clinical signs are suggestive.
- Perform aspiration cytology to rule out post-surgical infection.

Treatment

Explore the orbit to remove retained secretory tissue, approaching anteriorly through the eyelids.

Other Causes of Exophthalmos

Anecdotal reports attribute other causes of exophthalmos to the hormonal influences of estrus and to the edema caused by hypoproteinemia or systemic hypertension.

ENOPHTHALMOS

Enophthalmos refers to the recession of the eye within the orbit. Differentiate the condition from the relative enophthalmos that accompanies periorbital swelling or edema of the eyelids and conjunctiva.

Enophthalmos may be accompanied by mucoid-to-mucopurulent discharge because of the exaggerated conjunctival cul-de-sac and by ptosis and entropion because of loss of eyelid support by the underlying globe. With the exception of transient enophthalmos accompanying ocular pain, restoration of the globe's normal position within the orbit is seldom successful.

Causes of enophthalmos include developmental abnormalities, retraction of the globe due to pain, atrophy of orbital tissues following debilitating disease or trauma, and loss of smooth muscle tone in the periorbita.

Developmental Disorders

Microphthalmos or Anophthalmos

The microphthalmic globe fails to develop to normal size in dogs and occasionally in cats. Anophthalmos refers to a rare condition in which all ocular tissues are absent.

Etiology

Microphthalmos is inherited in several breeds of dog, including the Australian shepherd, miniature schnauzer, Old English sheepdog, Akita, cavalier King Charles spaniel, Samoyed, American cocker spaniel, Bedlington and Sealyham terriers, beagle, Labrador retriever, and Doberman pinscher. Multiple ocular defects, including microphthalmos, are associated with partial albinism and deafness in the Great Dane and collie. Teratogenic influences during early pregnancy may affect ocular development. Causes of microphthalmos in cats are poorly characterized.

Clinical Signs

- The anomaly is characterized by varying degrees of enophthalmos.
- Because orbital development is influenced by globe size during skeletal maturation, the orbit may also appear small and the palpebral fissure may appear narrowed.
- Accompanying ocular defects include persistent pupillary membranes, cataracts, colobomas, retinal dysplasias, and orbital cysts. Multiple ocular anomalies may render the globe sightless, but on occasion small globes may be structurally and functionally normal.

Diagnosis

- Diagnosis is based upon clinical signs.
  - Differentiate microphthalmos from phthisis bulbi, an acquired atrophy of the globe. Evidence of scarring, inflammation, and normal-sized orbit accompany atrophy.
  - Anophthalmos is diagnosed only after serial histologic examination of orbital tissue has excluded the possibility of microphthalmos.

Treatment

- There is no treatment for microphthalmos.
- Enucleate if chronic irritation and discharge accompany the condition.
- Eliminate affected animals from breeding programs.

Breed-Related Enophthalmos

Etiology

The large orbits and deeply set eyes inherited as conformational traits of dolichocephalic breeds, such as the Doberman pinscher, Irish setter, and golden retriever, may create a relative enophthalmos.

Clinical Signs and Diagnosis

- The globe appears normal but deeply set within the orbit.
- The nictitans may be prominent.
- Mucoid-to-mucopurulent discharge, ptosis, and entropion are common sequelae.

Treatment

- The condition is incurable.
- Manage secondary conjunctivitis with intermittent applications of topical antibiotic-corticosteroid ointment.
- Correct accompanying entropion.

Acquired Disorders

Acquired enophthalmos is common, particularly in response to ocular pain and as a consequence of severe or recurrent inflammation of the globe itself.

Ocular Pain

The retractor bulbi muscle pulls the eye into the orbit when pain is present. The phenomenon is more apparent in the dog than the cat.

Etiology

Any painful ocular disorder may cause enophthalmos, especially ulcerative keratitis, anterior uveitis, and acute glaucoma. These conditions are discussed in other chapters.

Clinical Signs

In addition to enophthalmos, the animal demonstrates other nonspecific signs of ocular pain: excessive tearing, eye rubbing, blepharospasm, photophobia, and nictitans protrusion.

Diagnosis

- Examine closely for ectopic cilia, foreign body, corneal ulcer, or intraocular disease.
- Pain associated with ocular surface disorders, such as ulcers, may decrease following topical application of 0.5% proparacaine.

Treatment

Treat the underlying ocular disease.

Changes in Orbital Volume

Reduction in retrobulbar tissue mass or damage to the bony or soft-tissue structures forming the walls of the orbit causes the globe to recede. Orbital neoplasia occasionally produces enophthalmos, especially in cats.

Dehydration or Cachexia

- Loss of retrobulbar fat causes a mechanical sinking of the globe into the orbit. Pronounced weight loss and dehydration secondary to vomiting, diarrhea, or other debilitating conditions decrease the retrobulbar fat pad.
- Reduced orbital tissue mass may also be a feature of aging.
- Correct dehydration if present. Enophthalmos secondary to cachexia and loss of retrobulbar fat may not be reversible.

Atrophy Following Inflammation or Trauma

Reduction of the orbital tissue mass effectively enlarges the orbit, resulting in enophthalmos.

Etiology

- Atrophy of the temporal, masseter, and pterygoid muscles is relatively common in dogs following myositis or as an idiopathic phenomenon.
- Brain stem infections or injuries may produce alterations in the trigeminal motor nucleus and result in atrophy of the muscles of mastication.
- Similar lesions may develop as a consequence of trauma to the trigeminal nerve at the base of the ear or fractures in the temporomandibular joint or skull at the oval foramen.
- Chronic or recurrent orbital inflammation may lead to atrophy of orbital contents; trauma or inflammation of the globe may lead to phthisis bulbi.

Clinical Signs and Diagnosis

- Atrophy of the masticatory muscles alters the facial appearance, exaggerating the skull's bony protuberances.
- The animal is unable to open the mouth widely and often has difficulty prehending food.
- Enophthalmos and passive nictitans prolapse may cause visual impairment.
- The phthisic globe is small and blind, with a thickened sclera, opaque cornea, and profound disorganization and scarring of the intraocular structures.

Treatment

- Consult a veterinary ophthalmologist regarding autogenous fat transplants or implantable beads (strictly a cosmetic procedure) to modify the degree of post-inflammatory or post-traumatic enophthalmos.
- There is no effective treatment for phthisis bulbi. Control secondary conjunctivitis with regular irrigation and intermittent topical antibiotic-corticosteroid ophthalmic preparations.
- Enucleate phthisic globes in cats because of the potential for post-traumatic ocular sarcoma.

Orbital Fat Prolapse

Enophthalmos and nonpainful subconjunctival swelling are reported in dogs with prolapse of orbital fat. Subconjunctival fine-needle aspirates are diagnostic. Surgical resection of the displaced fat is curative.

Sympathetic Denervation

Horner's syndrome and feline dysautonomia cause loss of sympathetic tone in the periorbita, with varying degrees of enophthalmos.

Neoplasia

Pathologic expansion of the orbit due to loss of the lateral and ventral periorbita may account for the enophthalmos that accompanies orbital neoplasia in the cat.

STRABISMUS

Involuntary deviation of the globe from its normal visual axis may occur as a developmental or acquired abnormality.

Developmental Disorders

Conformational Strabismus

Strabismus is common in brachycephalic and toy breeds of dogs. Exotropia or lateral deviation is most likely to occur in the Boston terrier, Pekingese, Shih Tzu, and pug.

Albinism

In Siamese and Himalayan cats, esotropia (crossed eyes) is attributed to effects of the albino gene. An increased number of optic nerve fibers originating in the temporal retina decussate at the optic chiasm in affected animals. The strabismus is thought to be a compensatory mechanism for the accompanying abnormal retinotopic projections to the lateral geniculate and occipital cortex. A fine pendular nystagmus may be associated with the strabismus.

Extraocular Muscle Hypoplasia

Congenital extraocular muscle aplasia and hypoplasia are rare causes of strabismus in the dog. A single report in a miniature poodle described dramatic upward rotation of one eye and esotropia of the opposite globe. Only the medial rectus and ventral oblique muscles were present. Position of the globe improved with resection of the medial rectus muscle.

Hydrocephalus

Expansion of the calvarium into the dorsomedial orbit is responsible for the lateral and ventral deviation of the globes in hydrocephalic puppies.

Acquired Disorders

Postproptosis Strabismus

Although deviation can occur in any direction, dorsolateral strabismus is a common sequela of proptosis due to avulsion of the ventral and medial rectus muscles. The strabismus usually improves over a period of weeks to months, although position of the globe seldom returns to normal. Severe, persisting deviation may be treated by anchoring sutures to realign the globe or by partial tarsorrhaphy to protect the cornea and improve the overall appearance.

Restrictive Extraocular Myositis

Restrictive myositis presents as a rapidly progressive ventral to ventromedial strabismus in young, adult, large-breed dogs, including the Irish wolfhound, Shar-Pei, Akita, golden retriever, and the dalmatian. Patients demonstrate unilateral or bilateral clinical signs, rapid onset ranging from 1 week to 4 months, and vision loss secondary to the severe globe deviation. Abnormalities are restricted to the extraocular muscles with no detectable abnormalities in the masticatory or limb muscles. Histopathology is characterized by muscle fibrosis, myonecrosis, and mononuclear inflammation. Limited serology for immune-mediated disease, infectious agents, antibodies against 2M fibers, and muscle enzymes have been normal.

Treatment

- Despite histopathologic evidence of mild lymphocytic-plasmacytic inflammation, medical treatment of restrictive myositis has been ineffective. Immunosuppressive systemic therapy with prednisone or prednisone and azathioprine has no effect on the muscle fibrosis and strabismus already present at initial examination.
- Surgical resection of the affected extraocular muscles alleviates the strabismus but has no appreciable effect on the accompanying enophthalmos. Some patients require repeated muscle resection.

Neoplasia

Strabismus secondary to space-occupying orbital disease has been previously described. External ophthalmoplegia with strabismus has also been reported secondary to intracranial masses. An intracranial meningioma affecting the oculomotor nerve caused ventrolateral strabismus and pupillary abnormalities in a 15-year-old Belgian sheepdog. Oculomotor lesions have also been reported in several cases of cavernous sinus syndrome in dogs.

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Chapter

141 Neuro-ophthalmology

Randall H. Scagliotti

Clinical signs of ocular dysfunction may appear as disorders in the neuroanatomic pathways that allow normal vision. Vision is optimal when sufficiently protected eyes receive the proper amount of light while holding images steady on the retina. Many complex neurologic systems are involved in vision, including the visual sensory system (retina to visual cortex), the autonomic nervous system (pupillary function and lacrimation), the ocular motor system (neural control of eyeball, eyelid, and third eyelid position and movement), and the trigeminal somatic sensory system (pain sensation) of the eye and adnexa.

The diagnosis of abnormal neuro-ophthalmic signs is dependent upon acquiring a solid base of knowledge about the various neural substrates that enable normal vision. How these neural substrates interact determines the normal physical reflexes and responses that are observed during examination of each of the abovementioned neurologic systems. This chapter emphasizes the examination process for each system and the interpretation of normal and abnormal responses, and it discusses diagnostic tests that can aid lesion localization and diagnosis. Specific diseases of the eyes and nervous system that afflict each system are discussed in other chapters of this book.

NEURO-OPHTHALMIC ANATOMY

- The cranial nerves that enable normal vision are summarized in Table 141-1.
- The nerves of the petrous temporal bone are of two types: those in transit through the bone and destined for distant locations that subserve the eye or some of its supporting functions, like lacrimation, and those that mediate other functions, like hearing or taste. Those in transit to and destined for the eyeball or to protective and supporting structures for vision (e.g., the adnexa or the vestibular apparatus for head-eye coordination) include cranial nerve (CN) 5, 7, 8; postganglionic neurons of the sympathetic nervous system; and preganglionic and postganglionic fibers of the parasympathetic nervous system.
- The parasympathetic system (general visceral efferent [GVE] fibers) of the glossopharyngeal nerve (CN9) may be indirectly involved in ensuring ocular health and vision. The preganglionic parasympathetic fibers of CN9 form a synapse on a collection of cell bodies known as the *otic ganglion,* which lies within the ventrorostral petrous temporal bone. This ganglion is the source of postganglionic parasympathetic neurons that innervate the parotid and zygomatic salivary glands.
  - These glands may become denervated and dysfunctional (leading to xerostomia) by the same process and at the same time that lacrimation ceases or is diminished from the lacrimal gland (leading to keratoconjunctivitis sicca [KCS]). Be sure the parotid gland is normal before performing parotid duct transposition in cases of medically refractory KCS.
- Two neuroanatomic pathways modulate the pupillary light responses: the pupillary light reflex (PLR) pathway and the efferent sympathetic pathway (Fig. 141-1).
- The afferent arm of the PLR pathway from each eye is a three-neuron pathway. Each consists of a retinal chain neuron (photoreceptors and bipolar cells), optic nerve, and pretectal neuron that distribute information bilaterally (i.e., to both parasympathetic nuclei of the third nerve) as a result of the crossover that occurs at both the optic chiasm and the caudal commissure.
- *Note that the crossover of optic nerve fibers is unequal at the level of both the optic chiasm and the caudal commissure.*
- The afferent arms of the PLR are part of the central nervous system (CNS). Each efferent arm of the PLR is a two-neuron pathway from the autonomic nervous system (ANS) and consists of preganglionic and postganglionic parasympathetic neurons that are distributed as part of the oculomotor nerve (CN3). The efferent arms of the PLR do not cross to the opposite side en route to the iris sphincter muscles (for pupil constriction) and therefore do not distribute information to both eyes.
- The other pathway that controls the iris is the efferent sympathetic pathway. This pathway, which originates centrally in the posterolateral hypothalamus, remains unilateral throughout its course.
- The central neuron pathway (which may actually consist of several linked pathways leaving the brain stem) proceeds down the lateral cervical spinal cord

Table 141-1. SUMMARY OF NEUROANATOMY

Nerve	Nerve Type	Nerve Cell Body Location		Ganglion	Distribution	Function
		Gross	Micro			
Optic (CN2)	SSA	Retina	Ganglion cell Layer of retina	—	Lateral geniculate body	Vision
					Pretectal nucleus	Innervates parasympathetic nucleus of CN3 (miosis)
Oculomotor (CN3)	SE	Ventral mesencephalon	Motor nucleus of oculomotor nerve	—	Medial, dorsal, ventral recti, ventral oblique Levator palpebrae muscle	Ocular motility
	GVE	Ventral mesencephalon	Parasympathetic nucleus of CN3	Ciliary ganglion	Iris sphincter muscle Ciliary muscle	Miosis Regulates lens curvature
Trochlear (CN4)	SE	Dorsal mesencephalon	Motor nucleus of trochlear nerve	—	Dorsal oblique muscle	Ocular motility
Trigeminal (CN5)	SA	Cavum trigeminal of dura at apex of petrous temporal bone	Trigeminal ganglion (gasserian or semilunar)	—	Ophthalmic division—orbit Maxillary division—eyelids	Sensory to orbit, eyeball, and eyelid Sensory to eyelids
Abducens (CN6)	SE	Ventral metencephalon	Motor nucleus of abducens nerve	—	Lateral rectus muscle Retractor bulbi muscle	Ocular motility Globe retraction, third eyelid protrusion
Facial (CN7)	SVE	Ventral metencephalon	Motor nucleus of facial nerve	—	Orbicularis oculi Muscles of face	Eyelid closure Facial expression
	GVE	Ventral metencephalon	Parasympathetic nucleus of CN7	Pterygopalatine ganglion	Lacrimal gland	Tear secretion
Vestibulocochlear (CN8)	SP	Myelencephalon	Vestibular ganglion	—	Semicircular canals, utricle, sacculus	Coordinates eye with head movement
Glossopharyngeal (CN9)	GVE	Myelencephalon	Parasympathetic nucleus of CN9	Otic ganglion	Parotid salivary gland	Salivary secretion, used for PDT

CN, cranial nerve; SE, somatic efferents; GVE, general visceral efferents; SVE, special visceral efferents; PDT, parotid duct transposition; SA, somatic afferents; SSA, special somatic afferents; SP (SSA proprio.), special proprioception.

to synapse with preganglionic sympathetic fibers within the lateral-rostral thoracic spinal cord. After these fibers exit the vertebral column, they return to the head by ascending the neck in the vagosympathetic trunk, where they synapse on the cranial cervical ganglion medial to the tympanic bullae.

- The postganglionic sympathetic fibers course through the middle ear and base of the brain to reach the orbits from which they extend to the dilator muscle of the iris (for pupil dilation).

CLINICAL SIGNS OF NEURO-OPHTHALMIC IMPORTANCE

Absence of Reflex Blinking:

- Absence of reflex blinking is associated with eyelid closure abnormalities.

Ptosis or Blepharoptosis:

- Ptosis or blepharoptosis indicates insufficient opening of the eyelids. Differentiate from *pseudoptosis,* which occurs when the upper eyelid droops over an eye that is abnormal in size (microphthalmic), shape (keratoconus), or position (enophthalmic) (see Chapter 132).

Decreased Tear Production:

- A Schirmer tear test of less than 10 mm of wetting per minute may indicate a disorder of either the afferent arm (trigeminal nerve) or the efferent arm (parasympathetic neurons of the facial nerve) of the trigeminolacrimal reflex. Differentiate injury along the trigeminolacrimal reflex pathway from injury to the lacrimal gland proper (see Chapter 139).

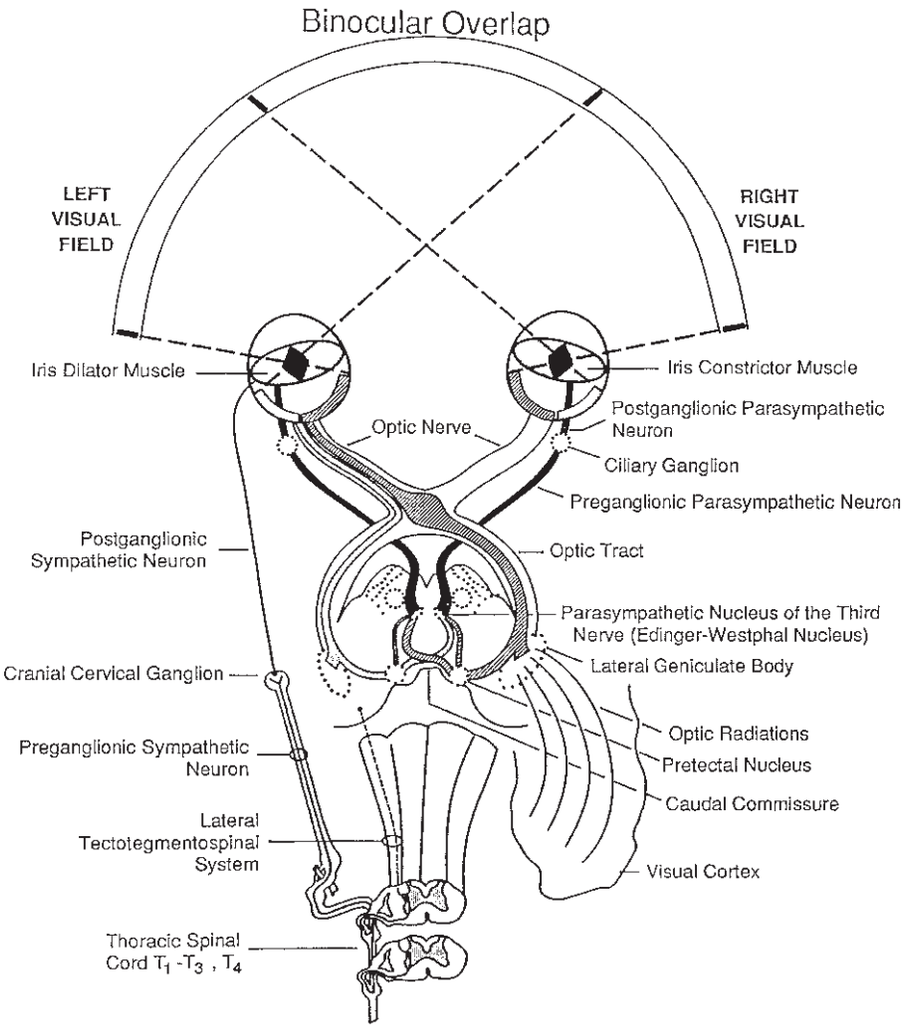

Figure 141-1. Pathways modulating the pupillary light response.

Decreased Parotid Salivary Gland Secretion:

- Decreased parotid salivary gland secretion can result from denervation of the parasympathetic fibers of the glossopharyngeal nerve (CN9). Parotid secretion must be adequate in the event that the parotid salivary duct is to be transpositioned to an eye for treatment of KCS (see Chapter 139).

Loss of Pain or Tactile Sensation to the Eye and Adnexa:

- Loss of pain or tactile sensation to the eye and adnexa occurs as a result of trigeminal sensory neuropathies. Differentiate ulcerative keratitis due to denervation of the trigeminal nerve (i.e., neuroparalytic keratitis) from other types of ulcerative keratitis.

Anisocoria:

- Anisocoria can result from developmental problems of the iris (e.g., aniridia) or acquired problems of the iris (e.g., posterior synechia). Differentiate from the anisocoria observed following neuropathology of the visual sensory system (CN2), PLR pathway, or efferent sympathetic pathway.

Strabismus:

- Strabismus indicates a problem with ocular alignment. This may occur due to a space-occupying mass in the orbit, mechanical restriction of extraocular muscles, extraocular muscle myopathy or junctionopathy, or neurologic dysfunction to the extraocular muscles.

Nystagmus:

- Nystagmus is an involuntary, repetitive, to-and-fro movement of one or both eyes that includes smooth sinusoidal oscillations (pendular nystagmus) and alternation of slow drift and corrective quick-phase oscillations (jerk nystagmus). Nystagmus occurs in any plane, can be permanent or transient, and may be either acquired (vestibular disease) or congenital (animals born congenitally blind).

Blindness:

- Blindness is a congenital or acquired condition in which there is complete loss of vision including all appreciation of or responses to light and dark. This may result from disorders of the eyes, visual pathways to the brain, or areas in the brain responsible for the sense of vision.

DIAGNOSIS

History

General History

- Obtain information about prior neurologic disturbances, systemic illness, head or neck disease, and drug use.
- Rubbing at the face or eyes with the paws or floor or furniture surfaces may indicate ocular pain. Orbital and ocular pain often lead to altered patterns of behavior. Most often patients with pain become secretive and reclusive; however, occasionally aggressive behavior is observed.

Ocular History

- Establish the specific nature of any ocular secretion; inflammation about the eye, eyelids, and orbit; and abnormalities in globe position and motility.
- When vision loss is incomplete, owners may characterize specific types of vision abnormalities. These descriptions include having difficulty observing stationary versus moving objects, seeing near versus far, or having loss of night or day vision.

General Physical Examination

Perform a complete physical examination including a thorough neurologic examination as described in Chapter 125, with particular emphasis on CN2 through CN9.

▼ ***Key Point*** Evaluate the ear, nose, mouth, pharynx, and paranasal sinuses, because they are intimately linked in disease to one another and to the eye. Disease involving any one these regions may directly or indirectly cause abnormal neuro-ophthalmic signs.

Visual Sensory System Evaluation

- Visual field testing, strictly speaking, cannot be performed in animals because their eyes will not hold a target (fixate) long enough to assess all visual fields. However, that should not preclude use of helpful clinical tests, albeit crude, to obtain information on vision quality or the integrity of the visual sensory system.
  - Although no one test should be relied upon to determine either aspect, use results from all the tests to make a good estimate of the type or degree of vision loss or the location of the lesion.

Ocular Examination

Use focal illumination and magnification to assess the anterior segment and direct or indirect ophthalmoscopy to examine the posterior segment.

Visual Placing Reaction

- This is a visually dependent postural reaction.
- Lift and support the patient under the abdomen and thorax while holding the head in a forward stationary position and advance toward a table edge. Present the table edge frontally (perpendicular to the long axis of the head and body) and then laterally (parallel to the long axis of the head and body). The normal response of a sighted patient is the forward advancement and placement of both feet on the table when the table edge is presented head-on and a lateral reaching movement with the leg nearest the table edge when it is seen by the *nasal hemiretina* (extreme lateral visual field).
- In lateral placing, have the nose extend beyond the corner of the table to ensure that only the most extreme portion of the nasal hemiretina (i.e., the most rostral portion of the nasal hemiretina referred to as the monocular crescent) is stimulated. When testing the visual fields, present the table edge from the front and side (laterally) under monocular and binocular test conditions.
- Visual placing requires an intact rostral portion of the striate cortex and foreleg region of the motor cortex.

Visual Cliff

- An indication of depth perception (stereopsis) ability can be obtained with a visual cliff.
- These are crudely created by using multiple variable height platforms or simply a table with variable height.
- A homogeneous texture and color has to cover all testing surfaces. Use a black-and-white checkered tablecloth.
- Normal dogs and cats will jump onto the lower platform (e.g., floor), whereas animals with poor depth perception will be unwilling to do so, will lower their bodies to the tabletop and slide off the table, or will

crash their chins into the floor as they miscalculate the depth of the jump.
- Monocular testing provides a reasonable control for determining whether monocular depth perception cues have been eliminated by the tablecloth. Most monocular patients are reluctant to jump, or they miscalculate the jump.

Visual Obstacle Course

- Use an obstacle course with a standardized layout based on the examiner's preference for most effective geometric design. This will result in more reliable deductions about the performance differences between sighted and non-sighted animals.
- Use five or six gray polyurethane foam cylinders, 2 feet tall and 4 inches in diameter, rather than the unprofessional and possibly injurious furniture objects customarily used, to ensure a safe, effective course.
- Run the course under monocular and binocular conditions using photopic (ambient room light) and scotopic (an incandescent red light bulb on a dimmer switch) illumination.
- Visually deficient animals will be reluctant to move in a strange environment under ambient light and/or scotopic light conditions or will move slowly through the course with their noses to the floor (i.e., "pick" their way). A few of the visually impaired will perform in a buoyantly bold manner yet run into many cylinders during each trial.
- Four or more trials through the obstacle course performed correctly under both photopic and scotopic illumination can be considered normal.

Dazzle Reflex

- This is a *subcortical reflex,* manifested as a bilateral partial eyelid blink in response to a bright light shined in one eye at a time.
- Use a powerful light source (halogen power with a Finoff transilluminator or, preferably, a fiberoptic light).
- It is present when the optic nerve is intact to the level of the midbrain. It also requires an intact facial nerve to elicit the blink.
- The closure is rapid and incomplete in the stimulated eye, and if present in the opposite eye, it is less extensive than in the stimulated eye.

Menace Response

- The menace response is a cortically mediated eyelid closure (i.e., cortical blink) and occasional head withdrawal originating in the cerebral cortex in response to a sudden threatening gesture in the near visual field. This response is complex and not totally understood.
- It requires intact peripheral and central visual pathways, including the cerebellum and facial nerves.
- Evaluation of the visual sensory system (CN2 and higher vision centers) requires isolating its function and integrity from the corneal blink reflex pathway (CN5 to CN7). If this is not achieved, a blink following a visual threat may elicit the corneal blink reflex afferently mediated by CN5, rather than the desired CN2-mediated menace response.
- Use a windshield (plastic shield or helmet visor) to block airwaves while still allowing the patient a view of the menacing threat.
- Menace the visual field of each eye (nasal and temporal hemiretina) after patching the other eye, which eliminates its participation in the response. Then evaluate the left and right binocular visual fields (i.e., the nasal hemiretina of one eye and the temporal hemiretina of fellow eye) by eliciting the menace response without patching.

Specialized Diagnostics

- *Electroretinography (ERG)* is a technique that differentiates retinal pathology from disorders of post-retinal anatomy (see Chapter 138).
- *Cerebrospinal fluid (CSF) pressure and analysis* is an invasive technique that assesses the status of the CNS when lesions are thought to be central in origin (see Chapter 125).

Autonomic Nervous System Evaluation

Pupillary Responses

Pupillary Light Reflexes

- This exam is best conducted in darkened conditions using a powerful light source (see Fig. 141-1). A halogen-powered light is minimally required to adequately evaluate the PLR, but a fiberoptic light source is best.
- The pupil under direct light stimulation (direct PLR) will constrict to a greater degree than the other eye. The constriction of the other eye is called the *indirect or consensual light reflex*. Thus, this pupil is said to react indirectly or consensually.
- Because the pupil receiving the direct light constricts to a greater degree than the other pupil (indirect pupil), an anisocoria exists during this active stimulation that is referred to as a *dynamic contraction anisocoria*. This is a normal physiologic response.
- Anisocoria is absent in ambient light unless there is heterochromia of the irides, iris disease, PLR pathway, or efferent sympathetic pupillary pathway pathology.

▼ ***Key Point*** Remember that iris muscle atrophy (as evidenced by light retroilluminating through holes in the iris) will weaken and, in some advanced cases, prevent the PLR.

Measurement of Pupil Size and Symmetry

- *Pupillary symmetry* is best obtained clinically using the direct ophthalmoscope as a crude pupillometer.
- Direct the light source at the interpupillary space on the bridge of the nose to observe the tapetal reflection of both eyes simultaneously.
- The overall size of the pupils and the existence of any inequality will be revealed quickly and accurately. Measure pupil size in ambient light using a hole sizing ruler or a caliper.

Swinging Flashlight Test

- This test measures the integrity of the retina and prechiasmal optic nerve.
- Perform in a darkened room because the PLR will be exaggerated.
- Immediately following direct light stimulation into one eye, swing the light source into the other eye, and then back again to the first eye directly stimulated. Repeat this procedure back and forth (thus the swinging flashlight) as often as necessary to be sure that both pupils constrict directly and indirectly.
- If a pupil dilates rather than constricts during direct stimulation immediately following its return from direct stimulation of the other eye, a unilateral retinal or prechiasmal optic nerve lesion exists. If dilatation of a pupil instead of pupil constriction occurs during the swinging flashlight test, this is referred to as positive for the dilating eye.

▼ ***Key Point*** A positive swinging flashlight test is pathognomonic for a unilateral retinal or prechiasmal optic nerve lesion.

Pharmacologic Testing

- Use topical drugs in cases of anisocoria to differentiate anatomic problems in the iris (e.g., synechia or iris atrophy) from neurologic problems. Also use topical drugs to localize the lesion to preganglionic or postganglionic fibers within each of the two efferent pathways (the efferent sympathetic pathway and the efferent parasympathetic pathway of the PLR).
- In an injured nerve whose terminals are allowed to degenerate, the structure supplied by it becomes supersensitive to the transmitter substance released by the terminals.
- Use pilocarpine (2%) and physostigmine (0.5%) to test the parasympathetic system and phenylephrine (10%) and hydroxyamphetamine (1–5%) to test the sympathetic system.

Lacrimation

Schirmer Tear Tests (Schirmer 1 and 2) (see Chapter 139)

- Use strips of Whatman paper to measure the autonomic innervation to the lacrimal gland (reflex tearing as measured by Schirmer 1 in the unanesthetized eye) and basal secretion from the lacrimal gland (by Schirmer 2 in the anesthetized eye). The contribution of the gland of the third eyelid is also figured into these measurements.

Trigeminolacrimal Reflex

- This reflex is responsible for reflex tearing as measured by Schirmer 1 values. The reflex-induced amount of tears is the difference between Schirmer 1 and 2 values. This difference is not as significant in the cat.
- The sensory nerve (CN5) of the eye conducts noxious stimuli centrally; the efferent arm of the reflex arises in the parasympathetic nucleus of CN7 in the ventral metencephalon (see Table 141-1) to course with branches of the facial nerve within the petrous temporal bone in route to the orbit. The pterygopalatine ganglion within the extraperiorbital sheath area of the orbit gives rise to postganglionic parasympathetic fibers that course with the zygomaticotemporal nerve (a branch of the maxillary division of the trigeminal nerve) to innervate the lacrimal gland with postganglionic parasympathetic fibers.
- It is assumed that the same reflex pathway is involved in the tear contribution made by the gland of the third eyelid.

▼ ***Key Point*** Lacrimation may be affected when the preganglionic parasympathetic fibers within the petrous temporal bone or the postganglionic parasympathetic fibers within the orbit are damaged during infectious or inflammatory disease in these regions.

Ocular Motor System Evaluation

Eyelid Position and Movement

Voluntary Eyelid Movement and Position

- Observing voluntary movement (blinks or eyelid elevation) in response to visual or auditory stimuli indicates much about normal eyelid closure and opening.
- Abnormal eyelid position is more easily observed because asymmetry of the palpebral fissures is more readily detected than eyelid movement. For instance, in facial paralysis, a lack of voluntary eyelid movement can be easily overlooked with certain head types (i.e., brachycephalic) that conceal the palpebral asymmetry associated with this disorder.

Eyelid Opening

- Motor neurons of the oculomotor nerve (CN3) innervate the levator palpebrae superioris muscle, the main muscle of upper eyelid elevation.
- In the dog, the levator anguli oculi medialis muscle (innervated by CN7) assists by elevating the medial portion of the upper eyelid and eyebrow. This muscle

action is readily assessed by leading the eyeball into a dorsal and medial position (intorsion) within the orbit. In order for an eye looking up and medially to maximize its visual field, the medial upper eyelid must be moved out of the way so that the eyebrow elevates during this eyeball movement. Evaluate both sides in a like manner.

Eyelid Closure

The facial nerve and the orbicularis oculi muscle mediate the final common neurologic pathway for all types of eyelid closure. The corneal blink reflex, dazzle reflex, and menace response all depend on a blink response and an intact facial nerve and afferent nerve supply. If any of the blinks are abnormal, determine whether it is an afferent or efferent arm problem.

- *Corneal blink reflex:* The corneal blink reflex is a subcortical reflex closure of the eyelids in response to a tactile or painful stimulus on the unanesthetized cornea. This reflex is afferently mediated by the trigeminal nerve (corneal sensory nerve) and efferently mediated by the facial nerve. Stimulation should come from outside the visual field to isolate this reflex from the menace response. A 3-ml syringe with a 27-gauge needle can provide a tight "air puff" stimulus across the corneal face outside the visual field.
- *Dazzle reflex:* See under "Visual Sensory System Evaluation."
- *Menace response:* See under "Visual Sensory System Evaluation."

▼ ***Key Point*** If all three types of blink responses are non-functional, it is most likely due to facial nerve paralysis.

Third Eyelid Position and Movement

- *Trigeminoabducent reflex and the third eyelid protrusion sign:* This reflex, in addition to protecting the eyeball by retraction (see trigeminoabducent reflex and the eyeball retraction response [ERR] below), is responsible for the active protrusion of the third eyelid through abducent nerve innervation of the lateral rectus muscle, which sends a slip of skeletal muscle to the third eyelid.
- *Passive protrusion of the third eyelid:* The third eyelid will passively protrude secondary to a variety of disorders, such as dehydration, atrophia bulbi, space-occupying mass, or displacement fractures of the bony orbit.
- *Active third eyelid retraction:* Sympathetic tone on the third eyelid retains the third eyelid in a retracted state in the ventral medial canthus. This is the normal position for the third eyelid.

▼ ***Key Point*** Protrusion of the third eyelid is indicative of pathology within the orbit, third eyelid, conjunctival surfaces, eyeball, or its innervation.

Eyeball Position and Movement

Duction Test

- The ability of one eye to rotate while it is viewing is referred to as a *duction.*
- Duction movements of an eye are evaluated by covering the other eye while the unpatched viewing eye is led through secondary and tertiary positions of gaze. Evaluate each eye in this manner for range of eye movement.

Version Test

- The ability of both eyes to move conjugately is referred to as *version movement.*
- Observe the eyes for conjugate movement and range of movement as they are led through the secondary and tertiary positions of gaze.

Forced Duction Tests

- These tests can be active or passive and are used in cases in which there is restricted range of eyeball movement.
- These tests help differentiate mechanical limitation of motion from paralysis of the extraocular muscles.
- In a passive forced duction test, grasp the anesthetized eye at the limbus with forceps on the side opposite to the direction in which the eye is to be moved and forcibly move the eye in the direction of gaze limitation. If no mechanical limitation is present, the eye can be moved fully into the direction of limitation. This indicates that the restricted movement of the eye is secondary to neurologic paralysis. If mechanical limitation is present, the eye will resist attempts to rotate it into the field of limitation.
- In the active forced duction test, grasp the anesthetized eye on the side of the gaze limitation. Hold the eye while the patient is coaxed into looking in the direction of gaze limitation. A tug on the grasped eye is felt if the nerve supply to the muscle is intact.

Trigeminoabducent Reflex and Eyeball Retraction Response

- This reflex is responsible for the protective eyeball retraction into the orbit from noxious stimulation of the eye and adnexa.
- This retraction can be sustained as long as needed because the motor neurons of the abducent nerve are stimulating retractor bulbi muscles, which are skeletal muscles.
- This reflex also causes active protrusion of the third eyelid. The enophthalmos created by active retraction also causes partial passive protrusion of the third eyelid (see the third eyelid position and movement discussion above).

Vestibulo-ocular Reflex

- This reflex maintains the eyes steady on a target during head rotation.
- This reflex is mediated through the vestibular apparatus, which compensates for the angular acceleration sensed by the semicircular canals. It is responsible for sustaining a clear visual image during head movement.
- It is often referred to as the doll's eye movement and is elicited by to-and-fro or up-and-down head rotation. One eyeball appears to move toward its medial canthus and the other eye simultaneously toward its lateral canthus during horizontal head rotation. During up-and-down movement of the head, both eyes will simultaneously move toward the center of the eyelids opposite the direction of the head movement.

Trigeminal Somatic Sensory System of the Eye and Orbit

- *Corneal blink reflex:* See eyelid position and movement above.
- *Corneal sensitivity:* The sensitivity of the cornea or the ability of the trigeminal nerve to feel and respond to discomfort is quantitatively measured with the Cochet-Bonnet aesthesiometer.

NEURO-OPHTHALMIC SYSTEM ABNORMALITIES

Abnormalities of the Visual Sensory System

Menace Response and Visual Fields

- Loss of a hemivisual field (homonymous hemianopia) and menace response in that visual field occur as a result of lesions that affect the ipsilateral nasal hemiretina and contralateral temporal hemiretina or higher in the CNS, a unilateral lesion in the contralateral striate cortex.
- Lesions of the rostral portion of the nasal hemiretina of one eye produce loss of the menace response and blindness in the ipsilateral monocular segment of the visual field.

Blindness

- Blindness broadly represents a loss of visual acuity and/or visual fields, and it may be complete or partial, unilateral or bilateral. Blindness can be categorized according to the location of the lesion. Lesions in the eye, brain stem, and cerebral cortex can result in blindness of neurologic origin.

Ocular Blindness

Ocular blindness is caused by any non-neurologic disorder that destroys the clarity of the ocular media (e.g., corneal scars or cataract) or any neurologic disorder (e.g., neuronal ceroid lipofuscinosis of the brain and retina) that interrupts the retinal processing of light. A lack of funduscopic abnormalities does not rule out the retina as the site of ocular blindness.

- Diseases of the retina can be divided into inherited and acquired. The inherited diseases are most frequently bilateral and may cause selective loss of vision (i.e., nyctalopia or hemeralopia) or progressive generalized loss of vision (i.e., generalized retinal atrophy and degeneration). Acquired retinal diseases (e.g., granulomatous meningoencephalitis [GME, reticulosis] of the ganglion cell layer and optic disc) may be unilateral or bilateral and can result in only partial or temporary loss of vision. Use electroretinography to assist in the differentiation of retinal diseases (see Chapter 138).
- The essential features of unilateral ocular blindness of retinal or prechiasmal optic nerve origin include loss of the dazzle reflex, menace response, direct PLR, and indirect PLR in the other eye. Static anisocoria (i.e., anisocoria present in steady ambient room light) and a positive swinging flashlight test are present in unilateral retinal disease, as well as in unilateral prechiasmal optic nerve disease. The above reactions (i.e., dazzle reflex, menace response, PLR, a positive swinging flashlight test) are lost in *advanced* bilateral retinal disease. In such advanced bilateral disease, the pupils are near maximum dilation and anisocoria may not be observed. In bilateral retinal disease at an *intermediate stage of progression,* the disease may be symmetrical or asymmetrical in its destruction of the retina; therefore, the reflexes will vary. The pupils will be larger than normal, with or without anisocoria (depending on the symmetry of retinal destruction), and the PLR can be absent, sluggish and incomplete, or paradoxical (see "Anisocoria in Optic Nerve Dysfunction" below). Ocular motility is normal in all positions of gaze.

Brain Stem Blindness

Blindness from acquired lesions in this region of the brain is the result of inflammation, infection, neoplasia, or vascular accidents. The areas of importance are those involved as vision relay centers (the dorsal lateral geniculate body) and visual pathways (the optic tracts or optic radiations [cerebral cortex]), and those responsible for visually guided behavior (rostral colliculi).

- The essential neuro-ophthalmic abnormalities will be variable depending on the lesion location and extent. The clinical features may include loss of visually guided behavior, blindness, anisocoria, loss of the dazzle reflex and menace response, and abnormal PLRs. Abnormal eye movement (gaze paresis) and eyeball position (strabismus) may be seen.
- Other neurologic signs referable to the brain stem may be present.

Cerebral Blindness

This is a generalized term describing the blindness caused by a disorder in any area of the cortex that plays a role in vision but that often results from a more rostral, cerebral cortical abnormality. In some cases cerebral blindness includes cortical blindness.

- The essential neuro-ophthalmic features may include complete loss of all visual sensation, including that for light and dark; a loss of the menace response and visual placing reactions; and the inability to detect a visual cliff. The eyes retain normal PLRs, dazzle reflexes, eye movements, and ocular alignment.

Cortical Blindness

This type of blindness indicates selective loss of the visual occipital cortex (striate cortex).

- The essential features include the loss of the menace response, problems with stereopsis, blindness in corresponding areas of the visual field, and abnormalities in the visual placing responses. The configuration of abnormalities is dependent upon the lesion site. The dazzle reflex (subcortical reflex) and PLR (subcortical reflex) remain normal. Ocular motility appears clinically normal, although ocular alignment may be abnormal, especially if the vision abnormality is congenital. For example, some Siamese cats have a congenital striate cortex abnormality that results in congenital bilateral esotropia with or without a pendular nystagmus. Although they do not have motion or visual field blindness, they are stereoblind (i.e., lack depth perception) (Table 141-2).

▼ ***Key Point*** Distinguish vision loss occurring from lesions in the striate cortex from that occurring from lesions in the motor cortex. Lesions of the motor cortex result in behavioral responses (e.g., falling off a visual cliff or running into objects) that are clinically used to indicate whether vision is present.

Table 141-2. LESION DIFFERENTIATION BASED ON BLINK REFLEX

Lesion	Optic Dazzle Reflex*	Tactile Corneal Reflex†	Menace Response	Vision
CN2 lesion	–	+	–	–
CN5 lesion	+	–	+	+
CN7 lesion	–	–	–	+
Visual cortex lesion	+	+	–	–
Large cerebellum lesion	+	+	–	+

*The dazzle and corneal reflexes are subcortical responses.
†The menace response requires an intact visual cortex.

- Unilateral lesions of the motor cortex in the regions for eyelid closure in response to a menace and in the region for visual placing in response to presentation of a table edge within the visual field result in the contralateral loss of the menace response and visual placing reaction. A loss of these responses usually is interpreted as a loss of vision. If the striate cortex is intact, both the menace and the table are seen in the contralateral visual field, but the lesion in the appropriate areas of the motor cortex prevents the appropriate behavioral response, a blink, and a placing reaction. For the same reason, a patient may fall off a visual cliff even if it is seen by the striate cortex. Thus, care must be taken in evaluating and defining the "blind" patient.

Abnormalities of the Autonomic Nervous System (Pupillary Light Reflexes and Lacrimation-Salivation)

Abnormalities of the Pupillary Light Reflexes

Lesions of the PLR pathways result in all or some of the following clinically detectable disturbances, depending upon the lesion site and extent: abnormalities in pupillary diameters and, in the cat, sometimes shape; abnormalities in response to dark adaptation; abnormalities in the PLR; and abnormalities in vision (Table 141-3).

Anisocoria in Ambient Light

- Unilateral pupillary pathway (i.e., afferent or efferent PLR pathway or efferent sympathetic pathway) lesions result in anisocoria of variable degrees. Some pupillary disorders that create anisocoria (e.g., feline spastic pupil syndrome and feline hemidilated pupil) also result in dyscoria.
- Unilateral lesions of the afferent arm of the PLR create subtle (i.e., the pupil size difference is very small) anisocorias and vision defects. The subtle anisocoria in Horner's syndrome is similar in appearance to those created by lesions in the afferent arm of the PLR. Differentiate on the basis of the associated clinical signs in Horner's syndrome (e.g., ptosis, reverse ptosis, enophthalmos, and protruded third eyelid). In addition, vision is not impaired in Horner's syndrome unless the extent of the third eyelid protrusion mechanically blocks vision. However, all lesions that occur in the afferent arm of the PLR result in complete to partial vision loss. Horner's anisocoria partially or completely disappears in bright light, while afferent PLR defects do not.
- Anisocoria with *large differences* in pupil size occurs with unilateral lesions of the efferent arm of the PLR.

Anisocoria in Darkness

- All unilateral and bilateral lesions of the afferent arm of the PLR dilate maximally and equally in darkness.

Table 141-3. NEUROPATHIC AND OTHER CAUSES OF ANISOCORIA: DIFFERENTIAL SIGNS AND TESTS

Diseases	Pupil Affected Side	PLR DI		SFT	Dazzle Reflex	Menace Response	DAD Test	Tonometry	PT	Diagnostic SLB	Funduscopy	Vision	Special Tests
Anterior uveitis	Miotic	±	±	–	+	±	Unequal	Hypo	No	+	–	Poor	–
Glaucoma (advanced)	Dilated (fixed)	–	–	–	–	–	Unequal	Hyper	No	±	+	Blind	–
Afferent arm lesions													
Retina/optic nerve	Dilated	–	–	+	–	–	Equal	Normo	No	–	±	Blind	–
Chiasm	± Dilated	±	±	–	±	±	Equal	Normo	No	–	–	Variable	–
Optic tract	Miotic	+	+	–	+	+	Equal	Normo	No	–	–	Homonymous hemianopia	–
Efferent arm lesions													
Atrophic iris disease	Dilated	–	+	–	+	+	Variable	Normo	Yes	+	–	Normal	PT
Traumatic iridoplegia	Dilated	–	+	–	+	+	Unequal	Hypo/normo	Yes	±	–	May be poor	PT
Pharmacologic blockade (atrophine-induced mydriasis)	Dilated	–	+	–	+	+	Equal	Normo	Yes	–	–	Normal	PT
Postganglionic denervation	Dilated	–	+	–	+	+	Dog, unequal Cat, equal	Normo	Yes	–	–	Normal	PT
Preganglionic/ central denervation		–	+	–	+	+	Unequal	Normo	Yes	–	–	Normal	PT
Efferent sympathetic nerve lesions													
Preganglionic denervation	Miotic	+	+	–	+	+	Unequal	Normo	Yes	–	–	Normal	PT
Postganglionic denervation	Miotic	+	+	–	+	+	Unequal	Normo	Yes	–	–	Normal	PT
Polyneuropathy													
Spastic pupil syndrome	Variable	±	±		+	+	No	Normo	No	–	–	Normal	+FeLV

PLR, pupillary light reflexes; D, direct (in affected, stimulated eye) light reflex; I, indirect (in nonaffected, unstimulated opposite eye) light reflex; SFT, swinging flashlight test; DAD test, dark adaptation test; PT, pharmacologic test; SLB, slit lamp biomicroscopy; FeLV, feline leukemia virus; Hypo, <15 mm Hg; Hyper, 0.25 mm Hg; Normo, 15–25 mm Hg.

- In cats with lesions of the efferent arm (both preganglionic and postganglionic parasympathetic fibers) of the PLR, the pupils dilate maximally and equally in darkness. This occurs because the efferent arm, including the short ciliary nerves, consists of purely parasympathetic fibers up to the point of entering the sclera where they are joined by the long ciliary nerves (containing sensory trigeminal neurons and postganglionic sympathetics). Thus, injury to the short ciliary nerves rarely involves the sympathetic system in cats.

▼ ***Key Point*** Maximal and equal dilation in darkness distinguishes lesions of the afferent arm (dog and cat) of the PLR and efferent arm of the PLR (cats only) from all other pupillary abnormalities, including those caused by physical restriction of iris movement (synechia).

- In dogs with ciliary ganglion or short ciliary nerve injury, anisocoria persists in darkness because the short ciliary nerves in the dog are mixed nerves containing both sympathetic and parasympathetic postganglionic fibers in addition to sensory nerves. The smaller pupil is ipsilateral to lesions in the ciliary ganglion or short ciliary nerves.
- The anisocoria of Horner's syndrome becomes more pronounced in darkness because the intact innervation to the dilator muscle opens the normal eye in darkness but not the Horner's pupil.
- Cats with feline spastic pupil syndrome will retain their anisocoria and dilate minimally or not at all in darkness.

Anisocoria in Optic Nerve Dysfunction

- A complete unilateral prechiasmal lesion, which involves the retina or prechiasmal optic nerve, creates anisocoria with the smaller pupil contralateral to the side of the lesion (see "Anisocoria in Darkness" and Table 141-3).
- Lesions of the chiasm lead to anisocoria when the fiber destruction is asymmetrical. The PLR may be paradoxical (i.e., the pupil of the eye opposite to that which is directly stimulated will constrict to a greater extent than the eye under stimulation). The reaction may still be paradoxical when the other eye is stimulated. The pupils are generally larger than normal in ambient light (see "Anisocoria in Darkness" and Table 141-3).
- A unilateral lesion of the optic (post-chiasmal) tract always appears with a subtle anisocoria with the smaller pupil ipsilateral to the side with the lesion (see "Anisocoria in Darkness" above and Table 141-3).

Anisocoria in Oculomotor Dysfunction

Injury to the oculomotor nerve's (CN3) preganglionic or postganglionic parasympathetic fibers (GVEs) that constitute the efferent arm of the PLR leads to anisocoria without any visual loss. The pupil on the affected side is widely dilated and fixed (will not move) to direct and indirect light (see "Anisocoria in Darkness" and Table 141-3).

Anisocoria in Oculosympathetic Dysfunction

Lesions in the efferent sympathetic pathway lead to the signs of Horner's syndrome, with anisocoria (miosis on the affected side) as its most diagnostic feature (see Table 141-3). Any or all of the other signs of Horner's syndrome, including the narrowed palpebral fissures from oculosympathetic ptosis (and reverse ptosis), third eyelid protrusion, and enophthalmos, may be present.

Abnormalities of Lacrimation

Loss of reflex tearing, which results in decreased Schirmer 1 tear test values in the unanesthetized eye, occurs with disorders (e.g., inflammation, infection, and neoplasia) of the trigeminal nerve (afferent arm of the trigeminolacrimal reflex) or of the preganglionic or postganglionic parasympathetic neurons of the facial nerve (efferent arm of the trigeminolacrimal reflex) (see Chapter 139).

Topical Diagnosis of Lacrimation Disorders

- *Central facial nerve paralysis:* Paralysis of the proximal portion of the facial nerve containing the preganglionic parasympathetic fibers to the lacrimal gland may lead to a reduction of reflex tearing. The cerebellopontine angle and the petrous temporal bone are likely locations for nerve injury.
- *Otitis media:* Chronic middle ear disease can injure the major petrosal nerve containing the preganglionic parasympathetic fibers (GVEs) of the facial nerve, which innervate the lacrimal gland. This is a leading cause of KCS.
- *Pterygopalatine ganglion injury:* The cell bodies of the postganglionic parasympathetic fibers of the facial nerve are vulnerable to injury from penetrating foreign bodies to the floor of the orbit and from suppurative and non-suppurative extraperiorbital sheath myositis (temporalis and pterygoideus muscles).
- *Lateral orbit injury:* Head trauma can injure the zygomaticotemporal nerve, an eyelid sensory nerve (a branch of the maxillary division of the trigeminal nerve) containing the postganglionic parasympathetic (GVEs of the facial nerve) innervation to the lacrimal gland.
- *Ophthalmic nerve:* Injury to this division of the trigeminal nerve results in corneal anesthesia, loss of the trigeminolacrimal reflex, and diminished Schirmer 1 tear test findings.
- *Xeromycteria:* A dry nasal mucosa occurs in some cases of KCS, leading to an accumulation of dried mucus at the nares on the affected side. This mucus accu-

mulation is often erroneously thought to result from the exit of mucus from an eye with KCS via the nasolacrimal duct. In fact, it is the result of damage to the postganglionic parasympathetic fibers from the pterygopalatine ganglion that course with the caudal nasal nerve (maxillary branch of CN5) to innervate the lateral nasal gland. The lateral nasal gland located near the maxillary sinus functions as a thermoregulatory gland by keeping the nasal cavity moist. Denervation of the lateral nasal gland leads to compensatory hyperplasia and production of the mucus-producing glands within the nasal mucosa, just as the conjunctival goblet cells hypersecrete mucus with KCS. Only a small percentage of KCS cases have mucus collection about the nares as a result of xeromycteria.

- *Paradoxical gustolacrimal reflex:* Crocodile tears are unilateral, profuse tearing in response to stimulation of the taste receptors.

Abnormalities of Salivation

The gustosalivary reflex is demonstrated by patients that have had a successful parotid duct transposition each time they eat. The profuse "tearing-salivation" is mediated afferently by taste receptors on the tongue and efferently by the parasympathetic nervous innervation of the parotid and zygomatic salivary glands. Medical treatment failure for KCS or for circumstances preventing its adequate medical therapy results in the need for parotid duct transposition to sustain a healthy cornea. The same conditions that cause a dysfunctional lacrimal gland may also affect the salivary glands, thereby rendering the parotid gland unsuitable for parotid duct transposition. Determine the health of the parotid gland by assessing parotid secretion prior to duct transposition. The bitter taste of atropine sulfate ophthalmic solution applied directly to the buccal mucosa immediately stimulates the gustosalivary reflex to elicit parotid gland secretion. A pulse-like squirting of parotid secretion from the parotid duct papilla is indicative of adequate secretion. If the parotid secretion slowly flows from the duct orifice without the pulse-like squirting, successful transposition is more problematic.

- *Otitis media:* Disease of the middle ear can injure the preganglionic parasympathetic fibers of the minor petrosal nerve and the otic ganglion and its postganglionic parasympathetic fibers located in the dorsolateral aspect of the auditory tube. These fibers lead to the parotid gland.
- *Otitis externa:* Diseases of the external ear, especially those that ossify the external auditory canal and lead to periauricular tissue damage, can injure the auriculotemporal nerve, a branch of the mandibular division of the trigeminal nerve. This sensory nerve conducts the glossopharyngeal postganglionic parasympathetic fibers arising from the otic ganglion to the parotid gland that is situated between the ear and the angle of the mandible.

▼ ***Key Point*** The otic ganglion and minor petrosal nerves lie close to the major petrosal nerve and may be injured in lesions that injure the major petrosal nerve. Lesions of the dorsorostral middle ear (e.g., from eustachian or auditory tube disease) will lead to KCS, xeromycteria, and xerostomia.

Abnormalities of the Ocular Motor System (Eyelid, Third Eyelid, and Eyeball)

Eyelid Position and Movement Abnormalities

Eyelid Closure Abnormalities

The eyelids will reflexively close to protect vision when the eyes are confronted with bright illumination (dazzle reflex), with a threatening image (menace response), and with noxious tactile stimulation (corneal blink reflex). The muscle responsible for all three closures is the orbicularis oculi innervated by the facial nerve. Observing voluntary eyelid closure prior to testing indicates that the facial nerve and the orbicularis oculi are intact. Failure of one of the eyelid closure responses may result from a disrupting lesion of the afferent arms (optic nerve or trigeminal nerve) of these reactions. Denervation of the orbicularis oculi results in the absence of all three eyelid closure responses. Determine the cause for failure of reflex eyelid closure by separate testing of the various nerve components of the reflex to isolate each nerve.

- *Absent corneal blink reflex:* Test this reflex as described above for eyelid position and movement. Presenting the stimulus (noxious) outside the visual fields avoids stimulating the optic nerve (visual image) and therefore isolates the trigeminal nerve. If the corneal blink reflex is absent but a voluntary blink is present, the trigeminal nerve is dysfunctional (see Table 141-2). Absence of voluntary blink suggests facial nerve dysfunction. When the corneal blink reflex is absent as a result of facial nerve paralysis, there frequently are associated deficits in some or all of the functions served by this nerve.
- *Topical diagnosis of facial nerve disease:* Topical diagnosis along the facial nerve is beyond the scope of this chapter. Schirmer tear testing, facial nerve conduction studies, acoustic reflex testing (to evaluate the facial nerve at the level of the stapedius muscle in the middle ear), brain stem auditory evoked responses (BAER), and magnetic resonance imaging (MRI) can be used to localize the lesion. The BAER is used because CN8 is close to CN7 within the petrous temporal bone, and a lesion at CN7 may therefore be demonstrated by a BAER deficiency in CN8.
- *Eyelid signs with facial nerve paralysis:* Denervation of eyelid closure leads to a widened palpebral fissure, an

increased amount of visible sclera (i.e., scleral showing), and the illusion of proptosis.

- *Absent dazzle reflex:* The dazzle reflex is a subcortical reflex mediated afferently by the optic nerve and efferently by the facial nerve. It produces a bilateral partial eyelid closure (blink or squint) in response to a bright light shined in one eye at a time. To isolate the dazzle reflex (CN2 to CN7) from the corneal blink reflex (CN5 to CN7), avoid touching the cornea or eyelid hair when shining the stimulating light in each eye. The loss of the dazzle reflex when a voluntary blink or the corneal blink reflex is present indicates that the facial nerve is intact and that there is unilateral retinal disease or unilateral optic nerve disease along the afferent pathway to the midbrain (see Table 141-2).
- *Absent menace response:* The menace response is not a reflex but rather a cortically mediated rapid eyelid closure response, with or without head withdrawal, in response to a threatening or unexpected image suddenly appearing within the near visual field. This response requires intact peripheral and central visual pathways, including the cerebellum and the facial nerves.
- In general, the menace response is abolished in the visual fields contralateral to unilateral lesions in specific areas of the cerebral cortex.
- Unilateral lesions in the caudal striate cortex, eyelid region of the motor cortex, and parietal lobe situated between the striate cortex and the motor cortex will cause unilateral disappearance of the contralateral menace response (see Table 141-2).

▼ ***Key Point*** While all three cerebral cortex lesions cause loss of the menace response, only striate cortex lesions cause the ensuing hemianopia.

- Absence of the menace response resulting from destruction of the eyelid region of the motor cortex is due to a partial supranuclear facial palsy and loss of menace response. Parietal lobe lesions entail no visual disturbances or partial facial palsy (voluntary blink remains).
- In dogs, the ipsilateral menace response can be lost and vision can be retained with large unilateral cerebellar lesions. Diffuse cerebellar cortical degenerative lesions cause a failure of the menace response bilaterally, without any visual deficit (see Table 141-2).

▼ ***Key Point*** The menace response (cortical) may be lost when the corneal blink and dazzle reflexes (subcortical) persist.

Eyelid Opening Abnormalities

Neuroanatomic diagnosis of ptosis is dependent upon clinical signs and evidence of neuropathic, neuromuscular, or myopathic disease. Consider the following types:

- *Oculomotor ptosis:* This ptosis results from injury to the oculomotor nerve at any level from the cerebral cortex to the levator palpebrae superioris muscle. Oculomotor ptosis is exaggerated in the lateral two-thirds of the eyelid during eyebrow elevation in the dog if the facial nerve, which innervates the levator anguli oculi medialis muscle, remains intact. This latter muscle assists in lifting the nasal portion of the eyelid and erects the long tactile hairs (pili supraorbitales) of the eyebrow. This muscle action is readily assessed by leading the eyeball into a dorsal and medial position (intorsion) within the orbit, which requires elevation of the eyebrow. Topical diagnosis of oculomotor lesions is enhanced when other functions (e.g., GVEs for PLR and motor fibers for ocular motility) of the oculomotor nerve are disturbed.
- *Oculosympathetic ptosis:* This is a component of Horner's syndrome and results from nerve damage along the efferent sympathetic pathway that innervates the smooth muscles of the eyelid. The lower lid often has an "upside-down ptosis," which creates a narrowed palpebral fissure. Differentiate from oculomotor ptosis. It helps when all or some of the other signs of Horner's syndrome (ipsilateral miosis, enophthalmos, protrusion of the third eyelid) are present.
- *Myopathic ptosis:* This is usually an acquired condition caused by damage to the levator muscle by inflammation, infiltration, or orbital trauma.

Third Eyelid Position and Movement Abnormalities

- *Hyperactive trigeminoabducent reflex:* Painful stimulation of the eyeball and/or adnexal surface (e.g., ectopic cilia) or a trigeminal neuritis will lead to the eyeball retraction response and third eyelid protrusion sign, both mediated by the trigeminoabducent reflex. Third eyelid protrusion leading to third eyelid protrusion sign is strictly active protrusion. Third eyelid protrusion may be assisted by active retraction of the eyeball(s) by the retractor bulbi muscle action, causing an enophthalmos. The enophthalmos leads to passive protrusion of the third eyelid. Although the final common pathway for each reflex (i.e., third eyelid protrusion and eyeball retraction) is mediated by the CN6, each acts independently of the other.
- *Denervation of third eyelid sympathetics (Horner's syndrome):* Denervation of sympathetic neurons to the third eyelid leads to passive protrusion of the third eyelid. This, like the complete Horner's syndrome, is usually unilateral.
- *Third eyelid dysautonomia (so-called Haw):* Any imbalance in the sympathetic-parasympathetic system that innervates the muscles of the third eyelid may lead to protrusion of the third eyelids. This condition is usually bilateral and the protrusion is usually partial, but it may be extensive enough to impair vision. It is more frequently seen in cats but can be seen in dogs,

especially golden retrievers. The cause is unknown. Gastrointestinal dysfunction may antedate the protrusion of the third eyelids or be concomitant.

- *Third eyelid protrusion of tetanus:* Tetanus infections lead to contraction of the skeletal muscles, which is caused by the potent neurotoxin liberated by *Clostridium tetani*. The third eyelids protrude in tetanus as a result of contraction of the lateral rectus muscles, which *actively* protrude the third eyelids. Tetanus also causes contraction of the retractor bulbi muscles, along with all the other extraocular muscles, which leads to enophthalmos and a *passive* protrusion of the third eyelids. The antagonistic contraction of the facial muscles, including the opposing muscles of the eyelid, the orbicularis oculi muscle, and the levator palpebrae superioris muscle, creates a sardonic smile with almond-shaped eyelids.

Eyeball Position and Movement Abnormalities

Ocular Position and Alignment

Strabismus (abnormal eye position) may be congenital or acquired. It is the result of CNS dysfunction, as is commonly observed in Siamese cats, or from peripheral abnormalities to the motor nerves of the eye (CN3, CN4, and CN6). Disorders of the neuromuscular junction and extraocular muscle myopathy may also result in strabismus.

- *Comitant strabismus:* This is an ocular deviation that does not vary with different positions of gaze or with either eye fixating.
- *Incomitant strabismus:* This ocular deviation varies when the direction of gaze changes and/or when either eye fixates.

Ocular Movement

- *Range of movement:* When the range of movement is restricted during version and/or duction movements, *restriction caused by muscle paresis must be distinguished from mechanical restriction*. Such differentiation is accomplished by performing passive and active forced duction tests (see "Forced Duction Tests" under "Eyeball Position and Movement").
- *Oculomotor nerve (CN3) dysfunction:* Damage to the oculomotor (CN3) motor neurons (somatic efferents) leads to ptosis and an inability to rotate the eye upward, downward, or inward. When the unaffected eye is fixating straight ahead (primary position of gaze), the eye is held in a position of divergent (outward and downward) strabismus. The eye can be returned to midline by having the gaze directed to the side opposite the paralysis. The strabismus therefore is incomitant.
- *Trochlear nerve (CN4) dysfunction:* Trochlear nuclear lesions produce effects in the contralateral dorsal oblique muscle. Paralysis of the trochlear nerve results in extorsion (outward rotation) of the eye. This palsy can be readily seen in the cat because the dorsal apex of its elliptical pupil is tilted toward the lateral canthus (12 o'clock position of the eyeball is rotated temporally), whereas in species with round pupils like the dog, the dorsal retinal vessels can be used as one of the indicators of dorsal oblique dysfunction. Since the dorsal oblique muscle normally acts as a depressor on inward and downward gaze, in trochlear nerve dysfunction, leading the eye into this tertiary position of gaze reveals an inability to lower the eyeball in this direction of gaze. During normal outward movement the dorsal oblique muscle acts as an intorter (tilts the 12 o'clock eyeball position nasally). During outward gaze with trochlear palsy, the unopposed ventral oblique muscle exaggerates the extorsion of the eyeball.
- *Abducent nucleus and nerve (CN6) dysfunction:* Abducent nerve (CN6) lesions cause denervation of the lateral rectus muscle and ipsilateral palsy of horizontal gaze. This results in a convergent (incomitant type) strabismus when the normal eye is fixating in the primary position of gaze.
  - In abducent *nucleus* lesions, there is ipsilateral palsy of horizontal gaze during version movements toward the affected side. Neither eye crosses the midline during such version movements.
  - Lesions of the abducent *nerve* usually cause paralysis of both the lateral rectus and the retractor oculi muscles. When the abducent nerve is damaged, the contralateral eye crosses the midline during version movements toward the affected side.
  - The *trigeminoabducent reflex* can be lost if the motor neurons to the retractor bulbi muscles are disturbed.
  - The *vestibulo-ocular reflex* (see Chapter 125) is abnormal with a paralysis of any extraocular muscle.

Nystagmus

Nystagmus is a to-and-fro movement of the eyes and is a normal response to vestibular and optokinetic stimuli. Pathologic nystagmus occurs in disorders of the systems that stabilize images of objects on the retina during head rotations (vestibular system and optokinetic system) or stabilize images of moving objects on the retina (pursuit system).

Congenital Nystagmus

This type is caused by metabolic dysfunction or structural abnormalities of the brain or eye.

- *Sensory congenital nystagmus* is of either the jerk or the pendular type and is associated with disease in the visual sensory system (cataracts, persistent hyperplastic primary vitreous, retinal detachment, aberrant sensory visual pathways). The nystagmus of some Siamese cats serves as an example of congenital sensory nystagmus.

- *Motor congenital nystagmus* is of either the jerk or the pendular type and lacks any primary disease of the visual sensory system. Any decrease in vision is secondary to the nystagmus.

Acquired Nystagmus

This type of nystagmus is often associated with other neurologic signs. *Vestibular nystagmus* is an acquired jerk nystagmus caused by imbalance within the vestibular apparatus, with the corrective quick phases directed away from the side of the lesion.

- In *peripheral vestibular disease,* the nystagmus is mixed because the axis around which the eye rotates relates to the geometric relationships of the semicircular canals. *Vertical-torsional nystagmus* indicates posterior or anterior semicircular canal irritation depending upon the direction of the corrective quick phase's vertical movement. *Horizontal-torsional nystagmus* occurs from complete unilateral labyrinthitis. Positional nystagmus can also be seen in peripheral vestibular disease.
- In central *vestibular disease,* the nystagmus is more purely torsional, horizontal, or vertical. Positional nystagmus can be present.

Abnormalities of the Trigeminal Somatic Sensory System of the Eye and Orbit

If the corneal blink reflex is absent but a voluntary blink is present, the trigeminal nerve is dysfunctional. Evaluate corneal sensitivity with a Cochet-Bonnet aesthesiometer to quantify the extent of sensory loss. Corneal denervation as a result of injury to the trigeminal nerve causes *neuroparalytic (neurotrophic) keratitis,* which results in ulcerative keratitis, corneal degenerative changes, and loss of corneal sensation. Head withdrawal during noxious stimulation of the cornea is also lost because the relay of ocular pain information to the cortex via the thalamus for conscious perception of pain is interrupted. The eyelid position in neuroparalytic keratitis is symmetrical with that of the other eye. Absence of voluntary blink and the dazzle reflex, along with the loss of the corneal blink reflex, supports the diagnosis of facial paralysis.

TREATMENT

Treatment depends upon the type of pathology and the location, the extent, and the duration of the condition. Treatment often involves a combination of modalities, including both surgical and medical. Refer to other chapters in this text for specific treatment for the various afflictions of the eye and nervous system.

PROGNOSIS

In general, patients with diseases manifesting neuro-ophthalmic signs have a better prognosis if the pathology is only inflammatory. The prognosis in infectious diseases and cerebral vascular accidents is more guarded. Neoplastic conditions, although sometimes successfully treated, in general have a poor prognosis.

SUPPLEMENTAL READING

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Section

11 Cardiopulmonary System

John D. Bonagura

Chapter

142 Auscultation and Physical Diagnosis

Robert L. Hamlin

Physical examination follows the obtaining of a complete history and the consideration of the species, age, breed, and sex (see Chapter 1). Diagnosis, or at the very least a number of plausible diagnoses, may be made in many instances by history and signalment; however, following a thorough physical examination, a single, "most likely" diagnosis can be made with reasonable assurance in most patients with cardiac problems.

Physical examination is best performed in a systematic manner, initially conducting those portions that are least likely to aggravate or to cause discomfort to the patient. Physical examination of the cardiovascular system can be separated into four steps: *inspection, palpation, percussion,* and *auscultation*. What separates the physical examination from the remainder of the cardiac examination is the close relationship between the veterinarian and the patient, and, with the exception of the stethoscope, the absence of elaborate instrumentation such as radiography, electrocardiography, or echocardiography.

INSPECTION

Inspect the patient while obtaining the history. Perform the inspection while the animal enters the room; while the pet stands, sits, or walks; while the owner supports the pet; and while the pet stands alone.

Condition, Attitude, and Posture

- *Body condition* of the patient is classified according to the degree of fat.
  - Normal overweight animals usually are not ill from heart failure but may manifest signs caused by pulmonary disease (e.g., chronic obstructive lung disease, pulmonary fibrosis).
  - Animals with moderate to long-standing heart failure are often thin to cachectic.
- *Attitude* of an animal with heart failure is usually depressed.
- *Posture* of animals with heart failure is often:
  - Standing—reluctant to lay down—with thoracic limbs abducted and neck extended to ease ventilation.
  - Swayback with the tail between the legs because of muscular weakness or occasionally caused by digitalis toxicity (from overdosage or impaired renal excretion related to dehydration or primary renal disease). Swayback can also result from electrolyte imbalance—in particularhypokalemia—caused by prolonged or excessive use of diuretics without consumption of sufficient electrolytes.
- Dogs with cardiomyopathy often have weakness of skeletal muscles and dogs with heart failure are often exhausted owing to the work of breathing.

Mucous Membrane Color

- Mucous membranes may be *pink*, *pale*, or *cyanotic*.
- Normal mucous membranes have a deeply saturated pink color. Gentle pressure on the gums will lead to blanching (whiteness) of the membranes. The *capillary refill time* needed to regain normal coloration is about 2 seconds or less.
- Delayed refill time generally indicates peripheral vasoconstriction, often as a compensatory response to reduced arterial blood pressure.
- Bright red membranes associated with a very short refill time may indicate peripheral vasodilation, as might occur with septic shock or during treatment with potent arterial vasodilator drugs.
- Mucous membranes are pale in some patients. *Pallor* indicates anemia or low cardiac output with reflex vasoconstriction (e.g., low output heart failure, severe aortic stenosis, cardiac tamponade), but without pulmonary congestion that often causes cyanosis.

Cyanosis

Cyanosis indicates the finding of dark-blue to purple colored mucous membranes caused by poorly oxygenated (desaturated) hemoglobin. The main reasons for cyanosis are respiratory disease and right-to-left shunting due to congenital heart disease.

- *Methemoglobinemia* (congenital or acquired from drug toxicity) may also alter the color of the mucous membranes.
- Cyanosis to the mucous membranes may be observed in late stages of congestive heart failure or in puppies or young dogs with tetralogy of Fallot or other congenital heart defects with right-to-left shunts. (see Chapter 154)
- Cyanosis occurs much more commonly in all types of pulmonary disease.
- Mucous membranes may be dark red in stages just prior to frank cyanosis.
- Long-standing cyanosis most commonly indicates pulmonary disease, since an animal cyanotic from heart disease usually either dies from the severity of the disease or the cyanosis is relieved with therapy.

Abdominal Distention and Edema

- Abdominal distention may be a result of gas in the gastrointestinal (GI) tract from aerophagia associated with chronic pulmonary disease, respiratory failure, primary GI disease, obesity, abdominal wall weakness (e.g., Cushing's disease) or fluid accumulation.
- Ascites and enlargement of abdominal organs (especially the liver) may indicate systemic venous hypertension or passive congestion due to right-sided heart failure or pericardial disease.
- Primary disease of abdominal organs (e.g., neoplasia) also can cause abdominal distention.
- Pitting edema of the limbs, brisket, and prepuce can be caused by severe right-sided heart failure.

▼ ***Key Point*** Subcutaneous edema in the absence of ascites or jugular distention *argues* against a diagnosis of congestive heart failure

Pattern of Ventilation

Observing the pattern of ventilation is extremely important. Characterize the rate and depth of breathing, and identify dyspnea.

- *Rate of breaths per minute* should be between 12 and 20 for dogs and only slightly higher for cats, but may increase from excitement, fever, anxiety, warm environment, chronic respiratory disease, respiratory failure, left-sided heart failure, or pulmonary injury.
- *Depth of ventilation* is difficult to quantify, but hyperpnea (increased depth) is often a sign of blood gas derangement (e.g., response to metabolic acidosis). It is not often observed in heart disease except with severe pulmonary edema. In upper airway obstruction both the inspiratory and expiratory phases of ventilation may become slower and exaggerated. In pleural diseases, the depth is generally shallow and the rate rapid. An exaggerated expiratory phase is typical of bronchial obstruction.
- *Dyspnea* (labored ventilation or respiratory distress) may occur as increased rate and/or depth of ventilation or merely as increased effort. With dyspnea one observes:
  - Bulging eyes.
  - Flaring nares.
  - Outward motion of thoracic limbs.
  - Reluctance to lay down.
  - Abdominal "pumping."
  - Extension of neck and open mouth breathing
  - A sucking in of the copula (the indentations at the thoracic inlet) during inspiration
- *Pulmonary retraction* is an indention of the thoracic wall caused by fatigue of muscles of ventilation. Regions of the thoracic wall affected must generate greatest tension during ventilation and do not have assistance from thoracic limbs. Pulmonary retraction produces an "hourglass" configuration to the thorax (most evident when viewing the dorsoventral radiograph).

Cough

Cough is a sign of both heart and lung disease. It may be characterized as follows:

- A hacking, honking, brassy cough indicates disease of the large airways, such as tracheobronchial collapse, compression of the left mainstem bronchus due to mitral regurgitation or generalized cardiomegaly, tracheobronchitis, or bronchopulmonary parasitism. This type of cough is seldom due to injury of the parenchyma of the lung and therefore is uncommon in pulmonary edema or pneumonia.

- Subtle or "half-hearted" coughing may be caused by pulmonary edema, pneumonia, or diaphragmatic hernia.
- So-called moist or truly productive coughs usually indicate an exudative process; however, in *late stages of left-sided congestive heart failure* it is common to have serosanguineous pulmonary edema fluid expectorated to gush from the nares and/or mouth.

Jugular Vein Evaluation

Analysis of the *jugular* vein (Fig. 142-1) is simpler if the hair is clipped from around the jugular furrow or if it is moistened with 70% alcohol. Look for pulsations in the vein and estimate the pressure distending it.

- The jugular vein normally collapses totally when the long axis of the head is tilted up at an angle of 45 degrees with the horizontal.
- The jugular vein also normally collapses during inspiration and immediately after the second heart sound.
- If the jugular vein does not collapse, the venous pressure may be elevated owing to heart failure, chronic obstructive pulmonary failure (COPD)/pulmonary fibrosis (PF), or ventricular filling restriction due to pericardial disease.
- A firm, distended jugular vein that collapses briefly immediately after the second heart sound is consistent with cardiac tamponade from pericardial disease. (see Chapter 151) Causes in dogs include hemorrhage into the pericardial sac due to a bleeding neoplasm or rupture of the left atrium with severe mitral regurgitation. Constrictive pericarditis and chronic respiratory disease also can cause similar jugular venous changes.

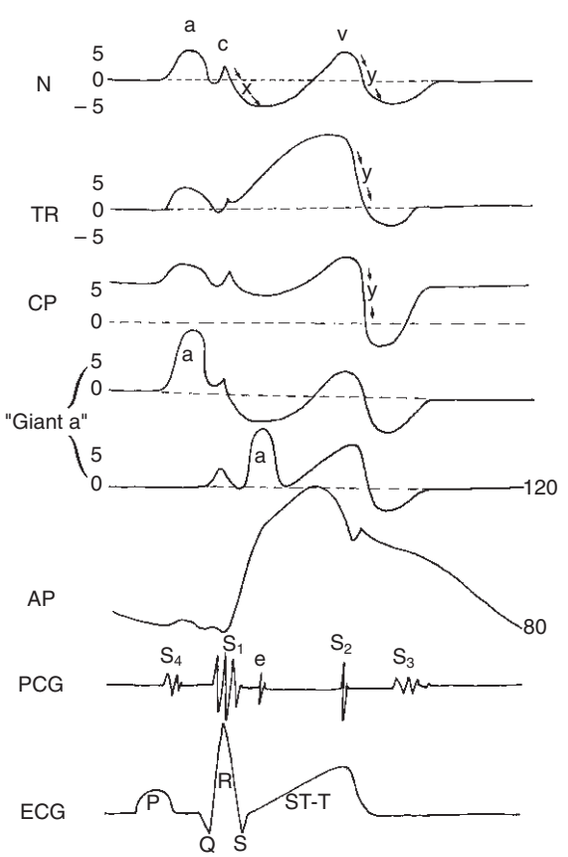


Figure 142-1. Analysis of venous pulses. A normal pulse is shown for reference (N), as are systemic arterial pressure (AP), phonocardiogram (PCG), and electrocardiogram (ECG). Abnormal pulses shown are those produced by tricuspid regurgitation (TR) and constrictive pericarditis (CP); also shown are two types of cannon, or giant, *a* waves.

Vigorous Pulsation of the Jugular Vein

- Jugular venous pulses ("cannon *a* waves") occurring at rates exceeding 120/min with a very slow ventricular rate slow (usually below 60/min) indicates third-degree (complete) or high-grade second-degree atrioventricular block.
- If *cannon a-waves* occur just before the first heart sound it may rarely indicate tricuspid stenosis or possibly stiffness of the ventricles (e.g., pulmonic stenosis).
- Cannon waves (*giant c-v waves*) observed between the first and second heart sounds indicate tricuspid regurgitation.

Hepatojugular Reflux

- Pushing on the abdomen of a standing dog displaces the liver dorsad and "milks" blood from the liver to the right side of the heart, increasing systemic venous return.
- If the right ventricle cannot pump the extra blood through the lungs, or if right ventricular filling is restricted owing to pericardial tamponade or constriction, the extra venous return "wells up" in the atrium and systemic veins. This situation produces added jugular venous distention or a positive hepatojugular reflex.

Miscellaneous

- Inspect the pharynx and mouth to identify: tonsillitis, pharyngitis, salivary mucocele (rannula), elongated soft palate, neoplasia, or periodontal disease.
- Watch the animal walk to identify and to quantify:
  - Exercise intolerance related to heart failure or chronic respiratory disease.
  - Weakness due to heart failure or conditions such as severe aortic stenosis.
  - Neuromuscular or skeletal disease.

PALPATION

Technique

Perform palpation with the animal standing and being held by an assistant with the assistant's hands cupped gently around the patient's neck.

- The examiner stands at the side or back of the animal.
- The examiner places his or her hands in the axilla and slides them caudad stopping at:

1. The second to third intercostal space.
2. The fourth to sixth intercostal spaces.
3. Just caudad to the rib cage.
4. All points on the abdomen.
5. The femoral arteries.

Thorax

- Determine where the heart "thumps" most vigorously against the thoracic wall. The point of maximal impulse is normally at the fifth intercostal space 2–3 fingerbreadths from the left sternal border *and* at the right third intercostal space near the right sternal border.
- The apical impulse starts at the first heart sound and peaks at the time of aortic opening. This impulse can be counted to obtain a heart rate, identify arrhythmias, and compare the frequency to the pulse rate (to detect pulse deficits).
- Cardiomegaly or space-occupying intrathoracic masses may displace the cardiac impulse.
- Ventricular hypertrophy may create a more prominent cardiac impulse.
- Precordial thrills (vibrations from murmurs) indicate the presence of a loud murmur and generally correlate to the point of maximal murmur intensity during auscultation.
- Gently palpate the trachea and then the thorax while observing the pattern and effort of ventilation.

Abdomen

- Gently palpate under caudal ribs to identify hepatomegaly.
- Palpate the abdomen for ascites, organomegaly, or neoplasia.

Femoral Pulses

- *Rate*—Palpate the femoral arteries for pulse rate, which in dogs and in cats is relatively independent of body size.

Heart Rates	Dog	Cat
Quiet (asleep)	50–90	90–120
During examination	80–160	140–220
Exercise	230	230

- *Rhythm*—Evaluate the cardiac rhythm by careful palpation of the pulse rate and regularity.
- *Respiratory sinus arrhythmia*—The average rate is usually as described previously for sleep. The rate speeds up during inspiration but seldom more than three or, at most, four heartbeats during an inspiration. More than four beats during inspiration may indicate abnormal ventilation caused by chronic pulmonary disease. Pulse rate slows during exhalation, occasionally to as low as 30 beats/min but only very briefly.

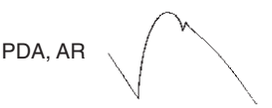
Pulse Rate and Rhythm

- *Atrial fibrillation* or frequent short bursts of supraventricular or ventricular tachycardia are characterized by rapid pulse rate; irregularly irregular rhythm (i.e., *not* in sync with ventilation); variable intensity; and *pulse deficits* (fewer femoral pulses than heartbeats).
- Rapid and irregularly irregular pulses are found with atrial fibrillation or with supraventricular or ventricular tachycardias in brief bursts.
- However, pulse rate in atrial fibrillation may not be rapid in large-breed dogs with concurrent hypothyroidism; when there is preserved myocardial function; in dogs with relatively slow-conducting atrioventricular nodes approaching complete heart block; or in dogs taking drugs that block atrioventricular nodal conduction (digoxin, beta-blockers, diltiazem).
- Occasionally supraventricular or ventricular *premature beats* occur singly and are characterized by apparent single skipped pulses followed by a pulse stronger than usual.
- Regularly irregular pulses in sync with respirations are found with *sinus arrhythmia.*
- "*Skipped" beats* (when combined with cardiac auscultation) are found with single premature depolarizations.

Pulse Character

- *Force*—Assess the force of the arterial pulse as normal, bounding (hyperkinetic), weak (hypokinetic), or sharp and brief (see Table 142-1 and Fig. 142-1).
- Weak pulses are found in:
  - Heart failure.
  - Aortic stenosis.
  - Dilated cardiomyopathy.
- Extremely bounding (water-hammer) pulses are found in:
  - Patent ductus arteriosus.
  - Aortic regurgitation.
  - Complete heart block with very slow ventricular rate.
- Sharp, "tapping" pulses are often found when the arteries are relatively stiff due to contraction of vascular smooth muscle in response to neuroendocrine activation in heart failure.
- *Absent pulses*—Loss of palpable femoral pulses are found in cats or cats with aortic embolism. In most cats the underlying cause is cardiomyopathy or endocarditis.
- Measurement of *arterial blood pressure* is a logical extension of the physical examination. This procedure is described in Chapter 153.

Table 142-1. TYPICAL SYSTEMIC ARTERIAL* PULSES FOR ANIMALS WITH VARYING PHYSIOLOGIC AND/OR PATHOLOGIC STATES

	Character	Pressure Systolic/ Diastolic	Pressure Differential	Rate	Pulse Character
Normal animal	Normal	120/80	40	Normal	
Patent ductus arteriosus (PDA) or aortic regurgitation (AR)	Bounding	160/40	120	Increased	
Aortic stenosis (AS) or early heart failure (HF)	Weak	90/60	30	Increased	
Mitral regurgitation (MR), ventricular septal defect (VSD), late heart failure (HF), or hyperkinetic ventricle (HK)	Sharp, brief	120/80	40	Rapid	

*For example, femoral artery.

PERCUSSION

This is the technique (Fig. 142-2) of thumping on the thorax and/or abdomen to determine the relative density of structures underneath the points of percussion (see also Chapter 166).

Thoracic Percussion

- The normal notes of percussion may be learned by percussing thoraces from many normal male and female animals of varying ages and body conformations. Regions of cardiac dullness are less obvious in quadrupeds than in primates, but large pulmonary lesions or pleural effusion may be detected effectively by percussion.
- Hyper-resonant notes sound like a tympany drum and indicate air-trapping in the lung (as with COPD) or a gas-filled structure (e.g., pneumothorax, gas-filled stomach) underneath. (Hyper-resonant sounds may be illustrated by drinking a can of carbonated beverage, jumping up and down for 15 seconds, and then thumping on the left side of your abdomen just over your stomach.)
- Dull notes sound "dead," like thumping one's skull, and indicate a dense, usually water-filled structure (e.g., pneumonia, pleural effusion, pulmonary edema, consolidation) underneath.
- See Figure 142-2, which integrates the findings of percussion and auscultation for the differential diagnoses of edema/pneumonia; pneumothorax;

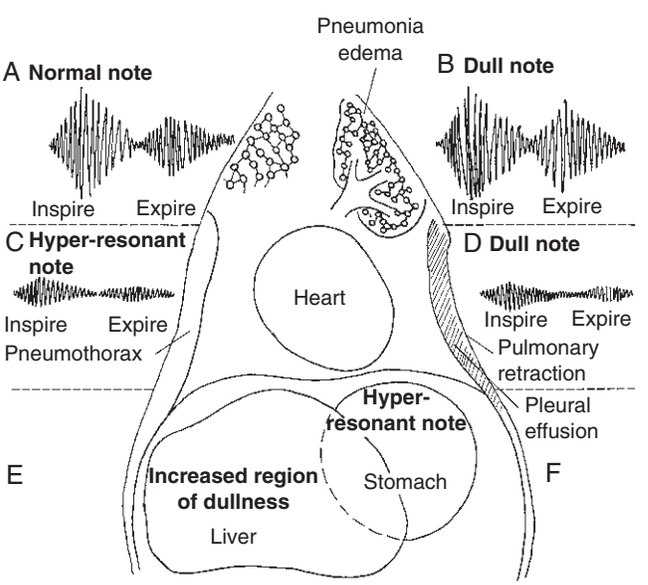


Figure 142-2. Schematic diagram of thorax and cranial portion of the abdomen viewed from the ventral aspect. *A* indicates the normal breath sounds and percussion. *B* shows a dull percussion note and louder than expected inspiratory and expiratory sounds due to pneumonia or edema. *C* represents the hyper-resonant percussion note and diminished breath sounds caused by pneumothorax, as illustrated by air between the thoracic wall and collapsed lung. *D* demonstrates a dull percussion note and diminished breath sounds due to pleural effusion, shown as density between thoracic wall and lungs. *E* indicates dull percussion notes because of an enlarged, dense liver. *F* is a hyper-resonant percussion note caused by gas in the stomach.

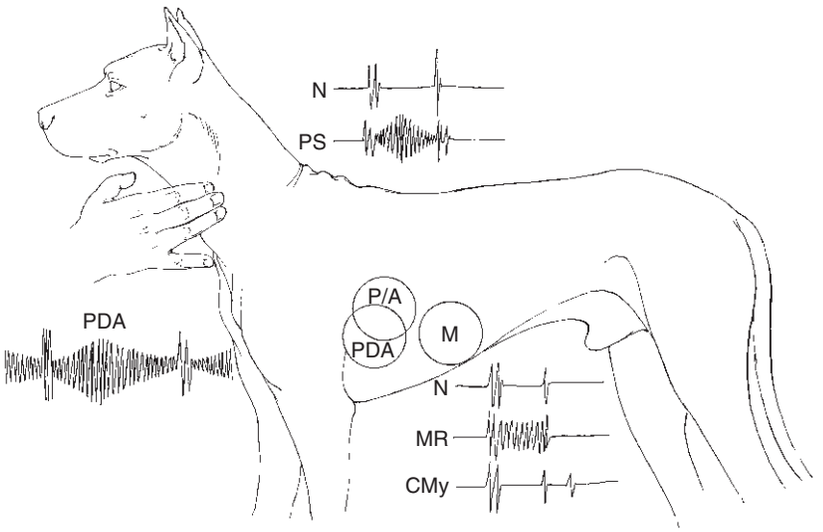


Figure 142-3. Regions where murmurs are heard best on the left hemithorax. Diagrams of murmurs typical of specific defects are shown. Normal (N) heart sounds are indicated above the murmurs of pulmonic stenosis (PS) and mitral regurgitation (MR). The diastolic gallop heard with dilated cardiomyopathy (CMy) is shown below the murmur for mitral regurgitation. PDA is the continuous murmur of patent ductus arteriosus. P/A is the ejection murmur of pulmonic stenosis or aortic stenosis. (Note: Loud murmurs of aortic stenosis may be heard equally on the right base as well.) M demonstrates systolic regurgitant murmur of mitral regurgitation.

pleural effusion; lung consolidation/neoplasia; and COPD/PF.

Abdominal Percussion

- *Hepatic enlargement* generates a dull note over a larger area than expected because the liver is an exceptionally dense structure.
- *Bloated (air-filled) stomach* is distended and generates a hyper-resonant percussion note because skin serves as the head of the drum and the gas in the stomach serves as the air-filled kettle of the drum. The abdomen bloated with gas produces an hourglass configuration with pulmonary retractions. It can be differentiated from organomegaly and/or ascites by the following:
  - It is tympanic (hyper-resonant).
  - It comes and goes quickly.
  - Air is often noted in the esophagus on thoracic radiography.

AUSCULTATION – OVERVIEW

- Auscultation is defined as listening to heart and breath sounds, usually with the aid of a stethoscope.

Methods of Auscultation

Optimal examinations are fostered by:

- A quiet environment, a quiet patient, and a tranquil examiner.
- An animal that is standing and restrained by an assistant standing to the front of the patient and, in dogs, holding the mouth closed to discourage panting.
- Positioning of the auscultator to the back or side of the patient while keeping a hand or arm between the pet's mouth and his or her face.
- A systematic approach to examination of the chest (Figs. 142-3 and 142-4).
- Appropriate use of the stethoscope.
- Understanding of normal heart and breath sounds.
- Integration with other findings—observation, palpation, and percussion.

Stethoscope

- Preferably use a stethoscope with ear pieces large enough to occlude most of the external acoustic meatus but not so large as to be airtight. The internal canal of the ear piece must be clean, and the outside should be sanitized if used by more than one person.
- Two tubes of commercial stethoscope tubing extend from ear pieces to chest piece (these may be wrapped within a single tube).
- There are a wide variety of stethoscope chest pieces used in modern instruments, but they represent variations of the traditional diaphragm and the bell.
- In traditional stethoscopes there is a single hard rubber or plastic diaphragm for characterizing high-pitched sounds and a bell—preferably a deep trumpet bell—for relatively low-pitched sounds.
- The diaphragm does not amplify high-pitched sounds but simply attenuates low-pitched sounds; whereas the bell—particularly the deep trumpet bell—does not preferentially attenuate sound of either frequency.
- Some newer models employ "tunable" diaphragms wherein varying pressure on the chest piece deter-

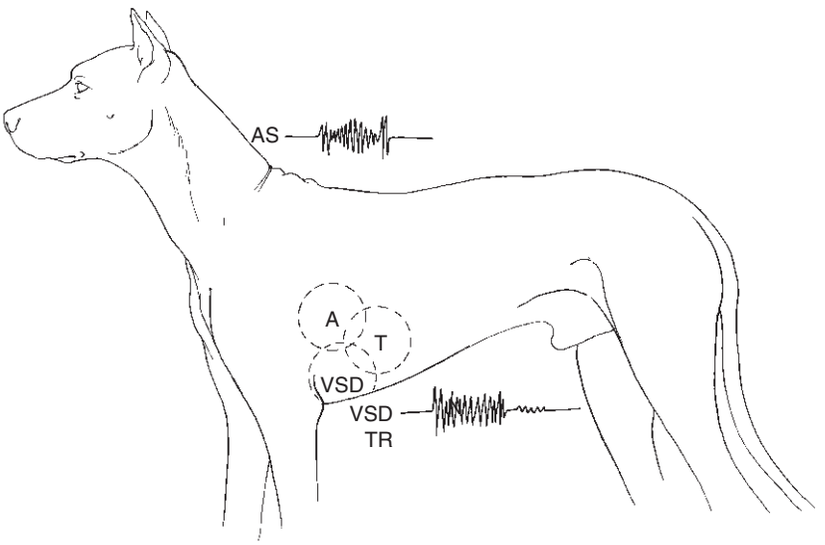


Figure 142-4. Left lateral view demonstrating where murmurs are heard best on the right hemithorax. A is the systolic ejection murmur of aortic stenosis (AS) and may be equally loud at left and right hemithorax. Systolic regurgitant murmur of ventricular septal defect (VSD) is heard best at the right sternal border. A soft diastolic murmur may also be heard from concurrent aortic regurgitation or increased flow across the mitral valve. T indicates where the systolic murmur of tricuspid regurgitation (TR) is heard best.

mines the frequency response characteristics of the system.

Auscultation of the Lungs

Examine the lungs to detect normal breath sounds and abnormal pulmonary sounds. Auscultate over the larynx, trachea, thoracic inlet, and along a number of ventral and dorsal, cranial and caudal locations on each side of the thorax. When possible, keep the patient's mouth closed to prevent panting. Gentle pressure over a nostril may encourage a deeper breath. See Fig. 142-2 for normal and abnormal breath sounds and percussion.)

- Normal *vesicular breath sounds* (sounds made by air tumbling through airways) are heard with sounds of inspiration being louder than sounds of expiration. They are transmitted best in the direction that the air flows, thus inspiratory vesicular breath sounds are heard over the basilar lobes whereas expiratory sounds are either absent or very soft.
- The percussion note of normal resonance is not too dull and not too resonant.

▼ ***Key Point*** In order to know what is "normal," you must auscultate and percuss hundreds of normal animals of various ages, breeds, and conformations.

Auscultation of the Heart

Examine the heart to detect the heart sounds, cardiac rhythm, sound intensity, murmurs, and other abnormalities. Begin by listening over the left apex and the move the stethoscope craniodorsally to the aortic valve area. Identify the first and second heart sounds and make note of any additional sounds such as a midsystolic click or a diastolic gallop sound. Systematically listen across the various areas of auscultation (shown in Figures 142-3 and 142-4). Once identified, classify heart sounds according to:

- *Frequency*—to assess autonomic tone and heart rhythm.
- *Regularity*—to detect arrhythmias.

▼ ***Key Point*** An animal ill from heart disease usually manifests low vagal tone and a reduced—or absent—sinus arrhythmia. Conversely, patients ill from lung disease often manifest an exaggeration of the sinus arrhythmia.

- Intensity
  - The normal first sound (S_1) is longer and duller and most prominent over the left apex. The normal second heart sound (S_2)is higher pitched and louder over the aortic and pulmonary valve areas. Occasionally in dogs, a subtle splitting of the normal second sound may be detected during inspiration.
  - A "booming" S_1 heart sound indicates forceful contraction, rapid atrioventricular conduction (short PQ interval in the ECG), or skinny thorax. A loud first sound also may be detected in dogs with advanced mitral regurgitation with preserved left ventricular function.
  - A "soft" S_1 heart sound indicates weak ventricle, long atrioventricular conduction (PQ interval), obesity, hyperinflation of lungs, pleural effusion, or pneumothorax.
  - A loud S_2 may indicate systemic or pulmonary hypertension.
- Presence of murmurs or a corresponding precordial thrill—a murmur is a prolonged audible vibration during a usually silent period of the cardiac cycle; a thrill is a palpable manifestation of a murmur. A

precordial thrill indicates a murmur of at least grade IV (out of VI).

CLINICAL ABNORMALITIES OF AUSCULTATION, PERCUSSION, AND PALPATION

Findings in Respiratory Disease

Bronchial Disease (see Chapter 162)

- Expiratory wheezes are considered relatively specific for narrowing of intrathoracic airways, particularly in the bronchial tree. Potential causes include:
  - Narrowing of multiple bronchi, as with bronchitis and bronchial asthma
  - Cuffing of bronchi or reactive bronchoconstriction from pulmonary edema or left-sided heart failure
  - Obstruction or collapse of a principal bronchus at the level of the carina. This may indicate heart enlargement (left atrial), compression from hilar lymph nodes, or primary bronchial wall disease/collapse
- Sonorous rhonchi (rattling sounds), localized to the chest, may be indicative of fluid in larger airways as with bronchitis or bronchopneumonia.

Abnormal breath sounds may be evident even before use of the stethoscope. In general, major airway obstruction leads to loud, audible ventilation; whereas, detection of pleural space or lung parenchymal disease often requires intense concentration and good technique.

Upper Airway Obstruction (see Chapter 161)

- Stertor or loud, inspiratory snoring sounds often indicate upper airway obstruction (redundant soft palate; soft tissue mass; nasopharyngeal obstruction). The origin of these sounds must be localized with the stethoscope to the laryngeal and pharyngeal area, as they are likely to be referred to the chest and be confused with pulmonary rhonchi.
- High pitched, inspiratory stridor localized to the larynx usually indicates glottic obstruction or laryngeal paralysis.
- Reversed sneezing is typically due to nasopharyngeal disease or fluid accumulation caudal to the nasal cavity.
- Auscultation or palpation of "honks" related to tracheal wall vibrations may be identified in dogs with tracheal collapse.

Pulmonary Edema, Pneumonia, and Fibrosis

- Breath sounds are termed bronchial or bronchovesicular (i.e., sounds are louder in both inspiration and expiration but are much louder and higher pitched during expiration). The increased intensity arises from these sounds being "made" normally at larger airways but being transmitted better than usual via fluid-logged parenchyma.
- Crackles or rales are also considered signs of parenchymal or very small airway disease.
- Crackles may be audible without the stethoscope, especially in cases of severe pulmonary fibrosis.
- In most instances, detection of crackles requires careful auscultation during inspiration.
- Crackles are indicative of pulmonary parenchymal diseases including edema, pneumonia, hemorrhage, and fibrosis.
- Percussion note is dull when the lung density is increased owing to fluid-filled parenchyma.

Pneumothorax (see Chapter 166)

- All breath sounds are softer than normal because the free air space between the stethoscope chest piece and the lung insulates against the transmission of sound.
- Percussion note is hyper-resonant (i.e., sounds like thumping on a tympany drum) because the thoracic wall acts like a drumhead stretched over an air-filled chamber underneath.

Pleural Effusion (see Chapter 164)

- All breath sounds are softer than normal because free liquid between pulmonary parenchyma and chest wall reflects sound away from its pathway to the stethoscope chest piece.
- Percussion note is dull because the water-filled cavity vibrates at high frequency and low amplitude and is dampened rapidly.

Findings in Heart Disease

The approach to auscultation is somewhat personal and may include examination of specific "valve areas" or more general regions over the heart. Auscultation in the cat differs somewhat from that of the dog because the feline heart is relatively small, more horizontal in axis, and discrete valve areas are more difficult to identify. Some of the key points of cardiac auscultation are indicated below. Other details can be found in chapters throughout this section.

Mitral Valve Region (see Fig. 142-3)

- This region is also known as the left apical region and is at the left fifth intercostal space approximately 2 to 3 fingers' breadth from the left sternal border. In the cat it is close to the sternum at the level of the palpable apical impulse.
- Here S_1 is louder, longer in duration, and lower pitched than S_2. S_1 is mimicked as a "lub;" S_2 is mimicked as a "dup."
- Sounds of mitral valve disease are usually most evident here, but do tend to radiate to the right directly across from the left apex.

- Mid-systolic clicks are often detected in dogs with early mitral valve degeneration and prolapse of the mitral valve.
- The murmur of mitral regurgitation extends from S_1 to, and often through, S_2, and is louder during expiration.

▼ ***Key Point*** The intensity of the murmurs of mitral and tricuspid regurgitation does *not* consistently correlate with the severity of the regurgitation and is influenced profoundly by the force of contraction of the ventricle.

- In dogs and cats with dilated cardiomyopathy, there is often an S_3 gallop producing a set of sounds like lub-dup-uh, especially when heart failure has developed.
- In case of left ventricular hypertrophy with preserved atrial function there may be a prominent S_4 gallop, evident at the apex and often at the base as well.

Craniodorsal Cardiac Base (Pulmonary Artery Region)

- Sounds in this area tend to originate in the aortic valve area caudally, the pulmonic valve area cranioventrally, the ascending aorta, or the main pulmonary artery. This is normally where S_2 is heard best. In cats, the "base" extends more ventrally than in dogs and many feline ejection murmurs are evident close to the sternum but cranial to the apex beat.
- There may be splitting of S_2 caused by the pulmonic valve closing later than the aortic valve—this is particularly pronounced during inspiration during relatively slow heart rates. Wide splitting may be detected with an atrial septal defect or severe pulmonary hypertension, especially when there is also a right bundle branch block.
- Functional ejection murmurs from sympathetic drive, anemia, fever, bradycardia, and the athletic heart are loudest here. Innocent puppy and kitten murmurs are also most likely to be detected in this region.
- The murmur of pulmonic stenosis (see Chapter 154) is heard loudest in this region. It is usually very loud and radiates dorsad, it is shorter in duration than mitral regurgitation, often very rough, and accentuated during inspiration.
- The murmur of aortic stenosis (see Chapter 154) is heard equally loudly here and at the same position on the right hemithorax, but it is usually louder during expiration. Very soft aortic flow murmurs tend to be louder at the left cardiac base.

▼ ***Key Point*** The intensity and duration of the murmur of pulmonic or aortic stenosis generally correlates well with the severity of the stenosis.

Patent Ductus Arteriosus Region

- The continuous murmur of the patent ductus arteriosus (PDA) is heard the loudest at the left third intercostal space over the base of the heart. With this murmur, S2 may not be heard because the murmur of blood rushing through the PDA is loudest during late systole. See Chapters 154 and 155 for more on PDA.

Right Hemithorax

- At the region of the right fourth intercostal space at the sternal border, S_1 is louder than S_2. The systolic murmur of typical perimembranous ventricular septal defect is heard best here, and is louder during exhalation.
- At the region of the right fifth intercostal space above the costochondral junction the systolic murmur of tricuspid regurgitation is heard best and is louder during inspiration. This murmur may be particularly intense with a palpable thrill in the setting of pulmonary hypertension.
- At the region of the right base the systolic murmur of aortic stenosis is almost as loud as at the left base and is louder during exhalation than during inhalation. In cases of severe aortic stenosis, the murmur is frequently louder on the right side.

Chapter

143 Cardiovascular Radiography

John D. Bonagura / Valerie F. Samii

Thoracic radiography and echocardiography are useful in the recognition and assessment of cardiovascular diseases. Other imaging modalities, such as cardiac magnetic resonance imaging, gated computerized tomography, and radionuclide studies, are uncommonly used in routine cardiology practice and have limited indications at this time. This chapter emphasizes the use of radiography in cardiac diagnosis.*

When combined with the results of the clinical examination, thoracic radiographs may contribute to the specific cardiac diagnosis, verify the presence of congestive heart failure (CHF), and assist in the differential diagnosis of respiratory signs such as coughing and dyspnea. Analysis of thoracic radiographs in the diagnosis of respiratory diseases is discussed in more detail in Chapter 159. Essential principles in the application of echocardiography are considered at the end of this chapter. More specific applications of radiography and echocardiography are discussed in other chapters throughout this section.

GENERAL PRINCIPLES OF CARDIAC RADIOGRAPHY

▼ ***Key Point*** The importance of the technical quality of thoracic radiographs is often underestimated. A radiograph with inadequate penetration, exposure during expiration, or poor patient positioning can be very misleading.

Technical errors can be avoided by addressing the following technical points prior to radiographic evaluation for cardiac disease.

Technical Considerations

- The practice should develop routine protocols for thoracic radiography of the cardiac patient.
  - At a minimum, two views, a right or left lateral projection and either a dorsoventral (DV) or a ventrodorsal (VD) projection, are needed for thoracic evaluation.
  - In general, a DV and right lateral projection are usually recommended for cardiac evaluation.
  - In some situations, both right and left lateral projections and VD and DV views are obtained.
- Radiographic technique (see Chapter 4):
  - Expose films at the peak of inspiration.
  - Remember that expiratory films are ineffective for evaluating the lung parenchyma for interstitial pulmonary edema.
  - A long gray-scale (high kilovolt peak, low milliampere-second) technique is most helpful for assessing thoracic disease. Underexposure mimics pulmonary disease by increasing apparent lung density, whereas overexposure leads to an underestimation of the severity of pulmonary changes.
  - Rotation often accentuates normal structures such as the main pulmonary artery on the VD projection or the left atrium or right ventricle on the lateral projection.
  - False apex shifting due to patient rotation on the VD projection may cause overestimation of ventricular size.
  - Consistent positioning and exposure techniques should be used when obtaining follow-up radiographs. This is particularly important when following patients with CHF.

Normal Lateral Radiograph (Fig. 143-1)

Dogs

The following are guidelines for understanding the normal canine lateral thoracic radiograph:

- The cardiac outline is roughly tear-shaped with a narrowed, ventral apex.
- *Orientation*—The long axis creates approximately a 45-degree angle with the sternum (varies with breed).
- *Location*—The cardiac silhouette extends from the third to sixth ribs, and the heart and diaphragm usually touch or overlap.
- *Size*—Ventricles occupy approximately three intercostal spaces. Using the vertebral score method (discussed below) the vertebral heart score (VHS) ranges from 8.5 to 10.6 (mean, 9.7), although studies in specific breeds have demonstrated breed-specific variation.
- The cardiac borders on the lateral projection represent the following:

*The contribution to this chapter made by Dr. C. Wendy Myer, Diplomate ACVR, is gratefully acknowledged.

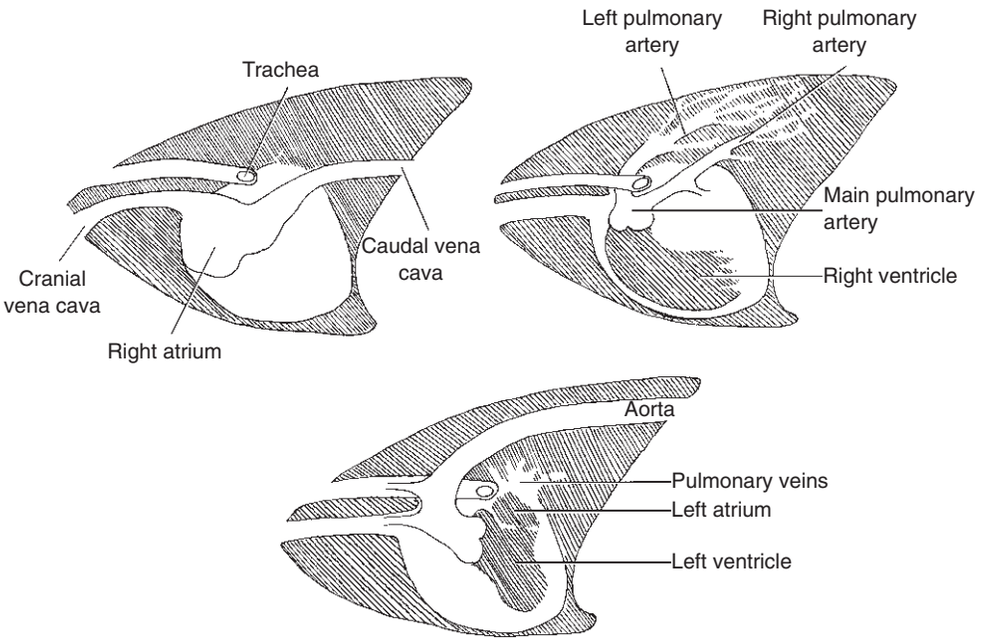


Figure 143-1. Three lateral views of the normal heart showing chamber location.

- Cranial—Rounded border, right ventricle and auricle
- Caudal—Straight border, left ventricle and atrium
- Dorsal—Both atria, pulmonary arteries, cranial and caudal vena cava, and aorta

- *Quadrants*—The cardiac silhouette can be divided into sections on the lateral radiograph by drawing a line from the tracheal bifurcation to the apex parallel to the cardiac axis and a second horizontal line at the level of the vena cava.
  - Atria are dorsal to the horizontal line.
  - Ventricles are ventral to the horizontal line.
  - Right-sided heart structures make up the cranial three-fifths of the heart shadow (remember that the two ventricles overlap owing to the curved ventricular septum).
  - Left-sided heart structures make up the caudal two-fifths of the heart shadow.
- There are some differences between right and left lateral films. Importantly, the left atrial border is more prominent and the cardiac apex appears slightly more elevated on left lateral films.

Cats

The following are guidelines for understanding the normal feline lateral thoracic radiograph:

- The cardiac outline is more elongated and elliptical than that in the dog.
- Cardiac borders are similar to those in the dog.
- *Orientation* is more variable than that in the dog, with a more horizontal major cardiac axis.
- *Location*—The heart and diaphragm are separated by one to two intercostal spaces.
- *Size*—The ventricles occupy approximately 2 to 2.5 intercostal spaces and the heart extends about two-thirds of the VD height of the thorax. The VHS is typically 8.5 to 9.0 in cats.

Normal Ventrodorsal or Dorsoventral Radiograph (Fig. 143-2)

Dogs

The following are guidelines for understanding the normal canine VD or DV thoracic radiograph:

- The cardiac outline has a curved (convex) right border and a relatively straight left border.
- *Orientation*—The apex is slightly to the left of midline, approximately at a 30-degree angle with the spine. The cardiac apex appears slightly closer to the midline on the DV as opposed to the VD projection.
- *Location*—The cardiac silhouette extends from the third to the eighth vertebrae, often overlapping the diaphragm.
- *Size*—The cardiac-thoracic index is about 60% to 65% of the thorax as measured from right to left.
- Cardiac borders (using the clock face analogy):
  - 11 to 1 o'clock—Aortic arch (seen better on the DV projection)
  - 1 to 2 o'clock—Main pulmonary artery
  - 2 to 3 o'clock—Left auricular appendage
  - 3 to 6 o'clock—Left ventricle (includes the apex)
  - 6 to 9 o'clock—Right ventricle
  - 9 to 11 o'clock—Right atrium

Cats

The following are guidelines for understanding the normal feline VD or DV thoracic radiograph:

- The cardiac outline is slightly more elongated than that in the dog.

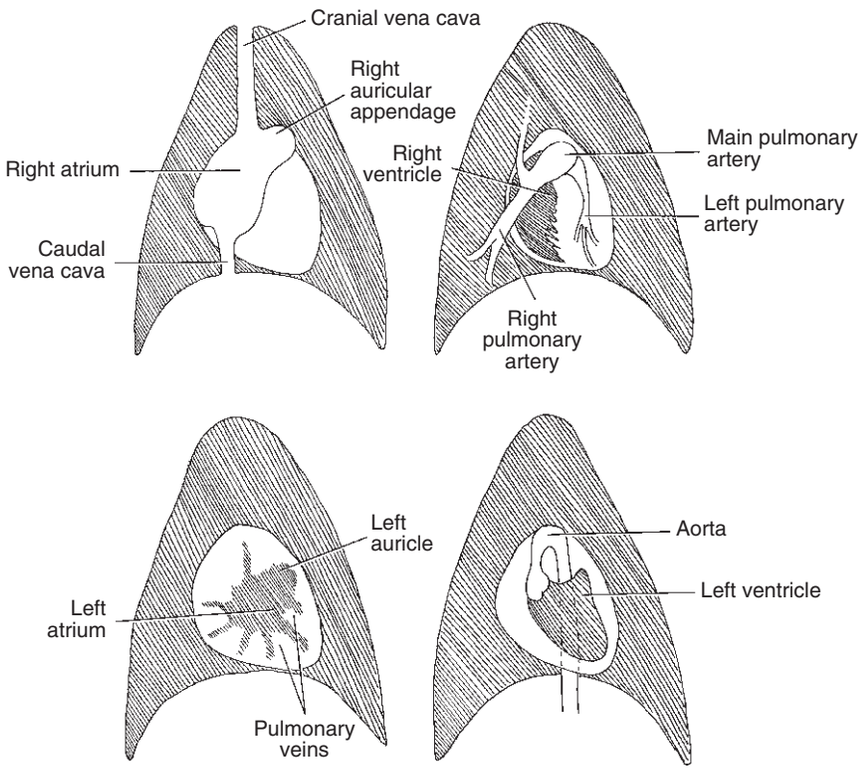


Figure 143-2. Four ventrodorsal views of the normal heart showing chamber location.

- *Orientation*—The apex is at or slightly to the left of midline.
- *Location*—The heart and diaphragm are separated by one to two intercostal spaces.
- Cardiac borders are similar to those in the dog, except that the main pulmonary artery does not contribute to the 1- to 2-o'clock border.

Normal Pulmonary Arteries and Veins

Location and Size

- The cranial lobe artery is dorsal to the bronchus which is dorsal to the vein on the lateral view.
- Arteries are lateral to the bronchus and vein, and originate cranial to the carina on the VD or DV view.
- Veins terminate in the left atrium caudal to the carina (veins are ventral and central).
- Vascular markings are often very prominent in healthy, deep-chested dogs, as well as in cats with hyperinflated lungs.
- Arteries and veins are approximately equal in size.
- Overlapping or superimposition of vessels from both cranial lung lobes can create a misleading appearance regarding vessel size on the lateral view.
- Normal, average vessel-to-rib ratio on the lateral projection is about 0.75 when comparing the artery with the proximal one-third of the fourth rib. However, the range of normal values is quite expansive (0.5–1.25).
- Pulmonary vessels on the VD or DV view should not exceed the width of the ninth rib at the point of intersection. Generally, this intersection creates a "square" as opposed to a rectangle.
- The caudal lobe arteries and veins appear larger on DV views because of distance from the cassette and subsequent magnification. In obese cats, magnification can be substantial and lead to overinterpretation of true vascular size.

Appearance

- Vessels are best seen on the lateral view as they extend into the cranial lobes.
- Vessels in the lung farthest from the cassette are magnified.
- Arteries are denser than veins, are slightly curved, and have dichotomous branching (branches of equal size).
- Veins are less visible, are straighter and blunter than arteries, and have branches of unequal size.

INTERPRETING THORACIC RADIOGRAPHS IN CARDIAC DISEASE

Once an adequately positioned and exposed radiograph has been obtained, the radiographs must be interpreted in a systematic manner. Optimally, the films would be assessed without knowledge of the patient and then reassessed after reading the signalment, clinical history, and examination findings. In most instances this is impractical, but it is clear that including the clinical findings will both assist the evaluation (by provid-

ing a clinical perspective) and hinder an objective assessment (by prejudicing the reader with the clinical diagnosis).

Initial Approach to Interpretation

The following general questions should be addressed during the radiographic assessment of cardiac disease:

- *Are the radiographs of sufficient technical quality?* Is the positioning straight, is the exposure appropriate, and was the film exposed during inspiration?
- *Is cardiomegaly present or absent?* If present, is this cardiac enlargement mild, moderate, or severe?
  - Species and conformational variations are important in this assessment (e.g., barrel-chested dogs normally have wider and more rounded hearts, and the cardiac size appears large relative to the thoracic volume, whereas deep-chested dogs have a narrower, more vertically oriented heart shadow).
  - Owing to marked breed variation, the subjective appearance of heart size may differ between projections. For example, cardiomegaly may be suspected on one view but may not be confirmed on the complementary projection.
  - Concentric ventricular hypertrophy may be underestimated by cardiac size as viewed by radiography.
  - It may be useful to calculate a VHS in dogs, particularly in cases of equivocal cardiomegaly. This score is especially helpful in toy-breed dogs, which often appear to have cardiomegaly by subjective evaluation. The technique is described more fully below.
- *Which specific cardiac chambers are abnormal?* Is more than one cardiac chamber affected? Is the abnormality restricted to one side of the heart, or is it generalized? (See below and Figs. 143-3–143-6.)
- *Is the cardiac apex in its normal position?* If not, is this shift due to poor patient positioning or true cardiomegaly?
  - Left heart enlargement may shift the apex to the right (typical of cats) or to the left. Typically, the heart will also be elongated in the left heart enlargement.
  - Right-sided enlargement may shift the apex to the left but in general does not elongate the heart.
  - Rotation of the heart and shifting of the apex often leads to overestimation of the size of other cardiac chambers. Evaluating the heart on both views may prevent erroneous conclusions in the case of apex shifting.
- *Are the great vessels (aorta and main pulmonary artery) normal or abnormal in appearance?*
- *Are the pulmonary vessels normal, small, or enlarged?* (Also see Chapter 159.) If enlarged, are changes restricted to the arteries (e.g., heartworm disease) or veins (e.g., left heart failure), or are both altered in size (e.g., pulmonary undercirculation or overcirculation)?
- *Is the radiographic opacity of the lung normal, decreased, or increased?* Are areas of increased opacity generalized or focal? If diffuse, what is the distribution of the pulmonary infiltrates (generalized, dorsal-caudal, or cranial-ventral)? What is the radiographic pattern of abnormal density? (See Chapter 159.)
- *Is there pleural effusion?*
  - Pleural effusion can stem from CHF or a noncardiogenic origin.
  - Thoracocentesis is necessary to determine the type of fluid present (see Chapters 3 and 164).
  - The cardiac silhouette is more obscured on a DV projection than on a VD projection in the presence of a mild to moderate amount of pleural fluid due to the effect of gravity on fluid distribution.
  - Patient stress may preclude a complete radiographic examination initially, but further films may be possible following thoracocentesis. If possible, both DV and VD projections should be obtained, as the latter will better delineate the cardiac silhouette.
- *Are the diaphragm and extrathoracic structures normal?* If not, are the changes most likely congenital (e.g., peritoneopericardial hernia) or acquired (e.g., acquired diaphragmatic hernia with related rib fractures)?

Enlargement Patterns for Specific Cardiac Chambers

Signs of Right Atrial Enlargement (Fig. 143-3)

Lateral View

- Right atrial enlargement usually is not seen on this view.
- Loss or filling in of the normal concave angle between the ventral edge of the craniodorsal mediastinum and the cardiac silhouette (the cranial "waist") may be seen due to bulging of the right atrial appendage (right auricle).
- In some cases the cranial waist may become accentuated due to discrete auricular enlargement.

Dorsoventral or Ventrodorsal View

- Bulging of the cranial right heart border (9–11 o'clock) is typical of right atrial dilation.
- Right atrial dilation is often masked by concurrent right ventricular enlargement.
- In cases of severe right atrial dilation, as with tricuspid valve malformation or primary atrial muscle disease (silent atrium), the apex may shift to the left and the craniodorsal mediastinum may bulge on the VD view because of cranial vena caval dilation.

Signs of Right Ventricular Enlargement (Fig. 143-4)

Lateral View

- Increased overall width of the heart
- Rounding of the cranial heart border
- Elevation of the cardiac apex and caudal vena cava
- In severe right ventricular enlargement, elevation of the trachea cranial to the carina and some degree of cardiac elongation

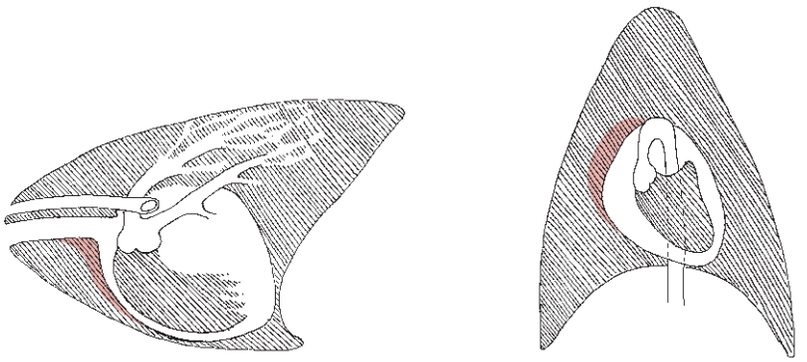


Figure 143-3. Radiographic appearance of right atrial enlargement. The red areas denote the abnormal region.

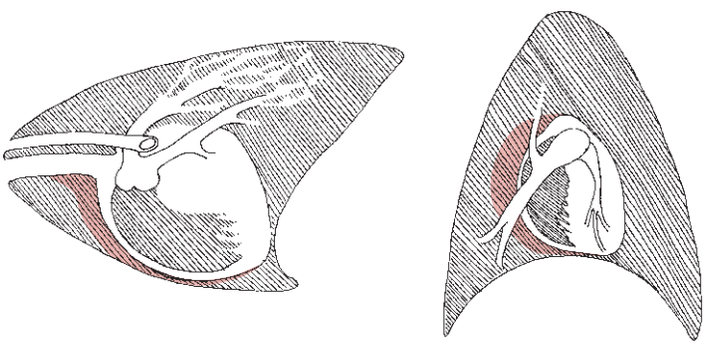


Figure 143-4. Radiographic appearance of right atrial and ventricular enlargement. The red region denotes the abnormality.

Dorsoventral or Ventrodorsal View

- Rounding of the right heart border (6–11 o'clock)
- "Reversed D" appearance if the main pulmonary artery is also dilated
- Increased overall width of the heart
- Decreased distance between the right side of the heart and the thoracic wall or shifting of the apex to the left side

Causes of Right-Sided Enlargement

- Right atrial enlargement (usually normal right ventricle):
  - Right atrial tumor
  - Tricuspid stenosis
  - Cor triatriatum dexter (caudal atrial dilation extending to caudal vena cava)
- Right atrial and right ventricular enlargement:
  - Atrial septal defect (ASD)
  - Atrial myocardial disease
  - Tricuspid regurgitation from any cause
  - Right ventricular cardiomyopathy
  - Chagas myocarditis
  - Pulmonic stenosis
  - Heartworm disease
  - Pulmonary hypertension (some cases)
  - Arrhythmias—Chronic bradycardia, relentless tachycardia, and atrial fibrillation
  - Plasma volume expansion—CHF, circulatory overload, and high output heart disease as with anemia, hyperthyroidism, or systemic arteriovenous fistula
- Right ventricular enlargement (usually normal right atrium):
  - Tetralogy of Fallot
  - Pulmonary hypertension (some cases)

Signs of Left Atrial Enlargement (Fig. 143-5)

Lateral View

- Elevation of the distal end of the trachea with dorsal displacement and compression of the left main stem bronchus between the left atrium and the descending aorta
- Bulging of the caudal-dorsal heart border (dorsal to the caudal vena cava)
- Filling in and loss of the normal caudal indentation of the cardiac border (the caudal waist), or, with marked dilation, accentuation of the caudal waist as the atrium projects caudodorsally

Dorsoventral or Ventrodorsal View

- The left atrium proper is a midline structure and does not normally contribute to the heart border on this view.
- There is displacement and separation of the main stem bronchi as they approach the cranial border of the left atrium and bifurcate around this chamber (producing a "bow-legged cowboy" appearance to the bronchial tree).
- On a well-exposed DV view, the enlarged atrium may be seen as a round, soft tissue mass summated on the caudal heart border.

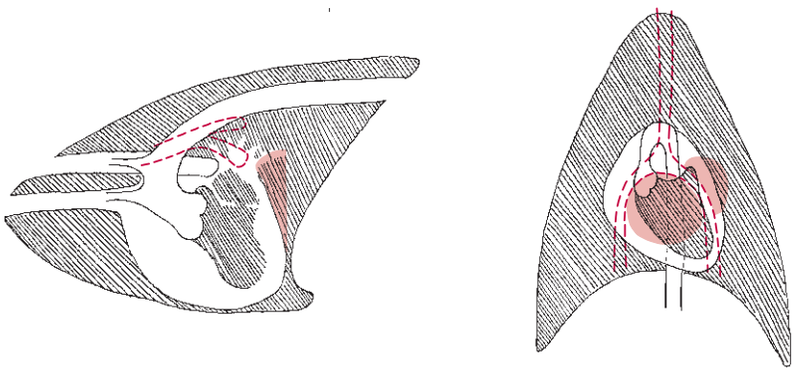


Figure 143-5. Radiographic appearance of left atrial enlargement. The red region denotes the abnormality. (Dotted red lines outline the trachea and main stem bronchi.)

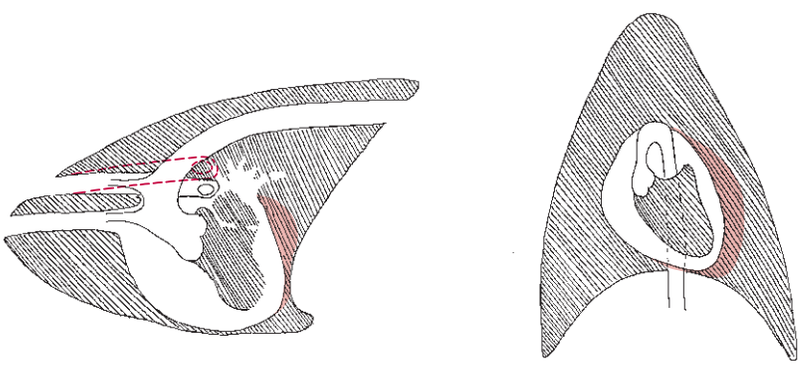


Figure 143-6. Radiographic appearance of left ventricular (with or without atrial) enlargement. The red region denotes the abnormality. (Dotted red lines outline the trachea.)

- Left auricular dilation is seen in dogs as bulging of the left heart border from 2 to 3 o'clock and in cats as a bulge from 1 to 3 o'clock.

Signs of Left Ventricular Enlargement (Fig. 143-6)

Lateral View

- Elongation of the cardiac silhouette and possibly widening of the silhouette
- Rounding of the caudal heart border
- Elevation of the carina and distal end of the trachea (causing the trachea to more closely parallel the spine than the sternum; this finding depends on chest conformation and breed)

Dorsoventral or Ventrodorsal View

- Elongation, rounding, and expansion of the left heart border
- Rounding of the cardiac apex
- Decreased distance between the left heart border and the thoracic wall or shifting of the cardiac apex to the right (especially common in cats)

Causes of Left-Sided Enlargement

- Left atrial enlargement (usually normal left ventricle):
  - Cor triatriatum (sinister)
  - Mitral stenosis
  - Supravalvular mitral ring (supravalvular mitral stenosis)
- Left atrial and left ventricular enlargement:
  - Mitral valve disease—Mitral regurgitation from any cause (endocardiosis, endocarditis, malformation, cardiomyopathy)
  - Left to right shunts—Patent ductus arteriosus (PDA), ventricular septal defect (VSD), and some ASDs, particularly when there is AV valve malformation (endocardial cushion defects)
  - Multiple systemic to pulmonary shunts (bronchial artery to pulmonary vascular tree)
  - Cardiomyopathy (all forms)—Dilated, hypertrophic, restrictive, and unclassified
  - Myocarditis
  - Chronic hyperthyroidism
  - Chronic systemic hypertension
  - Aortic stenosis (left atrial enlargement develops with impending CHF)
  - Aortic regurgitation (left atrial enlargement develops with CHF)
  - Arrhythmias—Chronic bradycardia and relentless tachycardia
  - Plasma volume expansion—CHF, circulatory overload, and high output heart disease as with anemia or hyperthyroidism

Signs of Biventricular Cardiac Enlargement

- This is a relatively common feature of many cardiac disorders.
- It usually is difficult to determine which ventricle is most enlarged on survey films alone; echocardiogra-

phy is very helpful in assessing chamber size and ventricular function.
- The heart appears generally rounded, and usually there is increased sternal contact on the lateral view.

Causes of Biventricular Cardiac Enlargement

Common causes include the following:

- Chronic degenerative valvular heart disease (mitral and tricuspid regurgitation)
- Left-sided heart failure (any cause) with secondary pulmonary hypertension
- Large VSD
- Dilated cardiomyopathy
- Mild to moderate pericardial effusion (mimics cardiomegaly)
- High-output heart failure (moderate to severe anemia, arteriovenous fistula, hyperthyroidism)
- Overinfusion of intravenous fluids

Signs of Microcardia

- A generalized decrease in cardiac size is most often associated with plasma volume contraction, shock, or trauma.
- Decreased cardiac size allows the heart to shift off the midline when the patient is in lateral recumbency, making the heart appear elevated from the sternum similar to the radiographic appearance of pneumothorax.
- Pulmonary circulation often appears diminished.

Causes of Microcardia

- Hypovolemic shock
- Addison's disease
- Hemorrhage
- Protracted vomiting or diarrhea
- Obstructive hepatic circulation (cirrhosis, caudal vena cava obstruction)

Enlargement of the Great Vessels

Aortic Enlargement (Fig. 143-7)

The direction of aortic bulging depends on the underlying etiology, as in the examples that follow.

Causes

- *PDA:* Some cranial bulging of the aortic arch is seen, but the most pronounced bulging is toward the left side at the site of the patent ductus ("ductus bump") (best seen on the DV view). In deep-chested dogs the aortic dilation may be observed just caudal to the aortic arch on the lateral projection.
- *Aortic stenosis:* There is dilation of the ascending aorta (cranioventrally), and often the brachiocephalic artery and aortic arch (in the cranial mediastinum) are dilated secondary to poststenotic turbulence.
- *Tetralogy of Fallot and pulmonary atresia:* Dilation of the ascending aorta due to aortic malalignment and dextropositioned aorta.
- *Persistent right fourth aortic arch:* On the VD or DV view, the aorta may be observed to arch to the right side (mirror-image arch) before connecting to the descending aorta.
- *Age:* Dilation and tortuosity of the ascending aorta, the aortic arch, and the arch extending into the descending aorta may be observed in older cats. Many of these cats also have hyperthyroidism or systemic hypertension, but cause and effect have not been established. Idiopathic dilatation of the ascending aorta and aortic arch also has been observed in many dogs. The appearance can resemble that of a mediastinal mass.

Pulmonary Artery Enlargement

Enlargement of the main pulmonary artery leads to bulging of the left cranial cardiac border at 1 o'clock (DV or VD view) in the dog. Only extreme main PA dilation will be evident in cats.

Causes

- Increased blood flow into the main pulmonary artery (PDA, VSD, ASD): Pulmonary vascular markings are usually increased as well.
- Post-stenotic dilation (pulmonic stenosis): Pulmonary circulation is normal to reduced.
- Pulmonary hypertension (heartworm disease, severe pulmonary thromboembolism, or related to congenital pulmonary vascular disease): Also dilation of lobar pulmonary arteries.

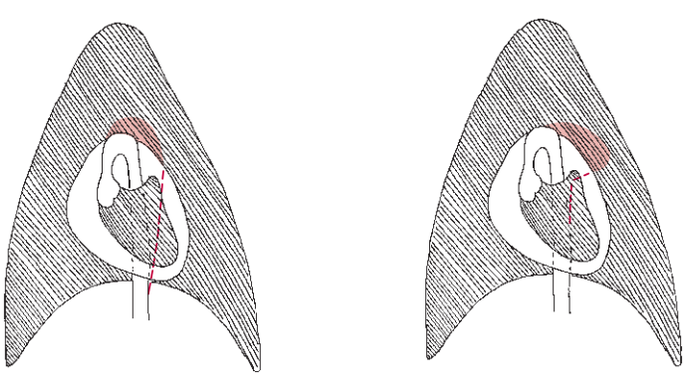


Figure 143-7. Radiographic appearance of aortic enlargement. *Left,* Aortic stenosis. *Right,* Patent ductus arteriosus.

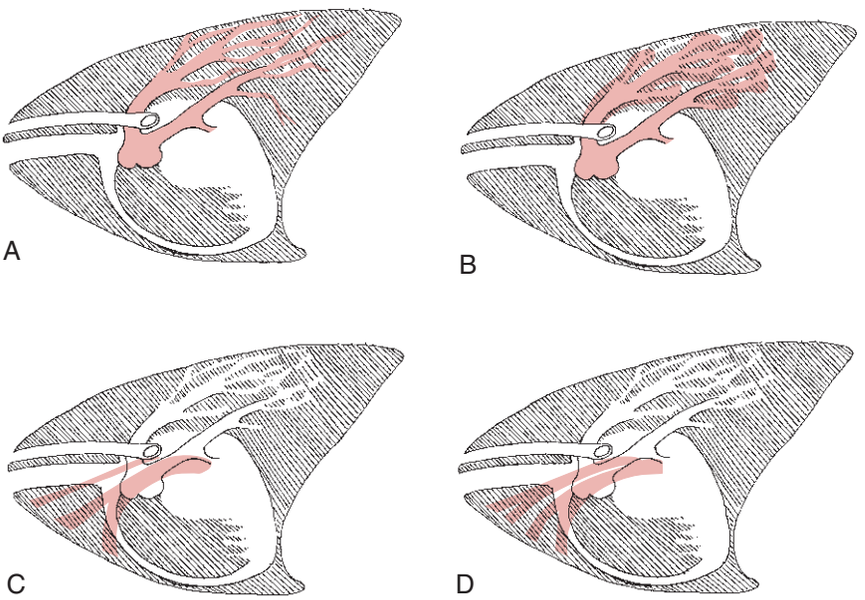


Figure 143-8. Radiographic appearance of pulmonic circulatory disorders. *A,* Normal pulmonary circulation. *B,* Pulmonary arterial hypertension caused by heartworm disease. *C,* Effects of venous congestion due to mitral insufficiency. *D,* Signs of pulmonary overcirculation caused by left-to-right shunt or pulmonary hypertension due to left-sided congestive heart failure.

Pulmonary Vascular Patterns (Fig. 143-8)

- Assessment of pulmonary vascularity requires judgment and evaluation of other cardiac structures.
  - On the lateral view: Evaluate vessels as they extend into the cranial lobes.
  - On the DV or VD view: Evaluate vessels as they extend beyond the heart border. The lobar artery is lateral to the bronchus and vein.
- As indicated above, the lobar artery and vein should be of the same diameter at adjacent levels. On the lateral view, the *average* vessel diameter at the fourth rib is 75% of the width of the proximal one-third of that rib. On the VD projection, the vessels should create a "square" summation density over the ninth rib.
- *Decreased pulmonary vascular markings* (small arteries and veins) are typical of decreased perfusion due to the following:
  - Right-to-left cardiac shunts (e.g., tetralogy of Fallot and Eisenmenger's physiology)
  - Severe pulmonic stenosis
  - Low cardiac output from volume contraction (e.g., shock and Addison's disease)
  - Cardiac tamponade
  - Pulmonary thromboembolism (regional, reduced blood flow to affected areas)
- *Increased pulmonary vascular markings* (large arteries and veins) is often caused by the following:
  - Pulmonary overcirculation (left-to-right shunts such as PDA, VSD, ASD, aorticopulmonary window, and bronchial artery to pulmonary shunts)
  - High output states (thyrotoxicosis)
  - Volume overload (excessive fluid therapy)
  - Possibly enhanced vascularity in the peripheral lung fields
- *Prominence of lobar pulmonary arteries* (arteries > veins) is usually related to pulmonary hypertension caused by the following:
  - Heartworm disease
  - Pulmonary thromboembolism
  - Pulmonary hypertension from parenchymal lung disease (cats > dogs)
  - Eisenmenger's reaction in congenital heart disease
  - Left-sided CHF with pulmonary hypertension (pulmonary veins and venous distention also are prominent)
- *Prominence of lobar pulmonary veins* (veins > arteries) is usually related to venous congestion:
  - Left-sided CHF
  - Compression of pulmonary venous return (regional, from a mass lesion)
  - Cor triatriatum (sinister)
  - PDA (arteries also are enlarged, but lobar veins are often more enlarged than lobar arteries)

Congestive Heart Failure

The clinical diagnosis of left-sided CHF is substantiated by thoracic radiography. Radiographic diagnosis of right-sided CHF is more difficult and must be interpreted with physical examination findings of right heart failure. In advanced disease there may be biventricular CHF with generalized cardiomegaly (Fig. 143-9).

- Left-sided CHF is characterized by left-sided cardiomegaly, pulmonary venous distension, and increased pulmonary density.
- Initially, perivascular interstitial densities that blur vascular margins are observed. These progress to a diffuse interstitial density with airway cuffing prior to alveolar flooding.

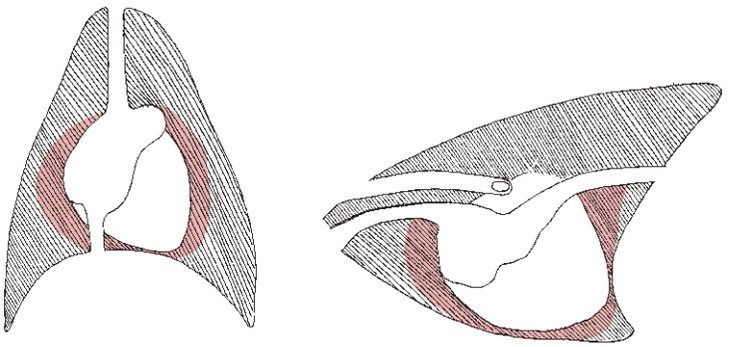


Figure 143-9. Radiographic appearance of generalized cardiomegaly. The red regions denote the abnormalities.

- Alveolar patterns are recognized as fluffy, coalescing densities with increased air-filled bronchi contrasted with the fluid-filled lung (air bronchogram sign). Fluid density structures such as the heart and diaphragm may be obscured (border effacement or silhouetting).
- Distribution of cardiac edema is usually perihilar, dorsal, and bilateral; however, right-sided prominence is common in severe edema due to different lymphatic drainage between the right and the left lungs. Diffuse or dependent infiltrates may be observed in fulminant cardiogenic edema.
- In cats, pulmonary edema is more likely to be localized to the dependent portions of the perihilar caudal lung lobes.
- Expect mobilization of alveolar edema within 48 to 72 hours following aggressive therapy for CHF (see Chapter 147). Radiographic changes often lag behind clinical improvement or deterioration by 12 to 18 hours. Failure to resolve increased pulmonary densities following appropriate treatment should prompt a reconsideration of the diagnosis of cardiogenic lung edema.
- Development of pleural fissure lines and pleural effusion is usually a sign of biventricular CHF and a fluid retentive state. Severe pleural effusion may indicate right ventricular decompensation associated with congenital right heart disease or atrial fibrillation. Cardiac tamponade is another cause of pleural effusion.

Interpretation Pointers

The radiographic features of many cardiac disorders are described in detail in other chapters within this section. Table 143-1 summarizes typical features of common conditions. There are always exceptions. The following statements are designed to assist the clinician in interpreting thoracic radiographs from dogs and cats with cardiac disease.

Verifying Cardiomegaly with the Vertebral Heart Score

As described above, detection of cardiomegaly would seem straightforward; however, in many instances there is uncertainty about heart size. It is critical to obtain an overall opinion based on study of both DV and lateral views. Cardiac elongation usually indicates left ventricular enlargement. Cardiac widening can occur with either left or right ventricular enlargement. When there is doubt, the VHS is invaluable. This can be calculated in about 3 minutes (Fig. 143-10) by following these steps:

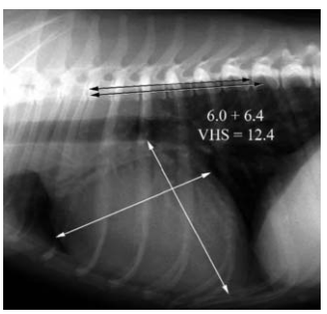


Figure 143-10. Lateral radiograph from a dog with cardiomegaly demonstrating the vertebral heart score.

- Measure the apical-basilar length from the ventral border of right bronchus at level of circular carina to the apex of the heart. This is the major axis measurement.
- Then draw a line perpendicular to your first measurement, extending from the cranial to the caudal heart border. This is the minor cardiac axis. Select the greatest length, but do not extend the measurement into the caudal vena cava or dorsal left atrium.
- Identify the fourth thoracic vertebral body; inspect the dorsal spinous processes to assist localization.
- Measure the VHS from the cranial edge of T4 caudally.
- Count the number of vertebral bodies encompassed in the major + minor axis lengths. Extrapolate to the nearest decimal point.
- A VHS that exceeds 8.0 in a cat is suspicious for cardiomegaly (average value is 7.5 vertebral bodies).
- A VHS that exceeds 10.7 in a dog is likely to indicate cardiomegaly (the normal average is about 9.7 vertebral bodies).

Table 143-1. TYPICAL RADIOGRAPHIC FEATURES OF HEART DISEASE

Disorder	LV	LA	Ao	RV	RA	MPA	Pulmonary Circulation	Additional Findings
Patent ductus arteriosus	+	+	+ Desc Ao	0*	0		+ Artery + Vein	Left-sided CHF
Ventricular septal defect	+	+	0	+†	0†	+	+ Artery + Vein	Left-sided CHF
Atrial septal defect	0	0‡	0	+	+	+	+ Artery + Vein	Right-sided CHF
Mitral regurgitation	+	+	0	+†	0	0	+ Vein 0/+ Artery†	Left-sided CHF
Tricuspid regurgitation	0	0	0	+	+	0	0	Dilated vena cava Right-sided CHF
Aortic stenosis	+	0/+	+ Asc Ao	0	0	0	0/+ Vein 0/+ Artery†	Left-sided CHF
Pulmonic stenosis	0	0	0	+	+	+	0/− Artery 0/− Vein	Right-sided CHF
Tetralogy of Fallot	0	0	+§	+	+	‖	− Artery − Vein	
Dilated cardiomyopathy	+	+	0	+	+	0	+ Vein 0/+ Artery	Biventricular CHF
Hypertrophic cardiomyopathy	+	+	0	0/+†	0/+†	0	+ Vein 0/+ Artery†	Left-sided or biventricular CHF
Restrictive cardiomyopathy	+	+	0	+	+	−	+ Vein 0/− Artery†	Variable findings
Pericardial effusion	+	+	0	+	+	0	0/− Artery 0/− Vein	Possible mass lesion
Hyperthyroidism	+	+	+	+	+	0	0/+ Artery 0/+ Vein	Dilated or tortuous aorta
Pulmonary hypertension	0/+¶	0/+¶	0	+	+	+	−/0/+ Artery −/0/+ Vein¶,#	Lungs may be abnormal or undercirculated
Heartworm disease	0	0	0	+	+	+	+ Artery 0 Vein	Pulmonary infiltrate

*Although the RV may appear enlarged, the echocardiograph demonstrates that LV dilatation accounts for ventricular enlargement; in the rare case of reversed patent ductus arteriosus, the radiograph resembles that of pulmonary hypertension.
†Right-sided cardiomegaly develops if there is pulmonary hypertension due to increased pulmonary flow, increased pulmonary vascular resistance, or both. Otherwise, right-sided cardiomegaly is variable.
‡In the typical ostium secundum (high) atrial septal defect (ASD), blood flows immediately into the RA and the LA doesn't enlarge substantially. In cases of primum ASD with concurrent ventricular septal defect, or mitral dysplasia (endocardial cushion defect), LA dilation also develops.
§The aorta is dextropositioned and receives the most blood flow; this causes widening of the ventrocranial mediastinum on the lateral projection.
‖The pulmonary artery is not dilated because blood preferentially shunts across the ventricular septal defect into the aorta.
¶In cases of pulmonary hypertension secondary to left-sided CHF, left-sided heart structures are enlarged.
#In cases of pulmonary hypertension secondary to left-sided CHF, pulmonary venous distention is also present; in pulmonary hypertension caused by pulmonary vascular disease (e.g., reversed patent ductus arteriosus, primary pulmonary hypertension), peripheral pulmonary vascularity is decreased, whereas central lobar vessels are dilated from pressure.
Ao, aorta; CHF, congestive heart failure; LA, left atrium; LV, left ventricle; MPA, main pulmonary artery; RA, right atrium; RV, right ventricle; 0, no change; +, enlarged or increased; −, decreased; desc, descending; asc, ascending.

- As with any diagnostic test, there will be some false-negative and false-positive results.

Atrial Dilatation in Chronic Mitral Regurgitation

The degree of left atrial dilation seen radiographically usually corresponds to the severity of chronic valvular regurgitation; however, in acute heart failure or with a ruptured chorda tendinea, left atrial enlargement may be underwhelming in the face of life-threatening alveolar infiltrates. Compression of the left main stem bronchus by the enlarged left atrium may cause coughing and persist following resolution of lung edema. This finding is often associated with recurrent coughing.

Canine Dilated Cardiomyopathy

Dilated cardiomyopathy is the second most important cause of CHF in dogs. There is no specific radiographic finding for this disease, and features are similar to those of chronic valvular endocardiosis. Generalized cardiomegaly is typical. Echocardiography is needed for definitive diagnosis.

Valentine-Shaped Hearts in Cats

This finding on the VD/DV radiograph is not specific for any one condition and can be observed with a variety of congenital and acquired diseases. It typically indi-

cates left ventricular enlargement and left auricular dilation, along with an apex shift to the right.

Rupture of the Left Atrium

Acute pericardial effusion in dogs with chronic mitral valve disease may indicate left atrial rupture. Typically, the pulmonary vascularity is reduced and the caudodorsal border of the left atrium becomes rounded.

Peritoneopericardial Hernia

This is a relatively common malformation in cats and can be readily confused with cardiomegaly from cardiomyopathy (see Chapter 150). A persistent mesothelial remnant is often evident ventral to and parallel to the caudal vena cava (which is displaced dorsally).

Pericardial Effusion from Congestive Heart Failure

Cats with CHF often develop pericardial effusion that clears with effective medical therapy. This can lead to relatively dramatic differences in cardiac size in "before and after" films.

Diuretic Therapy and Heart Size

Effective diuretic therapy of severe CHF is usually associated with reductions in both heart and lung volumes.

GENERAL PRINCIPLES OF ECHOCARDIOGRAPHY

Echocardiography is an advanced imaging modality that has become the gold standard for noninvasive cardiac diagnosis. A number of different echocardiographic formats are used in clinical practice, including the two-dimensional, M-mode, and Doppler examinations (color Doppler, pulsed wave, tissue Doppler, and continuous wave). Echocardiography has become increasingly sophisticated, and the combined modalities have largely replaced cardiac catheterization and angiocardiography for diagnosis and assessment of cardiac lesions. Appropriate use of the technology requires understanding of heart diseases, along with advanced training in diagnostic imaging. Specific echocardiographic findings in cardiac disease are discussed in a number of chapters within this section.

A detailed discussion of echocardiography and the various imaging planes and modalities used in diagnosis is beyond the scope of this book. However, the following comments are offered to place this imaging technique into an appropriate context.

- Veterinarians often find referral for echocardiography helpful or even essential for establishing a cardiac diagnosis. Examples include the following:
  - Definitive diagnosis of congenital heart disease
  - Assessment of cats with signs of heart disease (murmurs, gallops, cardiomegaly)
  - Recognition of dilated cardiomyopathy in dogs
  - Diagnosis and evaluation of pericardial disease
  - Diagnosis of pulmonary hypertension
  - Evaluation of dogs with chronic valvular heart disease
  - Assessment of dogs and cats with persistent arrhythmias
- Echocardiography should be performed and echocardiograms should be interpreted by individuals that appreciate pertinent issues and questions regarding specific cardiovascular diseases.
- The echocardiographic examination is not a substitute for a careful clinical examination or assessment. A veterinarian capable of integrating information from all sources, including the history and physical examination, radiography, and laboratory tests, should direct the treatment plan. These decisions should not be abdicated to any sonographer unless that individual has a full understanding of the entire clinical situation and has physically examined the patient.
- While limited echocardiographic examinations have their place, a referring veterinarian should expect an echocardiographic (with Doppler) examination to generate the following information:
  - Pertinent congenital or acquired anatomic lesions (morphologic diagnosis)
  - Estimates of cardiac great vessel and chamber size (dilatation and hypertrophy)
  - Quantitation of ventricular systolic function
  - Estimates of ventricular diastolic function
  - Evaluation of blood flow and valvular function
  - Estimates of hemodynamics (pressure/flow)
  - Overall significance of a lesion

SUPPLEMENTAL READING

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Suter PF: Thoracic Radiography: A Text Atlas of Thoracic Diseases of the Dog and Cat. Wettswil, Switzerland: Peter F. Suter, 1984, pp 351–516.

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Chapter

144 Electrocardiography

Francis W. K. Smith, Jr. / Larry Patrick Tilley / Michael S. Miller

Electrocardiography is the graphic representation of the electrical activity of the heart with time displayed on the x-axis and voltage displayed on the y-axis. Electrocardiograms (ECGs) are easy to perform and readily available to practicing veterinarians. There are numerous indications for performing ECGs, and the examination provides information that is useful and often pivotal to the diagnosis and management of cardiac and systemic disturbances. Veterinarians or their technicians can perform and interpret their own ECGs or utilize readily available fax, transtelephonic, or computer consultation services.

GENERAL PRINCIPLES OF ELECTROCARDIOGRAPHY

Indications for Performing Electrocardiography

Electrocardiography is the examination of choice for diagnosis of a normal cardiac rhythm and arrhythmias and for monitoring the effect of antiarrhythmic therapy. There are a number of clinical indications for recording and interpreting an ECG:

- To diagnose an arrhythmia detected on physical examination (auscultation, arterial pulse deficits, palpable precordial heart beat irregularities, or abnormal jugular venous pulsations).

▼ ***Key Point*** Perform an ECG on all animals with tachycardia or bradycardia and on all cats with any irregularity in rhythm. Perform an ECG on any dog with an irregularity in rhythm that is related to a pulse deficit or is not related to phases of respiration.

- To identify arrhythmias or conduction disturbances in patients with a history of syncope, seizures, or exercise intolerance.
- To monitor the effectiveness of antiarrhythmic therapy. In this regard, the ambulatory (Holter) ECG is the best approach for monitoring effectiveness of antiarrhythmic therapy for ventricular arrhythmias.
- To assess cardiac size in patients with known or suspected cardiac disease. While the ECG is not a very sensitive indicator of heart size, a cardiac enlargement pattern usually correlates with cardiac chamber enlargement or hypertrophy. The more criteria for heart enlargement present in a patient, the more likely the heart is enlarged. Most dogs with normal hearts will not exhibit heart enlargement patterns on ECGs.

▼ ***Key Point*** A normal ECG does not rule out a diagnosis of heart enlargement. Thoracic radiographs and echocardiography are more sensitive tests for evaluating heart size.

- To help individualize and monitor therapy in patients with heart failure by accurately assessing cardiac rhythm. It is important to understand that a diagnosis of congestive heart failure (CHF) cannot be made based on an ECG alone.

▼ ***Key Point*** An arrhythmia or a heart enlargement pattern supports the diagnosis of heart disease but does not confirm CHF. Obtain thoracic radiographs, along with an ECG, in a patient suspected of having CHF. The ECG is useful in patients with heart failure for the diagnosis and treatment of associated arrhythmias.

- To evaluate patients with suspected digoxin or other cardiac drug toxicity.
- To screen for electrolyte disturbances, especially hyperkalemia, hypercalcemia, and hypocalcemia.
- To look for evidence that may support the diagnosis of pericardial effusion, hypothyroidism, hyperthyroidism, or hypoadrenocorticism (Addison's disease).

Technique for Recording an Electrocardiogram

- For accurate measurements, place the patient in right lateral recumbency.

▼ ***Key Point*** If the animal is dyspneic or if restraint would be dangerous to the patient, obtain a rhythm strip with the animal supported in any comfortable position.

Table 144-1. ELECTRODE PLACEMENT

Chest Lead	Placement of the V Lead
CV_5RL (rV_2)	Fifth intercostal space on the right side near the sternum
CV_6LL (V_2)	Sixth intercostal space on the left side near the sternum
CV_6LU (V_4)	Sixth intercostal space on the left side at the costochondral junction
V_{10}	Over the dorsal spine of the seventh thoracic vertebra

- Wet the skin with alcohol or ECG electrode gel and attach the electrodes just above the elbows and stifles.
- Hold the upper limbs perpendicular to the long axis of the patient and parallel to the floor. If the thoracic limbs are not parallel and perpendicular to the long axis of the animal, the mean electrical axis will be altered.
- Record approximately three to four complexes in each of the six limb leads, and then record a long lead II strip for rhythm evaluation. Push the standard calibration button at the beginning and end of each recording.
- Chest leads can be obtained using the lead V electrode while keeping the limb leads attached. See Table 144-1 for electrode placement.
  - Chest leads are not necessary for all patients. However, they may be quite useful when the ECG complexes in the limb leads are small and difficult to evaluate. Often, P waves that cannot be seen in the limb leads become apparent on a chest lead.
  - Evaluation of chest leads may also be helpful in evaluating heart enlargement patterns.
  - The chest leads most commonly used in veterinary patients are CV_5RL (rV_2), CV_6LL (V_2), CV_6LU (V_4), and V_{10}.

Normal Cardiac Conduction

The ECG records the electrical activity of the heart. Electrical impulses originate in specialized pacemaker tissue in the sinus node of the right atrium. The impulse rapidly traverses the atrium, causing atrial contraction, and then slows as it passes through the atrioventricular (AV) node located at the proximal portion of the interventricular septum. Electrical activity then rapidly passes through the bundle of His, the anterior and posterior branches of the left bundle branch, the right bundle branch, and the terminal Purkinje fibers. This causes activation of the interventricular septum and the left and right ventricular myocardium (Fig. 144-1).

Components of the Electrocardiographic Tracing (Fig. 144-2)

- P wave indicates atrial depolarization.
- P-R interval indicates time for conduction of the impulse from the sinoatrial (SA) node to the AV node and delay of the impulse in the AV node, His bundle, bundle branches, and Purkinje system.
- QRS complex indicates ventricular myocardium depolarization.
- Q wave (lead II) is associated with depolarization of the interventricular septum.
- R wave (lead II) is associated with depolarization of the left ventricle.

Figure 144-1. Normal conduction pathway in the heart. (From De Sanctis RW: Disturbances in cardiac rhythm and conduction. In Rubenstein R [ed]: Scientific American Medicine, section 1, subsection VI. © 1991 Scientific American, Inc. All rights reserved.)

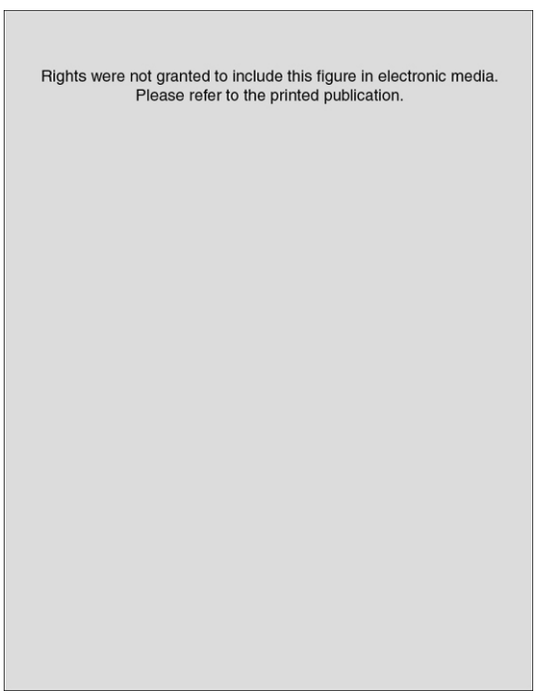

Figure 144-2. Normal electrocardiogram with components labeled. (From Tilley LP: Essentials of Canine and Feline Electrocardiography, 3rd ed. Philadelphia: Lea & Febiger, 1992.)

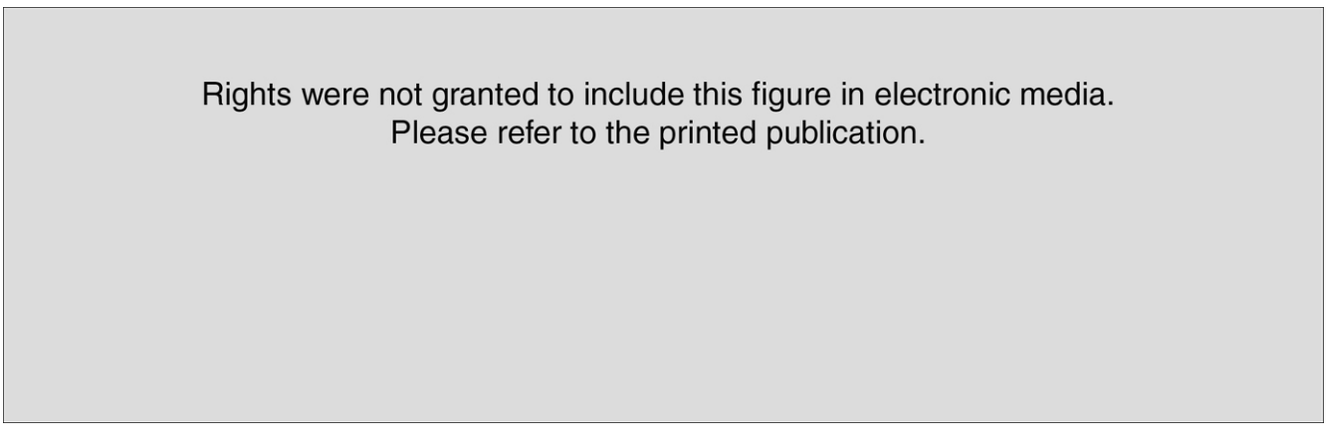

Figure 144-3. Electrocardiogram from a cat. Lead aVR is isoelectric. Lead III is perpendicular to aVR. The QRS deflection in lead III is positive, making the axis +120 degrees. If lead III had been negative, the axis would have been −60 degrees. (From Tilley LP: Essentials of Canine and Feline Electrocardiography, 3rd ed. Philadelphia: Lea & Febiger, 1992.)

- S wave (lead II), when present, is associated with depolarization of the right ventricle.
- T wave indicates ventricular repolarization.
- Q-T interval indicates an approximate interval of ventricular systole.

How to Evaluate the Electrocardiogram

- Always evaluate the ECG from left to right.
- Identify and label the ECG waveforms (P-QRS-T).
- Calculate the approximate heart rate (HR) by counting the number of R-R intervals in 3 seconds (two sets of time markers at 50 mm/second) and multiplying by 20.
- Determine the mean electrical axis.
  - One of the easiest ways to approximate the axis is to identify the isoelectric lead (sum of the positive and negative deflections of the QRS complex closest to zero).
  - Determine the perpendicular lead, and evaluate that lead to see if the complexes are positive or negative.
  - The axis is in the direction of the main deflection of the perpendicular lead (see Fig. 144-3 for an example).
  - If all leads are isoelectric, an axis cannot be determined in the frontal plane.
  - An alternative approach is to identify the frontal plane lead with the largest net positive QRS complex. In dogs, the frontal axis is normal if lead II or aVF is largest, the axis is deviated to the left if lead I or lead aVL is most positive, and the axis is deviated to the right if lead III or lead aVR is most positive.
  - A normal axis does not exclude the possibility of a cardiomegaly pattern or conduction disturbance.
- Determine the rhythm.
  - A sinus rhythm has nearly constant P-R and R-R intervals (usually varying by <10%).
  - A sinus arrhythmia has a nearly constant P-R interval, but the R-R interval varies, usually with the phase of respiration.
- Measure the height and width of the complexes.
- Determine the P-R and Q-T intervals and evaluate the S-T segment.
- Compare the heart rate, rhythm, and sizes of the complexes with the normal values (Table 144-2).

ELECTROCARDIOGRAPHIC ABNORMALITIES

Electrocardiographic abnormalities can be divided into those involving heart rate and rhythm and those involving the configuration of the complexes. This chapter discusses abnormalities involving the ECG complexes. Arrhythmias are discussed in more detail in Chapter 145.

Intraventricular Conduction Disturbances

- The right bundle branch is thinner and therefore more susceptible to injury than the left bundle branch.
- Injury to more than one bundle branch may result in first-, second-, or third-degree AV block.
- A bundle branch block does not cause significant hemodynamic changes and therefore does not warrant therapy.
- Rate-related bundle branch blocks can occur intermittently in association with either bradycardia or tachycardia. The right bundle branch cells have a longer refractory period than the left bundle branch cells. This makes the right bundle more sensitive to abrupt changes in the heart rate.

Table 144-2. NORMAL CANINE AND FELINE ELECTROCARDIOGRAM VALUES*

	Canine	Feline
Heart rate (HR)	Puppy: up to 220 bpm Toy breeds: up to 180 bpm Standard: 70–160 bpm Giant breeds: 60–140 bpm	120–240 bpm
Rhythm	Sinus rhythm Sinus arrhythmia Wandering pacemaker	Sinus rhythm
P wave		
Height	Maximum: 0.4 mV	Maximum: 0.2 mV
Width	Maximum: 0.04 sec (giant breeds 0.05 sec)	Maximum: 0.04 seconds
P-R interval	0.06–0.13 sec (>0.13 sec in giant breeds)	0.05–0.09 sec
QRS		
Height	Small breeds: 2.5 mV maximum Large breeds: 3.0 mV maximum†	Maximum: 0.9 mV
Width	Small breeds: 0.05 sec maximum Large breeds: 0.06 sec maximum	Maximum: 0.04 sec
S-T segment		
Depression	No more than 0.2 mV	None
Elevation	No more than 0.15 mV	None
Q-T interval	0.15–0.25 sec at normal HR	0.12–0.18 sec at normal HR
T waves	May be positive, negative, or biphasic Amplitude range ± 0.05–1.0 mV in any lead	Usually positive and <0.3 mV
Electrical axis	+40° to +100°	0° to ±160°
Chest leads		
CV_5RL (rV_2)	T positive; R < 3.0 mV	
CV_6LL (V_2)	S < 0.8 mV; R < 3.0 mV	R < 1.0 mV
CV_6LU (V_4)	S < 0.7 mV; R < 3.0 mV	R < 1.0 mV
V_{10}	QRS negative; T negative except in Chihuahua	T negative; R wave/Q wave <1

*Measurements are made in lead II unless otherwise stated.
†Not valid for thin, deep-chested dogs <2 years of age.
bpm, beats per minute; HR, heart rate; mV, millivolts; sec, seconds.

Right Bundle Branch Block (Fig. 144-4)

- ECG characteristics of right bundle branch block (RBBB) include the following:
  - QRS width greater than 0.07 second (dog) or 0.06 second (cat)
  - Right axis deviation
  - Wide S waves in leads I, II, III, and aVF and lower left precordial leads, such as CV_6LL and CV_6LU
  - W-shaped pattern in V_{10}
  - Terminal QRS complex positive in aVR and aVL and M-shaped in CV_5RL
- Incomplete RBBB may be present if the aforementioned criteria are present but complexes are of normal width. Incomplete RBBB can be a normal variant in beagles. The pattern may be confused with a left posterior fascicular block (for which criteria are not firmly established).
- Differentiate RBBB from right ventricular enlargement by radiographs or echocardiography. Right ventricular enlargement and RBBB can occur together.
- RBBB has been associated with the following conditions: congenital malformations such as pulmonic stenosis, cardiac surgery, cardiac needle puncture or cardiac arrest, cardiac neoplasia, trauma, *Trypanosoma cruzi* infection (dog), cardiomyopathy, hyperkalemia (cat), acute ventricular dilation, balloon valvuloplasty, and doxorubicin cardiotoxicity. RBBB may be an incidental finding in patients without apparent cardiac disease.

Left Bundle Branch Block (Fig. 144-5)

- ECG characteristics of left bundle branch block (LBBB) include the following:
  - QRS width greater than 0.07 second (dog) or 0.06 second (cat)
  - QRS positive in leads I, II, III, aVF, CV_6LL, and CV_6LU
  - QRS negative in leads aVR, aVL, and CV_5RL
  - Absent or small Q wave in leads I, CV_6LL, and CV_6LU (dog)
  - Q wave absent in leads I and CV_6LU (cat)
- LBBB indicates greater cardiac damage than RBBB—often cardiomyopathy.
- Differentiate LBBB from left ventricular enlargement by radiographs or echocardiography. Left ventricular enlargement and LBBB also can occur together.

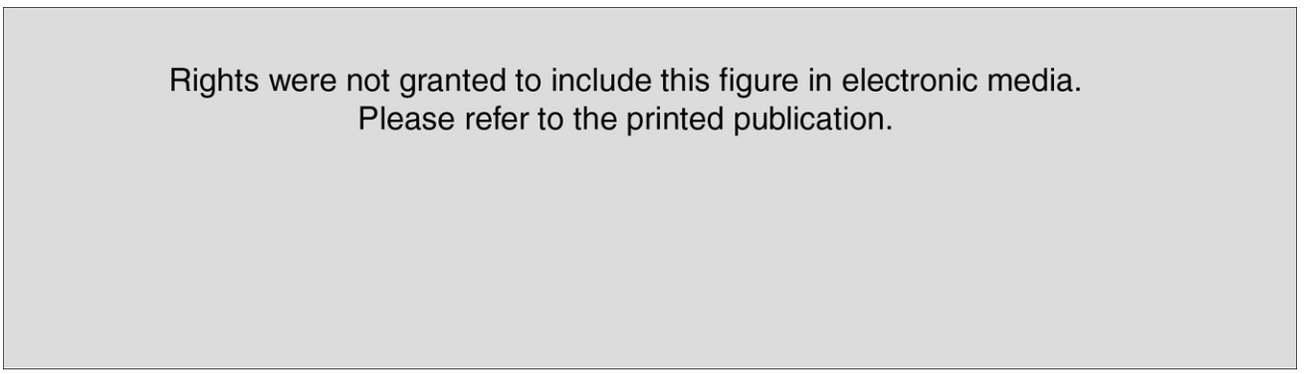

Figure 144-4. Example of right bundle branch block in the dog. Note the right axis (−110); the wide S wave in leads I, II, III, and aVF; and the M-shaped CV_5RL and W-shaped V_{10}. (From Tilley LP: Essentials of Canine and Feline Electrocardiography, 3rd ed. Philadelphia: Lea & Febiger, 1992.)

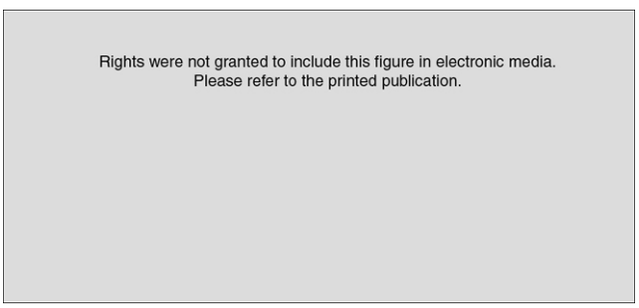

Figure 144-5. Left bundle branch block in a dog. Note the wide QRS complexes (0.08 sec). This electrocardiogram could also be consistent with left ventricular enlargement. (From Tilley LP: Essentials of Canine and Feline Electrocardiography, 3rd ed. Philadelphia: Lea & Febiger, 1992.)

- LBBB is most often associated with the following conditions:
  - In dogs—Cardiomyopathy, cardiac needle puncture, subaortic stenosis, and doxorubicin cardiotoxicity
  - In cats—Uncommon but associated with hypertrophic cardiomyopathy

Left Anterior Fascicular Block (Fig. 144-6)

- ECG characteristics of left anterior fascicular block include the following:
  - QRS width normal
  - Left axis deviation (dog < +40 degrees, cat < 0 degrees)
  - Small Q and tall R in leads I and aVL (small Q not essential)
  - Deep S wave in leads II, III, and aVF (exceeding the R wave)
- Associated conditions include hypertrophic cardiomyopathy, causes of left ventricular hypertrophy, hyperkalemia, ischemic cardiomyopathy, and cardiac surgery.
- Differentiate from left ventricular enlargement, altered position of the heart within the thorax, hyperkalemia, and ventricular preexcitation.

Left Anterior Fascicular Block and Right Bundle Branch Block (Fig. 144-7)

- ECG characteristics include the following:
  - QRS width greater than 0.07 second (dog) or 0.06 second (cat)
  - Left axis deviation
  - S waves deep and wide in leads I, II, III, aVF, and CV_6LU
  - Small Q and tall R in leads I and aVL
  - M-shaped QRS in lead CV_5RL
- Associated conditions are the same as for left anterior fascicular block.

Aberrant Conduction

- A sinus or premature atrial complex that is conducted through a bundle branch or myocardium during the absolute or relative refractory periods may result in an abnormal QRS-T complex. The resultant condition is called (phasic) aberrant ventricular conduction. The abnormal complex may assume the appearance of an RBBB or LBBB pattern or a more subtle widening or altered morphology of the normal QRS complex.
- Aberrancy is more common at slower heart rates or during sudden changes in R-R intervals, as might occur with atrial fibrillation or premature atrial complexes. Aberrant complexes usually have an RBBB pattern because of the longer refractory period of the right bundle branch cells.
- Aberrant beats are frequently confused with ventricular premature complexes (VPCs).
  - Look for P waves to differentiate the two.
  - An aberrantly conducted beat will have an associated P wave with a normal or slightly prolonged P-R interval.

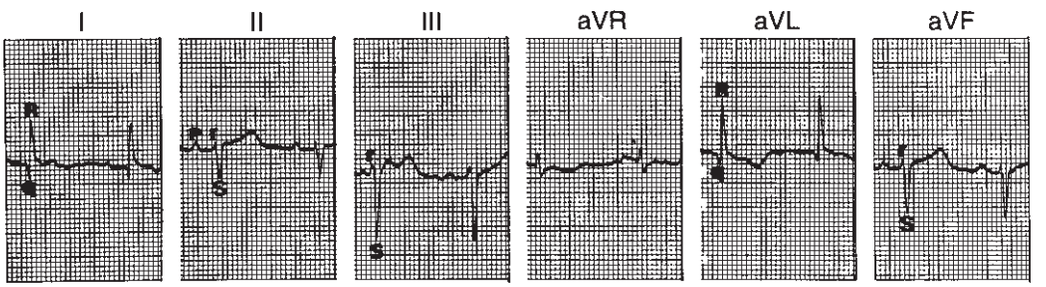

Figure 144-6. Left anterior fascicular block in a cat with hypertrophic cardiomyopathy. (From Tilley LP: Feline electrocardiography. Vet Clin North Am 7:257, 1977.)

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Figure 144-7. Left anterior fascicular block and right bundle branch block in a cat with hypertrophic cardiomyopathy. (From Tilley LP: Essentials of Canine and Feline Electrocardiography, 3rd ed. Philadelphia: Lea & Febiger, 1992.)

- VPCs do not have associated P waves with consistent P-R intervals. Refer to Chapter 145 for further discussion.

Preexcitation

Anatomy

In some patients, additional electrical pathways are present that allow electrical impulses to bypass the AV node and go directly to the bundle of His or ventricular myocardium. Electrical impulses in these patients simultaneously go through the AV node. Traditionally these accessory pathways have been called by their eponyms, particularly the bundles of Kent (that allow direct AV conduction) and the James fibers (that bypass the AV node and connect to the bundle of His) (Fig. 144-8). Today these eponyms have been largely replaced by the more encompassing term *accessory pathway.*

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Figure 144-8. Anatomy of accessory pathways. (From Tilley LP: Essentials of Canine and Feline Electrocardiography, 3rd ed. Philadelphia: Lea & Febiger, 1992.)

Electrocardiogram Characteristics

Electrical conduction through these accessory pathways is faster than through the AV node, resulting in a shortened P-R interval. If impulses are conducted over the bundles of Kent, the QRS complexes will be of longer duration and preexcitation of the ventricle will be manifested as a delta wave at the beginning of the complex (Fig. 144-9). The *delta wave* indicates the direct depolarization of the ventricular myocardium via the bypass tract. If the preexcitation impulse is conducted by the James fibers, the P-R interval will be of short duration but the QRS complexes will be of normal duration with no delta waves. This finding is due to the impulses bypassing the AV node but still activating the ventricles through the bundle of His, the bundle branches, and the Purkinje system. P waves are normal, and a 1:1 relationship exists between P waves and QRS complexes. In most patients, no clinical signs are seen with this conduction disturbance. However, reentrant supraventricular tachycardia can develop in association with

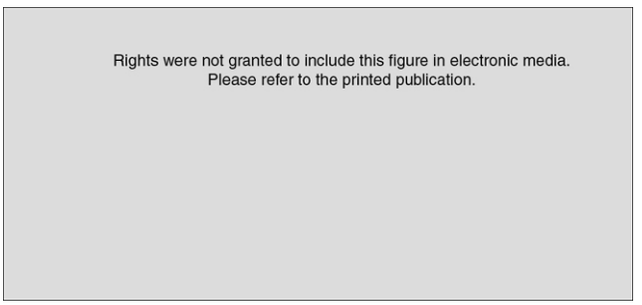

Figure 144-9. A dog with ventricular preexcitation and a history of syncope. The arrow points out the delta wave. (From Tilley LP: Essentials of Canine and Feline Electrocardiography, 3rd ed. Philadelphia: Lea & Febiger, 1992.)

preexcitation, and when associated with a "Kent" bundle is often termed the Wolff-Parkinson-White syndrome. These rhythms are discussed in Chapter 145.

Associated Conditions

Preexcitation is often noted as a congenital finding without other evidence of organic heart disease. Preexcitation may be seen in conjunction with other congenital cardiac diseases, such as atrial septal defect. In cats, preexcitation has been associated with hypertrophic cardiomyopathy.

Abnormalities of the QRS Complexes

Electrical Alternans (Fig. 143-10)

- Electrical alternans is a pattern of alternating configurations of the ECG complexes. The most common pattern is a variation in the height (taller to shorter) of the QRS complexes.
- Electrical alternans is classically associated with a large pericardial effusion that allows pendulous swinging of the heart. Electrical alternans is not present in all cases of pericardial effusion and is not considered a sensitive finding.
- An often-overlooked reason for electrical alternans is supraventricular tachycardias, often propagated through an accessory pathway. Atrial tachycardia or atrial flutter with a high rate of AV nodal conduction may also cause electrical alternans.
- Other reasons for this ECG finding are alternating bundle branch block and myocardial disease.
- Tachypnea (e.g., pleural effusion) can cause "pseudoalternans" when cardiac and respiratory rates are synchronized.

Small Complexes

Low-amplitude QRS complexes (R wave < 0.5 mV in lead II in dogs) may be a normal variant and may be associated with pericardial effusion, pleural effusion, pulmonary edema, hypothyroidism, obesity, pneumothorax, and hypoalbuminemia and with any cause of severe myocardial damage and loss of cardiac muscle mass. Axis deviation will also reduce the R wave amplitude in dogs, although larger voltages should be observed in the lead parallel to the axis shift. Some dogs with cardiomyopathy (e.g., boxers) demonstrate relatively low QRS voltages.

Increased Amplitude Complexes

High-amplitude complexes are generally defined in dogs as a Q wave > 0.5 mV or an R wave > 2.5 to 3.0 mV (using lead II). This finding may be a normal variant, especially in young, deep-chested dogs. Some breeds, such as the Doberman pinscher, may normally have deep Q waves. In most cases, high amplitude suggests cardiomegaly as described below.

Splintered, Notched, or Slurred QRS Complexes

Splintered or notched QRS complexes may be observed in conduction disorders and are best seen in leads I, II, and aVF. In some cases notching or splintering represents a nonspecific conduction disturbance related to old age or myocardial disease. There are some recognized associations. Tricuspid valve malformation may lead to splintered R waves, and some dogs with ventricular septal defects have wide, notched Q waves. When the R wave of a QRS complex ascends rapidly but the

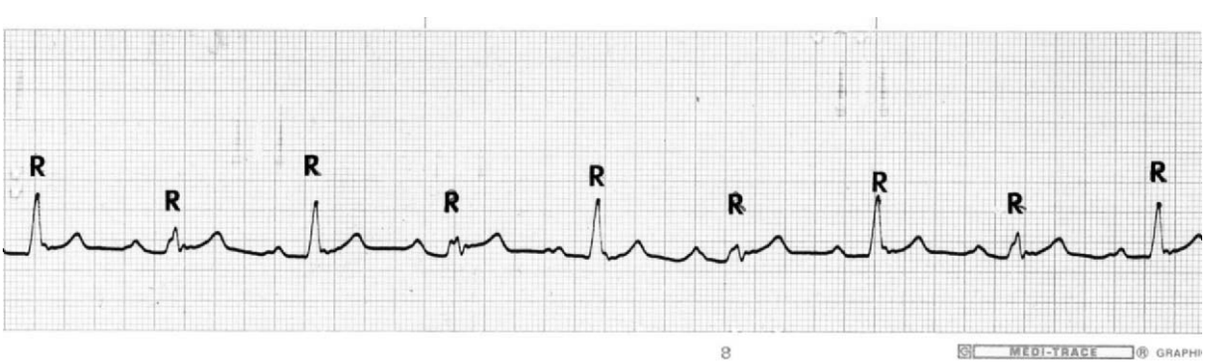

Figure 144-10. Electrical alternans in a dog with pericardial effusion.

descent is slower and slurred, the possibility of myocardial disease or conduction delay should be considered, particularly when the S-T segment is also abnormal (see below).

Abnormalities of the S-T Segment

The S-T segment and T waves represent periods of repolarization of the ventricles. In general, abnormalities can be primary disorders of repolarization (as with ischemia) or secondary changes caused by an abnormality of the QRS complex. The normal S-T segment should be approximately the same horizontal level as the baseline, considered the segment immediately in front of the P wave.

S-T Elevation

- S-T elevation (dog > 0.15 mV in lead II, III, or aVF or those leads with dominant R waves) is seen with myocardial hypoxia, pericarditis, some cases of pericardial effusion, and digitalis toxicity.
- Transmural myocardial ischemia causes S-T segment elevation in leads overlying the injured myocardium.

S-T Depression

- S-T depression (dog > 0.2 mV in lead II, III, or aVF or those leads with dominant R waves) is seen with myocardial hypoxia, hyperkalemia or hypokalemia, and digitalis toxicity.
- Subendocardial myocardial ischemia causes S-T segment depression in leads overlying the ischemic and infarcted myocardium.
- Pseudodepression of the S-T segment is common and is due to prominent T_a waves (atrial repolarization waves). Atrial enlargement, atrial disease, or sinus or atrial tachycardias can lead to prominent atrial repolarization waves, depressing the segment between the P wave and the QRS complex below the baseline and leading to S-T segment depression.

Other S-T Changes

- S-T segment changes can occur secondary to bundle branch blocks, myocardial hypertrophy, and VPCs. The changes in the S-T segment are in the opposite direction from the main QRS deflection. The S-T segment change in these conditions is often one of slurring or coving of the S wave into the T wave.
- Artifact related to baseline motion.
- Normal variant.

Abnormalities of the Q-T Interval

- Q-T interval changes are relatively nonspecific. The Q-T interval is inversely related to the heart rate, being shorter with more rapid heart rates. As a general rule, the Q-T interval should be less than half the preceding R-R interval.
- Q-T prolongation is associated with hypokalemia, hypocalcemia, hypothermia, quinidine administration, intraventricular conduction disturbance (associated with prolongation of the QRS complex), bradycardia, ethylene glycol toxicity, strenuous exercise, and central nervous system disturbance.
- Q-T interval narrowing is associated with hypercalcemia, hyperkalemia, and digitalis administration.

Abnormalities Involving the T Waves

- T wave changes are relatively nonspecific and often the consequence of an abnormal QRS complex. In general, the T wave in dogs should not be more than one-fourth the height of the associated R wave (Q or S wave, if either is larger than R) or more than 1.0 mV in any lead.
- In most leads, normal T waves may be positive, negative, or biphasic.
- Polarity is usually consistent on serial ECGs if heart rate is constant. T waves should be positive in CV_5RL in dogs older than 2 months of age and negative in V_{10}, except in the Chihuahua.
- *Large T waves* can be seen with myocardial hypoxia, intraventricular conduction disturbance, ventricular enlargement, and hypothermia and in animals with heart disease and bradycardia.
- *Large and sharply pointed (positive or negative) T waves* are associated with hyperkalemia.
- *Small biphasic T waves* can be seen with hypokalemia.
- *Nonspecific T wave changes* can be seen secondary to metabolic disturbances (hypoglycemia, anemia, shock, fever), drug toxicities (digitalis, quinidine, procainamide), and neurologic disease.
- *T wave alternans* (alternating positive and negative T waves) has been reported secondary to hypocalcemia, high levels of circulating catecholamines, and sudden increases in sympathetic tone and may be a risk factor for ventricular arrhythmias.

Electrolyte Disturbances

Electrocardiography is not very sensitive or specific in diagnosing systemic disturbances. However, it can be useful as a rapid screening test for certain electrolyte disturbances (particularly moderate to severe hyperkalemia).

Hyperkalemia

ECG changes vary with the degree of hyperkalemia.

- The earliest change is the development of sharply pointed (spiked) T waves (Fig. 144-11), followed by a reduction in the height of the P waves and a prolongation of the P-R interval.
- The QRS complexes then start to widen, and the P waves disappear (atrial standstill).

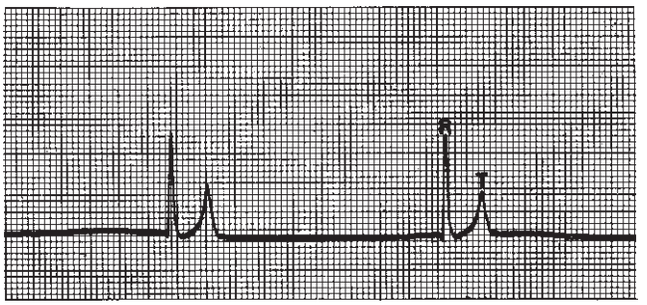

Figure 144-11. Atrial standstill and tall spiked T waves in a dog with severe hyperkalemia associated with Addison's disease.

- The QRS complexes become progressively wider and more bizarre in shape, and cardiac arrest or ventricular fibrillation follows.
- AV block and escape beats may also be seen with hyperkalemia.

Hypokalemia

- Q-T prolongation may develop, along with prominent U waves. A U wave is a repolarization deflection of the Purkinje fibers that occurs after the T wave; however, U waves are uncommon in dogs and cats.
- T waves may be small and notched.
- The S-T segment becomes progressively depressed.
- P-R prolongation and an increase in the height and width of the P and QRS complexes may be seen.

Hypercalcemia

- Q-T interval may be shortened.
- S-T segment shortening and depression have been reported.

Hypocalcemia

- Q-T prolongation develops.
- Duration of S-T segment correlates with the severity of hypocalcemia.
- T wave alternans has been reported.

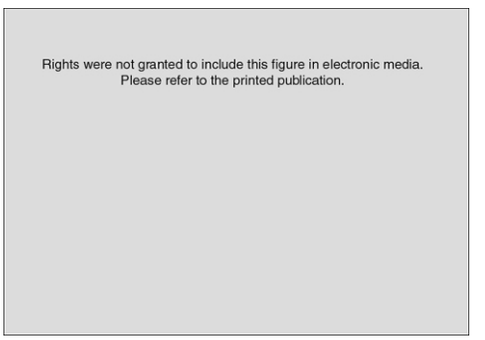

Figure 144-12. Wide and notched P waves in a dog with left atrial enlargement secondary to degenerative mitral valve disease. (From Tilley LP: Essentials of Canine and Feline Electrocardiography, 3rd ed. Philadelphia: Lea & Febiger, 1992.)

- Deep wide T waves, tachycardia, and tall R waves may be present.

Heart Enlargement Patterns

Left Atrial Enlargement

Left atrial enlargement is characterized by wider-than-normal P waves in lead II (Fig. 144-12).

- Dog and cat P waves are greater than 0.04 second (>0.05 second in giant-breed dogs).

Left Ventricular Enlargement

Left ventricular enlargement is characterized by one or more of the following (Fig. 144-13):

- Left axis orientation (dog < +40 degrees, cat < 0 degrees)
- S-T slurring or coving
- QRS duration > 0.06 second (dog) or 0.04 second (cat)
- Tall R waves
  - *Dog:* R greater than 3.0 mV in leads II, aVF, V_6LU (V_4), CV_6LL (V_2), and CV_5RL (rV_2). R greater than 1.5 mV in lead I. Sum of R wave amplitude in leads I and aVF greater than 4.0 mV.

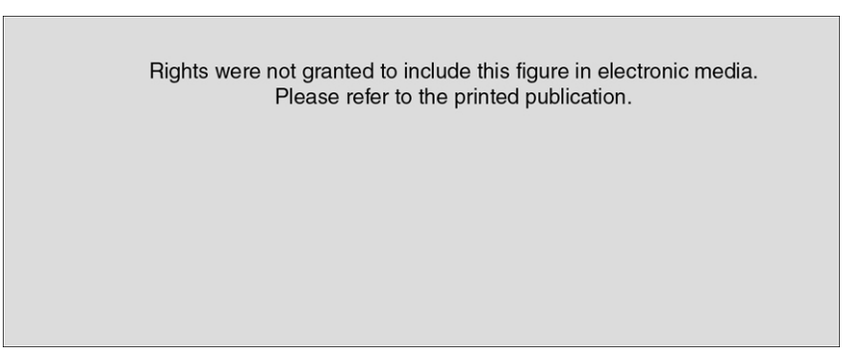

Figure 144-13. Tall and wide QRS complexes and S-T slurring *(arrow)* indicate left ventricular enlargement in this cat with hypertrophic cardiomyopathy. (From Tilley LP: Essentials of Canine and Feline Electrocardiography, 3rd ed. Philadelphia: Lea & Febiger, 1992.)

- *Cat:* R > 1.0 mV in CV_6LU (V_4). R > 0.9 mV in lead II or aVF. R wave or Q wave > 1.0 in V_{10}.

Right Atrial Enlargement

Right atrial enlargement is characterized by taller-than-normal P waves in lead II (Fig. 144-14).

- *Dog:* P > 0.4 mV (or prolonged P wave in some dogs).
- *Cat:* P > 0.2 mV (tall P waves may also indicate left atrial enlargement in cats).

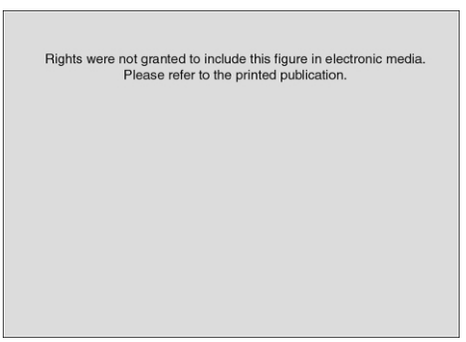

Figure 144-14. Tall P waves suggestive of right atrial enlargement. (From Tilley LP: Essentials of Canine and Feline Electrocardiography, 3rd ed. Philadelphia: Lea & Febiger, 1992.)

Right Ventricular Enlargement

Right ventricular enlargement is characterized by one or more of the following (Fig. 144-15):

- Right axis orientation (dog > +100 degrees; cat > +160 degrees)
- S wave in leads I, II, III, and aVF
- S wave in lead I greater than 0.05 mV (dog)
- Chest leads
  - *Dog:* S greater than 0.8 mV in CV_6LL (V_2). S greater than 0.7 mV in CV_6LU (V_4). R/S ratio less than 0.87. T positive (except for the Chihuahua) and W-shaped QRS complex in V_{10}.
  - *Cat:* Prominent S waves in CV_6LL (V_2) and CV_6LU (V_4); T positive in V_{10}.

SPECIAL DIAGNOSTIC PROCEDURES

Postexercise Electrocardiography

Patients with suspected cardiac disease or arrhythmia, based on auscultation or history of syncope or exercise intolerance, may have normal resting ECGs. Sometimes, an arrhythmia can be documented by repeating an ECG after vigorous exercise. T wave changes or S-T segment abnormalities may become apparent following exercise, suggesting underlying myocardial disease.

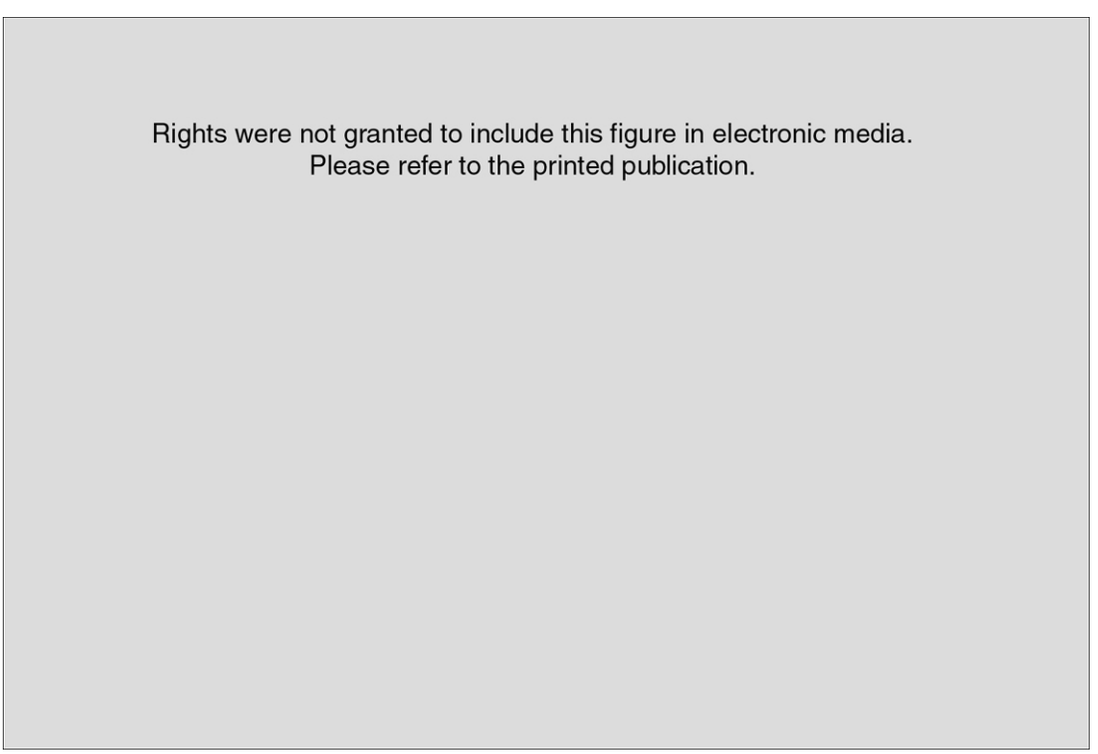

Figure 144-15. Marked right axis deviation in a dog with advanced heartworm disease and evidence of right-sided heart failure. (From Tilley LP: Essentials of Canine and Feline Electrocardiography, 3rd ed. Philadelphia: Lea & Febiger, 1992.)

Vagal Maneuvers

Indications

- Vagal maneuvers are sometimes useful in evaluating supraventricular tachycardias. A sudden surge of vagal tone may slow or block conduction down the AV node. This effect may terminate reentrant supraventricular tachycardia or "uncover" atrial flutter or tachycardia when there is regular AV conduction and atrial activity is buried within the ST-T.
- Vagal maneuvers may also help evaluate baroreceptor and sinus node functions.

Technique

- While running a lead II rhythm strip, vigorously massage the carotid sinuses that are located under the mandible in the jugular furrow.
- If this maneuver does not break the tachycardia, apply gentle, progressive ocular pressure.
- If still unsuccessful, apply ocular pressure and carotid sinus massage.

Interpretation

- If a supraventricular tachycardia breaks abruptly and the rhythm remains normal for at least a short time after stopping the vagal maneuver, the arrhythmia was probably reentrant atrial (supraventricular) tachycardia.
- If the rate gradually slows during the vagal maneuver and then speeds up again after the vagal maneuver, the rhythm is probably sinus tachycardia.
- If multiple P waves (>300/min) are observed, related to vagal-induced AV block, either atrial tachycardia or flutter is likely.
- If there is no change during the vagal maneuver, no conclusion can be made regarding the nature of the supraventricular tachycardia.
- Another area in which a vagal maneuver may be helpful is in trying to rule out bradyarrhythmia as a cause of syncope. If the vagal maneuver results in prolonged periods of sinus arrest or produces AV block, this supports sinus or AV nodal disease as a cause of syncope.

Holter Monitoring

Holter monitors provide a 24-hour ECG recording (Fig. 144-16). These recordings are ideal for identifying intermittent arrhythmias, determining the frequency and severity of arrhythmias, and monitoring the efficacy of antiarrhythmic drug therapy.

- Holter monitoring may be helpful in patients with syncope in which routine ECGs and laboratory evaluation do not confirm a diagnosis. If arrhythmias are identified on Holter monitoring of a patient with a history of syncope, the cause of the collapsing episodes may be discovered, although an event monitor is more specific in this situation (see below).

▼ ***Key Point*** The veterinarian cannot be certain that an arrhythmia identified on a Holter recording of an animal with syncope is the cause of the animal's problem, unless the animal has a syncopal episode or related clinical signs at the same time the arrhythmia is recorded.

- Holter monitoring is also used as a screening tool for the diagnosis of arrhythmogenic right ventricular cardiomyopathy (boxer cardiomyopathy) in boxers and occult cardiomyopathy in Doberman pinschers.
  - While in most breeds normal animals will have fewer than 25 VPCs in 24 hours, the threshold for normal may be higher in boxers The presence of greater than 100 VPCs, couplets, or runs is highly suggestive of arrhythmogenic right ventricular cardiomyopathy in boxers.
  - In Doberman pinchers, the presence of VPCs is a risk factor for development of dilated cardiomyopathy. In one study of Doberman pinschers with normal echocardiograms, all animals with greater than 50 VPCs per 24 hours, 94% with greater than 10 VPCs per 24 hours, and 94% with couplets or triplets of VPCs developed echocardiographic evidence of dilated cardiomyopathy within 1 year. However, not all Dobermans pinschers with VPCs develop cardiomyopathy and the absence of VPCs on a 24-hour Holter study does not rule out the subsequent development of dilated cardiomyopathy.
- When using Holter monitoring of antiarrhythmic therapy, a greater than 85% reduction in the frequency of VPCs in an indication of effective arrhythmia suppression.
- Holter monitoring is offered by some veterinary cardiologists and transtelephonic ECG services, and it sometimes can be arranged through a local medical cardiologist. Holter recordings should be reviewed by a veterinary cardiologist, as technicians trained to read human Holter studies often overinterpret atrial premature complexes on canine ECGs.

Event Recorders

Event or loop recorders are the best diagnostic tool for identifying arrhythmias as the cause of syncope. These are small digital ECG recorders that can easily be worn by even small dogs and cats.

- These units record a continuous 5-minute loop of an ECG. After the veterinarian attaches the system, the animal is sent home. When the animal has an event (e.g., syncope, collapse, or seizure) the owner pushes a button to activate the memory feature, which preserves the ECG in memory for a preprogrammed

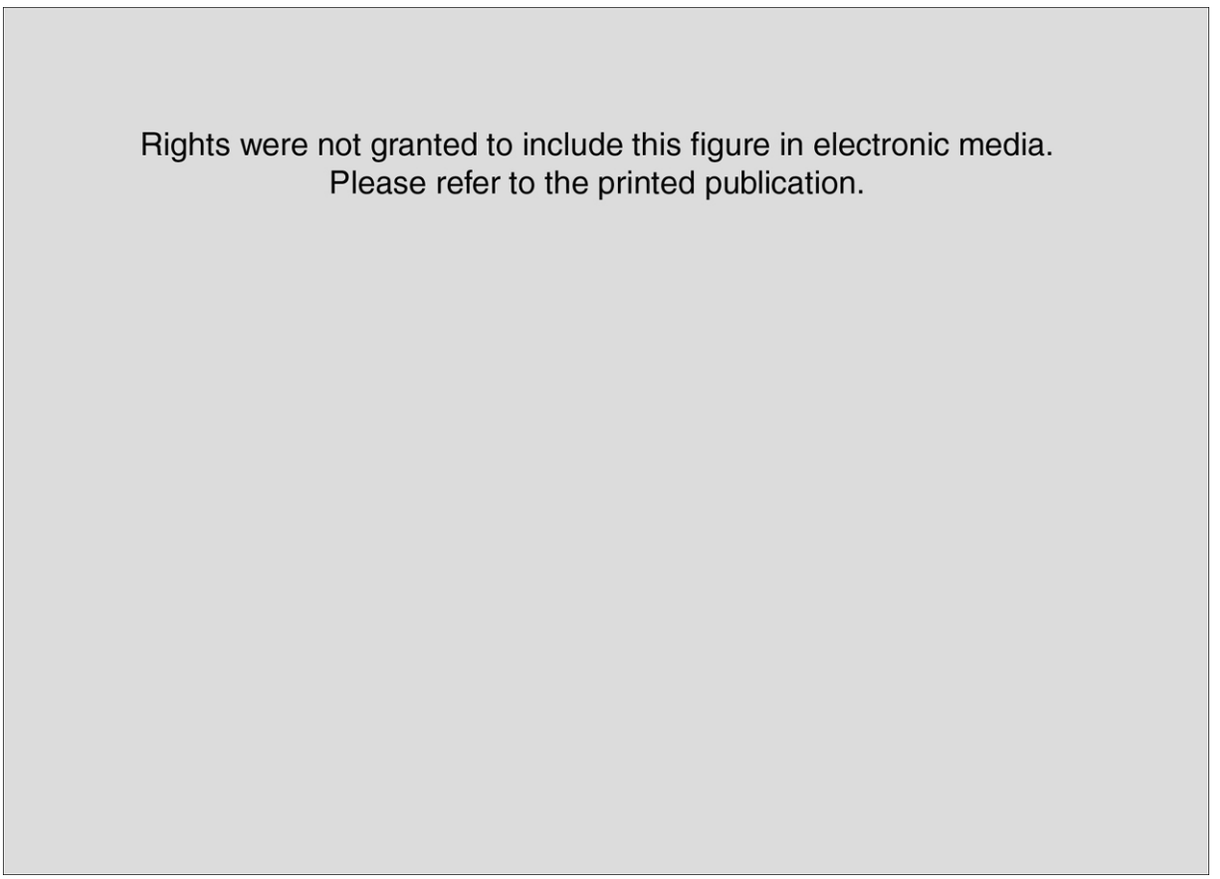

Figure 144-16. Printouts of three displayed time segments from a 24-hour electrocardiographic recording (Holter monitoring). The period of ventricular tachycardia can be easily recognized and correlated with the times of occurrence by referring to the digital time entries displayed adjacent to the electrocardiographic data. Detected ventricular ectopic activity can be efficiently enlarged, especially on the 15-second time segment (bottom frame) for more complete analysis and documentation. (From Tilley LP: Essentials of Canine and Feline Electrocardiography, 3rd ed. Philadelphia: Lea & Febiger, 1992.)

time before, during, and following the event. After the recording is made, it can be transmitted transtelephonically for printing and interpretation of the ECG.

- In animals with frequent syncopal episodes, an event monitor is preferable to a Holter monitor for making a diagnosis because the event recording is timed with the clinical signs. In a study of 60 collapsing animals, 51 tracings (85%) were diagnostic, ruling out arrhythmias in 65% and confirming arrhythmias in 35%.

Lidocaine Response Test

Patients with sustained, wide, complex tachycardia (ventricular tachycardia or atrial tachycardia with a bundle branch block) may be administered lidocaine (2–4 mg/kg IV) to help establish a diagnosis. Termination of the arrhythmia suggests the disturbance is a lidocaine-responsive, ventricular tachycardia. Occasionally, an atrial tachycardia will break following the administration of lidocaine.

Atropine Response Test

Patients with symptomatic bradyarrhythmia may be administered a test dose of atropine (0.05 mg/kg IM or SC) and undergo an ECG 30 minutes later. This test is helpful in determining the role of vagal tone in the bradyarrhythmia and whether or not oral anticholinergic drugs (e.g., hyoscyamine) might alleviate some symptoms associated with the bradycardia, particularly when pacing is not an option.

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Chapter

145 Disorders of Cardiac Rhythm

Michael S. Miller / Larry Patrick Tilley / Francis W.K. Smith, Jr.

Cardiac arrhythmias include disorders of cardiac impulse formation, conduction, rate, and regularity. Terms such as dysrhythmia, ectopia, and ectopy also are used to identify arrhythmias. Cardiac arrhythmias can be benign and clinically insignificant, or they can cause clinical signs. They can even progress to malignant arrhythmias that lead to heart failure, syncope, or sudden death.

Causes of cardiac arrhythmias include heart disease and disorders involving the autonomic nervous system, endocrine system, electrolytes, and other body systems. Anesthetic agents and other drugs can precipitate rhythm disturbances. Cardiac arrhythmias are diagnosed and classified electrocardiographically; see Chapter 144 for additional pertinent information regarding electrocardiography. A summary of the clinical pharmacology of drugs used in the treatment of congestive heart failure (CHF) is found in Chapter 146.

ETIOLOGY

- Cardiac arrhythmias are classified in Table 145-1. They occur with congenital or acquired cardiac disease or systemic disorders (Table 145-2).
- Cardiac pathology does not necessarily correlate with the type and severity of arrhythmias.
- Arrhythmia variation in animals with cardiac or systemic disorders may be explained by the complex interactions among cardiac cell transmembrane potentials, the autonomic nervous system, and body fluids.

MECHANISMS

- The normal cardiac impulse is generated automatically in the sinus node and is spread through the atria rapidly and sequentially via the His bundle, the bundle branches, and the intraventricular conduction system to the ventricular myocardium.
- The normal atrioventricular (AV) node serves as a bridge between the atria and the ventricles and slows the cardiac impulse prior to rapid impulse conduction through the ventricles.
- Cardiac rhythm disturbances develop from diverse electrophysiologic mechanisms.
- Enhanced automaticity in sinus node or subsidiary pacemaker cells can generate tachycardias or ectopic rhythms. Such activity may be influenced by sympathetic activity.
- Triggered activities are common causes of ectopic rhythms and tachycardias. Early or late afterdepolarizations follow a previously driven (sinus) depolarization. The premature impulses occur when the cell spontaneously depolarizes during or just after repolarization.
- Reentry, a common arrhythmia mechanism, typically is caused by functional dissociation of cardiac tissue, a unidirectional block in one pathway, and slowed conduction in the other pathway. The impulse then returns to the origination point by retrograde conduction through the unidirectionally blocked pathway.
- Electrophysiologic mechanisms, arrhythmia manifestations and accompanying clinical signs and symptoms may vary widely among dogs with specific inherited cardiac diseases. Arrhythmogenic mechanisms can be modified (for better or for worse) by autonomic activity, heart rate, and many cardiac and non-cardiac drugs.

DIAGNOSTIC APPROACH

Systematic Evaluation of the Electrocardiographic Strip

See also Chapter 144.

- Is sinus rhythm or an arrhythmia present?
- Is the heart rate rapid, slow, or normal?
- Are P waves present?
  - *Yes.* Do the P (atria) waves occur at regular or irregular intervals? What are the height, width, and direction?
  - *No.* What reason or abnormality explains the absence of the P wave? Is the P wave superimposed

Table 145-1. CLASSIFICATION OF CARDIAC ARRHYTHMIAS

Supraventricular Rhythms
Sinus rhythm
Sinus arrhythmia
Sinus bradycardia
Sinus tachycardia
Atrial premature complexes
Sinus block and/or arrest
Atrial tachycardia
Atrial/supraventricular tachycardia (reentrant)
Atrial flutter
Atrial fibrillation
Atrioventricular junctional rhythm

Ventricular Rhythms
Ventricular escape (rhythm)
Ventricular premature complexes
Idioventricular tachycardia
Ventricular tachycardia
Ventricular asystole
Ventricular fibrillation

Conduction Disorders
Atrial standstill
First-degree AV block
Second-degree AV block
Complete (third-degree) AV block

Arrhythmias and Conduction Disturbances
Sick sinus syndrome
Ventricular preexcitation and the Wolff-Parkinson-White syndrome

on a portion of the QRS complex, S-T segment, or T wave? Is the arrhythmia atrial standstill, atrial fibrillation, atrial flutter, AV junctional escape rhythm, or atrial tachycardia?
- Do the QRS (ventricular) complexes occur with regularity and uniformity? What is their morphology? If wide and bizarre, is this due to a ventricular arrhythmia or caused by a premature atrial impulse that is aberrantly conducted, or is bundle branch block evident?
- What is the relationship between the P waves and the QRS complexes? Is the relationship consistent?
- If AV dissociation is present, from where does the QRS complex evolve? Are AV junctional and/or Purkinje or idioventricular foci involved?

Questions To Be Answered in the Interpretation of Cardiac Arrhythmia

- What is the possible mechanism for the arrhythmia?
- Is it sinus, atrial, AV junctional, or ventricular in origin?
- Is there a conduction abnormality?
- What is the severity and frequency of the arrhythmia?

SUPRAVENTRICULAR RHYTHMS

Sinus Rhythm

Definition

- Impulses originate in the sinus node.
- The rhythm is regular with less than a 10% variation in the R-R interval.
- There is a normal P wave for each QRS complex, with a constant P-R interval.
- The heart rate is between 60 and 180 beats per minute (bpm) in dogs and between 120 and 240 bpm in cats.

Etiology and Clinical Significance

- Sinus rhythm is a normal resting rhythm in dogs and cats and requires no therapy.
- Animals with symptomatic cardiac disease or noncardiac disease may show a sinus rhythm.

Sinus Arrhythmia

Definition

- Impulses originate in the sinus node.
- The rhythm is irregular with more than a 10% variation in the R-R interval.
- There is a normal P wave for each QRS complex, with a constant P-R interval.
- A wandering pacemaker (a change in the morphology of the P wave due to a change in pacemaker location or conduction) is often present.
- Heart rates are similar to those for sinus rhythm.

Etiology and Clinical Significance

- Sinus arrhythmia is a normal rhythm variation in the resting dog, often correlated with varying levels of sinus node vagal tone, which changes with respiration (decreased vagal tone and increased heart rate during inspiration).
- Sinus arrhythmia is unusual in cats.
- Pronounced sinus arrhythmia occurs in the normal resting dog and in dogs and cats with respiratory disease.

Treatment

- No treatment is required unless there is symptomatic bradycardia, in which case anticholinergics or sympathomimetics may be helpful.

Sinus Bradycardia

Definition

- Impulses originate in the sinus node but at a slower-than-normal frequency.

Table 145-2. CAUSES OF CARDIAC ARRHYTHMIAS

Cardiac Causes in Dogs

- Heredity (genetics not documented in all cases)
  - Doberman (His bundle degeneration)
  - English springer spaniel (persistent atrial standstill)
  - Miniature schnauzer, dachshund, cocker spaniel, West Highland white terrier (sick sinus syndrome)
  - Pug, Dalmatian (sinus node disease)
  - Pug (stenosis and degeneration of the His bundle)
  - Wolff-Parkinson-White syndrome
  - Golden retriever (Duchenne muscular dystrophy)
  - German shepherd (ventricular tachyarrhythmia)
- Atrial and/or ventricular arrhythmias
  - Atrial enlargement, secondary to congenital defects or acquired disease
  - Cardiomyopathy
  - Congenital heart disease
  - Congestive heart failure
  - Mitral valve disease (congenital and acquired)
  - Myocarditis, endocarditis
  - Myocardial ischemia
  - Trauma
  - Drugs
- Conduction system disease
  - Acquired sinus and AV node disease (sick sinus syndrome)
  - Cardiomyopathy
  - Neoplasia
  - Surgical damage to conduction tissue
  - Trauma
  - Vascular (e.g., microscopic intramural myocardial infarction)
  - Ventricular septal defect and other congenital defects
  - Infection (Lyme disease)
  - Drugs
  - Degeneration

Cardiac Causes in Cats

- Heredity (rare)
  - Wolff-Parkinson-White syndrome
- Atrial and ventricular arrhythmias
  - Cardiac enlargement secondary to congenital heart defects
  - Cardiomyopathy
  - Neoplasia
  - Trauma
  - Systemic diseases
- Conduction system disease
  - Cardiomyopathy
  - Neoplasia
  - Idiopathic fibrosis in older cats

Noncardiac Causes in Dogs and Cats

Dogs and Cats

- Acidosis or alkalosis
- Autonomic nervous system imbalance (parasympathetic or sympathetic); central nervous system (pain, excitement, fear); respiratory, gastrointestinal, organic brain disease
- Drug toxicity (e.g., digitalis, preoperative sedatives, anesthetic agents, catecholamines, antiarrhythmic agents, bronchodilators)
- Electrolyte disorders (hyperkalemia, hypercalcemia, hypokalemia, hypocalcemia, hypomagnesemia)
- Endocrinopathies (hypothyroidism, hyperthyroidism, Addison's disease, pheochromocytoma)
- Hypothermia
- Hypovolemia
- Hypoxia, anemia
- Mechanical stimulation (cardiac catheterization, intravenous catheter)
- Neoplasia
- Shock
- Toxemia, sepsis
- Trauma

Adapted from Miller MS, Tilley LP: Treatment of arrhythmias and conduction disturbances. *In* Miller MS, Tilley LP, eds.: Manual of Canine and Feline Cardiology. Philadelphia: WB Saunders, 1995, with permission.

- The rhythm is regular.
- There is a normal P wave for each QRS complex, with a constant P-R interval.
- The heart rate is <70 bpm in dogs (<60 bpm in giant breeds) and <120 bpm in cats.

Etiology and Clinical Significance

- Sinus bradycardia may be a normal physiologic rhythm variation resulting from high levels of resting vagal tone.
- Hypothyroidism, sinus node disease (sick sinus syndrome), elevated cerebrospinal fluid pressure, and hypothermia are among the pathologic causes of sinus bradycardia.
- Drugs that can cause a sinus bradycardia include acepromazine, xylazine, other alpha$_2$-agonists (e.g., medetomidine), narcotics, digoxin, beta-blockers, diltiazem, pilocarpine, and general anesthetics.
- Animals with sinus bradycardia are often asymptomatic.
- Clinical signs of weakness, lethargy, and syncope may accompany sinus bradycardia.

Treatment

- Asymptomatic dogs or cats require no specific therapy.
- When correlated with signs of weakness or syncope, an atropine response test should be performed (0.04 mg/kg IM) followed by an electrocardiogram (ECG) in 15 to 30 minutes.
- If there is an increase in the cardiac rate following atropine administration, the animal may benefit from oral anticholinergic agents (Table 145-3).
- A poor clinical response to atropine suggests the need for a temporary or permanent cardiac pacemaker in symptomatic animals.

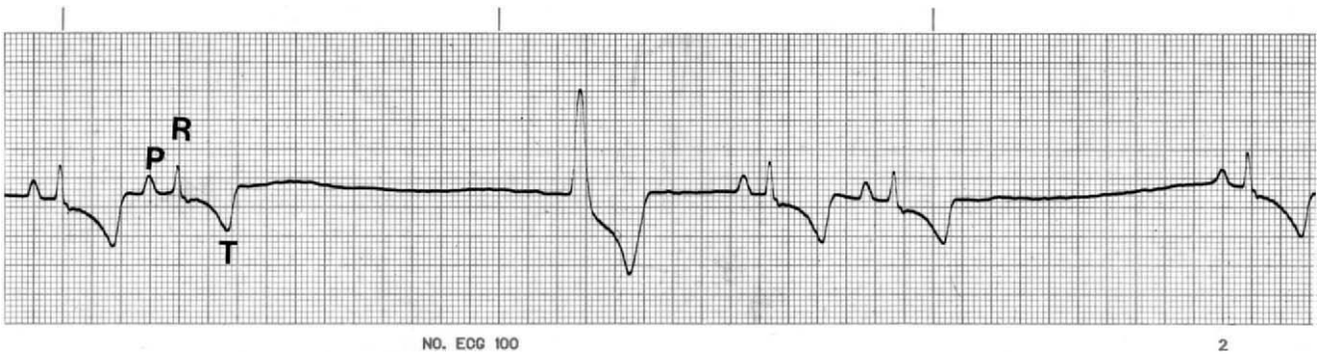

Figure 145-1. Sinus block and/or arrest with a ventricular escape beat in a dog. (Lead II rhythm strip, paper speed 50 mm/sec; 1 cm = 1 mV.)

- CHF may also develop, in which case consider diuretics and vasodilators as adjunctive treatment. Digitalis may exacerbate the sinus bradycardia in these cases. Hypotension may develop from vasodilator therapy.

Sinus Block and/or Sinus Arrest (Fig. 145-1)

Definition

- A primary disorder of the sinus node resulting in lack of generation of the cardiac impulse or its poor propagation across surrounding tissue.
- It is not possible to distinguish between sinus block and sinus arrest in dogs because of the normal variation in the R-R interval (sinus arrhythmia).
- The heart rate is variable and is often correlated with a bradycardia or slow sinus arrhythmia.
- The rhythm is regularly irregular or irregular with pauses.
- There is a normal P wave for each QRS complex with a pause equal to or greater than 2 times the normal R-R interval.
- The P wave may vary in shape if a concurrent wandering pacemaker is present.

Etiology and Clinical Significance

- Sinus arrest may be consistent with an increase in vagal tone (e.g., ocular pressure, irritation of the vagus nerve, brachycephalic breeds, or respiratory disease).
- Diseases of the atria (including fibrosis, cardiomyopathy, and neoplasia) and drug toxicity (e.g., digitalis, propranolol, quinidine, xylazine, and acepromazine) may result in sinus arrest.
- Sinus arrest is one of the arrhythmias of the sick sinus syndrome.

Electrocardiographic Differentials

- Sinus block and/or sinus arrest can be confused with marked sinus arrhythmia or with sinus bradycardia and non-conducted atrial premature complexes (APCs).

Treatment

- Treat the same as sinus bradycardia.

Sinus Tachycardia

Definition

- Impulses originate in the sinus node but at a faster-than-normal frequency.
- The rhythm is regular.
- There are normal P waves for each QRS complex.
- The heart rate is >140 bpm in the giant breeds, >180 bpm in toy-breed dogs, and >240 bpm in cats.

Etiology and Clinical Significance

- Sinus tachycardia may be a normal physiologic rhythm resulting from high sympathetic tone occurring with exercise or excitement.
- Sinus tachycardia may also occur with conditions such as stress, anxiety, pain, shock, fever, anemia, CHF, hyperthyroidism, and pheochromocytoma.
- Drugs (e.g., atropine, sympathomimetic agents, theophylline, ketamine, and light anesthesia) and intoxicants (caffeine, chocolate, cocaine) also can cause sinus tachycardia.

Electrocardiographic Differentials

- Other supraventricular tachyarrhythmias confused with sinus tachycardia include paroxysmal (atrial or AV junctional) tachycardia, atrial flutter with 2:1 AV block, and ventricular tachycardia when sinus tachycardia is associated with wide QRS complexes.
- A vagal maneuver (e.g., carotid sinus or ocular stimulation for 5 to 10 seconds) may result in a transient, gradual slowing of the sinus tachycardia.

Treatment

- Identify and treat the underlying cause of the sinus tachycardia.

Table 145-3. COMMON ANTIARRHYTHMIC DRUGS: FORMULATIONS, INDICATIONS, AND DOSAGES

Drug Trade Name	Formulation	Indications	Dosages	Comments
Amiodarone (Cordarone)	Tab: 200 mg	Class III antiarrhythmic agent; indicated for severe refractory atrial and ventricular arrhythmias	Dog: 10–20 mg/kg PO q12h Cat: None	Use as last resort for recurrent hemodynamically unstable ventricular tachycardia Takes weeks to achieve therapeutic levels
Atenolol (Tenormin)	Tab: 25, 50, 100 mg OS: 25 mg/ml Inj: 0.5 mg/ml	Atrial and ventricular arrhythmias, hypertrophic cardiomyopathy, hypertension, aortic stenosis	Dog: 0.25–1.0 mg/kg PO sid–bid Cat: 6.25–12.5 mg total dose PO sid–bid	Less bronchoconstriction, vasoconstriction, interference with insulin therapy than with non-selective beta-blockers Taper dose when discontinuing therapy Decrease dose with renal disease
Atropine sulfate*	Inj: 0.05, 0.1, 0.3, 0.4, 0.5, 0.8, 1.0 mg/ml	Sinus bradycardia, AV block, sick sinus syndrome, cardiac arrest	Dog: 0.01–0.04 mg/kg IV, IM, IO 0.02–0.04 mg/kg SC tid–qid (IT: double dose) Cat: Same	May transiently worsen bradyarrhythmia More potent chronotropic effects than glycopyrrolate
Digoxin* (Lanoxin)	Tab: 0.125, 0.25, 0.5 mg Inj: 0.25 mg/ml Elixir: 0.05 mg/ml Cap: 0.05, 0.1, 0.2 mg	Supraventricular arrhythmias, myocardial failure	Dog: *Maintenance dose*—0.22 mg/m^2 PO bid, 0.0055–0.01 mg/kg PO bid *IV loading dose*—0.0025 mg/kg IV bolus repeated hourly 3–4 times (total up to 0.01 mg/kg). Begin oral therapy 12 hours later *Oral loading dose*—Twice maintenance dose for first 24–48 hours Cat: 0.01 mg/kg PO qod (Tab preferred) 0.007 mg/kg PO qod (with furosemide and aspirin)	Toxicity potentiated by hypokalemia, hyponatremia, hypercalcemia, thyroid disorders, hypoxia Dose on lean body weight; reduce dose 10%–15% with elixirs Therapeutic range 1–2 ng/ml 8 hours after a dose Rapid digitalization not recommended except in emergency Reduce dose 50% with quinidine
Diltiazem (Cardizem, Dilacor)	Tab: 30, 60, 90, 120 mg Inj: 5 mg/ml Cardizem: 120, 180, 300 mg Dilacor: 120, 180, 240 mg	Supraventricular arrhythmias, hypertrophic cardiomyopathy, hypertension	Dog: 0.5–2.0 mg/kg PO tid (consider higher dose of 5 mg/kg based on recent studies) 0.1–0.2 mg/kg IV bolus, then 2–6 µg/kg/min IV CRI *Dilacor*—1.5–6 mg/kg PO sid Cat: 1.0–2.5 mg/kg PO tid 0.1–0.2 mg/kg IV bolus, then 2–6 µg/kg/min IV CRI *Dilacor*—30–60 mg PO sid	Less myocardial depression than verapamil Dilacor capsules contain 60-mg tablets used for dosing cats
Epinephrine* (Adrenalin)	Inj: 1:1000 conc (1 mg/ml) 1:10000 conc (0.1 mg/ml)	Cardiac arrest	Dog: 0.2 mg/kg IV, IO q3–5min Double dose for IT administration Cat: Same	Monitor with ECG Previously recommended dose of 0.02 mg/kg may be safer starting dose if defibrillator is not available
Esmolol (Brevibloc)	Inj: 10, 250 mg/ml	Supraventricular tachyarrhythmias, ventricular tachycardia, dynamic outflow tract obstruction	Dog: 50–500 (usually 50–100) µg/kg IV bolus every 5 minutes (up to 500 µg/kg) 50–200 µg/kg/min CRI Cat: Same	Ultra–short-acting beta$_1$-selective beta-adrenergic blocker
Glycopyrrolate* (Robinul)	Inj: 0.2 mg/ml	Sinus bradycardia, AV block, sick sinus syndrome	Dog: 0.005–0.01 mg/kg IV, IM 0.01–0.02 mg/kg SC Cat: Same	Longer duration of action with less of a chronotropic effect than atropine
Isoproterenol (Isuprel)	Inj: 1:5000 (0.2 mg/ml)	Short-term management of sinus bradycardia, AV block, sick sinus syndrome	Dog: 0.04–0.09 µg/kg/min IV (titrate up to effect) 10 µg/kg/min IM, SC qid Cat: Same	
Lidocaine* (Xylocaine)	Inj: 5, 10, 15, 20 mg/ml (without epinephrine)	Ventricular arrhythmias	Dog: 2–8 mg/kg slowly IV or IO (double the dose IT) in 2-mg/kg boluses followed by IV drip at a dosage of 25–75 (occasionally up to 100) µg/kg/min CRI Cat: 0.25–0.75 mg/kg IV over 5 min	Use with caution in cats Drug of choice for initial control of ventricular tachycardia Effects increased by high potassium and decreased by low potassium Seizures controlled with diazepam

Metoprolol (Lopressor)	Tab: 50, 100 mg/kg Inj: 1 mg/ml	Atrial and ventricular arrhythmias cardiomyopathy	Dog: 0.25–1.0 mg/kg PO tid Cat: Same	Less bronchoconstriction, vasoconstriction, interference with insulin therapy than with non-selective beta-blockers Taper dose when discontinuing therapy
Mexiletine (Mexitil)	Cap: 150, 200, 250 mg	Ventricular arrhythmias	Dog: 5–8 mg/kg PO bid–tid Cat: None	Reduce dose with liver disease Take with food to reduce GI side effects Synergistic effect when combined with beta-blockers
Procainamide* (Procan SR, Pronestyl SR, Procainamide CR)	Cap: 250, 375, 500 mg Tab: 250, 375, 500 mg Tab Procan, Pronestyl SR; 250, 500, 750, 1000 mg Inj: 100, 500 mg/ml	Ventricular and supraventricular arrhythmias, WPW syndrome	Dog: 10–30 mg/kg IM PO qid (Procan SR, Pronestyl SR, Procainamide CR; tid) 2 mg/kg IV over 3–5 min up to total dose of 20 mg/kg 20–50 µg/kg/min CRI Cat: 3–8 mg/kg PO, IM tid–qid	Beware of hypotension with IV administration Effects increased by high potassium and decreased by low potassium Monitor ECG: 25% prolongation of QRS is sign of toxicity Fewer GI and CV side effects than quinidine Use with caution in cats Reduce dose with severe renal and liver disease
Propranolol* (Inderal)	Tab: 10, 20, 40, 60, 80, 90 mg Inj: 1 mg/ml OS: 4, 8, 80 mg/ml	Atrial and ventricular arrhythmias, hypertrophic cardiomyopathy, hypertension, thyrotoxicosis	Dog: 0.2–1.0 mg/kg PO tid 0.02–0.06 mg/kg IV over 5–10 minutes C < 4.5 kg: 2.5–5 mg PO bid–tid C > 4.5 kg: 5 mg PO tid–tid 0.02–0.06 mg/kg IV over 5–10 minutes	Non-selective beta-blocker Start with low dose and titrate to effect Taper dose when discontinuing therapy Reduce dose with liver disease
Quinidine gluconate* (Quinaglute Dura-Tabs)	Tab: 324 mg Inj: 80 mg/ml	Ventricular and supraventricular arrhythmias, WPW syndrome, conversion of atrial fibrillation	D:† 6–20 mg/kg PO, IM qid 6–20 mg/kg PO tid with sustained release products 5–10 mg/kg IV (very slowly) Cat: None	Decrease digoxin dose 50% when using quinidine Effects increased by high potassium and decreased by low potassium Monitor ECG: 25% prolongation of QRS is sign of toxicity Has vagolytic, negative inotropic, vasodilating properties Reduce dose in CHF, hepatic disease, hypoalbuminemia Quinidine base (%) in each quinidine salt Quinidine gluconate (62%): 324-mg Tab = 200 mg of quinidine
Quinidine polygalacturonate (Cardioquin)	Tab: 275 mg			
Quinidine sulfate* (Quinidex)	Tab: 200, 300 mg Tab SR: 300 mg Inj: 200 mg/ml			
Sotalol (Betapace)*	Tab: 80, 120, 160, 240 mg	Ventricular arrhythmias	Dog: 1–3.5 mg/kg PO bid Cat: 1/8 of 80-mg Tab PO bid	Antiarrhythmic agent with class II (beta-blocking) and class III effects May be proarrhythmic when administered as sole agent in young German shepherds with inherited ventricular arrhythmias
Tocainide (Tonocard)	Tab: 400, 600 mg	Ventricular arrhythmias	Dog: 10–20 mg/kg PO bid–tid Cat: None	Oral analogue of lidocaine Giving with food may decrease GI upset
Verapamil* (Calan, Isoptin)	Tab: 40, 80, 120 mg Inj: 2.5 mg/ml	Supraventricular arrhythmias, hypertrophic cardiomyopathy	Dog: 0.05–0.20 mg/kg slow IV (1–2 minutes) in boluses of 0.05 mg/kg given at 10- to 30-minute intervals (to effect) Cat: None	Diltiazem is safer alternative in heart failure Potent vasodilator and negative inotrope

*Available in a generic preparation.

†Note: Dosage calculated for quinidine base equivalent, which varies with each quinidine salt. See Comment column.

AV, atrioventricular; Cap, capsules; CHF, congestive heart failure; conc, concentration; CRI, constant rate infusion; ECG, electrocardiogram; GI, gastrointestinal; Inj, injectable; IT, intratracheal; OS, oral solution; Tab, tablets; WPW, Wolff-Parkinson-White.

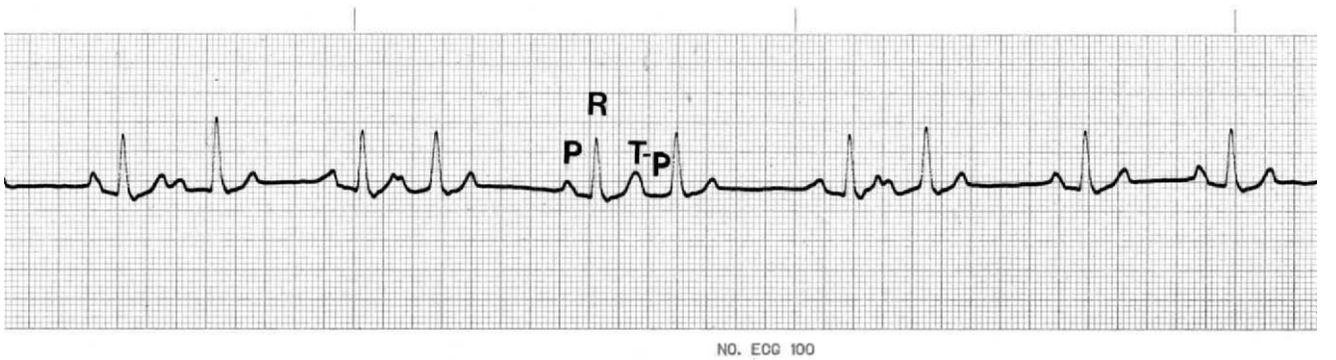

Figure 145-2. Atrial premature complexes in a dog. (Lead II rhythm strip, paper speed 50 mm/sec; 1 cm = 1 mV.)

- Antiarrhythmic drugs are seldom required.
- Administer atenolol (6.25 mg total dose q12–24h PO) or propranolol (2.5 mg total dose q8–12h PO) to hyperthyroid cats with intractable tachycardia (i.e., unresponsive to antithyroid medication).
- Administer digitalis for sinus tachycardia in CHF. Digoxin will reestablish normal baroreceptor function and lessen sympathetic tone.

Atrial Premature Complexes (Fig. 145-2)

Definition

- Impulses originate from an atrial focus, often other than the sinus node.
- The rhythm is irregular and the heart rate varies with the sinus node rate.
- There is usually an abnormal P' wave (premature P wave) followed by a normal QRS complex. The P'-R interval of the APC may vary from the sinus rhythm P-R interval. The P' wave may have various morphologies and may be fused with the T wave of the preceding beat.
- The P′ wave may occur so early in the cardiac cycle that the AV conduction system will be refractory and the impulse will not be conducted to the ventricles (e.g., APC with physiologic AV block).
- The pause following the APC is often less than fully compensatory because of premature depolarization and resetting of the sinus node. Full compensatory pause occurs when the R wave-to-R wave interval surrounding the APC is equal to two normal R-R intervals.
- The QRS complex is usually normal, but the intraventricular conduction system may be, in a relative or absolute refractory period, causing a bizarre (abnormal shape or direction) QRS complex. This abnormality is termed an APC with aberrant ventricular conduction.

Etiology and Clinical Significance

- APCs often indicate underlying cardiac disease (e.g., chronic valvular fibrosis, cardiomyopathy, congenital defect, or cor pulmonale) resulting in atrial enlargement.
- Other causes include electrolyte disturbances, thyrotoxicosis, hypoxia, anemia, drug toxicity (e.g., digitalis, dobutamine, or dopamine), toxemia, and increased sympathetic tone.

Electrocardiographic Differentials

- Sinus rhythm with APCs may be confused with marked sinus arrhythmia and ventricular premature complexes during auscultation, and with ventricular premature complexes on the ECG, when APCs are conducted with aberrant ventricular conduction.
- A P′ wave preceding the abnormal QRS complex and a similarity of the initial deflection of the QRS complex compared with a preceding normal beat supports the diagnosis of aberrant conduction.

Treatment

- Infrequent APCs may be a normal variation and do not require treatment.
- If this arrhythmia is associated with CHF, treat the arrhythmia with digoxin.
- If the APCs are associated with poor hemodynamic status without myocardial failure, prescribe digoxin, diltiazem, or a beta-blocker (e.g., propranolol or atenolol) (see Table 145-3).

Atrial Tachycardia (Figs. 145-3 and 145-4)

Definition

- Atrial tachycardia indicates rapid, abnormal impulses originating from an atrial site other than the sinus node.
- The atrium and/or AV junctional areas may be involved in a reentrant circuit that allows the impulse to restimulate the atrium, as well as to pass to the ventricles. (A vagal maneuver may abolish this arrhythmia.)
- An abnormal automatic focus in the atrium may also be responsible for this arrhythmia. (A vagal maneu-

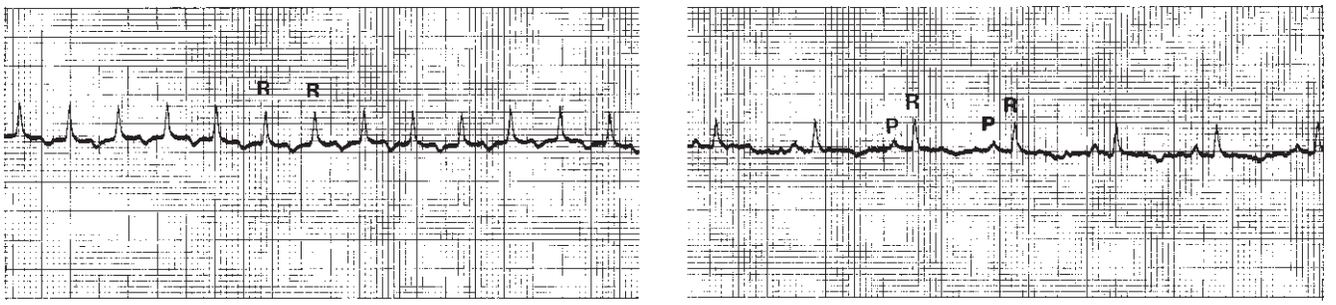

Figure 145-3. Paroxysmal atrial tachycardia *(left)* and after termination by a vagal maneuver *(right)* in a cat. (Lead II rhythm strip, paper speed 50 mm/sec; 1 cm = 1 mV.)

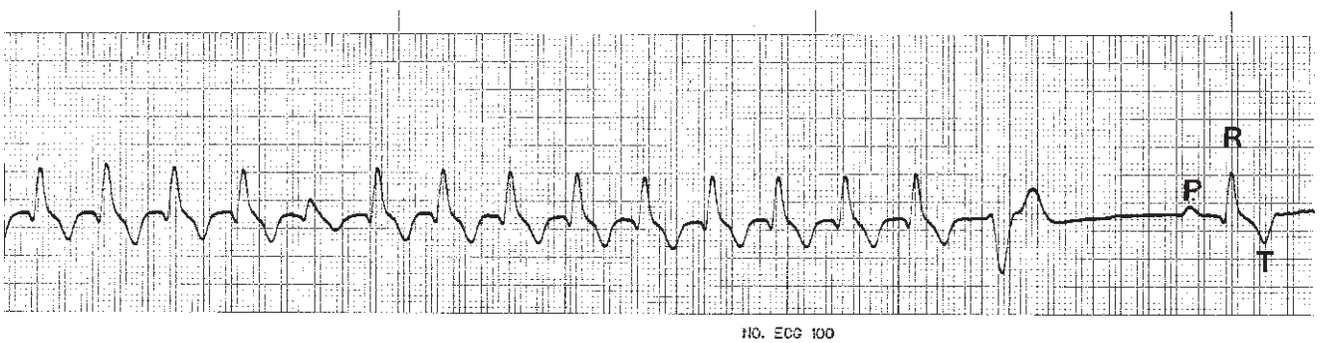

Figure 145-4. Paroxysmal atrial tachycardia terminated after a ventricular premature complex in a dog. (Lead II rhythm strip, paper speed 50 mm/sec; 1 cm = 1 mV.)

ver will cause AV block but not abolish the atrial tachycardia.)
- The heart rate is >140 to 180 bpm in dogs and >240 bpm in cats, in which it often approaches 300 bpm.
- The rhythm is usually regular but may be slightly irregular.
- There is a P′ wave for each QRS complex, although the P′ wave is usually of different morphology than the sinus P wave. The P-R interval is constant.
- The P′ wave may not be evident because it may be fused with the preceding T wave or occur simultaneously with the preceding QRS complex.
- The QRS complex may also be of different morphology because of aberrant ventricular conduction.
- An irregular R-R interval may be caused by concurrent AV block or by multifocal atrial tachycardia (P' waves varying in shape, the firing of two or more ectopic atrial foci).

Etiology and Clinical Significance

- Atrial tachycardia suggests severe myocardial or conduction system disease.
- This arrhythmia also may be secondary to digitalis toxicity or may occur under general anesthesia.
- Systemic disease that results in autonomic nervous systemic abnormalities also may be a cause.
- In cats, this arrhythmia is correlated with cardiomyopathy and hyperthyroidism.

Differential Diagnosis

- Atrial tachycardia can be confused with sinus tachycardia, AV junctional tachycardia, and atrial flutter.
- A vagal maneuver may be helpful diagnostically. Abrupt termination suggests AV nodal reentry, whereas transient AV block may develop with atrial tachycardia or atrial flutter, allowing abnormal P′ waves or atrial flutter waves to be identified at the baseline.

Treatment

- Sustained (non-paroxysmal) atrial tachycardia often is associated with weakness, hypotension, CHF, and syncope and requires immediate therapy.
- A vagal maneuver (ocular pressure or carotid sinus pressure) (see Chapter 144) may terminate an atrial tachycardia but generally only causes transient block of ectopic P' waves.
- If CHF is present, administer digitalis for the arrhythmia. IV digoxin, given cautiously, may slow the ventricular response and improve the clinical status (see Table 145-3).
- If digoxin is ineffective, IV diltiazem, verapamil, esmolol, or propranolol may convert supraventricular tachycardia (or atrial tachycardia) to sinus rhythm or slow the ventricular response rate. Use propranolol and verapamil with great caution because they

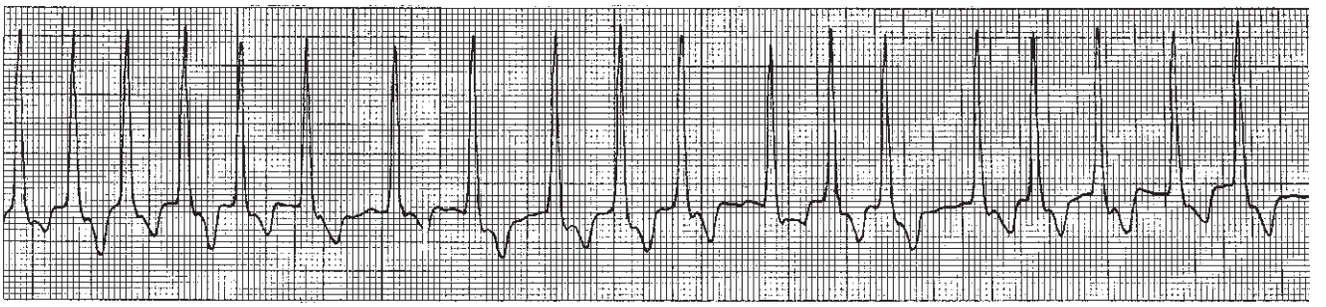

Figure 145-5. Atrial fibrillation in a dog. (Lead II rhythm strip, paper speed 50 mm/sec; 1 cm = 1 mV.)

may depress cardiac contractility and exacerbate CHF.

- For atrial tachycardia without CHF, initiate therapy with diltiazem, verapamil, or a beta-blocker (e.g., esmolol, atenolol, propranolol, or sotalol).
- Intramuscular procainamide or quinidine gluconate also have been used to convert atrial tachycardia to normal sinus rhythm in dogs with refractory atrial tachycardia.
- Atrial (supraventricular) tachycardia associated with accessory pathways (most commonly reported in Labrador retrievers) may respond acutely to IV therapy with diltiazem, verapamil, or procainamide. For long-term management, oral procainamide with or without a beta blocker is recommended. Digoxin is generally not recommended as it may preferentially direct current to the accessory pathway, which can be dangerous should atrial fibrillation develop. A class III antiarrhythmic such as sotalol or amiodarone can be tried in refractory cases.
- Radiofrequency catheter ablation following electrophysiologic mapping of reentrant or accessory pathway circuits is available at select referral centers for refractory symptomatic atrial tachyarrhythmias as a potential arrhythmia cure without permanent implantation devices.
- Reserve electrical cardioversion for refractory cases, to be administered only by an experienced veterinary cardiologist possessing the proper equipment.

Atrial Fibrillation (Fig. 145-5)

Definition

- A high number of disorganized atrial impulses, caused by a disorder of reentry within the atria, bombard the AV node, leading to an irregular rhythm.
- Many of these impulses approach the AV node in a refractory period and are not conducted to the ventricles, or they affect the conduction of subsequent impulses (concealed conduction).
- The heart rate is usually rapid (often >180 bpm in dogs and >240 bpm in cats), and the rhythm is irregular.

▼ ***Key Point*** The lack of P waves, an irregularly irregular rhythm on all ECGs leads, and an arterial pulse deficit are the hallmarks of atrial fibrillation.

- No P waves are seen, but there are normally shaped QRS complexes. Instead of P waves, small or large oscillations (f waves) are present.
- There may be some variation and widening of the QRS complexes due to aberrant ventricular conduction or bundle branch block. Subtle beat-to-beat variation may be observed in cats with atrial fibrillation.

Etiology and Clinical Significance

- Atrial fibrillation commonly occurs in patients with cardiomyopathy, advanced chronic valvular heart disease, pericarditis, and progressive congenital heart disease.
- Other rare etiologies include severe ischemia or shock (gastric dilatation-volvulus after cardiac arrest), atrial tumor (hemangiosarcoma), and electrolyte disturbances (hyperkalemia).
- Loss of atrial contraction decreases the stroke volume and cardiac output. The rapid ventricular rate also results in poor cardiac output.
- "Slow" atrial fibrillation (ventricular response rate <100 bpm) may signify drug toxicity (e.g., digitalis or a beta blocker), concurrent AV block, or very low sympathetic tone.
- Atrial fibrillation without echocardiographic evidence of structural heart disease is often termed lone atrial fibrillation. The ventricular response rate is relatively slow, typically in the 70- to 120-bpm range during a routine examination. Auscultation is more suggestive of sinus arrhythmia than atrial fibrillation. This condition develops most commonly in giant-breed dogs such as Irish wolfhounds.

Differential Diagnosis

- Atrial fibrillation can be confused with frequent APCs, AV junctional tachycardia with AV block, atrial tachycardia with AV block, and atrial flutter with AV block.

- Atrial flutter usually shows a regular R-R interval, and the atrial oscillations (F waves) are larger than f waves.

Treatment

- Since most dogs and virtually all cats with this arrhythmia have heart failure, digoxin is the initial treatment of choice to slow the ventricular response (see Table 145-3). Rarely, a sinus rhythm will return.
- After approximately 3 to 7 days, if the ventricular rate is not controlled, add a calcium channel antagonist such as diltiazem (begin with 0.5 mg/kg q8h) and increase the dose slowly until the resting ventricular rate is adequately controlled. The optimal ventricular response rate for dogs or cats with CHF and atrial fibrillation has not been determined, but most clinicians aim for rates of <140 to 160 bpm. Once CHF has been controlled, beta-blockers can cautiously be added to slow the rate further. Beta-blockers have greater negative inotropic effects than diltiazem and therefore are more likely to induce signs of CHF in marginally compensated patients with myocardial failure. However, studies in humans indicate that, when tolerated, long-term use of beta-blockers such as carvedilol and metoprolol actually improves myocardial function (see "Beta-blockers" in Chapter 146 for details).
- Although it is unusual to convert atrial fibrillation to normal sinus rhythm in dogs, the antiarrhythmic drugs (procainamide, quinidine) or calcium channel blockers (verapamil, diltiazem) may be useful for this purpose provided the dog is not in heart failure. In perioperative patients without CHF, IV or oral diltiazem is a good choice as it quickly controls the ventricular rate and may be associated with conversion to normal sinus rhythm. A normal-sized heart, recent onset of atrial fibrillation, and lack of CHF favor the use of these drugs (or electrical cardioversion). Quinidine use requires real caution as it may increase the ventricular response rate.
- Direct current, electrical cardioversion is another option for conversion of atrial fibrillation to normal sinus rhythm. Recent reports indicate a high rate of cardioversion with the newer biphasic cardioversion devices. General anesthesia is required. Maintenance of sinus rhythm requires chronic administration of amiodarone; otherwise, atrial fibrillation is likely to recur very soon in many dogs. The indications, risk-benefits, and selection of patients for this procedure should be discussed with a cardiac specialist.

Atrioventricular Junctional Rhythm

Definition

- Impulses are generated in the AV junctional tissue and spread backward (retrograde) through the atrium and forward (antegrade) to the ventricles.
- The heart rate varies with the mechanism—that is, a passive escape rhythm (60 bpm) versus an enhanced AV junctional rhythm (>60 bpm but <100 bpm) versus a junctional tachycardia (>100 bpm in the dog).
- The rhythm usually is regular.
- The negative P′ wave may occur before, during, or after the normal QRS complex. The P′-R or R-P′ interval is constant.
- The P′ wave location depends on the area of impulse generation and the relative speed of retrograde conduction through the atrium compared with antegrade conduction through the AV node, His bundle, and ventricular conduction system.

Etiology and Clinical Significance

- Digitalis toxicity may cause an AV junctional rhythm. When abnormally rapid, this arrhythmia is difficult to distinguish from atrial tachycardia.
- An AV junctional escape rhythm may occur in patients with depressed sinus node function, as in the sick sinus syndrome.
- Myocarditis may be associated with an enhanced AV junctional rhythm or AV junctional tachycardia. The rhythm has been observed in dogs with advanced heartworm disease.

Differential Diagnosis

- AV junctional rhythm can be confused with atrial standstill and slow atrial fibrillation.

Treatment

- Usually no treatment is needed and the rhythm reverts spontaneously, especially with correction of the underlying disorder.
- If weakness or syncope is associated with a slow AV junctional rhythm, atropine, dobutamine, or isoproterenol may be used in an attempt to accelerate the sinus node to help regain function as the primary pacemaker.
- Oral anticholinergic agents also may be useful for chronic therapy of junctional escape rhythm.
- If CHF is present with an enhanced AV junctional rhythm, administer digitalis.

VENTRICULAR RHYTHMS

Ventricular Premature Complexes

(Figs. 145-6–145-8)

Definition

Impulses arising from a focus below the AV node and AV junction create ventricular ectopic complexes. In some situations, these ectopic QRS complexes are normal mechanisms (escapes) that rescue the heart during sinus arrest or AV block. However, when ven-

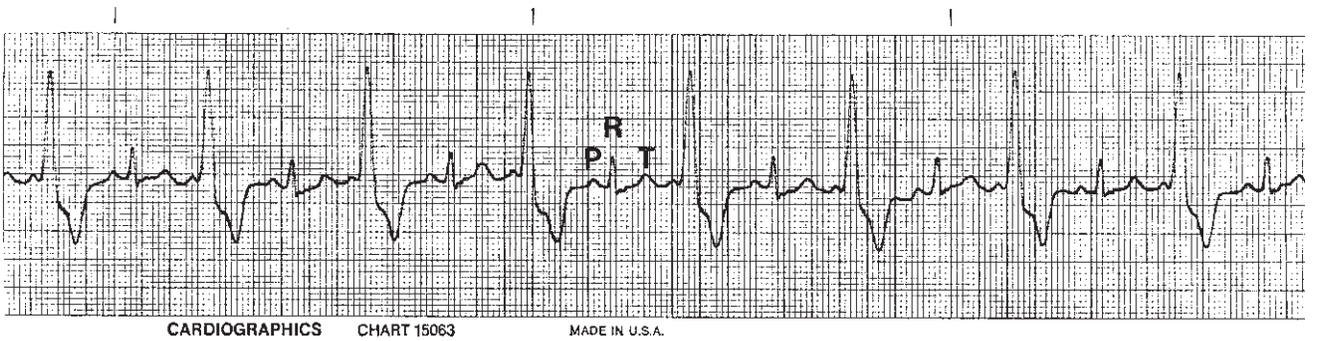

Figure 145-6. Ventricular premature complexes in a cat. (Lead II rhythm strip, paper speed 50 mm/sec; 1 cm = 1 mV.)

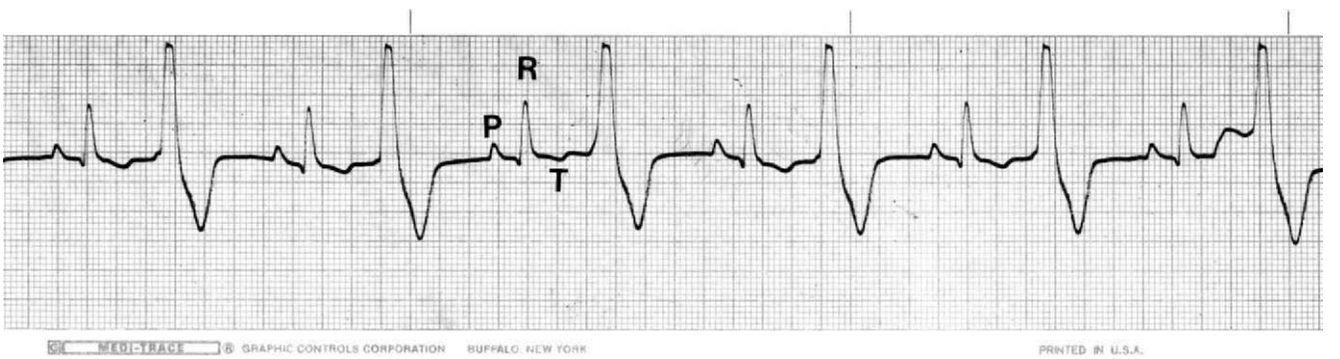

Figure 145-7. Ventricular premature complexes in a dog. (Lead II rhythm strip, paper speed 50 mm/sec; 1 cm = 1 mV.)

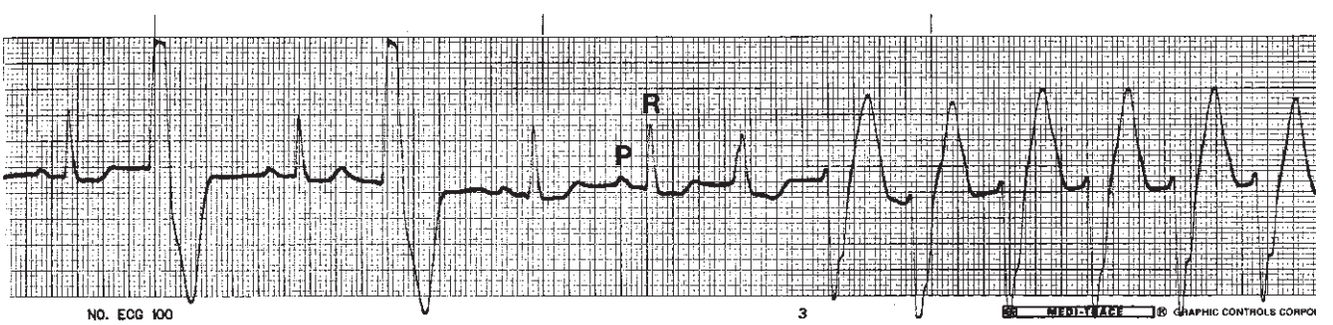

Figure 145-8. Sinus rhythm with ventricular premature complexes (right ventricular foci) and paroxysmal ventricular tachycardia (left ventricular foci) in a dog. (Lead II rhythm strip, paper speed 50 mm/sec; 1 cm = 1 mV.)

tricular ectopics are premature relative to the dominant cardiac rhythm, the ectopic impulses are called ventricular premature complexes (VPCs), also known as premature ventricular complexes or ventricular extrasystoles. The following are characteristics of VPCs.

- The heart rate is variable, depending on the frequency of VPCs; the rhythm is irregular.
- VPCs are usually related (coupled) to normal beats. If a VPC is not coupled to a normal beat, the origination site is referred to as a parasystolic focus.
- Usually there is a full compensatory pause following a VPC (i.e., the R-R interval of the two sinus complexes bounding the VPC is equal to two normal R-R intervals).
- Interpolated VPCs occur between normal beats and are not followed by a compensatory pause. The P-R interval of the next conducted sinus beat is slightly prolonged.
- P waves that are seen are normal in shape but are not associated with the QRS complex of the VPCs. The QRS complex often is wide and bizarre.

- The P-R interval of the sinus beat following a VPC may be prolonged due to retrograde conduction of the VPC into the AV node, resulting in conduction delay of the subsequent sinus beat. This is characteristic of an interpolated VPC.
- If the major deflection of the QRS complex is negative in lead II, the ectopic focus likely is in the left ventricle; if the major deflection is positive in lead II, the ectopic focus probably is in the right ventricle. Boxers with arrhythmogenic right ventricular cardiomyopathy typically have VPCs with predominantly positive deflections in lead II.

Etiology and Clinical Significance

- The ventricular arrhythmia may be due to cardiac disease (e.g., cardiomyopathy, CHF, myocarditis, or endocarditis; see Table 145-2).
- VPCs are often identified in the clinical settings of trauma, electrolyte disturbances, gastric dilatation and volvulus, pancreatitis, splenic disease, autonomic changes, hypoxia, systemic infections, ischemia, and drug toxicosis.
- Frequent VPCs or VPCs occurring during the preceding Q-T interval may be electrically unstable (depending on underlying heart disease) and may progress to ventricular tachycardia and/or fibrillation and sudden death.
- A 24-hour tape-recorded (Holter) ECG may be necessary to assess the severity of a ventricular arrhythmia (see Chapter 144, Fig. 144-16).

Differential Diagnosis

- VPCs can be confused with APCs with aberrant ventricular conduction and right or left bundle branch block.

Treatment

- VPCs do not generally require antiarrhythmic therapy.
- Consider antiarrhythmic therapy for:
  - Frequent *symptomatic* VPCs (>20–30 bpm)
  - Repetitive complexes or runs of VPCs at very rapid rates (e.g., >180 bpm), especially if causing signs or hypotension
  - Multifocal QRS configurations (not a definite indication)
  - R on T phenomena (vulnerable period for development of ventricular fibrillation), in which the VPC occurs during the Q-T interval of the previous complex
  - Associated clinical signs of poor cardiac output (e.g., weakness, dyspnea, and syncope) are probably the clearest indication for therapy.
- Do not treat ventricular escape complexes (while the QRS complex is similar to a VPC in configuration, these are not premature but occur at the end of pauses). Escapes represent a safety mechanism for maintaining cardiac output.
- Antiarrhythmic drugs commonly used to control VPCs in the hospital setting include IV lidocaine and parenteral procainamide (rarely quinidine) (see Table 145-3). Electrolyte imbalances and pain should be managed as these issues may contribute to VPCs in hospitalized patients.
- For chronic therapy of VPCs, the choice depends a great deal on the concern about repetitive rhythms and risk, as well as the appreciation of drug cost and toxicity. Beta-blockers such as atenolol, sotalol, and propranolol are often chosen for isolated VPCs, and in cats are the beta-blockers are the principle drugs used. Mexiletine, procainamide, and (rarely) tocainide are other options, but they have more side effects and are probably better reserved for more malignant arrhythmias (see Table 145-3 for dosages and Chapter 146 for a discussion of the clinical pharmacology of these drugs).

Ventricular Tachycardia (Figs. 145-8–145-10)

Definition

- Repetitive ventricular impulses (more than three VPCs in a row) are discharged from one or more ventricular foci and capture the ventricles.
- This arrhythmia may be paroxysmal (non-sustained) or sustained.
- The rate usually is >100 bpm in dogs and >150 bpm in cats.
- Once established, the rhythm tends to be regular unless the arrhythmia is intermittent or variable exit block develops (between Purkinje cells and ventricular myocardium).
- The P waves that are seen are normal in shape but have no fixed relationship to wide and bizarre QRS complexes. This independence is described as *AV dissociation*. Rarely, retrograde P waves are observed in the S-T segment because of ventricular to atrial conduction.
- A sustained ventricular rhythm faster than an escape (idioventricular) rhythm but slower than the above mentioned rates is termed an idioventricular tachycardia.

Etiology and Clinical Significance

▼ ***Key Point*** Ventricular tachycardia can be well-tolerated or represent a life-threatening arrhythmia that, if sustained, may lead to hypotension, myocardial ischemia, syncope or seizures, shock, and sudden death. Each case must be individually evaluated.

- Some patients with ventricular tachycardia show no clinical signs, especially if there is no underlying

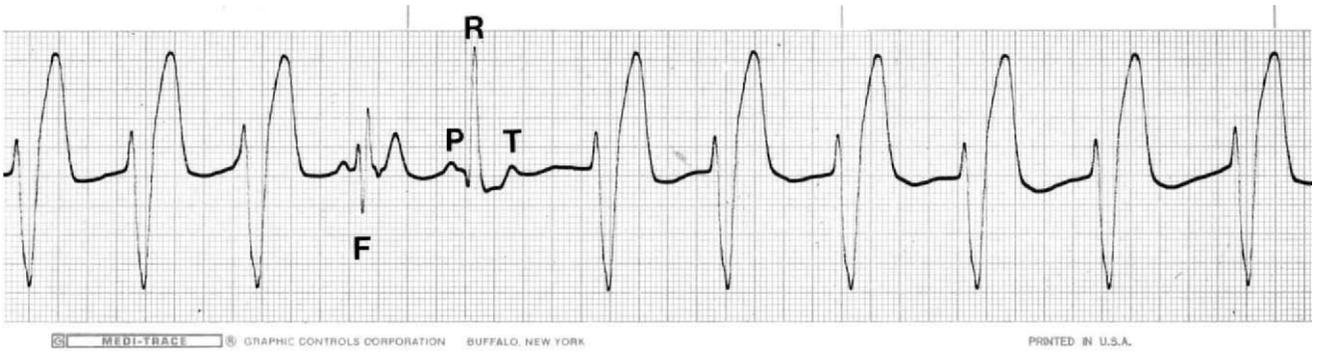

Figure 145-9. Paroxysmal ventricular tachycardia showing fusion beat (F) in a dog. (Lead II rhythm strip, paper speed 50 mm/sec; 1 cm = 1 mV.)

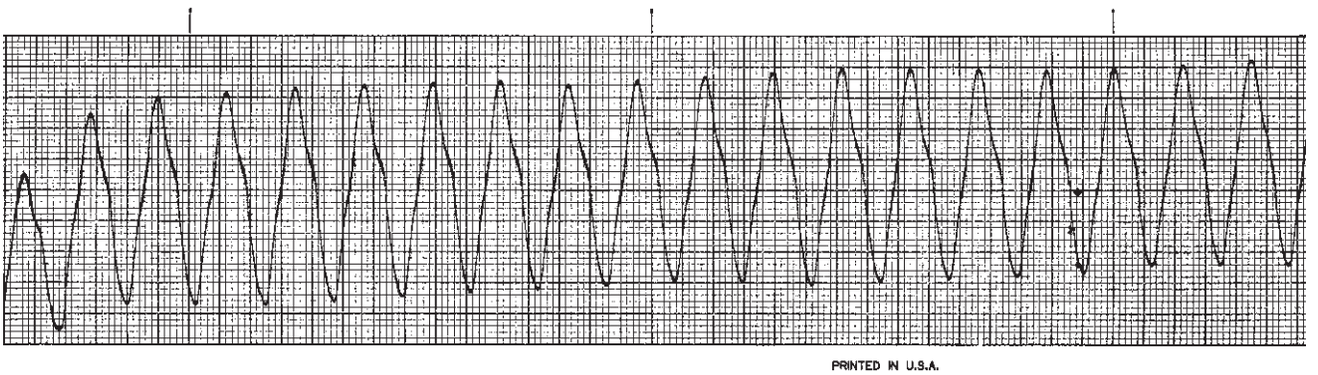

Figure 145-10. Ventricular tachycardia-flutter in a dog. (Lead II rhythm strip, paper speed 50 mm/sec; 1 cm = 1 mV.)

primary cardiac disease and the rate is not too rapid.
- All etiologies of VPCs (e.g., primary and secondary cardiac disease; see Table 145-2) may lead to a ventricular tachycardia; however, not all are dangerous to the patient.

Differential Diagnosis

- Ventricular tachycardia can be confused with supraventricular rhythms—sinus tachycardia, atrial tachycardia, or atrial fibrillation—when ventricular conduction is abnormal (as with left or right bundle branch block).

Treatment

- Antiarrhythmic therapy is required for some patients with sustained ventricular rhythms. Exceptions include patients with the following:
  - Complete heart block in which the ventricular rhythm may be an escape mechanism
  - "Slow" ventricular rhythms (also called idioventricular tachycardias) in which the ectopic rate is <180 bpm, the rate does not cause hypotension, and the rhythm alternates with the sinus rhythm
  - Acid-base or electrolyte disturbances, such as hypomagnesemia, hypokalemia, or hyperkalemia, that may respond to specific electrolyte or fluid therapy.
  - Hypomagnesemia can cause or potentiate ventricular tachycardia. Magnesium chloride (1–2 mg/kg/min for 20–30 minutes) can also exert a primary antiarrhythmic effect.

▼ ***Key Point*** Cats with ventricular tachycardia associated with hypokalemia may respond to simple KCl therapy (IV in fluids, oral) (see Chapter 5).

- Lidocaine hydrochloride without epinephrine (2–3 mg/kg) via slow IV administration is the initial treatment of choice in the dog.
  - If necessary, repeat the lidocaine bolus several times at 5- to 10-minute intervals. Higher dosages will increase the likelihood of toxicity.
  - Lidocaine also may be used in the cat (initial bolus of 0.25 mg/kg, slowly IV); beware of seizures.
  - The maximum total dosage for dogs is 8 mg/kg over 10 to 15 minutes. Seizures and vomiting may occur in dogs with toxic doses.
  - Administer diazepam IV for seizures.

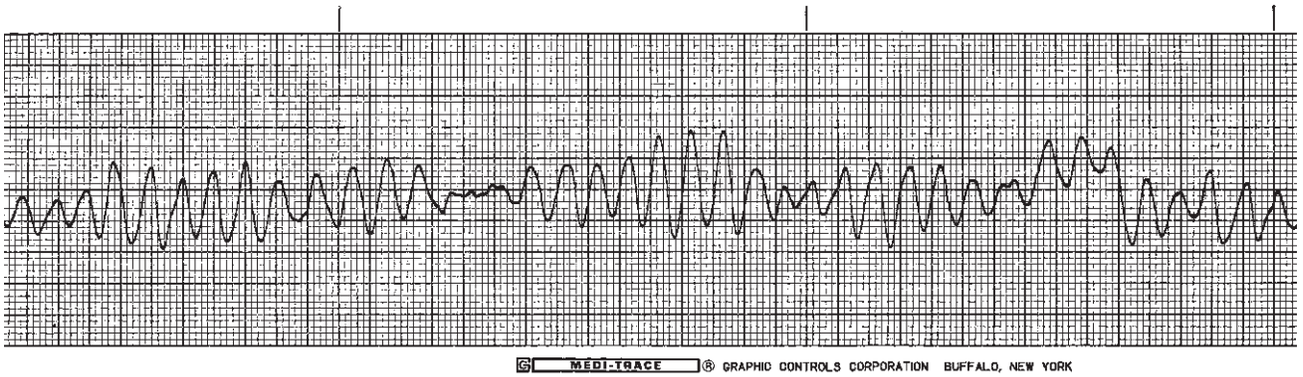

Figure 145-11. Ventricular fibrillation in a dog. (Lead II rhythm strip, paper speed 50 mm/sec; 1 cm = 1 mV.)

- Hypotension or sinus arrest also may occur if the bolus is administered too rapidly (especially in cats).
- The therapeutic effect of lidocaine is short lived, and repeated boluses or constant rate infusion may be required for a sustained antiarrhythmic effect. To calculate the amount of lidocaine to be added to IV fluids over 6 hours, use the following equation for any given infusion rate of 30 to 80 µg/kg/min:

$$\text{Body weight (kg)} \times 30 \text{ to } 80\,\mu\text{g/kg/min} \times 0.36 = \text{Lidocaine (mg)}$$

- Once the arrhythmia is controlled with lidocaine, initiate intramuscular or oral therapy with procainamide, or begin oral therapy with mexiletine or sotalol (see Table 145-3), and slowly reduce the lidocaine infusion over a 24- to 48-hour period. Alternative but less frequently used drugs include tocainide, quinidine, and amiodarone. Also manage hypokalemia, hypomagnesemia, and acidosis because they may cause therapeutic failure.
- When lidocaine therapy is contraindicated or impractical, either procainamide or quinidine, administered intramuscularly, may provide initial control of ventricular tachycardia.
- Prolonged oral therapy may be necessary in dogs with structural or primary heart disease. Most cardiologists prescribe sotalol or mexiletine plus a beta blocker such as atenolol for long-term control. For example, sotalol or a combination of mexiletine and atenolol are often effective for treatment of ventricular tachycardia associated with boxer arrhythmogenic right ventricular cardiomyopathy. Effective arrhythmia suppression is supported by a greater than 85% reduction in the number of VPCs on a Holter monitor following initiation of therapy.
  - Other antiarrhythmic drugs that may be useful include propranolol, quinidine, procainamide, tocainide and rarely amiodarone. See Chapter 146 for information about the various adverse effects of these drugs.
- Reserve electrical cardioversion for refractory or life-threatening ventricular tachycardia that will not respond to medicine.
- If a ventricular arrhythmia worsens with therapy, consider that antiarrhythmic drug toxicity (proarrhythmia) may be the cause, rather than worsening disease. For example, German shepherds may be prone to a proarrhythmic effect when sotalol is used as a single agent therapy. Sotalol combined with mexiletine reduces the frequency of VPCs in young German shepherds with inherited ventricular arrhythmias.
- Multiform ventricular tachycardia (torsades de pointes) due to procainamide or quinidine toxicity may be a life-threatening complication of antiarrhythmic medication.
- If the arrhythmia is well controlled, consider discontinuing the antiarrhythmic agent after a 2- to 3-week period. This may avoid complications of long-term therapy and the expense of antiarrhythmic drugs. Evaluate the ECG before each decrease in dosage, or within 1 week after stopping the medication. A Holter monitor (long-term ambulatory ECG) is the best way to determine antiarrhythmic drug efficacy and to guide withdrawal of therapy.
- In cases of refractory or recurrent ventricular tachycardia, consult a cardiologist.
- Radiofrequency catheter ablation following electrophysiologic mapping of ventricular tachyarrhythmic circuits is available at select referral centers for refractory symptomatic ventricular tachyarrhythmias as a potential arrhythmia cure without permanent implantation devices.

Ventricular Fibrillation (Fig. 145-11)

Definition

- Cardiac impulses are generated and propagated in the ventricles in a chaotic, asynchronous manner.
- The heart rate is rapid and disorganized.
- The rhythm is irregular.

- There are no P waves present, and there are no recognizable QRS complexes. There are continuous positive and negative oscillations that are chaotic and bizarre. The oscillations may be large (coarse) or small (fine).

Etiology and Clinical Significance

▼ ***Key Point*** The most common arrhythmia associated with cardiac arrest is ventricular fibrillation.

- There is no effective cardiac output.
- Conditions such as myocardial ischemia, electrolyte imbalance, autonomic nervous system imbalance, hypoxia, hypothermia, slow conduction, increased automaticity, drug toxicity, and unstable ventricular arrhythmias cause electrical instability and trigger ventricular fibrillation.
- Ventricular fibrillation is associated with a very grave prognosis.

Differential Diagnosis

- Differentiate ECG artifacts (e.g., 60-cycle electrical interference, respiratory movement, or use of electrocautery during surgery) from the ventricular fibrillation. A palpable arterial pulse and rhythmic precordial heartbeat rule out ventricular fibrillation.

Treatment

- Perform cardiopulmonary resuscitation (CPR) immediately (see Chapter 157).
- Electrical defibrillation is mandatory.
- Intracardiac lidocaine or other drugs are rarely successful in converting ventricular fibrillation to normal sinus rhythm.
- Open-chest cardiac massage may be effective in converting ventricular fibrillation to normal sinus rhythm if no defibrillation equipment is available (particularly in the cat). External blows to the chest (thumpversion) are far less effective.

Ventricular Asystole

Definition

- No impulses are generated from atrial, junctional, or ventricular pacemakers.
- There is no cardiac rate or ventricular rhythm.
- No QRS complexes are seen.

Etiology and Clinical Significance

- Ventricular asystole is associated with cardiac arrest and if left untreated is a lethal arrhythmia.

Differential Diagnosis

- Differentiate ECG artifacts (e.g., electrocardiograph is not on a proper lead or is connected improperly) from ventricular asystole.

Treatment

- Perform CPR immediately (see Chapter 157).
- Epinephrine, along with CPR, may be lifesaving.

CONDUCTION DISORDERS

Atrial Standstill

Definition

- Impulses are not generated in the sinus node and any native atrial activity is poorly conducted or non-conducted through the atrial tissues.
- The heart rate is <60 bpm in dogs and <160 bpm in cats.
- No P waves are seen, and the QRS complexes are normal or bizarre depending on the intraventricular conduction. The S-T segment may be elevated or depressed. The T wave may be tall due to shortened repolarization (see Chapter 144, Fig. 144-11).
- The rhythm may be regular or irregular.

Etiology and Clinical Significance

▼ ***Key Point*** Atrial standstill is a life-threatening abnormality when associated with hyperkalemia (hypoadrenocorticism, acute renal failure, urinary obstruction, and diabetic ketoacidosis).

- Persistent atrial standstill occurs in English springer spaniels (it may be correlated with a muscular dystrophy), as well as other breeds; it develops occasionally in cats with dilated cardiomyopathy in which there is degeneration and fibrosis of the atrial myocardial cells.
- There is cardiac enlargement, but electrolytes are normal with persistent atrial standstill.

Differential Diagnosis

- Differentiate atrial standstill on multiple lead ECGs from AV junctional rhythm, idioventricular rhythm, and atrial fibrillation with complete heart block.

Treatment

- If hyperkalemia is present, deliver emergency therapy to dilute and transfer extracellular potassium into the cells, thereby restoring normokalemia.
- Administer 0.9% saline, 40 to 90 ml/kg/hour, until hyperkalemia and hypovolemia are corrected.
- In addition, administer 2 mEq/kg of sodium bicarbonate very slowly IV. This may restore more narrow QRS complexes and increase myocardial contractility; repeat the dose if needed within 15 to 30 minutes. Beware of paradoxical cerebral acidosis.
- As an alternative therapy to sodium bicarbonate, administer 0.5 U of regular insulin per kilogram of

body weight coupled with 2 g of dextrose (in a 5–10% dextrose drip) per unit of insulin, slowly IV.
- For life-threatening conditions, give calcium gluconate (1 ml of 10% solution per 10 kg of body weight, slowly IV) to counteract the cardiotoxic effects of hyperkalemia. Administer with ECG monitoring.
- If hypoadrenocorticism is the cause of hyperkalemia, mineralocorticoid and glucocorticoid replacement is necessary (see Chapter 33).
- In the English springer spaniel with symptomatic atrial standstill, a permanent cardiac pacemaker is required. Consult a cardiologist.

Incomplete (First- and Second-Degree) Atrioventricular Block

Definition

- The cardiac impulse is delayed or intermittently blocked in the region of the AV node or AV junction.
- The heart rate is variable, depending on the rate of the sinus node pacemaker and the AV conduction sequence.
- The rhythm usually is regular in first-degree AV block (unless other arrhythmias are present) and irregular in second-degree AV block.
- *First-degree AV block* shows a prolonged but constant P-R interval (AV conduction) with normal P wave and QRS complexes at a 1:1 ratio.
- *Second-degree AV block* has normal P wave and QRS complexes with a constant P-R interval and with intermittent P waves not followed by QRS complexes.
  - In *Mobitz type I (Wenckebach) AV block,* the P-R interval is gradually prolonged before a dropped ventricular beat occurs. The rhythm is regularly irregular.
  - In *Mobitz type II AV block,* a consistent P-R interval occurs prior to a dropped ventricular beat. The rhythm often is irregular.

Etiology and Clinical Significance

- First-degree and Mobitz type I second-degree AV blocks often are caused by an increase in vagal tone (e.g., in brachycephalic breeds and in patients with respiratory, gastrointestinal, or neurologic disease), digitalis, and sedatives (e.g., xylazine and acepromazine).
- Antiarrhythmic drugs (beta-blockers, quinidine, procainamide, diltiazem, digoxin, and verapamil) and AV nodal disease are associated with these types of AV block.
- Physiologic AV block may occur following ectopic beats or atrial tachyarrhythmias that occur during the AV node's absolute or relative refractory periods (will slow or block the impulse).
- Mobitz type II AV block is a more advanced degree of block occurring in the AV junction, His bundle, or below. It may progress to a complete heart block. Causes include the following:
  - Idiopathic fibrosis (older dogs and cats), hereditary stenosis of the His bundle in the pug and Doberman pinscher, and hypertrophic cardiomyopathy in dogs and cats
  - Neoplastic infiltration secondary to metastatic neoplasia
  - Profound electrolyte disorders
  - Infection (e.g., Lyme disease or aortic valve endocarditis)
- The development of clinical signs (e.g., weakness, syncope, and CHF) depends on the degree of AV block, ventricular rate, and ventricular function.
- In cats there may be abrupt fluctuation among sinus rhythm, incomplete, and complete AV block. Older cats (>12 years) may tolerate second- and third-degree AV block very well, and these bradyarrhythmias may be incidental findings.

Differential Diagnosis

- Differentiate complete AV block from advanced second-degree AV block on the ECG.

Treatment

- Treatment usually is not required for Mobitz type I AV block. If the block is related to drug toxicity, stop the drug or lower the dosage.
- Therapy for Mobitz type II AV block depends on the clinical signs. If the cardiac rate is slow and weakness or syncope is evident, begin therapy with atropine, dobutamine, isoproterenol, or a temporary or permanent cardiac pacemaker. Oral therapy with hyoscyamine or theophylline may be helpful for long-term therapy if pacemaker implantation is not possible.

Complete (Third-Degree) AV Block (Fig. 145-12)

Definition

- The cardiac impulse is completely blocked in the region of the AV junction and/or the His bundle.
- The atrial rate (P-P interval) is within normal limits, and there is a slow idioventricular escape rhythm. The rhythm is usually regular. In dogs, an idioventricular escape rhythm has a rate of 40 to 60 bpm.
- An enhanced AV junctional or idioventricular rhythm (AV dissociation) has a more rapid rate, with the ventricular rate approaching the atrial rate.
- In cats, the escape rhythm is often quite a bit faster, between 80 and 120 bpm.
- The P wave is completely dissociated from the QRS complex.
- The P-R interval is variable, and usually there are many P waves with few QRS complexes.
- The morphology of the QRS complexes varies depending on the origin of the ventricular escape rhythm.

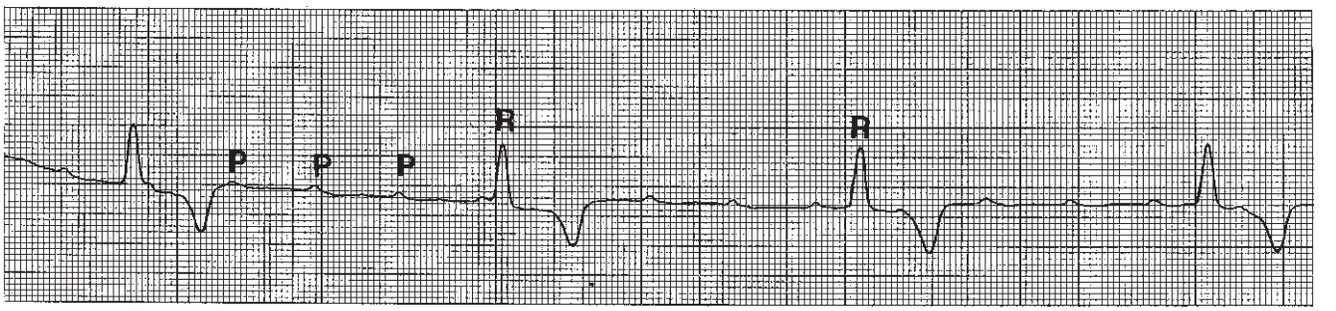

Figure 145-12. Complete (third-degree) atrioventricular block in a cat. (Lead II rhythm strip, paper speed 50 mm/sec; 1 cm = 1 mV.)

Etiology and Clinical Significance

- Complete AV block often is associated with the clinical signs of weakness, syncope, and CHF in dogs. This rhythm is often well tolerated in cats and often is detected as an incidental finding during routine exams of geriatric cats.

Differential Diagnosis

- Differentiate complete AV block on the ECG from advanced second-degree AV block, atrial standstill, and ventricular tachycardia (idioventricular rhythm).

Treatment

- A permanent cardiac pacemaker is the only consistently effective long-term treatment in symptomatic animals. A temporary transvenous pacemaker is indicated for life-threatening AV block. This condition can arise in the setting of a complete block with concurrent runs of ventricular tachycardia that is then followed by periods of ventricular asystole.
- Drugs that may be tried for short-term stabilization and treatment include atropine, isoproterenol, dobutamine, and corticosteroids (anti-inflammatory). It is rare to achieve conduction from drug therapy. An IV dobutamine or isoproterenol infusion may be useful for increasing the rate of the ventricular escape rhythm during required surgical procedures.
- In situations in which pacemaker implantation is not an option, oral therapy with methylxanthines (e.g., theophylline or aminophylline) or sympathomimetics (e.g., albuterol or terbutaline) may accelerate the ventricular escape rhythm.

Intraventricular Conduction Disturbances

Right bundle branch block, left bundle branch block, left anterior fascicular block, and combined right bundle branch–left anterior fascicular blocks are described and illustrated electrocardiographically in Chapter 144.

OTHER ARRHYTHMIAS AND CONDUCTION DISTURBANCES

Sick Sinus Syndrome

Definition

- In sick sinus syndrome (SSS), cardiac impulses are generated in the sinus node at a slower-than-normal rate or are blocked from exiting the sinus node.
- The atria and AV node may also be involved, resulting in an atrial tachyarrhythmia (e.g., atrial tachycardia, flutter, or fibrillation).
- A bradycardia-tachycardia syndrome may occur, with alternating periods of slow and rapid heart rates caused by sinus or ectopic atrial tachycardia.
- There is a normal P wave for each QRS complex. The P-R interval is constant unless the bradyarrhythmia-tachyarrhythmia syndrome is present.

Etiology and Clinical Significance

- SSS occurs predominantly in geriatric, small-breed females. Miniature schnauzers, cocker spaniels, West Highland white terriers, and dachshunds are overrepresented.
- Clinical signs of SSS are variable but often include weakness and syncope.

Differential Diagnosis

- Differentiate the multiple ECG abnormalities included in SSS from isolated sinus bradycardia, sinus block and/or arrest, and atrial tachycardia due to other causes. A poor (blunted) response to atropine (<50% increase in heart rate) supports the diagnosis of SSS.

Treatment

- If the animal is asymptomatic, no therapy is required.
- Anticholinergic drugs are rarely successful in symptomatic dogs.
- In animals with bradycardia-tachycardia syndrome, an artificial ventricular-demand pacemaker may be

required for long-term control of bradyarrhythmias and digoxin, propranolol, or diltiazem may control the tachyarrhythmia; however, do not use these drugs unless a pacemaker is implanted.

Ventricular Preexcitation and Wolff-Parkinson-White Syndrome

Definition

- In ventricular preexcitation the cardiac impulses are generated in the sinus node but spread to the ventricle simultaneously across an anomalous conduction pathway (accessory pathway or bundle of Kent), as well as the AV node. The QRS complex is essentially a fusion beat from two sources. (See Chapter 144 for additional information.)
- In Wolff-Parkinson-White (WPW) syndrome, a premature impulse finds the bypass pathway or AV node during its refractory period but traverses the other pathway, allowing the development of a macroreentry circuit that contributes to a tachycardia. The current moves in a circle: from atrium, to AV node, to ventricle, to accessory pathway, back to the atrium (or it travels in the opposite direction).
- During ventricular preexcitation, the cardiac rate and rhythm are normal. During the tachycardia of the WPW syndrome, the rate may be very rapid (e.g., 300 to 400 bpm).
- The P waves are normal in ventricular preexcitation and are retrograde and often unrecognizable in WPW syndrome (they are usually buried in the S-T segment).
- Depending on the type of accessory pathway present, the QRS complex may be widened with notching of the R wave (delta wave) or with a discrete wave just in front of the QRS (see Chapter 144 and Fig. 144-9). During the tachycardia of WPW syndrome, the QRS complex may be normal (typical), wide, or bizarre, depending on the direction and location of the circuit of the reentrant tachycardia.
- The P-R interval is short during sinus rhythm with ventricular preexcitation. During the WPW tachycardia, there is one retrograde P wave that follows each QRS complex (1:1 AV conduction).
- A short P-R interval may be correlated with a normal QRS complex if the anomalous pathway bypasses the AV node to the area of the His bundle (Lown-Ganong-Levine syndrome in humans).

Etiology and Clinical Significance

- Ventricular preexcitation and WPW syndrome may be congenital problems in the dog or cat that occur with or without other congenital heart defects (e.g., atrial septal defect, valvular dysplasia, or hypertrophic cardiomyopathy). Labrador retrievers are predisposed.

Differential Diagnosis

- Differentiate the tachycardia of WPW syndrome from AV junctional tachycardia, atrial tachycardia, and ventricular tachycardia.

Treatment

- Ventricular preexcitation without tachycardia requires no therapy.
- In animals with WPW syndrome, control and conversion of the sustained tachycardia can be attempted with a vagal maneuver (e.g., ocular or carotid sinus pressure); with drugs that block the AV node, such as diltiazem, verapamil, or adenosine; with drugs that effect the accessory pathway (procainamide or sotalol); or with direct current shock that depolarizes the entire circuit.
- Long-term control is best obtained by referral for radiofrequency catheter ablation of the accessory pathway.

THERAPEUTIC PRINCIPLES

- Determine a precise diagnosis for the arrhythmia. In most cases, the precise mechanism of the arrhythmia will not be known.
- Eliminate non-cardiac causes (e.g., acid-base and electrolyte abnormalities, hypothermia, hypovolemia, hypoxemia, anemia, infections, and other systemic problems) before using an antiarrhythmic drug.
- Stop other drug therapy if it may be the cause of the arrhythmia (e.g., digitalis, xylazine, or acepromazine).
- Treat heart failure if present.
- Drug therapy for cardiac arrhythmias is intended to prevent clinical signs such as weakness, syncope, seizures, personality changes, and CHF. Also, drug therapy may decrease electrical instability and the likelihood of progression to a lethal arrhythmia (e.g., ventricular fibrillation).
- Select the antiarrhythmic drug best suited to the underlying cause of the arrhythmia. See Chapter 146 for descriptions of the various antiarrhythmic cardiac drugs and refer to Table 145-3 for dosages.
- The benefit or complications of similar antiarrhythmic therapy may vary widely among breeds, such as ventricular tachyarrhythmias in German shepherd puppies (may be ineffective), boxers (variably effective), and Doberman pinschers (variably effective).
- Although arrhythmia frequency and complexity may be reduced, and clinical signs lessened, no antiarrhythmic studies to date have shown sudden death prevention in any canine or feline breed.
- An abolition or reduction in clinical signs or symptoms remains the key reason for the administration and expense of antiarrhythmic drugs.

- Be aware of synergistic effects of antiarrhythmic drugs (e.g., digoxin and propranolol may additively delay AV conduction) and of antagonistic effects (e.g., quinidine may cause serum digoxin levels to rise, increasing the possibility of digoxin toxicity).
- Refractory arrhythmias may require a combination of antiarrhythmic agents, although these may increase the possibility of drug-related toxicity (e.g., digoxin and diltiazem or atenolol for atrial fibrillation and mexiletine and atenolol or sotalol and mexiletine for ventricular tachycardia).
- Be aware that some arrhythmias may require antiarrhythmic drugs in addition to other therapeutic modalities (e.g., for SSS with bradyarrhythmia-tachyarrhythmias, a pacemaker for the bradyarrhythmia and an antiarrhythmic drug for the tachyarrhythmia).
- Be aware of the proarrhythmic potential of antiarrhythmic drugs.
- Digoxin can cause any arrhythmia and conduction disturbance. Monitor ECGs frequently.

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Chapter

146 Cardiovascular Drugs

John D. Bonagura / Karsten E. Schober

Pharmacologic interventions allow the veterinarian to impact pathophysiologic processes in animals with cardiovascular (CV) diseases. To effectively use drugs affecting the heart and circulation, the clinician must understand the pathophysiology of the disease and appreciate the relevant pharmacology of the drugs prescribed. This chapter reviews aspects of cardiovascular pharmacology that are particularly applicable to clinical small animal veterinary practice. Most drugs used to treat CV diseases in dogs and in cats prescribed in an extra-label manner and dosages are at best approximate for many of these agents. Specific drugs and commonly recommended dosages are listed in Table 146-1. Drugs used in management of cardiopulmonary-cerebral resuscitation are discussed in Chapter 157. Management of shock is discussed in Chapter 156.

DIURETICS

Diuretics are a standard of chronic congestive heart failure (CHF) therapy and are administered for two main purposes: (1) diuresis of the patient with pulmonary edema or body cavity effusions and (2) prevention of the chronic sodium and water retention that characterizes chronic CHF. Diuretics are also antihypertensive agents but do not represent an important treatment approach for high arterial blood pressure (ABP) in dogs and cats. Diuretics should be administered with a sodium-restricted diet that is proportional to the severity of CHF.

Furosemide

Furosemide is the most often used diuretic. It acts by inhibiting the co-transporter of chloride in Henle's loop with resultant losses of chloride, sodium, water, calcium, magnesium, potassium, and water-soluble vitamins in the urine. Bumetanide and torsemide are related human drugs infrequently used in veterinary practice.

- Parenteral administration of furosemide is associated with a rapid onset of diuresis, usually within 30 minutes of injection. IV administration also may be associated with release of beneficial venodilating prostaglandins. However, fast intravenous administration may also acutely stimulate the sympathetic nervous system and the rennin-angiotensin-aldosterone system, leading to an initial increase in systemic vascular resistance, blood pressure, heart rate, and left ventricular filling pressure; therefore, IV use should be reserved for severe CHF.
- Furosemide is a "high-ceiling" diuretic, demonstrating a graded dose-response effect. The drug must be delivered by renal blood flow to be effective. Reduced renal blood flow from CHF or volume depletion; renal failure; an NSAID such as aspirin; or hypoproteinemia can negatively impact delivery of furosemide to the proximal tubule. Malabsorption or decreased delivery of furosemide may be relevant in explaining refractory ascites in cases of severe right-sided CHF.
- Furosemide preparations include proprietary veterinary and generic veterinary formulations of 12.5 and 50 mg tablets; 20, 40, and 80 mg tablets (for human patients); injectable 1% and 5% solutions (10 mg/ml and 50 mg/ml); and 1% syrup (10 mg/ml).
- The usual parenteral dosage range for hospital therapy is 1 to 4 mg/kg; IV, IM, SC two to four times daily as needed. Cats tolerate lower dosages of diuretics when compared to dogs and are more likely to develop hypokalemia and azotemia.
- In life-threatening CHF, furosemide should be given by slow IV bolus. An alternative method of administration that may be more effective is constant rate IV infusion of furosemide. Following an initial bolus of 0.5 to 1 mg/kg, the dose earmarked for the next 24 hours can be constantly infused with a small volume pump.
- Oral furosemide is used for long-term treatment of CHF. Dosages are typically 2 to 6 mg/kg one to three times daily, titrated to the magnitude of fluid retention. Oral furosemide seems less potent (presumably from poorer absorption or renal delivery) when compared to parenteral furosemide at equal doses. One strategy for treating refractory ascites or pulmonary edema in the chronic CHF patient involves intermittent subcutaneous administration of furosemide at home. Injections are given in place of the regularly

Table 146-1. CARDIOVASCULAR DRUG DOSING—CANINE AND FELINE PATIENTS

Drug	Preparation(s)	Usual Dosage*
Amlodipine	Norvasc, 2.5-mg tablet size	DOG: 0.05–0.2 mg/kg q12h–24h CAT: $^1/_4$–$^1/_2$ tablet dose, once or twice daily
Amiodarone	Cordarone injection, 50 mg/ml Cordarone and USP scored tablets, 200 mg	DOG: Loading dose of 10 mg/kg PO q12h for 1 week; thereafter 5 mg/kg PO q12–24h For IV use: 3–5 mg/kg over 60 min, followed by 5–10 mcg/kg/min CRI
Amrinone	Inocor, 5 mg/ml (20-ml vials)	DOG: 1–3 mg/kg IV followed by 30–100 mcg/kg/min constant rate infusion
Atenolol	Tenormin and USP tablets, 25 and 50 mg	DOG: 0.25–1.5 mg/kg PO q12h CAT: 6.25–12.5 mg dosage, once or twice daily (up-titrate dosages for both species)
Atropine	USP: 0.4 and 0.5 mg/ml for injection	0.01–0.04 mg/kg, IV, IM, SQ
Benazepril hcl	Lotensin tablets, 5, 10, 20, 40 mg	DOG: 0.25–0.5 mg/kg PO q12–24h (initial daily dose typically 0.5 mg/kg daily) CAT: 0.25–0.5 mg/kg PO q12–24h (as per dog)
Butorphanol	Torbutrol 0.5 mg/ml for injection Torbutrol tablets, 1, 5, 10 mg	DOG: 0.25–0.5 mg/kg, SQ, IM for sedation DOG: 0.5 mg/kg PO q6–12h as an antitussive CAT: 0.2–0.3 mg/kg in a cocktail with acepromazine (0.05–0.1 mg/kg), SQ, IM
Carvedilol	Coreg tablets, 3.125, 6.25, 12.5 mg	DOG: initiate dosage in canine DCM at 0.05–0.1mg/kg PO q12h for 2 weeks; up-titrate the dose every 2–4 weeks provided marked lethargy, progressive CHF, or relative bradycardia develop (HR < 100/minute during examination) do not develop. Typical dose target is 0.2–0.4 mg/kg PO q12h for canine DCM.
Digoxin	Lanoxin, Cardoxin, USP tablets, 0.125, 0.25 mg Elixirs of 0.05 mg/ml and 0.15 mg/ml Lanoxin for injection, 0.25 mg/ml	DOG: 0.0055–0.0075 mg/kg q12h, PO CAT: $^1/_4$ of a 0.125 mg Lanoxin tablet q48 to 72 hours
Dihydrocodone	Hycodan, 5-mg tablets	DOG: 1.25–5.0 mg, PO q8–24h for cough
Diltiazem	Cardizem and USP tablets, 30, 60, 90, 120 mg Dilacor XR capsules 120, 180, 240 mg Cardizem CD capsules 120, 180, 240 mg Diltiazem for injection 50 mg/ml	DOG: 0.5–2.0 mg/kg PO q8h (up-titrate dose) DOG/CAT: 0.1 mg/kg IV (can repeat every 15 minutes to 0.5 mg/kg while monitoring arterial blood pressure). CAT: 0.5–2.0 mg/kg PO q8–12h for standard diltiazem; $^1/_2$ of a 60 mg Dilacor pellet (taken from the capsule) q12–24h PO; or compounded Cardizem CD starting at 30 mg PO q12h
Dobutamine	Dobutrex for injection, 250 mg (20 ml vial)	DOG: 2.5–20 mcg/kg/min, constant rate IV infusion. CAT: 2.5–10 mcg/kg/min CRI
Dopamine	Intropin, USP for injection, 200 mg, 400 mg vials	2–10 mcg/kg/min, constant rate IV infusion
Enalapril	Enacard, USP tablets: 1.25, 2.5, 5, 10, 20 mg	DOG: 0.25–0.5 mg/kg PO q12–24h (initial daily dose typically 0.5 mg/kg daily) CAT: 0.25–0.5 mg/kg PO q12–24h (as per dog)
Epinephrine	Adrenaline, USP 1:1,000 (1 mg/ml), 1:10,000	DOG, CAT: 0.05–0.2 mg/kg, IV or intratracheal (only for status asthmaticus or cardiopulmonary-cerebral resuscitation)
Esmolol	Brevibloc for injection, 100 mg/ml (10-ml vial)	DOG, CAT: Initial IV loading dose of 100 to 500 mcg/kg administered over one minute, followed by a 25–150 mcg/kg/min constant rate infusion.
Furosemide	Furosemide for injection, 10 mg/ml and 50 mg/ml Veterinary Lasix tablets, 12.5, 50 mg Furosemide USP tablets, 20, 40, 50, 80 mg Furosemide 1% oral syrup (10 mg/ml)	DOG: 2–6 mg/kg q8–12h as needed, IV, IM, SQ, PO CAT: 1–4 mg/kg q12h as needed, IV, IM, SQ, PO Following initial bolus, CRI can be used to deliver 24h dose
Heparin USP	Heparin USP for injection	CAT: 150–250 units/kg initial dose, SQ, IV 50–200 units/kg q8h, SQ
Hydralazine	Apresoline, USP tablets, 10, 25, 50 mg	DOG: 1–3 mg/kg PO, q12h (up-titrate dose to ABP effect)
Hydrochlorthiazide	Hydrodiuril, USP tablets, 25, 50 mg	DOG, CAT: 1–4 mg/kg q24–48h, PO
Isosorbide dinitrate	Sorbitrate, Isordil, USP tablets, 5, 10 mg	DOG: 2.5–5 mg orally bid
Lidocaine	Xylocaine, USP for injection, 2% (20 mg/ml, without epinephrine)	DOG: 2 mg/kg IV bolus, can repeat up to 8 mg/kg over a 10-minute period; 25–75 mcg/kg/minute constant rate IV infusion (check blood potassium concentration if no effect); CAT: 0.25–1.0 mg/kg, slow IV injection over a 3–5-minute period

Table 146-1. CARDIOVASCULAR DRUG DOSING—CANINE AND FELINE PATIENTS—cont'd

Drug	Preparation(s)	Usual Dosage*
Lisinopril	Prinivil unscored tablets, 2.5, 5, 10, 20, 40 mg	DOG: 0.25–0.5 mg/kg q12–24h, PO
Magnesium	20% $MgCl_2$ solution for injection (contains 1.97 mEq of Mg++ per mL)	DOG: 0.75–1 mEq/kg/24h IV infusion (50% of total dose can be given in 2–4 hours if necessary) For ventricular fibrillation: 0.15–0.30 mEq/kg IV over 5–10 min
Metoprolol tartrate	Toprol-XL scored tablets, 25 mg	DOG: Start at $^1/_4$ of a 25 mg tablet once daily; up-titrate every 2 weeks to 12.5 mg q12h, PO (for a 20–30 kg dog)
Mexiletine	Mexitil, USP capsules, 150, 200, 250 mg Mexitil, 250 mg for injection	DOG: 5–8 mg/kg q8h, PO DOG: 2.5 mg/kg bolus IV given over 10 min, followed by 30 mcg/kg/min for 3 hours CRI, followed by 5–8 mcg/kg/min CRI for 24–48 hours IV (currently available in Europe)
Nitroprusside sodium	Nitropress, Nipride 50 mg/vial	Usual dosage range is 2–10 mcg/kg/min CRI Begin at 0.5–1 mcg/kg/minute and uptitrated If possible limit infusion to 24 hours
Nitroglycerine ointment (2%)	Nitrol, Nitro-bid, Nitrostat, USP 15 mg per inch Minitran transderm patches 2.5, 5, 10, 15 mg/24 hr	DOG: $^1/_4$–1 inch topically q12h; Patch: 2.5–10 mg (small–giant dog) CAT: $^1/_4$ inch topically q12h
Pimobendan	Vetmedin capsules, 1.25, 2.5, 5 mg	DOG: 0.3–0.6 mg/kg/day, divided; usual dose is 0.25 mg/kg q12h PO (give 1 hour before feeding)
Prazosin	Minipress, 1-, 2-, 5-mg capsules	1 mg/15 kg q8–12h PO
Procainamide	Pronestyl, USP for injection, 100 mg/ml; 500 mg/ml Procainamide SR, USP capsules and tablets, 250, 375, 500 mg	DOG: 2 mg/kg (IV) to a maximum total dose of 20 mg/kg over a 30-minute period; 25–40 mcg/kg/min IV infusion; 8–20 mg/kg, IM or SQ q4–6h; 10–20 mg/kg q8h PO (sustained release preparation) CAT: 3–8 mg/kg q6–8 h IM or PO
Propranolol	Inderal, USP for injection, 1-mg ampoule Tablets, 10, 20, 40, 60, 80 mg Inderal LA capsules, 60, 80, 120, 160 mg	DOG, CAT: 20–60 mcg/kg over 5–10 min, IV DOG: 0.5–1.0 mg/kg q8h, PO (use with caution in CHF) Can up-titrate dose from 0.1 mg/kg q8h, PO CAT: 2.5–5.0 mg dose q8h, PO (use with caution in CHF)
Spironolactone	Aldactone, USP tablets, 25 mg	DOG: 0.5 mg/kg–1.0 mg/kg q12–24h, PO
Sotalol	Betapace, USP scored tablets, 80, 160, 240 mg	DOG: 1–2 mg/kg q12h, PO
Tocainide	Tonocard, USP tablets, 400, 600 mg	DOG: 10–20 mg/kg q8h (rarely prescribed today; available in Europe)
Verapamil	Isoptin, 5-, 10-mg ampoules for injection; Isoptin, Calan, 40-, 80-, 120-mg tablets	DOG: 0.05 mg/kg, IV every 10–30 minutes to a maximum cumulative dose of 0.2 mg/kg
Warfarin	Coumadin 1-, 2-mg scored tablets	CAT: 0.5 mg PO, initial daily dose; compounding may be needed

Check dosing information and standard textbooks for specific dosing recommendations.
Prescription of many of these drugs in small animal patients constitutes an *extra-label* use and vary across different countries; Clients should be so advised.
Recommendations are based on current standards of veterinary practice.
Many drugs must be titrated to effect, especially in dogs and cats with congestive heart failure.
Consider drug interactions when prescribing multiple drugs.

scheduled oral treatment. This can be initiated three times weekly and increased or decreased as necessary. Chronic subcutaneous administration may lead to granuloma like swellings in some dogs.

▼ ***Key Point*** Chronic monotherapy with furosemide leads to sodium and volume depletion and activates homeostatic vasoconstricting (renin-angiotensin) and sodium retaining responses. These effects are deleterious in the heart failure and are countered by co-administration of an angiotensin converting enzyme inhibitor (ACEI) and control of dietary sodium intake.

Adverse Effects

Adverse effects of furosemide and other diuretics relate mainly to volume depletion and electrolyte loss.

- Consequences in the patient may include azotemia, hypochloremia, metabolic alkalosis, and potentially hypokalemia (though this effect is usually blunted by adequate food intake and by an ACEI).
- Magnesium depletion also may develop.
- Hypokalemia and hypomagnesemia predispose to premature complexes, digitalis intoxication, loss of efficacy of class I anti-arrhythmic drugs, and increased likelihood of drug-induced ventricular arrhythmias in animals treated with class III anti-arrhythmics.
- Excessive diuretic doses can be detected by regular measurement of blood pressure and the serum BUN, creatinine, and electrolytes.
- Azotemia is very common in dogs and especially in cats requiring daily furosemide treatment. Mild to moderate azotemia is acceptable in a patient with persistent fluid accumulation because the edema or effusion is likely to worsen if furosemide dosage is

decreased. In contrast, the dose of furosemide should be reduced in a patient with azotemia and no evidence of edema.

Spironolactone

Spironolactone is a potassium- (and magnesium) sparing diuretic that antagonizes the effects of aldosterone by binding to mineralocorticoid receptors in the distal collecting duct. Though a weak diuretic, it is often added to a comprehensive CHF therapy regimen that includes furosemide, an ACEI, and a positive inotrope. Eplerenone is a related drug that is not widely used in veterinary practice.

- Spironolactone prevents sodium reabsorption, spares potassium and magnesium, and most importantly, it antagonizes the cardiotoxic effects of aldosterone on the myocardium. Early use of this drug should be considered in CHF owing to potentially favorable effects on preventing myocardial fibrosis.
- Spironolactone, like digoxin, also improves baroreceptor function in dogs with CHF.
- Spironolactone is available in 25- and 50-mg tablets. Typical dosages for cardioprotection range from 6.25 to 25 mg once or twice daily and generally fall within a dosage range of 0.5 to 2 mg/kg daily. Dosages are somewhat empiric and related to severity of CHF and patient size; in human patients, even low dosages are cardioprotective.
- Hyperkalemia occasionally occurs from the combined effects of the spironolactone added to an ACEI. For this reason, potassium supplements should not be administered concurrently with spironolactone.
- Use of spironolactone in occult dilated cardiomyopathy without overt CHF is not of proven value and there is no substantive diuretic effect in dogs without CHF.

Hydrochlorothiazide

Hydrochlorothiazide (HCT) is occasionally used in combination with furosemide and spironolactone for management of refractory fluid retention. HCT primarily blocks the sodium transporter in the distal convoluted tubule and the connecting segment but also has action across the proximal tubule. This effect inhibits sodium, chloride, and water reabsorption. HCT is a moderately potent diuretic, but when used in combination with furosemide, the diuretic impact is greatly magnified as HCT prevents distal sodium reabsorption that escapes the effects of the loop diuretic.

- HCT is a "low ceiling diuretic" because the maximal response is reached at relatively low dosage.
- HCT is available in a variety of tablet sizes, some of which represent combination products. HCT is often formulated with spironolactone (25 mg of each in the 50-mg tablet) or triamterene (to spare potassium) as these combinations increase the diuretic effect while sparing potassium.
- The usual dose of HCT is 1 to 2 mg/kg daily provided the drug can be tolerated. Unfortunately, the "sequential nephron blockade" of fluid and electrolyte reabsorption during combination diuretic therapy is frequently too potent: the result is rapid volume and electrolyte depletion.
- To minimize the risk of acute renal failure and electrolyte disturbances, HCT is administered every other day for the first week of therapy, and serum chemistries and blood pressure are then reevaluated.
- If renal function and electrolytes remain stable, the frequency of dosing can be increased to once daily administration, added to the previously established furosemide-spironolactone regimen.

Adverse Effects

Profound hyponatremia, hypokalemia, and hypochloremia may develop with HCT, regardless of treatment with spironolactone or an ACE inhibitor. These consequences often promote withdrawal of HCT therapy.

Nesiritide

Nesiritide, or synthetic human brain natriuretic factor (h-BNP), has been developed as a "smart diuretic" and this drug may be applicable to veterinary practice. Naturally occurring BNP is released from the heart during volume expansion and leads to natriuresis and vasodilation.

- Nesiritide (labeled for human use) appears to be effective in dogs. It enhances urinary output and reduces aldosterone effects in furosemide-treated dogs; increases urine volume in normal dogs and those with experimental CHF; and demonstrates minimal electrophysiologic effects on the canine heart.
- There is potential for volume depletion and azotemia, so renal function should be followed.
- Currently the drug is too expensive for routine use, but it may be considered in stabilization of life-threatening pulmonary edema.

Monitoring of Diuretic Therapy

Diuretics contract plasma volume and dosing must be adjusted to control fluid accumulation while preventing hypotension, weakness, dehydration, electrolyte disturbances, and azotemia. In most cases, simple monitoring of ABP along with serum creatinine and BUN are sufficient to ensure the dose is not excessive.

Most adverse effects develop within the first two to three weeks unless other medications change or complications develop (e.g., digoxin toxicity with vomiting).

Monitor diuretic therapy as follows:

- Examine the jugular veins. If prominent or distended, volume depletion is not likely an issue and higher diuretic doses are likely to be tolerated.

- Measure the total protein, PCV, BUN/creatinine, and ABP to assess the plasma volume status.
- Measure the serum electrolytes to screen for hyponatremia, hypochloremia (disregard if mild), hypokalemia (never disregard). Hypomagnesemia often tracks hypokalemia.
- Metabolic alkalosis may be evident by increased or normal bicarbonate concentration in the face of a low serum chloride. As with hypochloremia, this abnormality is typically ignored unless moderate or severe.
- Diuretic complications are treated by reducing the diuretic dosage and, if necessary, infusing crystalloids (5% dextrose in water or 0.45 NaCl/2.5% dextrose; either fluid should be supplemented with potassium chloride at 10–20 mEq KCl per 500 ml fluid).
- Patients with primary renal disease and CHF pose a treatment challenge, as volume depletion reduces renal blood flow. It is difficult to support renal function and still control edema or effusions in patients with advanced CHF.
- Provided the patient is drinking, chronic administration of subcutaneous fluids is illogical, as the same effect can be obtained by simply lowering the diuretic dosage (which generally worsens the CHF).
- Mild to moderate azotemia often must be accepted if CHF therapy is to be successful. Hemodialysis would be optimal for controlling uremia and volume status but is not widely available or accessible.
- Progressive azotemia and accompanying signs of uremia (anorexia, vomiting, and depression) frequently prompt the euthanasia of affected patients.

POSITIVE INOTROPIC DRUGS (CARDIOTONICS)

Positive inotropic drugs increase the availability of calcium to cardiomyocytes, thereby enhancing the strength of heart contraction. This class of drugs includes the digitalis glycosides (digoxin, digitoxin), catecholamines (dobutamine, dopamine), phosphodiesterase inhibitors (milrinone), and calcium sensitizers (pimobendan).

Digoxin

Digoxin is the oldest inotropic drug in common use. (Digitoxin is used rarely and will not be discussed.) Digoxin is indicated in therapy of moderate to severe CHF caused by dilated cardiomyopathy, chronic valvular heart disease, or untreated congenital heart disease in dogs. It is rarely prescribed to cats. Digoxin is especially useful when CHF is complicated by atrial fibrillation or frequent premature atrial complexes. The cardiac glycosides have *not* been shown to prolong survival in CHF.

- Following oral or IV administration, digoxin inhibits the sodium–potassium ATPase that activates a sodium calcium exchanger, which increases calcium influx. The inotropic effect is mild when compared to potent drugs such as dobutamine or pimobendan.
- Digoxin also sensitizes arterial baroreceptors, leading to a withdrawal of sympathetic activity and increased vagal efferent tone to the heart. This effect slows the sinus node rate at rest and decreases the ventricular rate response to atrial fibrillation (by impairing AV nodal conduction).
- Canine data suggest that digoxin may inhibit the renin–angiotensin system and decrease sympathetic nerve discharge.
- Digoxin administered orally decreases systemic vascular resistance, venous tone, and central venous pressure and induces diuresis in patients with CHF.
- Digoxin given IV may cause systemic and coronary vasoconstriction and can produce transient myocardial ischemia. Therefore, IV administration is not recommended.
- Digoxin is mainly a drug for management of advanced CHF caused by predominately systolic dysfunction. The drug is particularly indicated in the setting of atrial fibrillation and CHF.

▼ ***Key Point*** Digoxin is unlikely to provide satisfactory control of ventricular response rate to atrial fibrillation unless used in combination with diltiazem or a beta-blocker. However, as a positive inotrope, digoxin is the first drug used in treatment of atrial fibrillation in the setting of CHF.

While some veterinarians use the examination heart rate to decide if they will prescribe digoxin, there is no established basis for this approach or for predicting the potential benefit of the drug. Digoxin does little to mitigate heart rate due to high sympathetic tone, stress, or exercise; heart rate benefits of increased vagal tone are most evident in the resting state.

- Digoxin should not be used in some clinical settings and is contraindicated in others.
- Digoxin plays no role in the acute hospital therapy of CHF unless it is complicated by atrial fibrillation.
- Digitalis is not prescribed for isolated diastolic problems such as pericardial disease or HCM.
- We do not prescribe digoxin for occult (asymptomatic) heart disease as other drugs (ACEI and beta-blockers) are more likely to be cardioprotective and digoxin may aggravate ventricular ectopy.
- Overt contraindications to digitalization include frequent or complex ventricular ectopy; moderate to severe renal failure (reduced elimination); myocarditis, sinus node disease, or heart block (vagal effects can depress nodal functions); hypokalemia (increases potential for arrhythmias); ventricular pre-excitation (AV block may lead to preferential conduction

down the accessory pathway); and known individual hypersensitivity (typically anorexia) to the drug.
- Drug interactions may occur with quinidine, verapamil, and amiodarone resulting in increased serum digoxin concentration.
- Digoxin is administered typically by the oral route. Intravenous use is uncommon today in small animals. Available digoxin preparations include tablets (0.125, 0.25, 0.5 mg) and elixirs (0.05 and 0.15 mg per ml). The usual daily dose for the dog is 0.0055 to 0.0075 mg/kg, PO, twice daily.
- Monitoring of therapy can be accomplished by client interview for adverse signs; auscultation for arrhythmias; an ECG when heart rhythm disturbances are detected; and most importantly, a serum digoxin level. Following a week of consistent treatment, a blood sample is obtained 8 to 12 hours post dosing; the therapeutic goal for a trough level is 0.8 to 1.2 ng/ml.

Adverse Effects

Common adverse effects of digoxin include anorexia, depression, vomiting, diarrhea, and cardiac arrhythmias. Arrhythmias are explained by either increased vagal tone (causing sinus node depression or AV block) or enhanced calcium entry into cells, leading to membrane oscillations, increased automaticity (particularly in the His-Purkinje fibers), and subsequently premature complexes. Ventricular bigeminy and ectopic junctional rhythms also have been observed in dogs with digitalis toxicity.

Catecholamines

The catecholamines used most often in emergent management of CHF are dobutamine and dopamine. These drugs stimulate cardiac beta- and alpha–receptors to increase contractility in a dose-dependent manner via the second messenger effect (increased generation of cyclic AMP or IP_3 for beta- and alpha–receptor stimulation, respectively). In patients with CHF, the heart rate generally increases slightly during infusion of catecholamines. The effects of catecholamines on systemic arterioles are dose dependent but include vasodilation at lower doses ($beta_2$ effect) and vasoconstriction (alpha effects) at higher infusion rates.

- Dobutamine HCl is an injectable catecholamine (synthetic analogue of dopamine) with dose-dependent positive inotropic effects that are far greater than digitalis glycosides. Effects on blood vessels are dose-dependent and depend on the predominant drug effect and availability of sympathetic receptors.
- Both beta and alpha effects are inotropic, but myocardial beta-receptor density is far greater in dogs and cats.
- Myocardial receptor density is altered in chronic canine CHF, and the beta-receptor density (especially $beta_1$) is reduced. Accordingly, the dose of dobutamine required for cardiac stimulation may be higher than that used for healthy dogs in other settings (as with anesthesia). Constant rate infusion can lead to further down regulation of beta-receptors occurring within several hours (tachyphylaxis), requiring higher doses to maintain the same inotropic effects.
- In resistance arterioles, the $beta_2$ effect of catecholamines causes vasodilation, while alpha-receptor stimulation constricts the vessels.
- Dopamine, the precursor to nor-epinephrine, has similar effects but causes more tachycardia and pulmonary and systemic vasoconstriction than dobutamine for equivalent inotropic doses. For these reasons, dopamine is used less often in CHF but is preferred if bradycardia or severe hypotension is present.
- *Indications for catecholamines*—The principal use of dobutamine or dopamine in CHF is therapy of cardiogenic shock, which can be defined clinically as severe CHF accompanied by hypotension (systolic ABP <80 mm Hg and a mean ABP <50 mm Hg) with evidence of poor perfusion (pale mucous membranes and elevated blood lactate). This situation is often accompanied by hypothermia and in cats is also associated with sinus bradycardia (HR <160/min). Dobutamine also can be used to support the dog with chronic refractory CHF that is retaining fluid and is unresponsive to high dose diuretic therapy.
- The immediate goal of catecholamine therapy in CHF is the short-term (24–48 hours) support of myocardial contractility to achieve a higher stroke volume and cardiac output. Such therapy, when administered with other drugs for heart failure such as diuretics and nitrates, frequently stabilizes the patient. Ideally this benefit will occur mainly through an increase in stroke volume, without excessive increases in heart rate or vascular resistance.
- Clinical measures of improvement during catecholamine infusion include increases in ABP and urinary output; enhanced tissue perfusion, as judged by heightened level of consciousness, normal rectal temperature, pink mucous membrane color, and shortened refill time; and improved muscle strength.
- Clinical use of dobutamine in dogs with CHF involves a constant rate intravenous infusion with initial suggested rate of 2.5 mcg/kg/min. Dobutamine is added to 5% dextrose solution and infusion controlled by an automated dose syringe or infusion pump.
  - The initial dose can be increased in 30 to 60 minutes to 3.75 or 5 mcg/kg/min and then uptitrated as needed to clinical effect.
  - Objective markers of drug effect are increases in rectal temperature and ABP. A target ABP of 90 to 100 mm Hg systolic is a reasonable goal, and the infusion should be maintained at a level to prevent higher ABP or tachycardia.
  - Rarely are infusions of >10 mcg/kg/min needed.

  - After 24 to 48 hours of dobutamine, the infusion can be reduced by 50% every 2 to 4 hours with monitoring of ABP. If blood pressure is maintained at >85 mm Hg systolic, the drip can be discontinued.
  - If ABP fails to increase in dogs with cardiogenic shock, consideration should be given to adding or substituting dopamine for more potent vasoconstriction. Dose rates are indicated in Table 146-1.
  - Atrial fibrillation is not a contraindication for use of dobutamine. In most cases, ventricular rate response is unchanged or actually slows during dobutamine infusion, presumably from improved ABP and withdrawal of endogenous sympathetic tone. Digoxin can be used in combination with dobutamine to help control ventricular response rate.
- Cats with CHF, hypotension, and bradycardia can benefit from infusions of dobutamine. This includes feline patients that have suffered a myocardial infarction superimposed on pre-existent cardiomyopathy.
  - Typically an infusion of 2.5 mcg/kg/min is initiated. Infusion rates exceeding >7.5 mcg/kg/min are uncommonly needed.
  - The infusion rate can be increased every 30 to 60 minutes to achieve an ABP of 90 to 120 mm Hg systolic. In most cases, heart rate also will increase to more appropriate levels for a cat with CHF.
  - Clinical assessment of benefit is similar to that for dogs. Most cats receive dobutamine for 24 to 36 hours.
- Contraindications for catecholamines are mostly relative. Ventricular ectopy may worsen and should be carefully monitored by ECG monitor. Hypokalemia may worsen with catecholamine infusion, so electrolyte imbalances should be corrected.

Adverse Effects

Adverse effects of catecholamines are predictable extensions of sympathomimetic stimulation and include sinus tachycardia; premature supraventricular and ventricular complexes; ventricular tachycardia that can progress to ventricular fibrillation; anxiety; tremors; elevated ABP; and seizures (mainly in cats). Simply stopping or lowering the infusion rate controls most adverse effects as the drug is rapidly hydrolyzed within minutes of administration. Life-threatening side effects can be treated with the ultrashort-acting beta-blocker esmolol (100–500 mcg/kg dose infused over 5–10 minutes with HR and ABP monitoring).

Inodilators

The word "inodilator" pertains to positive inotropic drugs that also demonstrate significant vasodilator effects. The combination of increased myocardial contractility and left ventricular afterload reduction result in a potent increase in ventricular stroke volume.

Milrinone and Amrinone

Milrinone and amrinone are PDE-III inhibitors that prevent the degradation of cyclic AMP, the second messenger of the beta-adrenoceptor. This leads to accumulation of the cyclic nucleotide and a potent positive inotropic effect. Cyclic AMP also functions as a peripheral vasodilator, especially in dogs, so that reduced left ventricular afterload further improves cardiac performance.

These drugs are administered by IV infusion, are relatively expensive, and are used infrequently in veterinary practice, though canine studies with oral and IV milrinone showed both acute and chronic benefit of this drug.

Clinical indications for IV milrinone would be the combination of severe systolic dysfunction and tachycardia (as PDE-III inhibitors have relatively little effect on heart rate, even at higher doses) or the patient with acute-on-chronic heart failure, already receiving beta blockade and in need of acute inotropic support that bypasses the beta-receptor.

Pimobendan

Pimobendan (Vetmedin) is classified as a calcium sensitizer, as well as a phosphodiesterase inhibitor with vasodilator properties. It is approved for veterinary use in many countries and completing clinical trials in other countries (including the USA). Pimobendan is an inodilator with a novel mode of action on contractility. Whereas digitalis and catecholamines increase the transport of calcium into the cardiomyocyte, pimobendan increases the *sensitivity* of the actin-myosin contractile apparatus to available calcium.

Compared to other inotropic drugs, pimobendan offers a number of advantages.

- It is far more potent than digoxin and does not cause anorexia. Furthermore, pimobendan is not reported to impact off-loading of calcium from the contractile apparatus, which suggests it will not impair diastolic function (a potential problem with digitalis).
- Pimobendan is superior to pure phosphodiesterase inhibitors in canine models of CHF, emphasizing the benefit of the calcium sensitization.
- Pimobendan is administered by the oral route yet still carries a potent inotropic effect. For this reason, it serves as a second choice to dobutamine (or dopamine) infusion for hospital treatment of low cardiac output. ABP must be followed to insure that excessive vasodilation does not develop secondary to PDE inhibition. Thus, while dobutamine is the drug of choice for cardiogenic shock, pimobendan may be more practical in many practice situations.
- Unlike digoxin, catecholamines, and pure PDE-III inhibitors, pimobendan is noteworthy for an apparent lack of sensitization to ventricular arrhythmias.
- One disadvantage of pimobendan is a relative lack of effect on heart rate in atrial fibrillation.

- Pimobendan is indicated in the therapy of heart failure in dogs caused by dilated cardiomyopathy and is also beneficial in treatment of CHF due to chronic valvular heart disease or untreated congenital heart diseases in dogs. It has also been used for "prevention" of CHF in breeds with advanced occult DCM such as that encountered in the Doberman pinscher. Where available, pimobendan has often replaced digoxin for treatment of canine CHF.
- There is no logical reason for prescribing pimobendan to the exclusion of "standard CHF therapy" of furosemide and an ACE-inhibitor, along with dietary sodium restriction. This trio provides an excellent pharmacologic profile for treatment of advanced CHF in dogs.
- It is likely that pimobendan will be useful in cats with CHF, though extra-label feline use requires far more study.
- Digoxin, diltiazem, or a beta-blocker (carvedilol) can be added for heart rate control in cases of atrial fibrillation.
- Pimobendan capsules (1.25, 2.5 and 5 mg) are available for veterinary use in many countries. The usual canine dose is 0.25 mg/kg PO q12h. In clinical trials doses ranging from 0.3 to 0.6 mg/kg daily (once or divided bid) have been effective. Pimobendan should be given at least 1 hour before feeding for maximal effect. The drug has demonstrated an anti-thrombotic effect in some *in vitro* studies, and this may prove useful in animals as well. Drug expense may limit its use.

Adverse Effects

Adverse effects of pimobendan appear to be minimal. Unlike other inotropic drugs, ventricular ectopy is not believed to worsen under pimobendan. The heart may literally "pound" under the influence of this inodilator, and impact on degree of mitral regurgitation is a theoretical concern that has not been established in studies of CHF in dogs.

VASODILATORS AND ANGIOTENSIN CONVERTING ENZYME INHIBITORS

The vasodilator drugs are a heterogeneous group of agents that dilate arteries or veins. Vasodilators act by varying cellular mechanisms, often with predominant effects on arteries or veins. The class of drugs includes the nitrates (nitroglycerin, sodium nitroprusside), hydralazine, calcium channel blockers (amlodipine, diltiazem), phosphodiesterase inhibitors (milrinone, pimobendan, sildenafil), and the numerous drugs that act as an angiotensin converting enzyme inhibitor (ACEI).

Overview

Vasodilators are used in both hospital therapy and chronic management of CHF.

- These drugs have hemodynamic effects that pertain mainly to reduction in preload or afterload. In addition, the clinician must consider the effects of any given vasodilator on neurohormonal activation.
- Venodilator drugs reduce *preload* (filling pressures) through venous pooling. Decreased filling pressures counteract edema formation and decrease ventricular wall tension by reducing preload.
- Arteriolar dilators are thought to decrease *afterload* of the left ventricle by lowering ABP and reducing vascular resistance (though afterload is not simply blood pressure). Because the failing left ventricle is very sensitive to afterload, the higher the load, the greater the wall tension and myocardial oxygen consumption and the lower the ventricular stroke volume. Reducing afterload with a vasodilator also decreases mitral regurgitant volume and increases cardiac output.
- As a consequence of sudden drops in ABP, the direct vasodilators often create an undesirable activation of the sympathetic and renin-angiotensin-aldosterone systems. In contrast, the ACEI exert favorable hemodynamic and neurohormonal effects by inhibiting these systems. Accordingly, direct vasodilators are usually administered with an ACEI.
- "Direct" vasodilators such as nitroglycerin and sodium nitroprusside are often used in hospital therapy of left-sided CHF (see below).
- While the calcium-channel blocker/vasodilator amlodipine occasionally is used in chronic CHF, an ACEI is the vasodilator of choice in chronic management of CHF due to valvular disease, cardiomyopathy, and congenital heart disease. ACEIs are considered "balanced" arterial and venous vasodilators; they also decrease the neurohormonal activity that has been associated with morbidity and mortality in CHF.
- Phosphodiesterase inhibitors are also vasodilators. This effect may explain part of the benefit of pimobendan in management of chronic canine CHF or sildenafil (Viagra) in treatment of pulmonary hypertension.
- The third-generation beta-blocker carvedilol (Coreg) is used increasingly in treatment of dilated cardiomyopathy and exhibits alpha-adrenergic blocking activities; this action confers vasodilator properties to carvedilol.

Nitroglycerine

Nitroglycerine (NTG) induces nitric oxide–mediated vasodilatation in the vascular endothelium. When applied topically (2% ointment) NTG acts mostly as a systemic venodilator. The potency of the drug administered IV in dogs is unchallenged, but the overall benefit

of topical administration on filling pressures requires further study.

- Systemic venodilation may reduce pulmonary venous pressure by translocating pulmonary venous blood to dilated splanchnic veins. However, there may be great individual variability in NTG effects with respect to redistribution of fluid.
- Nitrate tolerance develops if NTG is administered too frequently; therefore, the drug is usually given once or twice daily allowing a nitrate-free interval.
- *Indications* for NTG therapy include hospital therapy of pulmonary edema. Home use of NTG may be considered in dogs with nocturnal dyspnea (apply at bedtime) or in difficult to medicate dogs that will tolerate topical therapy.
- NTG comes as a 2% ointment with applicator dose sheets. There is approximately 15 mg NTG per inch of ointment, but the dose depends also on the surface area covered.
- The approximate canine dose (from toy breed to giant breed) $^1/_2$ to 2 inches, cutaneously, q12–24h.
- Alternative approaches include the use of nitrate patches (5, 10 mg) that are removed after 12 hours to provide a nitrate-free interval.

Adverse Effects

Adverse effects of NTG are apparently few, though potentially a reduced preload could lead to a lower cardiac output.

Sodium Nitroprusside

Sodium nitroprusside (Nipride) is a potent dilator of both systemic arterial and venous smooth muscle (generating NO in vascular smooth muscle). Benefits of therapy are rapid reduction in ABP and venous pressures (from venous pooling) with reduced mitral regurgitation fraction, decreased LV afterload (increasing forward flow), and less pulmonary edema.

- *Indications* for nitroprusside are hospital treatment of life-threatening pulmonary edema and severely reduced cardiac output when caused by cardiomyopathy or mitral valvular disease, as well as in the emergent treatment of systemic hypertension. In addition, controlled hypotension during surgery of patent ductus arteriosus or certain brain lesions may be accomplished by nitroprusside infusion.
- Therapy with sodium nitroprusside is usually prompted when initial doses of furosemide and nitroglycerin fail to provide relief from pulmonary edema, or when pulmonary edema is so fulminant that the patient is expectorating bloody froth or the chest x-ray demonstrates a "white lung" or "white-out."
- When used in the setting of pre-existing systemic hypotension, dobutamine (or dopamine) should be infused simultaneously to increase cardiac output and prevent further lowering of blood pressure.
- Nitroprusside may increase intracranial pressure. Therefore, it should not be used for the management of hypertensive encephalopathy.
- Nitroprusside must be given IV, and it is important to follow instructions regarding drug preparation and delivery (read the insert).
- For CHF, initial nitroprusside doses of 0.5 to 2.5 mcg/kg/min are generally well tolerated and the infusion rate can be increased to 5 mcg/kg/min (or higher) if necessary. However, doses > 5 mcg/kg/min are uncommonly required for dogs with only CHF. Titrate the dosage to a systolic ABP of 85 to 100 mm Hg, and avoid use for more than 48 hours.
- Wean the patient from the drug over a 4 to 6 hour period.
- Owing to the risk of hypotension, frequent monitoring of ABP is important when using this drug. An automated, ABP monitor can track the trends.

Adverse Effects

The most common *adverse effects* are related to hypotension, which is readily controlled by stopping or reducing the drip. After 24 to 48 hours of therapy, additional adverse effects including cyanide accumulation and toxicosis become a concern.

Sildenafil

Sildenafil (Viagra) is an inhibitor of phosphodiesterase-5 and demonstrates pulmonary arterial, as well as selective systemic arterial vasodilation. The mechanism of action is reduced degradation of cyclic GMP, the intracellular mediator of nitric oxide.

- The drug has been used effectively in some in human patients with pulmonary hypertension, and empiric use of the drug in canine pulmonary hypertension has been communicated using typical starting doses of 0.5 to 1 mg/kg, PO two to three times daily. Higher doses (2–3 mg/kg PO q8h) may be tolerated and are often required to reduce pulmonary vascular resistance.
- The drug is expensive and clinical trial data in animals are lacking.
- *Indications* for sildenafil are evolving but include the treatment of dogs with right-sided CHF and documented pulmonary hypertension (based on Doppler echocardiography or cardiac catheterization). Heartworm infected dogs with right-sided CHF or profound pulmonary hypertensive disease also might benefit, particularly during the adulticide treatment interval. Another indication for sildenafil may be management of pulmonary hypertension associated with congenital heart disease.

Adverse Effects

Adverse effects include systemic hypotension, so ABP should be monitored carefully.

Hydralazine

Hydralazine induces vasodilation in systemic arterioles, possibly by altering potassium channels in vascular smooth muscle.

- Hydralazine causes significant vasodilation within 2 hours of oral administration to dogs, usually reaching a near peak effect within 3 to 5 hours post administration.
- *Indications* for hydralazine are severe left-sided CHF in the setting of mitral regurgitation in dogs, particularly following rupture of a chorda tendineae, and in the therapy of refractory systemic hypertension in dogs or cats.
- Hydralazine is a potent arteriolar vasodilator and by decreasing systolic and diastolic ABP, left ventricular afterload decreases, mitral regurgitation decreases, and antegrade stroke volume increases. While not as potent or as rapid acting as nitroprusside, the combination of hydralazine plus nitroglycerin offers a combined vasodilator approach that is easier to deliver in the private practice setting.
- Hydralazine (Apresoline 10 and 25 mg tablets) is typically dosed at 0.5 to 2 mg/kg orally q12h. Higher doses may be tolerated. In acute CHF, the dose should be titrated to achieve a systolic ABP of 90 to 100 mm Hg.

Adverse Effects

Adverse effects of hydralazine include hypotension with reflex sinus tachycardia; anorexia; and activation of neurohormonal reflexes. The latter problem makes hydralazine a poor choice for chronic CHF therapy.

Angiotensin Converting Enzyme Inhibitors (ACEI)

The renin-angiotensin-aldosterone system (RAAS) is triggered by inadequate blood pressure, reduced renal blood flow, and sympathetic stimulation of the kidneys. RAAS activation is increased chronically in CHF and contributes to the morbidity and mortality of chronic CHF. An ACEI blocks the conversion of AT–I to AT–II by inhibiting the converting enzyme of angiotensin (a kininase). ACEIs also decrease aldosterone formation and may reduce sympathetic nervous system activity.

- The onset of vasodilation with an ACEI is not as abrupt or as marked as with IV nitroprusside or oral hydralazine; however, the ACEIs are arterial vasodilators (via inhibition of AT-II release) and also venodilators (by preventing degradation of kinins).
- Commonly used ACEIs are enalapril (veterinary products Enacard and Cardiovet), benazepril (veterinary product Fortecor; human product Lotensin), ramipril (veterinary product Vasotop, human product Altace), quinapril (Accupril), and lisinopril (Prinivil), with others available in various countries.
- Comparative ACEI trials with proven major end points (need for hospitalization, objective symptom scores, survival) are lacking in dogs and cats, making the choice of one specific ACEI over another relatively empiric and one of personal choice.
- Some ACEIs are pro-drugs and must be converted to active forms by transformation in the liver (e.g., enalapril to enalaprilat).
- Most ACEIs are eliminated by the kidney. Hepatic elimination of benazepril is a potential benefit for dogs and cats with renal failure.
- Some ACEIs may demonstrate greater cardiac tissue selectivity; however, major end-point benefits of one ACEI versus another (in terms of survival or CHF signs) have not been shown for dogs or cats.
- Principle *indications* for an ACEI include empiric cardioprotection in occult dilated cardiomyopathy (early heart failure); management of CHF; and treatment of systemic hypertension.
- Additional indications for an ACEI are treatment of renal disease with proteinuria and cardioprotection following the rare documented myocardial infarction.
- Because ACEIs may control or prevent secondary hypertrophy in models of pressure overload, there is some interest in treatment of asymptomatic ventricular hypertrophy with ACEIs; examples include subaortic stenosis, pulmonic stenosis, and hypertrophic cardiomyopathy. However, these uses currently are speculative, and ACEI treatment is generally limited to management of incipient or established CHF in these conditions.
- The use of ACEIs in dogs and in cats with CHF is discussed below.
- Management of *systemic hypertension* using ACEIs is well established in both dogs and in cats.
- ACEIs lower ABP and partially mitigate neurohormonal activation caused by high-renin hypertension or following direct vasodilator therapy with amlodipine.
- For dogs with hypertension, an ACEI is often the first drug chosen, particularly in cases where elevated pressure is associated with glomerular disease.
- In cats, amlodipine is a more effective antihypertensive for moderate to severe hypertension, but the combination of benazepril (or another ACEI) along with amlodipine makes good sense in the cat with hypertension and renal disease.
- It should be emphasized, however, that some cats do not respond effectively to monotherapy with an ACEI and require either amlodipine or a beta-blocker to achieve effective blood pressure control (for details, see Chapter 153).

ACE-Inhibitors for Heart Failure in Dogs

As a group, the ACEIs are helpful for long-term management of canine heart failure, increasing survival, and reducing clinical signs of CHF.

- In dogs with acute CHF, therapy with an ACEI is generally initiated following initial diuresis or at the time of release from the hospital.
- The combination of an ACEI, furosemide, spironolactone, and a positive inotropic drug (digoxin or pimobendan) represents the main treatment approach for chronic CHF in dogs.
- The use of an ACEI in dogs with asymptomatic heart disease is less defined.
- Current data (from three studies) indicate no clear benefit in the early use of ACEI in asymptomatic canine mitral valve disease in small-breed dogs. However, many cardiologists empirically initiate ACEI therapy once interval changes demonstrating progressive cardiomegaly are demonstrated by radiography or echocardiography.
- In contrast to degenerative mitral valve disease in small-breed dogs, most cardiologists do start empiric ACEI treatment (often with a beta-blocker) in dogs with proven occult dilated cardiomyopathy, which represents an early form of heart failure. A similar approach is taken in larger sized dogs with chronic mitral regurgitation and echocardiographic evidence of LV systolic dysfunction.
- Dosing for enalapril (Enacard), benazepril (Fortecor), and lisinopril is initially 0.5 mg/kg PO once daily and for ramipril (Vasotop), 0.125 mg/kg per day.
- In moderate to severe CHF, increasing the dosage of enalapril or benazepril to twice daily is recommended after one or two weeks of therapy.
- Under-dosing may reduce overall benefit of ACEI, as the effect is probably dose-related.

ACE-Inhibitors for Heart Failure in Cats

While there are no published, placebo-controlled trials of ACEIs in cats, both benazepril and enalapril appear useful clinically in management of feline CHF.

- Regardless of cause, the combination of furosemide and an ACEI is the current mainstay of therapy for CHF in cats as supported by a recent controlled clinical trial.
- Whether or not the angiotensin inhibitors can reduce myocardial hypertrophy in cats with primary cardiomyopathies is unknown, but there is no hard evidence for this. Therefore, empiric therapy with an ACEI in cats with cardiomyopathy is not recommended by us until there is LA dilation or convincing Doppler evidence of elevated LA pressure (both of which suggest impeding CHF).
- Reducing ABP in cats with asymptomatic HOCM is a potential concern, but treatment with an ACEI does not appear to worsen dynamic LVOT obstruction.
- The usual dosage of enalapril or benazepril in cats is 0.25 to 0.5 mg/kg q24h, but in advanced disease, it can be given bid.

Monitoring ACEI Therapy

ACEI therapy is monitored by measuring ABP and with periodic monitoring of renal function, serum sodium, and potassium.

- Consider published dosing guidelines when prescribing.
- Measure ABP at each visit (target range is a systolic pressure of 90–120 mm Hg).
- Follow renal function (BUN/creatinine), serum sodium, and potassium; measure these within 7 to 14 days of initiating therapy or after changing the dosage.
- Mild hyperkalemia is not an indication to discontinue therapy.

Adverse Effects

- Adverse effects of an ACEI are generally related to effects on blood pressure, intra-renal hemodynamics, and serum electrolytes. Combination of an ACEI with aspirin or a diuretic increases the likelihood of renal failure.
- Volume depletion superimposed on dilatation of the efferent arteriole in the glomerulus can lead to reversible renal failure, which can be acute in the occasional case. In most cases, mild to moderate azotemia develops.
- Therapy of ACEI-induced renal failure includes reducing the doses of diuretic and ACEI and administering fluid therapy judiciously. If systolic blood pressure is < 85 mm Hg, or if BUN/creatinine increase by 2 to 3 times over pretreatment levels, the dose of the ACEI, furosemide, or both, should be reduced by 33% to 50%.
- Some patients are seemingly dependent on angiotensin-II effects for maintaining glomerular filtration pressure, and these patients may not tolerate any dose of an ACEI. Such cases are unusual in dogs.
- Mild hyperkalemia is more likely in patients receiving spironolactone concurrently. Provided the potassium is < 6 mmol/L, the situation is not of great concern. Clients should be instructed to avoid potassium supplements.

BETA-ADRENERGIC BLOCKERS

Overview

The heart contains a rich supply of $beta_1$ receptors and a smaller number of $beta_2$ receptors. Stimulation of cardiac beta-receptors increases heart rate (chronotropy), contractility (inotropy), relaxation (lusitropy), conduction velocity (dromotropy), and subsidiary pacemaker excitability (bathmotropy). Blood vessels contain a

number of extrasynaptic beta$_2$ receptors; when stimulated the vessel undergoes vasodilation.

Beta-adrenergic blockers (beta-blockers) diminish each of the above effects of sympathetic stimulation on target organs. Beneficial and adverse effects of beta-blockade are readily understood by simply "reversing" the physiologic effects of beta-receptor stimulation.

When beta-receptors are chronically blocked the number of beta-receptors increases. This change explains some of the benefits of long-term beta-blockade in heart failure. Conversely, sudden withdrawal of beta-blocker therapy may expose the heart to excessive stimulation from catecholamines.

Treatment with a beta-blocker prolongs diastole as a function of a slower heart rate. This allows more time for ventricular and coronary arterial filling.

Beta blockers initially decrease resting cardiac output by about 10% to 20%, causing a compensatory reflex rise in the peripheral vascular resistance so that ABP is largely unchanged. Vascular resistance and ABP begin to fall 1 to 2 days after initiation of therapy. The overall effects of beta-blockers on blood pressure are complex, but in general ABP decreases.

There is a *reduction of myocardial oxygen demand* following beta-blockade, reducing so-called "demand ischemia." Beta-blockers reduce the myocardial oxygen imbalance (relative to the delivery of oxygen) that develops in hypertrophied hearts with sympathetically mediated tachycardia, hyper-contractility, or elevated blood pressure.

The net effect of beta-blockers on *diastolic function* of the heart, especially in cats with HCM or dogs with subaortic stenosis, is unknown. Beta stimulation improves relaxation (lusitropy) in healthy cardiac muscle and also in some canine models of cardiac disease; accordingly beta-blockers should not directly improve myocardial relaxation. However, indirect effects of beta-blockers, especially slowing of heart rate and reduction of myocardial oxygen demand, may be beneficial to diastolic function. Furthermore, in some studies beta-blockade has been shown to reduce diastolic calcium leakage from the sarcoplasmatic reticulum in cardiomyopathic hearts, reduce diastolic calcium overload, and improve ventricular relaxation.

The beta-blockers used in veterinary practice can be classified as first generation (non-selective beta-blockers such as propranolol); second generation (selective beta$_1$-blockers such as metoprolol and atenolol); and third generation blockers such as carvedilol (with alpha-adrenergic blocking effects and anti-oxidant properties).

Most beta-blockers are lipophilic, cross the blood-brain barrier, and are eliminated by the liver. Those beta-blockers that cross the blood-brain barrier may be more beneficial in prevention of sudden cardiac death. Compared to other beta-blockers, atenolol, sotalol, and nadolol are different, with hydrophilic nature and renal elimination.

Indications and Clinical Uses of Beta-Blocker Therapy

There are a number of indications and uses for beta-blockers in small animal practice. While most of the drugs in this class may be substituted for each other on a pharmacologic basis, clinical experience and limited research studies offer guidelines for the use of specific beta-blockers in certain situations. Some of the most common disorders treated with beta-blockers are indicated below.

Cardioprotection in cardiomyopathies, chronic heart failure, and with congenital heart defects

- Long term use of beta-blockers in *heart failure* can retard the progress of myocardial failure; support ventricular ejection fraction; reverse cardiac remodeling; and prevent sudden cardiac death in experimental canine models similar to spontaneous DCM. A variety of mechanisms have been proposed for this benefit, but the major effect is believed to be reduction in catecholamine injury to the heart and prevention of sympathetic-induced ventricular arrhythmias.
- While the precise value of beta-blockade in chronic canine cardiomyopathy or chronic valvular heart disease is under study, increasingly, cardiologists prescribe beta-blockers as "cardioprotection" against the injurious effects of the sympathetic nervous system on heart muscle.
- A beta-blocker is indicated in the dog with discovered, well-documented, "occult" dilated cardiomyopathy; such patients generally tolerate beta-blockers well.
- It is more difficult to initiate beta-blocker therapy in the dog with established CHF, largely because of the advanced state of heart failure observed in most canine patients. In addition, the available dosing forms of human drugs pose a limiting factor, since very small dosages must first be given.

▼ ***Key Point*** Since beta-blockers are *potent* negative inotropic drugs, never begin therapy until CHF is well controlled with diuretics and ACEI.

- In dogs that have received long-term beta-blockade, the eventual development of CHF should prompt a reduction, but not discontinuation, of the dose. Typically a 25% to 50% dose reduction is undertaken, and CHF is controlled with diuretics, ACEI, and inotropic drugs.
- Dogs with CHF caused by aortic or pulmonic stenosis may become dependent on heart rate to maintain cardiac output in the setting of a fixed obstruction. In these patients, the beta-blocker dose should be reduced to permit an examination heart rate of at least 100 to 120/min.
- While any beta-blockers could theoretically benefit the failing heart, *carvedilol and long-acting metoprolol*

are the beta-blockers most often used for cardioprotection in cases of dilated cardiomyopathy or chronic valvular disease in dogs (see below).

- Beta-Blockers also may confer cardioprotection in hypertrophic hearts *prior* to the onset of ventricular failure. One possible mechanism is *reduction of myocardial oxygen demand*, especially in times of exercise or stress. *Atenolol and propranolol* are most commonly used for cardioprotection in HCM and in concentrically hypertrophied hearts related to congenital heart disease.
  - Reduction of myocardial oxygen demand may be especially beneficial in diseases where "demand ischemia" develops during tachycardia; for example, with HCM and congenital heart diseases characterized by concentric ventricular hypertrophy.
  - The benefit of beta-blockers in long-term management of feline HCM has not been confirmed; nevertheless, atenolol is often used for cardioprotection and to reduce dynamic outflow obstruction.
- In *congenital subaortic stenosis* beta-blockers are cardioprotective and recent reports suggest that survival is prolonged in cases of severe SAS compared to untreated dogs. Presumably a similar benefit would be observed in severe pulmonic stenosis, but this has not been verified.
- In *congenital pulmonic stenosis* and in *tetralogy of Fallot*, beta-blockers decrease dynamic right ventricular outflow obstruction caused by hypercontractility of thickened myocardium.
  - Benefit also may be observed following balloon valvuloplasty wherein RV shortening might increase due to the sudden drop in afterload.
  - *Propranolol and atenolol* are the beta-blockers most commonly used for reducing RV dynamic outflow obstruction.
- Beta-Blockers *reduce dynamic left ventricular outflow obstruction*, including that associated with mitral-septal contact in cats and dogs with hypertrophic obstructive cardiomyopathy, with reduced LV cavity size, and associated with mitral valve malformation.
  - This benefit is attained by reducing the rate of myocardial contraction, especially under circumstances of heightened sympathetic tone, and delaying the onset of systolic anterior motion of the mitral valve.
  - *Atenolol* is most commonly used for reducing LV dynamic outflow obstruction.
- The beta-blockers are considered "broad-spectrum" *anti-arrhythmic drugs*.
  - Atrial and ventricular ectopic beats may be suppressed by effects on automaticity of fibers and reduction of sympathetically mediated calcium influx. Beta-Blockers are used often as co-therapy with another anti-arrhythmic drug such as mexiletine or digoxin.
  - In atrial tachyarrhythmias, such as atrial fibrillation, beta-blockers reduce ventricular response rate, especially when combined with digoxin or diltiazem. This effect is achieved by reducing conduction velocity across the AV node.
- Sinus tachycardia is blunted by beta-blockade, an effect that may be beneficial in feline HCM; congenital mitral stenosis; in thyrotoxicosis; pheochromocytoma; and in certain toxicities (cocaine, caffeine, chocolate).

The choice of beta-blocker varies:

- *Esmolol*, *propranolol*, and (in some countries) *sotalol* are available for IV use when needed.
- *Sotalol* is the most potent beta-blocker used for arrhythmia control.
- *Atenolol* is used more often as co-therapy with other anti-arrhythmic drugs, or as monotherapy when supression of frequent single premature complexes is a goal.
- *Atenolol and carvedilol* are most often used in control of heat rate in patients with atrial fibrillation.
- In *hyperthyroidism*, elevated sympathetic tone is a factor in the systemic clinical signs and in the cardiotoxicity of the condition; beta-blockers attenuate this effect. *Atenolol* is most commonly used for this purpose.
- Beta-Blockers are effective drugs for co-therapy of *systemic hypertension* and can be used with calcium channel blockers or ACEI. Blood pressure is reduced by effects on lowering heart rate and stroke volume, decreasing cardiac output, and possibly by central effects and reduction of beta-receptor mediated renin release. *Atenolol and carvedilol* are especially appropriate for this use.
- In *pheochromocytoma*, control of hypertension should begin with an alpha-blocker (phenoxybenzamine or prazosin); subsequently, as blood pressure falls, a beta-blocker can be added for heart rate and rhythm control. *Propranolol* is most often used for this purpose.
- In reflex mediated (vasovagal, neurocardiogenic) syncope, beta-blockers reduce the stimulation of ventricular mechanoreceptors, an effect that may blunt the resultant reflex bradycardia and vasodilation.

Contraindications for Beta-Blocker Therapy

- *Untreated CHF*, as inotropy and heart rate initially are depressed (don't give beta-blockers to "wet" patients).
- *Systemic hypotension*, as reduction of heart rate and contractility will worsen the situation.
- *Bradyarrhythmias* including sinus bradycardia, sinus node disease (sick sinus syndrome), and atrioventricular block, as beta-blockade suppresses nodal function.
- When long-cardiac cycles or slowing of the heart rate triggers ventricular ectopy (e.g., in the inherited ventricular tachycardia of German shepherd dogs).

- *Peripheral vascular disease* and *arterial thromboembolism*, especially the non-selective beta-blockers, because $beta_2$ blockade may lead to vasoconstriction.
- *Bronchial disease* and particularly reactive airway disease (*asthma*), as $beta_2$-blockade may promote bronchoconstriction.
- *Insulin-dependent diabetes mellitus*, because the sympathomimetic signs of hypoglycemia may be masked and therefore ignored.
- *Relative drug contraindications* are many, but include:
  - When a beta-blocker is combined with digoxin or diltiazem, as all three drugs suppress SA and AV nodal function.
  - When a beta-blocker is combined with diltiazem or class IA or class III anti-arrhythmics, as these drugs are all negative inotropic drugs.
  - When a beta-blocker is on board or administered during general anesthesia owing to depression of heart rate and myocardial function (in cases of long-standing beta-blocker therapy, the perioperative dose is reduced, but the drug is not stopped).
  - Use of a water-soluble beta-blocker, such as atenolol or sotalol, in patients with renal failure.

Clinical Pharmacology of Specific Beta-Blockers

There are a large number of beta-blockers available for hospital use or extra-label prescription. The drugs most often used in small animal practice are briefly described below, along with guidelines for choosing effective doses.

Propranolol

- *Propranolol* is a first generation, lipophilic, non-selective beta-blocker that is convenient to use in terms of dosing size (10-mg tablets that can be quartered) but not in terms of dosing frequency (tid is needed).
- Propranolol has more "inverse agonism" than other beta-blockers and this leads to greater depression of myocardial contractility. Therefore, it is not an optimal drug for use in patients with CHF.
- This non-selective, marked negative inotropic effect is useful in treatment of tetralogy of Fallot or in pulmonic stenosis wherein hyperdynamic RV contraction may contribute to outflow tract obstruction and to exercise-induced cyanotic spells. In addition, propranolol may help to control right-to-left shunting by blunting $beta_2$-dependent vasodilation that occurs with exercise.
- Usual dosing in non-CHF patients is approximately 0.5 to 1 mg/kg PO q8h.
- Propranolol can be used to up-titrate other beta-blockers as the propranolol tablet size permits conservative dosing while allowing the patient to acclimate to beta-blockade. For example, very small doses of 0.05 to 0.1 mg/kg, PO, q8h can be started; this is about $^1/_4$ of a 10-mg tablet in a large breed dog.

Atenolol

- *Atenolol* is a hydrophilic $beta_1$-receptor blocker, with renal elimination. It is one of the most commonly used beta-blockers in veterinary practice with numerous clinical indications for dogs and cats (discussed above).
- Atenolol (Tenormin and generic 25-mg tablets) is readily divided into quarters of 6.25 mg.
- The tolerated dose of atenolol depends greatly on ventricular function. In the setting of myocardial dysfunction, lower doses should be used. It should be used very cautiously, if at all, in the setting of CHF.
- The value of adding atenolol in cats with CHF due to HCM appears to be unfavorable, especially in the setting of recent-onset failure.
- In cats with well-controlled CHF (receiving furosemide and an ACEI) and with moderate to severe residual outflow tract obstruction, atenolol may be added cautiously if the cat is free of pulmonary edema.
- If CHF occurs in a cat that has received long-term beta-blockade, the dose should be reduced by 25% to 50%, but atenolol should not be stopped.
- To maintain a 24-hour effect, atenolol should be given on a bid. basis.
- In cats, atenolol is dosed initially at $^1/_4$ of a 25-mg tablet PO once daily for three days, then $^1/_4$ tablet q12h. The usual dosage range in cats is $^1/_2$ tablet in the AM and $^1/_4$ to $^1/_2$ tablet in the PM. Small cats may be well maintained on $^1/_4$ tablet q12h.
- Effective dosing in cats can be estimated by the examination heart rate. After 1 to 2 weeks of regular dosing, the examination heart rate should fall between 120 and 160/min, despite the stress of the veterinary environment. Lower rates prompt dose reduction; higher rates a dosage increase.
- Additionally, in cats with HCM with dynamic LV outflow obstruction and mitral regurgitation, the intensity of the heart murmur(s) and the outflow tract velocity as measured by Doppler echocardiography should be diminished.
- In dogs, the usual dose of atenolol is 0.5 to 1 mg/kg PO once daily for 3 days and then 0.5 to 1 mg/kg PO q12h. Dogs with normal LV function may tolerate higher dosages, in the range of 1.5 mg/kg PO q12h. Examination heart rates of <80/minute may indicate excessive dosing, and the heart rate should be reassessed following mild to moderate exercise.

Metoprolol Tartrate

- *Metoprolol tartrate* is a selective ($beta_1$), lipophilic, beta-blocker that has been best studied in experimental canine studies of cardioprotection. Sold only as a human drug (Lopressor, Toprol-XL, among others),

the sustained release preparation is especially cardioprotective.
- Despite these benefits, the smallest available long-acting tablet is the scored 25-mg Toprol-XL. This makes the initial dosing and up-titration difficult in CHF.
- In asymptomatic DCM or for cardioprotection, a dose of $^1/_2$ tablet PO q12h is a reasonable initial target for a large-breed dog.

Carvedilol

- *Carvedilol* (Coreg) is a nonspecific, lipophilic beta-blocker with mild alpha-adrenergic blocking properties. Carvedilol is also a highly potent anti-oxidant. Despite the cost, Coreg is used increasingly in veterinary practice for treatment of myocardial dysfunction in dogs.
- Carvedilol is used mainly for cardioprotection in heart failure. This drug may be better tolerated than other beta-blockers because alpha-blockade causes peripheral vasodilation and reduces left ventricular afterload.
- The anti-oxidant effects of carvedilol are believed to be highly beneficial in reducing myocardial injury caused by pro-inflammatory cytokines.
- The dose of carvedilol must be up-titrated over a number of weeks to months in dogs with CHF. Initially, the patient should be under heart failure therapy and free of edema.
- The suggested starting dose of carvedilol for a large breed dog with DCM is 0.05 to 0.1 mg/kg PO q24h (about $^1/_2$ to one 3.125 mg tablet q12h). The aim is to increase the dosage every 2 to 4 weeks provided the drug is tolerated (no worsening of CHF, not too lethargic, examination HR is >90/min and systolic ABP is >90 mmHg).
- As the dosage is increased larger tablets (6.25 mg, 12.5 mg) can be used.
- Heart rate may be a reasonable guide to an upper dosage with an arbitrary examination HR target of between 90 and 120/min for dogs in sinus rhythm.
- Should fluid retention worsen, the daily dosage must be lowered. Unfortunately, some dogs have difficulty tolerating even the lowest dosages of carvedilol and the drug must be discontinued.

Esmolol

- *Esmolol* (Brevibloc) is an ultrashort-acting, nonspecific beta-blocker available for IV use. The main value of esmolol relates to its short duration of action, as the drug is rapidly hydrolyzed by plasma esterases.
- Esmolol may be useful for patients requiring rapid intravenous control of arrhythmias; a brief infusion allows one to judge the efficacy and tolerability of the drug in that patient.
- Duration of action is typically less than 10 minutes after dosing.
- Dosing depends in part on ventricular function. If systolic function is normal, an initial 500 mcg (0.5 mg) per kg loading dose that can be administered over 1 to 5 min (use the longer interval in anesthetized animals). This is followed by a 50 to 150 mcg/kg/min constant rate infusion. ABP should be monitored during treatment.

Sotalol

- *Sotalol* is a beta-blocker with prominent Class III anti-arrhythmic effects. This drug is discussed under "Anti-arrhythmic Drugs."

Adverse Effects of Beta-Blockers

Toxicity of beta-blocker therapy is associated with the listed relatively predictable, anti-sympathetic effects. Treatment involves lowering the dose in most cases. Sudden withdrawal in cases of long-term therapy can be dangerous because beta-blockade allows up-regulation of beta-receptors. Bradycardia and cardiac depression can generally be overcome by administration of atropine or infusion of dopamine. If this fails, an alpha-adrenergic agonist (phenylephrine) can be used to raise ABP. Reversal of refractory cardiac depression also can be achieved with drugs that bypass the beta-receptor. Although glucagon has been suggested, the use of a PDE inhibitor like milrinone or a calcium sensitizer such as pimobendan (beware of vasodilator effects) may be better.

- Symptomatic hypotension with lethargy and depression
- Sinus bradycardia (examination HR < 120/min in cats; < 60/min in dogs)
- Reduced myocardial contractility
- Progressive cardiac chamber dilatation (including left atrial enlargement)
- Prolongation of the P-R interval on the ECG and AV blocks
- Precipitation of CHF
- Cough from bronchoconstriction following block of $beta_2$-receptors (mainly in cats)

CALCIUM-CHANNEL BLOCKERS

Overview

Calcium channels are critical to function of cardiac and vascular smooth muscle. Sinus and AV nodal cells are dependent on calcium-mediated depolarization. Calcium ions cross the cell membrane across calcium channels in the form of "slow current." Thus, pacemaker function and atrioventricular conduction are tied to calcium entry into these specialized cells. Calcium entry into cardiac and vascular myocytes triggers the intracellular release of stored calcium from the

sarcoplasmic reticulum. This event leads to muscle contraction or vasoconstriction.

The calcium channels are modulated by a number of receptors including the beta- and alpha-receptors in heart muscle and the alpha-receptor and angiotensin II receptor in vascular smooth muscle. Each of these receptors increases current flow across the calcium channel.

A calcium channel blocker (CCB) binds to L-type, voltage-dependent calcium channels and inhibits the entry and physiologic effects of calcium in cardiac and vascular cells.

The effects of CCB are predictable based on the mechanism of action:

- In general, the CCBs exert negative inotropic, chronotropic, and dromotropic (conductive) effects.
- Vascular smooth muscle is relaxed by CCBs, leading to peripheral vasodilation and coronary vasodilation.
- In some cases, peripheral effects will activate a baroreceptor reflex in response to lowered blood pressure. This may increase sympathetic tone to the heart, leading to indirect cardiac effects (that may in part be blunted by *direct* effects of the CCB on rate, contractility, and conduction).
- Therapy with CCBs often results in cardiac effects that are similar to those of beta-blockers; however, the CCBs are not considered cardioprotective in the same manner as beta-blockers.
- Different CCBs have varying degrees of vascular selectivity. Of the two most commonly used CCBs in veterinary medicine, the dihydropyridine CCB amlodipine has high vascular selectivity and is used mainly as a vasodilator drug. In contrast, diltiazem affects the heart and cardiac nodal tissues as well as effecting vasodilation. Diltiazem is used mainly for its effects on the heart.

Indications for Calcium Channel Blockers

Amlodipine

- *Amlodipine* is used exclusively as a vasodilator drug in veterinary small animal practice.
- As a potent, dose-dependent arterial vasodilator, amlodipine is useful in treating both cats and dogs with *systemic hypertension.*
- Amlodipine is also beneficial in advanced management of CHF due to mitral regurgitation, particularly when further ABP and afterload reduction are needed beyond that offered by an ACEI and diuretic. This situation may be encountered in end-stage CHF or when heart disease is complicated by systemic hypertension.

Diltiazem

- *Diltiazem* is used for two main purposes in small animal patients.
- Diltiazem is an effective *anti-arrhythmic drug* in the management of supraventricular arrhythmias. In particular, diltiazem is useful in treatment of *supraventricular* tachycardias.
- Diltiazem blocks AV nodal conduction and helps to control the ventricular response rate in *ectopic atrial tachycardia*, *atrial flutter,* and *atrial fibrillation* (usually as co-therapy with digoxin and possibly a beta-blocker). Compared to beta-blockers, diltiazem often provides better heart rate control and is less likely to exacerbate CHF but does not confer the same degree of cardioprotection against progressive myocardial disease.
- In atrial fibrillation/flutter of recent onset, IV administration of diltiazem controls ventricular response rate acutely and may also convert some patients back to normal sinus rhythm.
- When used to treat regular *supraventricular tachycardias*, diltiazem may break an orthodromic, re-entrant tachycardia that is AV nodal dependent. This situation develops when there is a functional accessory AV pathway (as in Wolff-Parkinson-White type syndrome).

▼ ***Key Point*** Diltiazem is a drug of choice for management of supraventricular tachycardias in dogs and in cats.

- Diltiazem may improve *ventricular filling* in cats with HCM.
- Diltiazem slows heart rate increasing filling time.
- Relaxation may improve (a positive lusitropic effect). Possible mechanisms for this benefit might include reflex activation of the sympathetic nervous system (in response to CCB induced vasodilation); improved coronary circulation; or other direct effects on calcium uptake into the sarcoplasmic reticulum.
- Although the chronic administration of diltiazem has been reported to decrease LV hypertrophy in cats with *very severe* HCM, initial enthusiasm for obtaining regression has been lost, and it is rare to observe regression of hypertrophy even with prolonged therapy.
- Diltiazem may exert an anti-platelet effect in cats; the clinical relevance of this is undetermined.

Contraindications for Calcium Channel Blockers

- Uncontrolled CHF, especially with diltiazem, owing to the negative inotropic and chronotropic effects.
- Systemic hypotension, with any CCB, as additional vasodilation will further lower ABP.
- Bradycardias, sinus node disease, and atrioventricular blocks, as CCB, especially diltiazem, will suppress nodal function.
- For amlodipine, the presence of tachyarrhythmias, as vasodilation may trigger a baroreceptor reflex with increased sympathetic traffic to the heart.

- Digitalis intoxication, as further block of the AV node may develop.

Clinical Use of Calcium Channel Blockers

Amlodipine

- Amlodipine (Norvasc) is a human drug commonly prescribed in extra-label treatment of hypertension in cats and dogs. Amlodipine is also used in advanced canine CHF as an afterload reducer. As the elimination half-life of this drug is long (about 24 hours in dogs), it may take a week to identify maximal benefit or side effects of therapy.
- The *anti-hypertensive effect* of amlodipine (Norvasc) is well established, and at usual feline dosages of $^1/_4$ to $^1/_2$ of a 2.5-mg tablet per cat, one to two times daily, ABP is often well controlled. In practice the combination of amlodipine (AM) with an ACE inhibitor (PM) is often chosen for cats with hypertension associated with renal disease.
- In dogs with hypertension, the initial starting dose is 0.05 to 0.2 mg/kg PO q12h. In dogs with refractory hypertension, the dosage may need to be much higher, up to 0.5 mg/kg PO q12h. Often amlodipine is used as co-therapy with an ACEI. This approach has merit for dogs with glomerular disease and also helps to control the high cost of Norvasc.
- In dogs with refractory CHF, amlodipine has been added to standard CHF therapy to further reduce afterload. Some dogs are better controlled when systolic ABP is maintained at approximately 90–100 mm Hg, and this level may not be achieved by ACEI alone. The doses required for this purpose are usually lower than for dogs with hypertension, and doses as low as 0.05 to 0.1 mg/kg PO once daily may improve pressure control and reduce load. The dose can be up-titrated to twice daily after a few days with strict attention to ABP.

Diltiazem

- Diltiazem (Cardizem) is the most commonly used CCB for treatment of arrhythmias and is effective for treatment of supraventricular tachycardias, including atrial fibrillation. This CCB is also used by some clinicians in the empirical management of feline HCM.
- Diltiazem is supplied as a solution for injection (5 mg/ml) and for oral use as 30- and 60-mg tablets. Sustained release diltiazem includes Dilacor, Cardizem-CD, generic diltiazem-CD, and diltiazem HCl extended release capsules.
- One also must be mindful that diltiazem is a negative inotropic drug, so the initial dose should be low and the drug dose up-titrated with attention to ABP and cardiac rhythm.
- For intravenous use, an initial bolus of 0.05 to 0.1 mg/kg, given IV over 5 to 10 minutes is appropriate for dogs and cats. Doses can be repeated every 15 to 30 minutes to a *cumulative dose* of 0.3 to 0.5 mg/kg, provided systolic ABP is >90 mm Hg.
- In *atrial fibrillation*, heart rate control can be gained by up-titration of the oral dosage.
- For initial oral therapy, 0.5 mg/kg q8h is appropriate. Provided CHF is under control, the dose of diltiazem can be rapidly increased (increasing each successive dose by about 0.25 mg/kg) to a target of about 1.5 mg/kg PO, q8h.
- Some patients require even higher doses (up to 2 mg/kg q8h, or greater), but care must be taken to prevent hypotension or excessive myocardial depression, particularly in the setting of CHF.
- The optimal target examination heart rate response in atrial fibrillation is between 100 and 150/min during clinical examination (or ECG).
- An alternative to three times daily dosing with standard diltiazem is twice daily treatment with a long-acting diltiazem preparation such as Cardizem-CD or Dilacor. These sustained release drugs may be compounded. Dilacor comes in tablet form (within a capsule that is readily opened), and can be cut in half. The same total daily dose of diltiazem should be given but now in two divided doses. The effects of breaking tablets on long-acting drug effects is uncertain.
- In cats under therapy for HCM, the usual dose of standard diltiazem is 7.5 mg ($^1/_4$ of a 30-mg tablet), PO q8h. This dosing interval is generally impractical for cat owners, and an alternative approach is to administer Dilacor, $^1/_2$ of a 60-mg tablet, once daily. Some clinicians use this drug on a bid. basis in cats, but there is a higher incidence of adverse effects. Cardizem-CD can be compounded into a palatable syrup, starting at 30-mg per cat once daily. However, preliminary pharmacokinetic studies reported a lower bioavailability and suggest the tolerated dosage might be as high as 10 mg/kg once daily. Unfortunately, detailed clinical studies with sustained release preparations are unavailable.
- Overall, diltiazem should reduce myocardial oxygen demand in HCM by decreasing contractility, blood pressure, and heart rate. (Though heart rate is less effectively controlled when compared to atenolol.)
- Effects on reducing dynamic outflow tract gradients have been disappointing at the doses commonly used. (Atenolol appears better for this purpose in HCM with obstruction.)
- Thus, the main reason to choose diltiazem therapy in cats with HCM is for potential improvement of diastolic function and for prevention or treatment of CHF in HCM.
- In a recent multicenter study of cats with recent onset CHF, the addition of diltiazem to background furosemide therapy did not provide any clear short-term benefits; however, some clinicians will establish diltiazem therapy at the time of follow-up, after initial stabilization of CHF with furosemide and an ACEI.

- As for beta-blockers, the long-term benefit of diltiazem in feline HCM has not been demonstrated.

Combined therapy of Calcium-Channel Blockers and Beta-Blockers

On occasion, the combination of a beta-blocker and a CCB will be considered. Since many of the pharmacologic effects on the heart are similar, the clinician must be mindful of adverse effects (see below).

- Diltiazem and carvedilol may be used in combination in dogs with CHF and atrial fibrillation. Initially digoxin and diltiazem are used to control heart rate; subsequently, carvedilol is up-titrated as described above. This may permit a dose reduction in diltiazem.
- Diltiazem and atenolol is sometimes considered for cats with HCM and severe dynamic LV outflow tract obstruction. This combination of drugs must be used with great care because of additive depressive effects on heart rate, AV conduction, contractility, and blood pressure.
- In patients with unresponsive hypertension, the addition of a beta-blocker (atenolol, carvedilol) to amlodipine or ACEI-amlodipine is generally well tolerated.

Adverse Effects of Calcium Channel Blockers

The adverse effects of CCB are extensions of their pharmacologic activities. Treatment involves withdrawing the drug or lowering the dose. Bradycardia and cardiac depression can generally be overcome by administration of atropine or infusion of dopamine. Hypotension from excessive vasodilation responds to infusion of an alpha-adrenergic or mixed alpha/beta agonist (phenylephrine, ephedrine, adrenaline). Calcium infusions may be beneficial but are proarrhythmic. Common adverse effects of CCB include

- Depression and weakness, usually from hypotension
- Hypotension from vasodilation or depression of cardiac output
- Worsening or precipitation of CHF from cardiac depression (reduced contractility and heart rate)
- Bradycardia from sinus or AV nodal depression (sinus bradycardia; AV block)
- Anorexia, salivation, and weight loss (cats)
- Skin reactions, including erythema and localized edema
- Constipation is often reported in human patients and may occur in some animals

ANTI-ARRHYTHMIC DRUGS

Overview

The anti-arrhythmic drugs are used to treat disorders of heart rhythm. These drugs can be classified based on their electrophysiologic characteristics (the Vaughan–Williams classification); however, this ordering is not ideal, and other schemes have been proposed.

The Vaughan-Williams classification places anti-arrhythmic drugs in one of four classes (or subclasses). As with any classification, it is limited and does not consider other potentially useful drugs with anti-arrhythmic effects. For example, the anti-cholinergic effects of atropine; the parasympathetic effects of digoxin; the delayed AV nodal conduction caused by (potassium-channel opening with) adenosine; and the membrane stabilizing effects of the magnesium salts are not included.

- *Class I* anti-arrhythmic drugs reduce the rate of Na+ influx by blocking the rapid sodium channel. These drugs generally decrease the rate of depolarization, slow conduction, and increase overall refractory period of cells; these are subdivided as follows:
  - IA (e.g., quinidine, procainamide, disopyramide) lengthen the action potential duration and the refractory period.
  - IB (e.g., lidocaine and mexiletine) shorten the action potential duration but increase the refractory period;.
  - IC (e.g., flecainide, propafenone) produces little effect on action potential duration but slows conduction.
- The *Class II* anti-arrhythmic drugs block beta adrenoceptors and decrease sinus node rate, slow AV nodal conduction, and reduce arrhythmias related to high sympathetic tone. Central effects may also be evident with some lipophilic drugs.
- The *Class III* anti-arrhythmic drugs prolong action potential duration by blocking potassium channels and also increase cell refractoriness. These include the drugs amiodarone and sotalol. These drugs generally do not change automaticity or conduction velocity.
- The *Class IV* drugs block the movement of calcium ions across the slow calcium dependent channel and include verapamil and diltiazem. Effects are a decreased heart rate, slowing of AV nodal conduction, and other less well-defined anti-arrhythmic effects.
- Effective use of any anti-arrhythmic drug depends on clinical response and experience. There is very little published information regarding anti-arrhythmic therapy of cats.

▼ ***Key Point*** Every drug used to treat arrhythmias is considered an extra-label drug use in veterinary practice, and treatment recommendations are based mainly on clinical experience with various arrhythmias.

Hypokalemia and hypomagnesemia decrease or nullify the beneficial effects of many anti-arrhythmic

drugs, especially class I agents. Electrolyte disorders can also predispose to pro-arrhythmic effects with Class IC and III agents.

The indications and drugs of choice for various arrhythmias are quite varied and are summarized in Chapter 145. Lidocaine, mexiletine, procainamide, sotalol, amiodarone, diltiazem, and the beta-blockers have been used most often in clinical practice with varying degrees of effectiveness and toxicity. Typical dosages of these drugs are summarized in Table 146-1 and "essential use" is summarized below.

Anti-arrhythmic drugs not only affect electrical activity of cardiac tissues but can also negatively reduce myocardial contractility. Additional effects may develop indirectly related to activation of the autonomic nervous system.

Aside from the beta-blockers, most anti-arrhythmic drugs demonstrate a pro-arrhythmic effect in a small percentage of patients. This and other potential adverse effects make the use of anti-arrhythmic therapy a true risk-benefit proposition.

▼ ***Key Point*** Anti-arrhythmic drugs must be used cautiously in the setting of CHF. Most anti-arrhythmic drugs are negative inotropes and are likely to worsen CHF.

Common Indications for Anti-arrhythmic Drugs

As discussed under the individual anti-arrhythmic drugs, more than one agent may be indicated for the treatment of a specific arrhythmia. Selection of one drug over another often is based on clinical experience, published trial, or simply personal preference. Some drugs are more likely to depress heart function and ABP, while others have a better adverse-risk profile. These various effects are often considerations in anti-arrhythmic drug choice. Some guidelines are indicated below:

Sinus bradycardia

- Atropine, glycopyrrolate, or catecholamines in the hospital; oral anti-cholinergic or sympathomimetic drugs can be tried for chronic oral management (cardiac pacing is better)

Supraventricular tachycardias

- Commonly used: digoxin (with CHF), diltiazem, beta-blockers
- Less often used: sotalol, amiodarone, procainamide

AV block

- Atropine or catecholamines can be tried for hospital management (cardiac pacing is preferred)

Ventricular arrhythmias

- Commonly used: lidocaine, procainamide, esmolol, magnesium salts for hospital therapy
- Commonly used: sotalol, mexiletine, beta-blockers for chronic therapy in dogs
- Less often used: procainamide, amiodarone, propafenone in dogs
- Commonly used: beta-blockers for chronic therapy in cats
- Less often used: sotalol or procainamide in cats

Arrhythmias in setting of CHF

- For atrial fibrillation, begin with digoxin and then add diltiazem; with control of CHF, a beta-blocker can be considered.
- Boxers, Doberman pinschers, and other breeds often develop CHF complicated by complex ventricular ectopy. Mexiletine or procainamide (+/– beta-blocker such as carvedilol) is most often used to control ventricular tachycardia in the CHF patient.
- Sotalol is an effective anti-arrhythmic, but demonstrates prominent beta-blocking properties, and should not be prescribed in the setting of uncontrolled CHF.
- Amiodarone is also a negative inotropic drug, but is probably preferable to sotalol in the setting of CHF and also may be better tolerated than mexiletine in some dogs.
- Mexiletine often leads to GI or neurological side effects in dogs with CHF.

The clinical pharmacology and clinical use of specific anti-arrhythmic drugs, based on the Vaughan Williams Classification (I–IV), are summarized below.

Procainamide

- Procainamide (Class IA) is a "broad–spectrum" anti-arrhythmic agent with potential value for the treatment of acute atrial fibrillation; suppression of atrial, junctional, and ventricular premature complexes; control of atrial and ventricular tachycardias; and potential suppression of AV nodal bypass tracts.
- The drug is available for injection, oral administration (capsules), and sustained release products. The short elimination half-life of 2 to 4 hours in the dog necessitates frequent administration. Limited sustained-release oral preparations of these drugs are available, allowing q6–8h oral dosing. Dosing guidelines are indicated in Table 146-1.
- Procainamide is sometimes administered to control PVC's and to maintain sinus rhythm following conversion of sustained or paroxysmal ventricular tachycardia in the dog and infrequently in the cats.
- Procainamide can be given to dogs already receiving or unresponsive to a lidocaine infusion. The drug is particularly versatile as it can be given IV, IM, or SQ, and then orally to maintain sinus rhythm.
- The long-term use of procainamide is considered in some dogs needing chronic treatment for ventricular tachycardia, though less often than for sotalol or

mexiletine. A sustained release preparation must be prescribed to maintain blood levels, and it is suggested that the drug be co-administered with a beta-adrenergic blocker unless there is CHF.

Adverse effects

- Procainamide is hypotensive when given too rapidly by intravenous bolus. This is explained by depressive effects on myocardial contractility and by peripheral vasodilation.
- As with other class IA drugs (and class III drugs), the prolongation of the action potential can serve as a proarrhythmic stimulus, worsening the ventricular rhythm.
- Atrioventricular block can occur (from the direct depressive effect on the infranodal bundle of His and bundle branches). Do not use procainamide in the setting or pre-existent AV block.
- Prolongation of the QRS and QT intervals can occur with eventual development of a polymorphic ventricular tachycardia or ventricular fibrillation (pro-arrhythmia). If the QRS complex prolongs to >25% of baseline, stop the drug and reduce the dosage.
- Procainamide can lead to lupus erythematosus in dogs and has been associated with immune mediated reactions and changes in hair color.

Lidocaine and Mexiletine

Lidocaine, mexiletine, and the rarely used tocainide (Class IB) have similar electrophysiologic properties. (Chronic tocainide use causes numerous side effects in dogs including renal failure and ocular injury; this drug should not be prescribed). Lidocaine (IV) and mexiletine (oral) are the drugs in Class IB most often administered for control of ventricular tachycardia in dogs. These drugs decrease automaticity of cardiac tissues by a class I effect (see above). Refractoriness is minimally prolonged. Lidocaine also reduces disparities in action potential duration preferentially in ischemic tissue, making it suitable for preventing re-entrant ventricular arrhythmias in the setting of myocardial ischemia. Lidocaine may also be used for acute cardioversion of atrial fibrillation into normal sinus rhythm in vagally induced atrial fibrillation.

- *Lidocaine* has a very rapid onset of action after IV administration and a terminal halflife in dogs of 0.9 hours. It is then quickly metabolized by the liver (1–3 hours). Intravenous boluses must be repeated (every 10–20 minutes) or supplemented with a constant rate IV infusion (see Table 146-1). Dosing guidelines are indicated in Table146-1.
- Effectiveness of therapy depends on the extracellular K+, which must be maintained in the normal range.
- Initial administration of lidocaine as a bolus (or loading infusion) followed by simultaneous use of smaller boluses with constant intravenous infusion is the usual method for controlling acute ventricular tachycardia in the dog. Lidocaine is relatively easy to control, and compared to other anti-arrhythmics, has minimal adverse hemodynamic effects, making it the drug of choice for hospital management of ventricular tachycardia.
- The cat is quite sensitive to the *neuroexcitatory* side effects of lidocaine, which must be given to this species slowly and at lower dosages.
- It is common for arrhythmias to become less responsive to lidocaine. This is particularly true when there is inattention to potassium (and magnesium) supplementation in hospitalized patients. When lidocaine does fail, it can be combined with procainamide if another injectable medication is required and may still provide anti-fibrillatory and analgesic effects to the patient.
- When long-term therapy is needed, lidocaine may be followed by treatment with sotalol or mexiletine and a beta-blocker.
- *Mexiletine* is used to suppress ventricular arrhythmias; unlike lidocaine, it can be given orally. The drug is often combined with a beta-blocker for chronic management of severe ventricular arrhythmias in the dog. Mexiletine can be effective but carries a higher side-effect profile than sotalol, an alternative treatment for chronic ventricular tachycardia.

Adverse effects

- CNS excitation including anxiety and twitching, often followed by depression
- Focal or generalized convulsions (control with diazepam)
- Depression of sinus or AV nodal function, particularly in the cat
- Hypotension is uncommon but can occur with too-rapid injection.
- Drug interactions
- Both propranolol and cimetidine reduce liver blood flow and delay excretion of lidocaine and mexiletine.
- CHF, hypotension, and halothane anesthesia may reduce lidocaine clearance and require lower dosages to prevent toxicity.

Beta-Adrenergic Blockers

Indications, contraindications, and clinical pharmacology of the beta-blockers (Class II) have been described previously. Sotalol is a beta-blocker with powerful Class III effects and is described below. The beta-blockers are "broad spectrum" anti-arrhythmic drugs, and key points regarding arrhythmia control of these drugs are summarized below:

- Treatment of severe sinus tachycardia in drug toxicities or hyperthyroidism.
- Suppression of atrial premature complexes and some atrial tachycardias.

- Depression of AV nodal conduction, decreasing the ventricular rate response to atrial flutter/fibrillation.
- Used as monotherapy to control isolated ventricular PVCs or combination with a Class I anti-arrhythmic drug for management of ventricular tachycardia or complex ventricular rhythms.
- Ultra-short acting IV beta blockade (esmolol) or graded IV doses (propranolol) can be used to control ventricular arrhythmias in the critical care setting (following trials of lidocaine and procainamide).
- Oral administration of a beta-blocker (atenolol, metoprolol, or propranolol) may be useful for long-term therapy of PVCs.
- Adverse effects have been discussed previously. Of highest importance is the negative inotropic effect of beta-blockers in the setting of uncontrolled CHF or hypotension.

Sotalol and Amiodarone

Sotalol and amiodarone (Class III) prolong the action potential duration by blocking potassium channels and also exert beta-blockers effects (sotalol > amiodarone).

- The principal indications for these agents are life-threatening or refractory ventricular arrhythmias.
- Class III drugs, particularly amiodarone, also have been used to prevent recurrence of atrial fibrillation in dogs following successful electrical cardioversion. Conversion of atrial fibrillation to sinus rhythm is possible, but relatively uncommon with either drug.
- *Sotalol* is the drug of choice for many clinicians for the long-term treatment of malignant ventricular arrhythmias. It is eliminated by the kidneys. In dogs peak plasma concentrations are attained within 2 hours. Oral dosages of 1 to 2 mg/kg q12h are well tolerated in dogs with normal ventricular function. Sotalol has been used occasionally in cats. Malignant ventricular arrhythmias can be exacerbated by hypokalemia in sotalol-treated patients.
- *Amiodarone* is a complicated drug (exhibiting varying degrees of class I, II, III, and IV activities) and considered an effective anti-arrhythmic drug with a prolonged duration of action (days) and an extremely long elimination half-life and hepatic metabolism.
- Bretylium and ibutilide are other drugs with class III properties. Bretylium tosylate is used in humans for prevention of ventricular fibrillation. Ibutilide has been used in people to rapidly convert atrial fibrillation to normal sinus rhythm; use in animals has been limited mainly to experimental models.

Adverse effects

- Amiodarone has an arm's length of side effects associated with chronic use, including impaired thyroid dysfunction, hepatotoxicity, neutropenia, corneal microdeposits, and potentially fibrosis of the lung. Lower dosages may be safer.
- Both sotalol and amiodarone depress myocardial contractility so use these drugs in CHF with caution. Sotalol in particular should be avoided in the setting of CHF or pronounced myocardial dysfunction. Amiodarone appears better tolerated in dogs with CHF.
- Lengthening of the QT interval from prolongation of the action potential duration offers both anti-arrhythmic benefit and proarrhythmic risk with all Class III drugs. A highly malignant form of polymorphic ventricular tachycardia (of the torsade de pointes variety) may develop.

Calcium Channel Blockers (Diltiazem)

The calcium channel blockers (Class IV) have been discussed previously. Diltiazem and the prototype drug verapamil block the L-type calcium channel and alter membrane responsiveness of SA and AV nodal cells, as these are highly dependent on slow (calcium) current for depolarization. The following comments pertain mainly to anti-arrhythmic effects of these drugs.

- Diltiazem is the CCB most often used in dogs and in cats with supraventricular tachyarrhythmias. Diltiazem has profoundly depressant effects on AV nodal conduction and therefore slows the ventricular response rate to ectopic atrial tachycardia, atrial flutter, and atrial fibrillation. This effect is typically greater than for beta-blockers at equivalent negative inotropic doses. Infrequently CCB therapy leads to conversion to sinus rhythm.
- Calcium channel blockers are also useful for supraventricular tachycardias that use the AV node as part of the re-entrant tachycardia circuit. By blocking the orthodromic (downward) path of current, the electrical circuit is abolished and sinus rhythm may resume.

Adverse Effects

Adverse effects have been described previously.

- Reflex sinus tachycardia, secondary to vasodilation may develop; however, diltiazem directly depresses sinoatrial nodal function so the effect may be blunted. Accordingly, a CCB should be used cautiously in sick sinus syndrome or in dogs with sinus node dysfunction.
- In the setting of pre-existent AV block, diltiazem (or verapamil) is contraindicated.

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Chapter

147 Heart Failure in Dogs

John D. Bonagura / Bruce Keene

Heart failure (HF) is a state wherein the cardiac output is inadequate to meet the perfusion needs of the metabolizing tissues and exercise capacity is limited. The causes of HF in dogs are diverse, but there are stereotypical cardiovascular and systemic responses to impaired cardiac function, regardless of cause. This chapter provides a brief overview of HF; considers the causes and diagnoses of HF in dogs; and reviews treatment plans for management of the cardiac failure patient. The clinical pharmacology and pathophysiologic rationale for drugs used in treatment of HF are detailed in Chapter 146. Management of HF in cats is discussed in the chapter "Cardiomyopathy" (Chapter 150).

OVERVIEW

Heart failure is a not a specific disease but a pathophysiologic disorder. Some of the key abnormalities of this condition are summarized below, and the pathophysiologic rationale for using particular cardiovascular drugs is summarized in Chapter 146. The reader is directed to other textbooks for a detailed review of pathophysiology of HF.

- HF is triggered by a cardiac lesion (or injury) that leads to *systolic* or *diastolic dysfunction* of the heart. Decreased cardiac output and blood pressure (often called "arterial underfilling") are pivotal events that initiate the syndrome of HF.
- The decrease in blood pressure is countered by adaptations of the neuroendocrine system, kidney, heart muscle, and blood vessels.
- There is increased activity of vasoconstrictor and sodium-retaining control systems; attenuation of vasodilator and natriuretic systems; activation of fetal-gene programs within the heart; and increased activity of tissue mediators that lead to myocardial and vascular hypertrophy, fibrosis, and inflammation.
- The well-compensated cardiac patient often maintains basal (resting) cardiac output and blood pressure within the normal range. This is achieved through vasoconstriction, mild volume expansion, and redistribution of blood flow.
- Vasoconstriction is a prominent feature of HF and is mediated by sympathetic nervous system activation, the renin-angiotensin system, release of arginine vasopressin, and local endothelial mediators such as endothelin. These systems represent therapeutic targets for both current and for future drug developments.
- The excess sodium and water retention characteristic of the syndrome of congestive heart failure (CHF) is mediated by sympathetic stimulation that alters renal blood flow, the release of aldosterone and vasopressin, and inhibition of natriuretic hormones that are released from the stretched heart. The need for diuretics and dietary sodium restriction in CHF stems from activation of these compensatory responses.
- The heart itself changes in structure and function in a process called cardiac remodeling. As heart disease progresses there is increasing dependence on myocardial hypertrophy, cardiac dilatation, and heart rate to maintain cardiac output. At the same time, structural alterations in the intercellular matrix of collagen and connective tissue impair the filling and pumping functions of the myocardium. Key mediators of cardiac injury include norepinephrine, angiotensin II, aldosterone, and pro-inflammatory cytokines. The increased use of "cardioprotective" drugs in HF are aimed at blunting these mediators and the tissue damage caused by them.
- Despite the effectiveness of these combined compensations for maintaining arterial blood pressure, these systems become increasingly *maladaptive*. This concept is central to the progression and the treatment of HF.
- Compensatory mechanisms activated in advanced heart disease are so effective that clinical signs of cardiac failure may be evident only with *exercise* when pulmonary venous pressure increases and perfusion of skeletal muscles becomes limited.
- With worsening cardiac function *hemodynamic* abnormalities become prominent.
- Decreases in cardiac output, systemic arterial blood pressure (ABP), and tissue perfusion develop, accompanied by increases in systemic and pulmonary vascular resistances.

Table 147-1. OVERVIEW OF MORPHOLOGIC/ANATOMIC DIAGNOSES

Developmental disorder or malformation
Vascular change: congestion, edema, hemorrhage, thrombosis, infarction
Inflammation
Degeneration
Necrosis
Apoptosis (programmed cell death)
Hypertrophy
Neoplasia
Disruptive defects such as trauma
These lesions may be encountered in the pericardium, myocardium, endocardium-valves, conduction system, or blood vessels of the heart or circulation.

Table 147-2. OVERVIEW OF ETIOLOGIC DIAGNOSES

D = developmental disorders; degenerative lesions
A = anomalies, autonomic dysfunction, anemia
M = metabolic diseases (endocrine diseases, electrolyte disturbances, renal failure), mechanical problems (such as a foreign body)
N = neoplasia or nutritional disorder
I = infectious, inflammatory, ischemic, immune, iatrogenic and idiopathic diseases
T = tumor, trauma or toxin

- Inadequate tissue perfusion contributes to exercise intolerance, azotemia, and metabolic disturbances such metabolic acidosis.
- Elevations in pulmonary arterial, venous, and capillary hydrostatic pressures lead to clinical signs of CHF.
- While hemodynamics may explain many clinical signs, morbidity and mortality of HF are related strongly to the tissue effects of accentuated neurohormonal and cytokine activities that develop in response to the failing heart.
- Chronic therapy of CHF is aimed at modulating and countering these responses to minimize clinical signs of CHF, protect tissues, and prolong life.

ETIOLOGY

Next in this chapter we will consider the key causes of heart disease in dogs, as well as an overview of cardiac disease classification and applicable diagnostic studies. The following are salient points regarding cardiac diagnosis and the clinical workup.

Classification

Identifying the predominant form and cause of heart disease and classifying the pathophysiologic mechanism of cardiac failure allows the clinician to direct appropriate therapy and render a more accurate prognosis. Cardiac diagnoses can be classified in a number of ways.

- The *morphologic* or *anatomic* diagnosis refers to the *lesions* one might observe during gross or microscopic examination of the heart or blood vessels (Table 147-1). It is also helpful to classify CV diseases relative to the *anatomic components* of the system affected; this is often included into the anatomic diagnosis as follows: pericardial diseases; myocardial diseases; valvular and endocardial diseases; disorders of the impulse forming and conduction system (arrhythmias); and vascular diseases.
- The *etiologic* diagnosis indicates the putative *cause* of cardiovascular disease and includes genetic disorders and errors of metabolism (Table 147-2). A sub-classification of the etiologic diagnosis includes general designations of "*congenital*" heart disease and "*acquired*" heart disease.
- The *physiologic* diagnosis represents the *disruption in cardiovascular function* that results from cardiovascular disease, including the clinical signs observed in the patient. This diagnosis can be general or relatively specific. For example, contractility failure, hemodynamic overloads, diastolic failure, and arrhythmia are considered general pathophysiologic mechanisms for reduced cardiac output and heart failure. Examples of more specific cardiovascular diagnoses include syncope, valvular regurgitation, left to right shunt, and cardiac murmur (Table 147-3).

Causes

The most important causes of *canine* heart disease involve a limited number of acquired disorders and a handful of important congenital heart defects. These conditions, as well as usual diagnostic findings, are summarized in Table 147-4 and in other chapters across this section. The most important acquired cardiac disorders responsible for HF in dogs are:

- *Mitral and tricuspid valvular endocardiosis*, which is characterized by progressive and chronic atrioventricular valve degeneration often with valve prolapse and ruptured mitral valve chordae tendineae. Atrial arrhythmias, left mainstem bronchial compression, CHF, left atrial rupture, and systemic hypertension may complicate the picture.
- *Dilated cardiomyopathy*, which is a primary myocardial disorder of progressive contractility failure leading to heart failure. Often associated with cardiac arrhythmias such as atrial fibrillation and ventricular tachycardia; the condition is "idiopathic" but certainly genetically predisposed in many dogs. Sudden death is common.
- *Pericardial effusion* causing cardiac tamponade (impaired filling of the heart from compression) is under-recognized. The main causes in dogs are idio-

Table 147-3. OVERVIEW AND DEFINITION OF PHYSIOLOGIC CV DIAGNOSES

Arrhythmia (dysrhythmia)—disorder of electrical impulse formation or conduction leading to an abnormal heart rate or rhythm.
Bradyarrhythmia—a cardiac arrhythmia characterized by a slow heart rate as with sinus bradycardia, sinus arrest, atrial standstill, or atrioventricular block.
Cardiac murmur: functional—a prolonged audible vibration associated with blood flow in the heart or great vessels but unrelated to structural heart disease (also termed physiologic or innocent murmur); functional murmurs are often caused by anemia, fever, thyrotoxicosis, elevated sympathetic tone, or protracted bradycardia.
Cardiac murmur: organic—audible vibration associated with abnormal blood flow in the heart or great vessels associated with structure disease; these murmurs typically indicate pathology affecting the heart valves or a congenital shunt.
Congestive heart failure—an advanced pathophysiologic state of heart failure characterized by renal sodium retention, elevated venous pressures, and fluid accumulation in the lung, subcutaneous tissues, or body cavities.
Contractility failure—a general mechanism of ventricular dysfunction; see myocardial failure.
Diastolic heart failure (diastolic dysfunction)—impairment of ventricular diastolic filling or distensibility as with concentric hypertrophy of the ventricle or pericardial disease; the ventricle must be filled by higher than normal filling (venous and atrial) pressures.
Heart failure—a pathophysiologic state caused by systolic or diastolic failure of the heart and characterized by neurohormonal activation and inadequate cardiac output relative to exercise and tissue perfusion demands.
Hemodynamic overload—a condition characterized by increased demand on the ventricle to pump a greater stroke volume or a higher pressure than normal; typically these are subdivided into volume overloads and pressure overloads (see the following).
Hypertension—elevated systemic arterial blood pressure; in dogs systolic values exceeding 160 mm Hg are suspicious and those >180 mm Hg are considered elevated
Hypotension—reduced systemic arterial blood pressure; when systolic ABP is <90 mm Hg, clinically significant hypotension is possible.
Myocardial failure—loss of ventricular myocardial contractility leading to systolic dysfunction as with dilated cardiomyopathy or chronic volume or pressure overload.
Pressure overload—condition wherein the ventricular systolic (pumping) pressure must be higher than normal to eject the stroke volume; usually associated with hypertension or obstruction to ejection as with aortic stenosis.
Pulmonary hypertension—elevated pulmonary arterial blood pressure generally caused by left-sided heart failure, pulmonary vascular or parenchymal disease, or marked increase in pulmonary blood flow (without concomitant decline in pulmonary vascular resistance).
Shock—an acute, life-threatening disorder characterized by diminished tissue perfusion, impaired oxygen delivery, altered metabolism, and tissue injury; various causes of shock include cardiogenic shock (from profound heart failure), hypovolemic shock (from fluid loss or hemorrhage), and distributive shock (excessive vasodilation secondary to sepsis, anaphylaxis, or spinal injury).
Shunting: left-to-right—abnormal flow of blood from the systemic to the pulmonary circulation as with ventricular septal defect or patent ductus arteriosus.
Shunting: right-to-right—abnormal flow of blood from the pulmonary to the systemic circulation as with tetralogy of Fallot or PDA with elevated pulmonary vascular resistance.
Sudden cardiac death—cardiac arrest due to asystole or ventricular fibrillation.
Syncope—sudden loss of consciousness and postural tone caused by reduced cardiac output, excessive vasodilation, or both.
Systolic heart failure (systolic dysfunction)—impairment of ventricular systolic pumping that limits stroke volume and cardiac output; typical of dilated cardiomyopathy, severe valvular heart diseases, and myocardial failure due to chronic volume or pressure overloads.
Tachyarrhythmia—a cardiac arrhythmia generally characterized by a fast heart rate, as with sinus tachycardia, atrial tachycardia/flutter/fibrillation, supraventricular re-entrant tachycardia, and ventricular tachycardia.
Valvular regurgitation—incompetency or insufficiency of the valve permitting backflow of blood during systole (mitral, tricuspid valves) or diastole (aortic, pulmonic valves).
Valvular stenosis—narrowing and obstruction to flow across a valve (or adjacent tissue) during systole (aortic, pulmonic valves) or diastole (mitral, tricuspid valves).
Volume overload—condition wherein the ventricular systolic (pumping) volume is higher than normal; usually associated with a left-to-right shunt, a regurgitant heart valve, or chronic bradycardia.

pathic pericardial hemorrhage in young dogs and cardiac tumors (e.g., hemangiosarcoma, chemodectoma, and mesothelioma) in older dogs.

- *Systemic hypertension* is most often secondary to chronic glomerular or renal tubular disease, Cushing's disease, or uncommon tumors such as pheochromocytoma. Essential or idiopathic disease is also recognized. Target organs in hypertension include the brain, eyes, heart, and kidneys.
- *Pulmonary hypertension* with right-sided heart failure is most often due to the preventable disorder dirofilariasis, but also can be secondary to chronic left heart failure or severe bronchopulmonary disease; some cases are idiopathic.
- *Arrhythmias* can be recognized that are unassociated with overt structural heart disease such as cardiomyopathy. These primary disorders of electrical impulse formation or impulse conduction include sinus node dysfunction (sick sinus syndrome), lone atrial fibrillation, atrioventricular blocks, and arrhythmogenic cardiomyopathy, such as arrhythmogenic right ventricular cardiomyopathy in the Boxer or English bulldog, or sustained reentrant supraventricular tachyarrhythmias in Labrador retrievers.
- *Bacterial endocarditis* (infection of the cardiac valves) is relatively uncommon in dogs but may lead to a variable clinical syndrome that includes bacteremia, systemic inflammation (fever, leukocytosis), constitutional illness (depression, anorexia, shivering), metastatic infection (brain, kidneys, bone), immunologic phenomena (polyarthritis, glomerulonephritis), thromboembolic disease, and cardiac injury (valvular regurgitation, arrhythmias, CHF).

Table 147-4. COMMON CANINE DISEASES

Disorder	Necropsy & Echo (Anatomic Diagnosis)	Typical Clinical Problems	Etiologic diagnoses
Pericardial effusion	• Hemorrhagic effusion (esp. dogs <8 years) • Neoplastic- related effusion (esp. in dogs >8 years of age) • Infective pericarditis • Cysts • **Echo:** echo-free space around heart; +/− mass lesions	• Hypotension and sudden collapse due to cardiac tamponade • Right-sided CHF (chronic pericardial disease)	• Idiopathic bleeding (may be recurrent) • Various cardiac and heart base neoplasms: hemangiosarcoma, chemodectoma (aortic body tumor), mesothelioma, ectopic thyroid carcinoma • Infection from a migrating foreign body or from a fungus (e.g., Coccidioidomycosis)
Dilated cardiomyopathy (DCM) phenotype	• Cardiac chamber dilatation (typically left sided chambers +/− right sided) • Myocardial fibrosis; wavy fibers or fibro-fatty replacement of myocytes • **Echo:** cardiac dilatation and loss of myocardial contractility	• CHF, left sided • CHF, biventricular • Atrial fibrillation • Secondary AV valvular regurgitation • PVCs • Sudden cardiac death • Less commonly: right ventricular cardiomyopathy with right-sided CHF	• Idiopathic dilated cardiomyopathy (genetic; giant breeds and spaniels; unrelated to structural lesions of the valves, congenital malformations, or ischemia) • Cardiomyopathy of chronic volume overload (related to chronic valvular regurgitation or shunt) • Tachycardia-induced DCM • Taurine deficiency DCM (spaniels, other breeds?)
Arrhythmogenic cardiomyopathy	• As per DCM above • Myocarditis is evident histologically in some dogs • Right ventricular fibro-fatty tissue replacement (Boxers) • No lesions (functional cellular defect) in others • **Echo:** no lesions; may progress to DCM	• PVCs • Ventricular tachycardia • PACs, PAT • Atrial fibrillation • Near syncope • Syncope • Sudden cardiac death	• Genetic in a number of breeds: • German shepherd dogs (young) • Boxers (arrhythmogenic RV cardiomyopathy) • Doberman pinschers (often occult DCM) • Irish wolfhounds (often show PACs, AF) • Giant breed dogs (PACs, VPCs, AF precede DCM) • English bulldogs, Mastiffs (similar to boxers?)
Chronic mitral and tricuspid valvular regurgitation	• Valvular endocardiosis (degenerative disease) of the mitral and tricuspid valves • Chordae tendineae stretch (mitral and tricuspid valves) or rupture (mitral valve) • Left atrial tears • **Echo:** thickened valve(s); prolapse; volume overload; LV function often preserved; PH	• Systolic murmur of MR or TR • Mitral systolic click • Left bronchial compression • Left-sided or biventricular CHF • PACs; atrial fibrillation • Pulmonary hypertension • Cardiac tamponade from ruptured LA	• Genetic predisposition; typically affects older, smaller breed dogs with marked predilection for some breeds such as small breed spaniels • Premature disease in cavalier King Charles spaniel
Endocarditis	• Infection (vegetation) of the mitral or aortic valve(s) • **Echo:** valvular thickening; shaggy oscillating mass (acute, subacute BE); hyperechoic thickened valve (chronic BE); variable degrees of left-sided cardiomegaly	• Systemic inflammation: fever, systemic signs of infection, elevated WBC • Metastatic infection • Immune mediated signs such as polyarthritis • Thromboembolism • Cardiac signs: heart murmur (systolic for MV; diastolic for AV), CHF	• Bacterial infection of the heart valve
Congenital valvular diseases	• Subaortic stenosis • Mitral valve dysplasia (MV malformation; generally causes MR; rarely MS) • Pulmonic valve stenosis • Tricuspid valve dysplasia (typically causes TR; rarely tricuspid stenosis) • **Echo:** valvular (or subvalvular or supravalvular) malformation; ventricular hypertrophy (concentric or eccentric); atrial dilatation (MVD, TVD); post-stenotic dilatation (SAS, PS)	• Systolic heart murmur • Cardiac arrhythmias from progressive cardiomegaly or concurrent electrical defects (TV dysplasia) • Development of CHF in severe cases • Syncope • Sudden cardiac death (especially with outflow obstruction) • Endocarditis (SAS) • Right-to-left shunting across PFO (PS, TVD)	• Congenital VHD is presumed to be genetic in origin: • SAS: especially in golden retrievers and Newfoundland dogs with many other breeds also affected • MVD: great Danes, German shepherds, bull terriers, others • PS: Labrador retrievers, terrier breeds, bulldogs, beagles, others • TVD: Labrador retrievers, OES, large breed dogs, others

Table 147-4. COMMON CANINE DISEASES—cont'd

Disorder	Necropsy & Echo (Anatomic Diagnosis)	Typical Clinical Problems	Etiologic diagnoses
Heartworm disease (Dirofilariasis)	• Pulmonary vascular disease • Secondary right-sided cardiomegaly (cor pulmonale) • Pulmonary complications (infarction, pneumonitis, fibrosis) • **Echo:** variable findings related to severity of PH; adult parasites in TV orifice in caval syndrome	• Signs related to pulmonary disease (cough, tiring) • Right-sided cardiac dysfunction (exercise intolerance, right-sided CHF) • Caval syndrome • Glomerular disease	• *Dirofilaria immitis*—adult parasites • Pathology related to microfilaria(?) such as eosinophilic pneumonitis
PDA	• Persistently patent ductus arteriosus • Left-sided cardiomegaly • Dilated aorta and PA • **Echo:** above lesions hypertension—shunt	• Continuous heart murmur • Left-sided CHF • Atrial fibrillation • Pulmonary hypertension and shunt reversal (rare)	• PDA is presumed to be a genetic disorder affecting many canine breeds such as poodles, schnauzers, Irish setters, dachshunds numerous other breeds

Arrhythmias:
• Sinus node disease (sick sinus syndrome)
• Atrial arrhythmias (premature complexes, atrial fibrillation, atrial standstill)
• Atrioventricular (AV) blocks
• Re-entrant SVT from accessory pathway
• Ventricular arrhythmias (premature complexes, ventricular tachycardia)
	PM or Echo may demonstrate cardiac lesions but often there is no overt structural lesion	• Bradycardia
		• Tachycardia
		• Irregular heart rhythm
		• Variable heart sounds
		• Sudden pauses
		• Weakness, syncope, CHF, sudden death
			• Structural heart diseases
			  • Myocardial fibrosis
			  • Myocarditis
			  • Myocardial ischemia or infarction
			  • Degeneration of the conduction system
			• Functional electrical disorders (no obvious anatomic substrate)
			  • Autonomic nervous system imbalance
			  • Metabolic and endocrine diseases
			  • Hypoxia, anemia
			  • Drugs
			  • Extracardiac diseases: splenic, GDV, sepsis

- Malformations or *congenital heart diseases* in dogs represent about 5% to 10% of patients seen in cardiology referral practices. Congenital heart defects are recognized in most cases by detection of a murmur during the puppy vaccination sequence. Malformations are definitively diagnosed by echocardiography with Doppler studies. Optimal management should involve a clinician experienced in congenital heart disease.

The most important of the canine congenital heart defects include the following:

- *Aortic stenosis* (generally subvalvular AS)—A subvalvular narrowing of the left ventricular outflow tract, leading to pressure overload of the left ventricle. Outcomes in severe disease include exercise intolerance, syncope, sudden death, and congestive heart failure. Dogs are at higher risk for bacterial endocarditis.
- *Patent ductus arteriosus*—The persistence of the fetal ductus arteriosus leading to a left-to-right shunt and volume overload of the left ventricle. Untreated cases are likely to die from left-sided CHF.
- *Pulmonic stenosis*—A subvalvular, valvular, or supravalvular narrowing of the right ventricular outflow tract, leading to pressure overload of the right ventricle. Outcomes in severe disease include exercise intolerance, syncope, sudden death, right-to-left shunting across a septal defect or foramen ovale, and right-sided congestive heart failure.
- *Mitral valve malformation*—Dysplasia of the mitral valve that can lead to progressive left-sided volume overload, atrial fibrillation, or CHF. Rarely the lesion causes mitral stenosis.
- *Tricuspid valve malformation*—Dysplasia of the tricuspid valve that can lead to progressive right-sided volume overload, atrial fibrillation, or right-sided CHF. Rarely, the lesion causes tricuspid stenosis.
- *Ventricular septal defect (VSD)*—A persistent opening between the ventricular cavities; clinical significance depends on the size of the defect.
- *Tetralogy of Fallot*—A large VSD, pulmonary stenosis, right ventricular hypertrophy, and dextropositioned aorta. A cause of cyanosis from right-to-left shunting but rarely leads to CHF.

- The *peritoneopericardial diaphragmatic hernia* is an uncommon pericardial defect in puppies.

▼ ***Key Point*** The most important reasons for CHF in dogs are degenerative valvular disease, dilated cardiomyopathy, pericardial diseases, and heartworm heart disease. These conditions can be complicated by systemic hypertension, pulmonary hypertension, and arrhythmias such as atrial fibrillation or ventricular tachycardia.

DIAGNOSIS

History and Clinical Signs

The diagnosis of heart disease involves a systematic examination that begins with consideration of *species, age, breed,* and *sex.*

There are obvious risks for cardiovascular disease relative to these factors. Young animals will be suspected of congenital heart disease; mature animals of acquired, degenerative, and neoplastic diseases. There are dozens of genetic breed predispositions to cardiovascular diseases. These tend to be tabulated in standard reference textbooks and are described in other chapters within this volume.

- The *history of clinical signs* in heart disease is variable. Many patients have no overt clinical signs until CHF develops. No historical sign is specific for HF.
- Signs of *low cardiac output*, such as exercise intolerance or syncope may be observed, but are subtle and may be overlooked by dog owners.
- Syncope—the sudden loss of consciousness and postural tone—is often observed with structural cardiovascular lesions and cardiac rhythm disturbances, from inappropriate reflex activation (neurocardiogenic syncope), in pulmonary hypertension, and following treatment with drugs that lower arterial blood pressure.
- Hypertensive heart disease may be overshadowed by injury to other target organs such as the eyes (blindness), brain (stroke or hypertensive encephalopathy), or kidneys (renal failure).
- Endocarditis results in multisystemic signs that include evidence of inflammation, immune system activation, cardiac injury, thrombosis, and metastatic infection.
- Respiratory signs such as cough and dyspnea are common in heart disease. These may stem from pulmonary edema, pleural effusion, heartworm disease, thromboembolism of the lung, or compression of the left bronchus.
- The most sensitive sign of heart failure is *exercise intolerance.* However, signs of *"congestive" heart failure* are more obvious and indicate problems related to fluid accumulation.
- Pulmonary edema and effusions in body cavities are typical of advanced heart disease with left-sided CHF. Chief clinical signs are tachypnea, dyspnea, and cough.
  - Right-sided CHF in dogs generally causes exercise intolerance and abdominal enlargement from hepatomegaly and ascites.

Physical Examination

The *physical diagnosis* is pivotal in heart disease and involves a systematic examination. Key aspects of the examination include

- Inspection for obvious signs of *right-sided CHF* and for cardiac *cachexia* (loss of lean muscle mass, typically along the spine).
- Examination for *jugular venous* distension or jugular pulse abnormalities. Elevated jugular venous pressure is indicative of right-sided CHF, pericardial disease, large pleural effusion, or cranial mediastinal mass. Jugular venous pulses may indicate a lesion on the right side of the heart (such as pulmonary hypertension or tricuspid regurgitation).
- Examination for *arterial pulse abnormalities*, including hypokinetic (small stroke volume), hyperkinetic (large pulse pressure), or pulse deficits (arrhythmias). Pulsus paradoxicus may be detected in cardiac tamponade.
- Measuring of *arterial blood pressure* by oscillometric methods or Doppler flow methods. Blood pressure should be measured in *every* cardiac patient to identify hypertension and hypotension and to monitor drug effects (diuretics, vasodilators, ACE inhibitors).
- Palpation of the *precordium* for the apical location, strength, and precordial thrills.
- *Auscultation* of the heart and lungs to detect abnormalities that include
  - Heart sounds that are too soft or too loud.
  - Cardiac arrhythmias (bradycardia, tachycardia, irregular rhythm).
  - Gallop sounds (loud atrial or ventricular filling sounds indicating ventricular diastolic dysfunction).
  - Clicks—most often indicative of mitral valve disease.
  - Murmurs (prolonged audible vibrations).
  - Abnormal breath or lung sounds—loud bronchial sounds or fine crackles are typical of pulmonary edema from left-sided CHF.
- Examination of *mucous membranes* and capillary refill time: If the membranes are pale, rule out anemia or systemic vasoconstriction; if cyanotic, evaluate for respiratory dysfunction, cardiogenic shock, or right-to-left shunting
- *Abdominal palpation* for hepatomegaly or ascites, which are typical signs of right-sided CHF.
- Ocular examination to identify *retinal hemorrhage* and *retinal detachment*, which are common consequences of systemic hypertension in dogs.

- It should also be noted that dental disease has *never* been proven as a cause of heart disease in dogs. However, periodontal disease may negatively affect the respiratory system by allowing recurrent aspiration of infected materials or possibly by stimulating the immune system.

Diagnostic Evaluations

A number of routine laboratory studies are useful in the diagnosis of cardiovascular diseases of dogs and these are discussed in more detail within other chapters of this text.

- *Thoracic radiographs* are important for evaluating the heart, lungs, and pleural space (see Chapters 4, 143, and 159).
  - Key points about radiographs include the presence of cardiomegaly, identification of vascular abnormalities, and observing for radiographic changes compatible with CHF.
  - Typical radiographic findings of left-sided CHF are left-sided cardiomegaly, pulmonary vascular (venous) prominence, and parenchymal densities compatible with CHF.
  - Radiographs are essential in the differential diagnosis of respiratory problems in small animals.
- The *electrocardiogram* (ECG, EKG) is especially important for diagnosing arrhythmias and conduction disturbances. The ECG also may demonstrate cardiomegaly patterns or abnormalities in pericardial disease or ischemia, but the true sensitivity and specificity of this examination is unknown (see Chapter 144).
  - Canine ECGs exhibit great differences in terms of normal voltages. Typically, the normal canine QRS complex is <3.0 mV in any limb lead, with 2.5 mV representing a more sensitive but less specific value for cardiomegaly. However, some normal deep chested dogs have very large voltages.
  - Right axis deviation usually indicates RV hypertrophy or conduction delay. Left axis deviation is either normal or indicative of left ventricular disease or partial conduction delay.
- The *echocardiogram* is the noninvasive gold standard for diagnosis of heart disease. Key aspects of the echocardiographic and Doppler studies include identification of cardiac lesions and cardiomegaly; measurement of ventricular systolic and diastolic function; assessment of valvular heart disease, identification of abnormal flow patterns, and quantitation of pressure gradients.
- Other *clinical laboratory tests* may be useful for identifying the causes or consequences of heart disease or heart failure in particular instances. Commonly used tests include heartworm tests, blood cultures, levels of serum troponin (CTnI), thyroid function tests, serum potassium (and electrolytes), renal function tests (BUN, serum creatinine), and striated muscle enzymes (CK, AST). In the future, greater reliance on biomarkers can be expected. For example, ANP and BNP and their pro-hormones are increased in heart failure and may be useful as screening tests for patients with dyspnea.

TREATMENT

A large number of drugs impact the heart and the vascular system. The clinical pharmacology of these drugs is summarized in "Cardiovascular Drugs" (Chapter 146).

- Some treatments for CHF demonstrate rapid *hemodynamic effects*, increasing cardiac output or reducing pulmonary venous pressures or left ventricular afterload. Examples include furosemide, dobutamine, sodium nitroprusside, and pimobendan.
- Others treatments modulate *neurohormonal* or *inflammatory mediators* of CHF. These are often considered "cardioprotective treatments." Examples include angiotensin converting enzyme inhibitors (ACEI), spironolactone, beta-blockers, and omega-3 fatty acids.
- Still other treatments represent mainly *symptomatic therapy*. For instance, sedatives, oxygen, and thoracocentesis all serve a specific therapeutic purpose.
- Understanding the clinical use of these drugs singly and in combination with others is critical. The clinician should be mindful of the indications and contraindications for drug use; drug dosing; findings that indicate drug benefit; and method to identify adverse drug effects.
- The following treatment recommendations are general approaches to management of CHF in dogs. In almost every case, the cause of CHF will be related to chronic mitral/tricuspid valvular disease or dilated cardiomyopathy, but the treatment plans are also applicable to CHF due to congenital heart disease or pulmonary hypertension. Management of cardiac tamponade does not involve drugs and is described in Chapter 151.

Acute Heart Failure: Standard Hospital Treatment Plans

Combining **F**urosemide, **O**xygen, **N**itroglycerine (or **N**itroprusside) and **S**edation represents a treatment plan applicable to most cases of CHF regardless of cause and is especially effective in mild to moderate pulmonary edema. In life-threatening pulmonary edema, additional consideration should be given to afterload reducers. In cardiogenic shock, potent positive inotropic drugs should be administered.

Basic Therapy for CHF

- The F-O-N-S therapy plan delivers the following benefits: diuresis is initiated; pO2 is increased; ventricu-

lar preload is reduced; the tendency towards pulmonary edema is reduced; and anxiety is relieved.
- If necessary, additional treatments can be added to this protocol.
- For life-threatening pulmonary edema, an afterload reducer such sodium nitroprusside, hydralazine, or enalapril can be initiated (see below).
- For cardiogenic shock (CHF with hypotension), a potent positive inotrope such as dobutamine or pimobendan can be administered (see below).
- Loop diuretics such as furosemide are generally effective in acute pulmonary edema. However, these drugs must be carried by renal blood flow to the proximal nephron where furosemide is actively secreted into the filtrate before passing to the loop of Henle. In severe CHF with impaired renal perfusion, furosemide may not be effectively delivered to the proximal nephron.
- For this reason, use a relatively high initial furosemide dose (4–5 mg/kg, IV) in cases of severe CHF. The dog should be checked every 30 minutes for evidence of diuretic effect (observation for urination and palpation of the urinary bladder).
- Once diuresis ensues, the dose is reduced to 2 mg/kg q8–12h, IV or IM.
- Alternatively, a constant rate IV infusion of furosemide can be instituted. Following a bolus injection, the total dosage anticipated for the next 24 hours in calculated and delivered evenly by a syringe or other type of infusion pump.
- Nitroglycerine ointment ($^1/_2$–2 inches, cutaneously, q12h), if effective, works by pooling blood in capacitance veins and away from the pulmonary veins.
- Butorphanol (0.25 mg/kg IM) is the recommended sedative of choice for dogs in CHF.
- Most mild to moderate cases of CHF will respond very well to this treatment plan.

Life-Threatening Pulmonary Edema

A more aggressive approach to afterload reduction should be undertaken in the situation of life-threatening pulmonary edema. In particular, a potent alternative to nitroglycerine is the "balanced" vasodilator *sodium nitroprusside*. The main indication for nitroprusside is life-threatening pulmonary edema from left heart failure. Other afterload reducers available for hospital treatment include hydralazine and ACEI.

- This clinical situation is often related to rupture of a mitral chorda tendinea or development of atrial fibrillation, creating so-called acute on chronic HF.
- Clinically life-threatening pulmonary edema is characterized by severe dyspnea, hemoptysis, expectoration of pink froth, marked alveolar infiltrates on the thoracic radiographs ("white-out"), or failure of furosemide and nitroglycerine to relieve clinical signs of respiratory distress.
- Another indication for afterload reduction in hospital treatment of CHF is the dog with concurrent systemic hypertension. High ABP increases both the load on the LV and the volume of mitral regurgitation.

▼ ***Key Point*** Reducing arterial blood pressure is one of the most effective methods for reducing the severity of mitral regurgitation.

- The main contraindication to afterload reducers such as nitroprusside is pre-existent symptomatic or severe hypotension (<80 mm Hg systolic).
- Nitroprusside sodium is dosed in canine CHF at 0.5 to 5 mcg/kg/min, by IV infusion (carefully follow label directions for formulation). Frequent ABP monitoring should be scheduled. One can titrate the dose of nitroprusside drugs to a systolic ABP of 85 to 100 mm Hg (as well as to clinical signs) and continue treatment for 24 hours or less in most cases.
  There are alternatives to the use of nitroprusside:
  - One approach is the combination of nitroglycerine ointment with oral hydralazine (starting at 1–2 mg/kg PO). Hydralazine is a potent afterload reducer with relatively rapid onset of action.
  - An ACEI (0.5 mg/kg of enalapril or benazepril PO) also can be used in this acute situation; however, the onset of effect is slower and the control of ABP less reliable when compared to nitroprusside or hydralazine. The ACEIs are generally used for transition to home therapy and then for long-term management of CHF.
- The decision to unload the left ventricle with an arterial vasodilator ultimately requires good clinical judgment, and the aggressiveness of afterload reduction should relate to the severity of the pulmonary edema.
- Once the pulmonary situation is stabilized, taper the nitroprusside over about 6 hours (or stop the nitrate/hydralazine). At that time, begin the ACEI that will be continued during the home care process (see below).

Cardiogenic Shock

The finding of cardiogenic pulmonary edema or pleural effusion with severe hypotension (ABP <80 mm Hg) and other indicators of low cardiac output (pallor, hypothermia, depression, elevated blood lactate) is highly suggestive of cardiogenic shock. Volume infusion is inappropriate to raise ABP in this setting, and in most cases there is a need to stimulate myocardial contractility to improve pump function and facilitate diuresis.

- Other potential causes of cardiogenic shock include myocardial infarction (rare) and massive pulmonary embolus, for example, after treatment for adult heartworms.
- Dogs with CHF due to dilated cardiomyopathy (often Doberman pinschers) represent the typical case of cardiogenic shock.
- Initial treatment is the same as discussed above.
- Begin with basic heart failure therapy F-O-N-S therapy, These patients are hypotensive and often

very depressed; sedation is rarely needed. Determine if thoracocentesis is needed, as dogs with cardiogenic shock may have both pulmonary edema and pleural effusion.

- If there is a moderate-to-large pleural effusion, tap the chest.
- The most important therapy to administer in cardiogenic shock is a potent positive inotropic drug. The goal is to increase ABP by augmenting cardiac output. In most cases, the catecholamine *dobutamine* is administered as a constant rate intravenous infusion.
- Dobutamine (or dopamine) can effectively increase ABP in these patients primarily by a positive inotropic effect (at lower doses), by arterial vasoconstriction, or through an increased heart rate (at higher doses, generally >5 mcg/kg/min).
- Neither vasoconstriction (afterload mismatch) nor sinus tachycardia (increased oxygen demand) represent an advantage to a failing left ventricle; thus, the main goal of catecholamine treatment is stimulating myocardial contractility (and filling) while minimizing increases in vascular resistance and HR.
- Following initial F-O-N-S therapy, allow the patient 30 minutes to stabilize while preparing the dobutamine solution. Place an IV catheter in a peripheral vein and attach ECG monitoring leads (if available) and a blood pressure cuff for repeated monitoring of ABP.
- One method for preparing a stock solution of dobutamine for dogs follows:
  - Obtain 5% dextrose in water solution and the needed infusion set(s).
  - Add potassium chloride (8 mEq KCl per 500 ml D5W).
  - Add 250 mg of dobutamine to the 500 ml of 5% dextrose solution, yielding an approximate concentration of 500 mcg dobutamine per ml.
  - Hang the bag of 500 ml D5W with additives, attach the appropriate infusion set for accurate delivery, and flush and prime the line with dobutamine solution.
  - Attach the infusion line to the infusion pump. Begin the dobutamine infusion at a rate of 2.5 mcg/kg/min, and increase the dose after 30 to 60 minutes to 5 mcg/kg/min if tolerated. Doses greater than 10 mcg/kg/min are rarely used in our hospital.
- One can use the following guide for a *5-mcg/kg/min–infusion rate*; adjust as needed:

Weight (kg)	Micrograms per min	Micrograms per hour	Total ml of fluid per hour
10	50	3,000	6
20	100	6,000	12
30	150	9,000	18
40	200	12,000	24
50	250	15,000	30
60	300	18,000	36

- Re-measure the clinical variables often to assess the trend.
- Therapeutic effects of dobutamine include increased cardiac output, elevated ABP, increased tissue perfusion (better color and shorter refill time, stronger pulse), increasing body temperature, and improvement in attitude and strength.
- Adverse effects, necessitating dose reduction, include increasing heart rate, excessive vasoconstriction, and induction of extrasystoles. Seizure activity and vomiting are infrequently observed.
- Once the ABP is stable (systolic pressure in the 90 to 100 mm Hg range), other vasoactive drugs can be added to unload the left ventricle. The approach is similar to that discussed in the previous section.
- As a minimum, an ACEI such as enalapril or benazepril (0.25–0.5 mg/kg, PO once or twice daily, depending on ABP) should be initiated since these drugs benefit neurohormonal status, reduce aldosterone secretion, and reduce afterload. This seems the most practical vasodilator to add in this setting, as it will also constitute part of the home treatment.
- Alternatively, sodium nitroprusside (see the previous section) can be initiated if there is life-threatening pulmonary edema, starting at the conservative dose of 0.5 mcg/kg/min and titrated in concert with the dobutamine to maintain a systolic ABP of 90 to 100 mm Hg.
- After 24 to 48 hours of dobutamine therapy, reduce the dobutamine rate by 50% every 2 to 4 hours until you have reached 1.25 mcg/kg for 4 hours, then stop the infusion. If you cannot wean the patient from dobutamine (i.e., ABP is too low), increase the infusion rate to increase ABP and either increase the enalapril (to 0.5 mg/kg PO q12h) or begin pimobendan (if available).
- Eventually *establish home therapy* with oral furosemide, an ACEI, and digoxin (or pimobendan).

Use of Positive Inotropes in Hospital Therapy of CHF

Positive inotropic drugs are mainly used in treatment of specific situations such as CHF with hypotension or when atrial fibrillation complicates HF.

- The use of *dobutamine* (or dopamine) for cardiogenic shock has been discussed.
- *Milrinone*, an IV inodilator that acts by PDE inhibition, is rarely used in veterinary practice but is both a potent inotrope and afterload reducer.
- Where available, the inodilator drug *pimobendan* should be considered strongly for both hospital and home therapy of CHF. Pimobendan is a calcium sensitizer/vasodilator.
  - The drug is very potent and may be considered in place of dobutamine, when IV therapy is impractical.
  - One risk of pimobendan therapy in the setting of cardiogenic shock is the potential to reduce blood pressure via vasodilation, so ABP should be monitored carefully.

- Alternatively, the patient can be started on dobutamine and then bridged over to pimobendan for potent oral inotropic support and afterload reduction.
- It should be noted that some dogs already receiving pimobendan have improved following dobutamine infusion; the drugs are not interchangeable.
- Generally, digoxin is not administered in the urgent care of CHF patients; however, in the setting of HF with atrial fibrillation *digoxin* should be started (see below).

Management of the Dog with CHF and Atrial Fibrillation

- After confirming the rhythm diagnosis with an ECG, administer digoxin (Lanoxin) using a modified loading dose (0.01 mg/kg PO q12h for two doses), and then begin maintenance treatment (0.005 mg/kg, PO, q12h).
- To gain better control of the heart rate, after 24 to 48 hours of HF stabilization, add the calcium channel antagonist diltiazem to block the AV node (starting at 0.5 mg/kg, PO, q8h). This will better control ventricular rate response.
- Provided ABP is >90 mm Hg, one can up-titrate the dose of diltiazem at each subsequent dosing interval.
- Usual target doses of diltiazem are 1.0 to 1.5 mg/kg, PO, q8h (though higher doses may be needed) in order to obtain a "resting" hospital heart rate of 120 to 160/minute.
- On follow up examination, determine if the dog can tolerate low-to-moderate doses of a beta-blocker such as carvedilol or metoprolol (see above). Beta-blockers are cardioprotective and also slow heart rate in atrial fibrillation.
- The clinician must be aware of the negative inotropic effects of diltiazem and beta-blockers.
- While beta-blockers have more theoretical benefits in terms of "cardioprotection," they depress myocardial function more than diltiazem for equivalent heart rate control.
- The author recommends controlling heart rate with digoxin and diltiazem initially and subsequently adding carvedilol for additional rate control once the patient is "dry."
- Another option for treatment of AF is DC cardioversion. Pros and cons of such therapy should be discussed with a cardiologist.

Management of the Dog with CHF and Ventricular Tachycardia

In settings of CHF with ventricular tachycardia, it may be worthwhile to consult with a cardiologist. Treatment of isolated ventricular premature contractions with anti-arrhythmic drugs is not recommended.

▼ ***Key Point*** Digoxin is contraindicated in the presence of complicated or repetitive ventricular arrhythmias.

- *Lidocaine* (2 mg/kg IV boluses; 40–60 mcg/kg/minute, IV infusion) or *procainamide* (2 mg/kg IV boluses to 10 mg/kg; or 10–20 mg/kg, IM, q6h; or 25–40 mcg/kg/min, IV infusion) are most often used to attain initial rhythm control.
- *Mexiletine* (5–8 mg/kg, PO, q8h) is an oral alternative treatment to lidocaine.
- Anti-arrhythmic drugs, in general, are problematic in the setting of HF. Most drugs (except lidocaine and mexiletine) significantly depress myocardial function.
- While lidocaine and mexiletine are the safest in terms of myocardial contractility, reduced hepatic blood flow could lead to drug accumulation and toxicity (tremors, anorexia, vomiting, seizures).
- Procainamide can be used in dogs that fail to respond to lidocaine, but procainamide exerts a negative inotropic effect and also may cause peripheral vasodilation.
- Since sotalol has significant beta-blocking actions, it should be avoided in this setting.
- Amiodarone is also a beta-blocker but is probably a better choice in this setting provided liver toxicity does not develop.
- Any of the ventricular anti-arrhythmic drugs may also be pro-arrhythmic in dogs (worsening the ventricular tachycardia).

Home Therapy of CHF

The transition from hospital to home therapy of CHF usually begins after 24 to 72 hours of hospital treatment, depending on severity of CHF. During that interval the initial diagnostic workup of thoracic radiographs, serum biochemical profile, ECG, and echocardiogram should have been completed. ABP should have been measured frequently during this time. Often a follow up "renal/electrolyte panel" will be done prior to release, as vigorous diuretic therapy may alter these serum biochemical values. In patients with severe pulmonary edema on admission, repeated thoracic radiographs should be obtained to insure control of the CHF.

Transition to Home Therapy

The following sequence is typical:

- Parenteral furosemide is replaced with oral furosemide.
- Oxygen is discontinued.
- Nitroglycerine is replaced with an ACEI, a balanced vasodilator with cardioprotection properties.
- A decision is made regarding initiation of digoxin or pimobendan.
  - Pimobendan is a very effective drug for therapy of CHF and works very well with the combination of furosemide and an ACEI.
  - Digoxin is a weak inotropic drug but is clearly useful in atrial fibrillation and should be considered where pimobendan is unavailable. Relative

contraindications to digitalis include complex ventricular ectopia, azotemia, sinus node dysfunction, or pre-existent atrioventricular block.
- Spironolactone (a weak, potassium-sparring diuretic) is initiated for cardioprotection against effects of aldosterone.

Initial Home Treatment Plan

For chronic CHF due to valvular heart disease or dilated cardiomyopathy, home therapy consists of the following:

- A maintenance dose of furosemide (typically 2–4 mg/kg, PO, q12h)
- An ACEI, usually enalapril at 0.25 mg/kg, PO, q12h)
- Spironolactone (0.5–2 mg/kg, PO, daily)
- Digoxin (0.005 mg/kg, PO, q12h) is prescribed for dogs with DCM or advanced CHF if not contraindicated.
- Where available, pimobendan (0.2–0.3 mg/kg, PO, q12h) is prescribed instead of digoxin for dogs with dilated cardiomyopathy or advanced valvular heart disease.
- Moderate dietary sodium restriction is discussed with the client; a prescription diet may be dispensed.

Initial Reevaluation

- The typical patient is reevaluated in 7 to 10 days.
- At that time the history is explored regarding appetite, attitude, exercise capacity, ability to sleep comfortably, and presence of "symptoms."
- A physical examination is conducted and ABP measured.
- A serum biochemical profile is performed.
- A serum digoxin concentration is measured (draw blood 8–12 hours post-dose; target concentrations are 0.8–1.2 ng/ml).
- Prior therapeutic results and current clinical signs will determine if another thoracic radiograph or an ECG is needed. Continual respiratory problems or abnormal thoracic auscultation are indications for radiography. An arrhythmia is the main indication for another ECG.
- A repeated echocardiogram is unnecessary and rarely guides adjustments in drug dosages in canine CHF.
- At this visit, dosage adjustments are made to current drugs:
  - Furosemide therapy is individualized to thwart fluid retention (increasing doses for progressive edema) or to mitigate azotemia or hypotension (decreasing doses to improve renal perfusion).
  - Spironolactone is continued.
  - The dosage of enalapril (or benazepril) is increased to the "optimal dosage" of 0.5 mg/kg, PO, q12h if renal function and ABP are satisfactory (i.e., BUN or creatinine have not increased by >1.5 to 2 times baseline and systolic ABP is >90 mm Hg). This upward adjustment is especially important in dogs with DCM or advanced chronic valvular disease.
  - If not prescribed initially, digoxin or pimobendan should be reconsidered for dogs with advanced CHF. Atrial fibrillation is an indication for digoxin.

Other Therapeutic Considerations

- If the patient is stable and CHF well controlled, consideration should be given to additional "cardioprotection" therapy with a beta-blocker such as carvedilol (Coreg) or metoprolol-long acting. Initial doses of carvedilol (also an alpha blocker and potent antioxidant) is about 0.05 to 0.1 mg/kg, PO, q12h.
- The dose can be increased every 2 to 4 weeks with a target of 0.2 to 0.4 mg/kg q12h for dogs with CHF due to dilated cardiomyopathy.
- The benefits of beta-blockade in small-breed dogs with valvular endocardiosis are uncertain and a topic of current study
- See Cardiovascular Drugs (Chapter 146) for a more complete discussion of beta-blockers, as well as side effects of these drugs.
- Weakness, bradycardia (HR <80), or worsening CHF may indicate inability to tolerate the beta-blocker. In these cases, the drug dose should be reduced slightly and other medications (furosemide, pimobendan) increased if possible.
- The dietary supplements with omega-3 fatty acids (EPA, DHA) may be of benefit in cardiac cachexia. The use of other nutriceuticals, such as taurine, L-carnitine, co-enzyme $Q_{10,}$ or L-arginine, should be considered on a case-by-case basis.
  - Currently there is little to no evidence to support widespread use of these supplements in canine CHF, and many are expensive.
  - Some prescription diets are supplemented with a number of these nutrients.
- Cough suppressants, such as hydrocodone or butorphanol, are useful for coughing in small breed dogs with bronchial compression or concurrent tracheal collapse, but first ensure that effective treatment of pulmonary edema has occurred.
- If atrial fibrillation develops, control it as discussed above, by adding diltiazem to digoxin initially and later up-titrating carvedilol or another beta-blocker.
- Treat serious ventricular tachycardia with mexiletine or other anti-arrhythmic drugs such as amiodarone (with care).

Progressive Left-Sided CHF

When left-sided CHF with pulmonary edema advances despite optimized initial therapy, other treatments can be considered.

- In dogs with left-sided CHF, the clinician should ensure that the patient is not hypertensive (as might occur with chronic renal disease or Cushing's disease).

Elevated ABP should be aggressively lowered if hypertension is found.
- First optimize the ACEI dosage to 0.5 mg/kg, PO, q12h.
- If this fails consider adding amlodipine (0.05–0.1 mg/kg daily as an initial dose).
- Alternatively, assess the effect of carvedilol (Coreg) on ABP.
- Even if the ABP is normal, cautiously reducing systolic pressure with the combination therapy of an ACEI and amlodipine can reduce afterload, MR, and left atrial pressure in refractory left-sided CHF due to MR.
- If pimobendan is not licensed, attempt to obtain extra-label permission for its use.
- Alternative approaches include increasing diuretic doses or using subcutaneous furosemide, as discussed below for right-sided CHF.

Progressive Right-Sided CHF

Chronic right-sided CHF with refractory ascites generally stems from one of the following problems: mitral valve regurgitation that is complicated by pulmonary hypertension and tricuspid regurgitation; superimposition of atrial fibrillation on any heart disease; dilated cardiomyopathy; or pulmonary hypertension (including dirofilariasis and idiopathic PH).

- In addition to standard therapy of furosemide, spironolactone, dietary sodium restriction, and digoxin or pimobendan, there should be increased emphasis on dietary sodium restriction. Exercise restriction also may be beneficial (controlled walks only).
- Thoracocentesis should be done for any dog with a large pleural effusion.
- Tense ascites should be partially drained (about $^1/_3$ to $^1/_2$ of the volume) to relieve discomfort, but be careful about distinguishing hepatomegaly from ascites. Recurring body cavity effusions indicate that adjustment in medical therapy will be needed.
- Spironolactone dosage can be increased to 1 to 2 mg/kg, PO, q12h.
- For pulmonary hypertension that has been documented by Doppler echocardiography, a trial course of sildenafil (Viagra) at 1 to 2 mg/kg, PO, q12h may be of some benefit, but clinical trials are lacking and the drug is expensive.
- Pimobendan clearly can benefit some dogs with chronic cardiac ascites and should be obtained whenever possible
- If these measures fail, consider prescribing hydrochlorothiazide, but remember that sequential nephron blockage can induce acute volume depletion and renal failure, so start with low every other day dosing (1–2 mg/kg, PO, daily) and recheck renal function and electrolytes after 3 or 4 doses have been given.
- An alternative (and safer) approach to more advanced diuretic therapy is to administer oral furosemide and spironolactone and enhance the furosemide effect by intermittent dosing of furosemide subcutaneously.
  - While this can be done through repeated hospital visits, in most cases, we preload syringes for clients and instruct them in proper techniques for subcutaneous injection.
  - Initially substitute one of the oral doses of furosemide with the same injectable dosage. Start with an every other day regimen.

PATIENT FOLLOW-UP

When assessing the effectiveness and tolerability of cardiovascular drug therapy, consider the following key points:

- The client **interview**—review the medications; consider the owner's overall assessment of quality of life; discuss the dog's appetite, activity, and ability to sleep comfortably; respiratory symptoms; and exercise capacity.
- Identify any signs of possible drug **intoxication.**
- Concentrate on the **physical examination** signs of CHF: elevated jugular venous pressure, hepatomegaly, ascites, thoracic auscultation, and overall body condition (cachexia).
- Measure the arterial **blood pressure.**
- Test **renal function** and measure **electrolytes** if indicated.
- Assess the **cardiac rhythm** by auscultation; record an ECG if indicated by auscultation.
- Determine if thoracic **radiography** is indicated; review the chest films for control of edema and effusions.
- Determine serum concentrations of drugs if indicated (e.g., **serum digoxin**).

CHF PROGRESSION

Congestive heart failure may become complicated or progressive for a number of reasons related to cardiac or extracardiac issues. Some of the factors to consider include

- Progression of valvular disease or myocardial dysfunction
- Heightened neurohormonal compensation
- In dogs with MR, cardiac complications of ruptured chorda tendinea, left atrial tear, atrial fibrillation
- Medication problems: insufficient or excessive therapy for stage of disease; poor client compliance or inadequate follow up; negative inotropic drugs (beta-blockers, calcium-channel blockers, anti-arrhythmics)
- Excessive exercise
- Poor or unpalatable diet, excessive sodium intake

- Medical conditions that increase cardiac demands and workload: hypertension, hyperthyroidism (iatrogenic in dogs), anemia, infections (especially with fever)
- Other medical conditions: neoplasia, renal failure, chronic respiratory disease
- Environmental stress (heat, high humidity)
- Iatrogenic causes: excessive or inappropriate drug therapy causing hypotension, dehydration, renal failure

PROGNOSIS

The prognosis of canine CHF depends on the cause, severity, and care received.

- Many dogs survive >1 year following the first signs of CHF provided they receive optimal veterinary and home care, including extra-label drugs such as carvedilol and pimobendan combined with "standard" therapy of furosemide-spironolactone, an ACEI, and dietary modifications.
- The prognosis for DCM is always more guarded, especially in Doberman pinschers. Once CHF has progressed to severe ("functional class IV") failure, the outlook is generally guarded-to-poor and a 3- to 9-month prognosis is typical.
- There are no critical studies that *prospectively* examine prognostic criteria across all groups. The multicenter enalapril (North America) and benazepril (European) studies clearly indicate improved survival and reduction of clinical signs in canine CHF caused by DCM or chronic valvular disease when an ACEI is added to background therapy of furosemide +/− digoxin.
- Where pimobendan is available to treat canine DCM or advanced valvular heart disease, the long-term outcome also appears more favorable when compared to "conventional" therapy with furosemide and digoxin or even furosemide and an ACEI. (Though it is illogical not to combine pimobendan with furosemide and an ACEI.)
- Beta-blockers slow the progression of cardiac dilatation and HF in experimental canine myocardial diseases, and a drug like carvedilol should be part of the long-term treatment regimen, especially in DCM, provided it is tolerated.

Causes of Death

The **causes of death** in chronic CHF vary but are most often related to one of the following:

- Sudden electrical event (such as asystole or ventricular fibrillation)
- Hypoxemia (pulmonary edema, pleural effusion)
- Pulmonary embolism leading to fatal hypotension
- Multi-systemic organ failure
- Client desire for euthanasia. This is a particularly common ending and pertains to many factors that include effectiveness of therapy, severity of signs, client (and veterinarian) perceptions about quality of life, and issues of care (medication frequency, visits to the veterinary hospital, costs) among other factors.

Chapter

148 Syncope

John D. Bonagura / Shianne L. Koplitz

OVERVIEW

Syncope, or fainting, is a sudden and unexplained *loss of consciousness and postural tone* usually related to inadequate delivery of oxygen to the brain. This chapter outlines a general approach to the diagnosis of the syncopal patient. Effective therapy of syncope is predicated on identifying and managing the underlying disorder.

Characteristics of Syncope

- The event is often precipitated by exercise, sudden activity, or excitement (sympathetic stimulation). However, syncope can occur during rest or even sleep, especially in cats.
- Along with a loss of consciousness, there is a failure to maintain postural tone, causing falling. If the dog or cat is recumbent at the onset of the event, it is common for the patient to fall backwards or to roll to lateral recumbency.
- Brief stiffening is common along with forelimb rigidity and opisthotonus.
- Minor convulsive activity may be observed, such as focal head twitching. This is more common in cats wherein syncope often resembles a true seizure event.
- Urination during the event is a frequent observation. Defecation may occur but is far less common.
- Mucous membrane color is initially pale pink to white when the cause is low blood pressure; subsequently, cyanotic, normal, or flushed membranes may be observed. If hypoxemia from respiratory disease or a right-to-left shunt is the cause of fainting, cyanosis may precede the spell.
- Following recovery of blood pressure and cerebral function, mentation and behavior are typically normal. However, if the syncope is related to a protracted cardiac arrhythmia or ongoing or progressive pathology, as with a stroke, there may be a longer period of listlessness, stupor, or profound weakness.
- Some patients with syncope also demonstrate pre- or near-syncope. This is characterized by a sudden jerk of the head and body. This apparent "lightheadedness" abates just in time to prevent falling.

Differential Diagnosis

- The *differential diagnosis* of syncope includes seizure disorder or epilepsy; sleep disorder, including narcolepsy; stroke or transient ischemic attack of the CNS; metabolic disease affecting the CNS; and drug intoxication.
  - Syncope is readily confused with *seizure disorders or epilepsy* (see Chapter 127). Facial fits, generalized tonic-clonic movements, and postictal behavioral abnormalities are more typical of true seizures. However, clients can readily confuse the two, and even after obtaining a careful history, an experienced clinician may remain uncertain about the nature of the event.
  - *Sleep disorders* such as narcolepsy are rare (see Chapter 127) but may be precipitated in dogs by eating. The event appears similar to actual sleep, and in some cases, dogs may chew their food and literally fall asleep on the food bowl. Cataplexy, a loss of postural tone with maintenance of consciousness, is rare in dogs and cats.
  - *Strokes or transient ischemic attacks* can cause true syncope or, more commonly, lead to progressive or episodic neurological dysfunction (see Chapter 126).
  - *Central nervous system disorders,* such as primary brain lesions, may lead to altered consciousness and episodic falling, which might be misinterpreted as a syncopal attack (see Chapter 126). Acute vestibular syndromes may lead to falling, but mentation is normal, and the signs are generally obvious during neurological examination (see Chapters 61 and 126).
  - Metabolic diseases may alter cerebral function and be associated with staggering or falling; these include hypoglycemia, hepatic encephalopathy, and hypoadrenocorticism when it causes profound hypotension.
  - Overdose of prescribed drugs or ingestion of human drugs or toxins in the household can at times lead to altered cerebral function as well as hypotension, ataxia, or weakness. The resulting fall may be interpreted as syncope. In some cases, drugs cause profound hypotension leading to true fainting.

ETIOLOGY

General Mechanisms

- Syncope is generally caused by *insufficient oxygen delivery* to the brain.
  - The arterial oxygen content of the blood depends on pulmonary function (arterial pO_2) and the hemoglobin concentration (PCV, hematocrit).
  - Delivery of oxygen-containing blood is achieved by cerebral blood flow, which depends on arterial blood pressure (ABP) and the integrity of the vascular supply to the brain.
- From a pathophysiologic perspective, general causes of impaired cerebral oxygen delivery include:
  - Low arterial pO_2
  - Anemia
  - Cerebrovascular disease
  - Hypotension (low ABP)
- The most common cause of syncope is a sudden fall in ABP. This is typically caused by a cardiac arrhythmia, impairment of cardiac filling, or malfunction of the baroreceptor reflex arc.
- Blood pressure depends on ca*rdiac output* and *systemic vascular resistance.*
  - Cardiac output is the product of heart rate and stroke volume.
  - Stroke volume is modified by ventricular preload (venous return), myocardial contractility (inotropic state), valvular function, and ventricular afterload (impedance to ejection).
  - Stroke volume also is influenced by heart rhythm. Arrhythmias can alter ventricular filling or reduce the effectiveness of ventricular contraction.
  - Systemic vascular resistance depends on autonomic tone to arterioles, local (metabolic) factors that dilate or constrict the vessels, and the baroreceptor reflex systems.
  - Vasoactive drugs also can affect vascular tone.

Non-Cardiovascular Causes of Syncope

Syncope may be caused by disorders other than heart disease. Non-cardiovascular etiologies include:

Cerebral Hypoxia

- Anemia—in particular, moderate to severe or acute anemia.
- Respiratory disease—such patients are usually cyanotic from airway obstruction, pulmonary disease, or pleural effusion.

Cerebrovascular Disease

- This is relatively uncommon in dogs but can occur with severe hypothyroidism and accompanying atherosclerosis of the cerebral vessels in dogs (see Chapter 31); transient ischemic attacks also have been reported in cats.

Stroke

- This is a disruption in cerebral function related to sudden loss of blood supply.
- Hemorrhagic stroke—this is most commonly related to systemic hypertension in dogs and cats.
- Ischemic (thrombotic) stroke—a rare cause of syncope, but it has been observed in cats with feline cardiomyopathy and with bacterial endocarditis in dogs.

Metabolic Disorders

- Hypoglycemia is a relatively uncommon cause of syncope and is more likely to cause weakness, seizures, or coma. However, hypoglycemia can also affect autonomic function, blood vessel tone, and vascular response to changes in posture, predisposing to true syncopal attacks.
- Addison's disease may lead to syncope, likely related to volume depletion (see Chapter 33).
- Plasma volume depletion from any cause, including vomiting and diarrhea, can reduce cardiac output and ABP.

Drugs

- Drugs that affect heart rate, rhythm, plasma volume, or vascular tone may lead to hypotension and syncope. Examples include inadvertent ingestion of a beta-blockers or illicit drugs (cocaine); over-zealous treatment with diuretics; and administration of vasodilator drugs.

Cardiac and Vascular Causes of Syncope

Among the many cardiovascular causes of syncope are the following disorders:

Right-to-Left Shunting

- This can occur with congenital heart malformations including tetralogy of Fallot (see Chapter 154).

Bradyarrhythmias

- Sinus arrest; persistent atrial standstill; high-grade, second-degree, or complete AV block; ventricular asystole (see Chapter 145).

Tachyarrhythmias

- Ventricular tachycardias (often >300 bpm); less often supraventricular tachycardias or atrial fibrillation.

Reduced Cardiac Preload

- This can be due to structural heart disease or reduced venous return.
- Pericardial disease—cardiac tamponade.
- Intracardiac tumor with obstruction to cardiac filling.

- Caudal vena cava obstruction.
- Severe plasma volume depletion.

Valvular Heart Disease

- If sufficiently severe, outflow tract stenosis, atrioventricular valvular stenosis, or mitral or tricuspid regurgitation can limit cardiac output sufficiently to cause or contribute to syncope.

Cardiomyopathy

- Syncope is related to limited cardiac output, development of arrhythmias, or obstruction to blood flow (hypertrophic cardiomyopathy) (see Chapter 150).

Pulmonary Hypertension

- Acquired and congenital causes of pulmonary hypertension represent a common cause of syncope, especially in dogs. This may relate to obstruction of blood flow from the right ventricle, arrhythmias, and inappropriate activation of the baroreceptor reflex.

Congestive Heart Failure

- As with pulmonary hypertension, there may be multiple reasons for syncope in dogs and cats with CHF (see Chapter 147).
- Ischemia as a trigger for inappropriate activation of the baroreceptor reflex is a potential cause of syncope.

Hemorrhage

- Sudden hemorrhage is more likely to lead to hypotension and collapse but can also lead to syncope, as with rupture of a splenic tumor or traumatic injury with blood loss.

Thromboembolism

- A cerebral embolus may lead to a stroke that may include loss of consciousness and falling. The likely cardiac causes would be bacterial endocarditis or, in cats, a form of feline cardiomyopathy.

Loss of Vascular Tone

- Inappropriate vasodilation may follow administration of drugs, hypoglycemia, or activation of the cardiac baroreceptors (see below).

Reflex-Mediated Syncope

Syncope can be caused by inappropriate and prolonged activation of the baroreceptor reflex; this is termed reflex-mediated syncope. A variety of other names for reflex-mediated syncope are encountered including: "vasovagal," "neurocardiogenic," "neural-mediated," "vasodepressor," "cardioinhibitory," and "situational" syncope. While seemingly common, this form of syncope is poorly described in veterinary medicine.

- Autonomic control mechanisms are central to blood pressure control:
  - The baroreceptor reflex controls heart rate, ventricular contractility, and systemic vascular resistance via the autonomic nervous system.
  - Baroreceptors located in the systemic arteries (aortic and carotid sinuses) are well appreciated, but pressure receptors are also present within the ventricular myocardium (unmyelinated C-fibers). The sudden stimulation of these myocardial receptors is capable of triggering a baroreceptor reflex. One of the main reasons for activation of these cardiac receptors is sudden vigorous contraction of the myocardium as might occur with surges of sympathetic tone, excitement, or exercise.
  - Activation of the baroreceptor reflex slows the heart rate and causes vasodilation (reduced vascular resistance) through increased vagal and reduced sympathetic tone. Inappropriate activation of this reflex can lead to excessive vasodilatation and bradycardia, reducing ABP markedly.
  - Syncope can occur when a baroreceptor reflex is triggered inappropriately by sudden sympathetic stimulation of the heart, especially with excitement, or by situations such as coughing, urinating, or vomiting. The reflex can be predominately that of sinus arrest/bradycardia ("cardioinhibitory syncope"), vasodilation ("vasodepressor syncope"), or a mixed response ("vasovagal syncope").
  - In people, this inappropriate reflex activation is most often related to sudden sympathetic surges (as with pain or fright) or from postural (orthostatic) changes that develop with sudden or protracted standing. The sympathetic surge stimulates the heart to maintain ABP and perfuse the elevated head. However, postural activation for this reflex in quadrupeds seems less important than other triggers.
  - Common disease associations for reflex-mediated syncope in dogs include aortic and pulmonic stenosis, pulmonary hypertension, acquired valvular heart disease, and congestive heart failure. The reflex is often triggered by excitement, activity, or coughing (a type of situational syncope).
  - There can be a "disconnect" between the recovery of the sinus node function and the return to normal systemic vascular resistance (which can be delayed). This point is pivotal because on first examination the owner or veterinarian may identify a heart rate that is more than sufficient to maintain ABP (generally >40 beats per minute). However, the arterioles may be persistently dilated, producing an unconscious or very weak animal, with pale or cyanotic mucous membranes.
- Multiple reasons for syncope may be operative in a patient. For example, in a dog with tight congenital subaortic stenosis, possible mechanisms for excitement- or exercise-induced syncope might include: (1) reflex-mediated from stimulation of ventricular

baroreceptors; (2) myocardial ischemia leading to ventricular tachycardia; (3) outflow tract stenosis limiting stroke volume and cardiac output; and (4) effects of a cardiovascular drug, such as high-dose enalapril, that leads to peripheral vasodilation and reduced vascular resistance.

DIAGNOSIS

A number of diagnostic studies are needed to establish a diagnosis of syncope and identify the underlying cause for fainting.

History and Physical Examination

The history should include a medication history and full description of the event(s) as discussed in the Overview.

- Perform a complete physical, ophthalmic, neurological, and cardiovascular examination.
- Measure resting ABP to identify pre-existent hypotension or hypertension. If the patient is taking cardiovascular drugs, measure the ABP a number of times during the day.
- If the patient is currently affected by CHF and receiving potentially hypotensive drugs (diuretics, ACE-inhibitors, vasodilators, beta-blockers), it may be helpful to hospitalize the patient, administer medications, and record the ABP throughout the day. Systolic pressures <60 mm Hg often lead to weakness and syncope.
- If possible, have the client videotape an event. This can be especially helpful if you are uncertain about the nature of the event. Also ask the owner to observe mucous membrane color and to palpate the apex beat during the spell to count a heart rate. Remember that vasodilation can persist beyond bradycardia and an arrhythmia that leads to syncope may be gone by the time the patient is actually touched by the client or veterinarian.

Laboratory Tests

- Routine laboratory tests—Obtain a CBC, full serum biochemistry panel, and urinalysis to screen for anemia and metabolic diseases.
- Perform a heartworm test in endemic areas.
- Endocrine studies (especially for Addison's disease or hypothyroidism) should be considered in dogs (see Chapters 31 and 33).

Diagnostic Imaging

- Obtain thoracic radiographs to evaluate the heart, lungs, and thoracic cavity.
- Obtain a 2D echocardiogram to exclude structural heart diseases, pericardial disease, and mass lesions.
- In some situations, a Doppler echocardiogram may be indicated to screen for evidence of pulmonary hypertension.

Electrocardiography

▼ ***Key Point*** It is pivotal that the clinician understands the cardiac rhythm occurring during a syncopal episode.

There are a number of ways to determine the rhythm.

- *Resting (baseline) ECG*—this is rarely diagnostic. If auscultation is normal, this examination will be positive for the cause of fainting <3% of the time.
- *Holter (ambulatory) ECG*—this 24 to 48 hour examination is better but is a suboptimal study unless the patient is fainting regularly or you strongly suspect a ventricular arrhythmia, sinus arrest, or transient heart block as the cause of the event. The diagnostic yield is between 20% and 40%, depending on the patient and frequency of the spells.
- *Event recorder ECG*—this is the optimal electrocardiographic examination for the syncopal patient.
  - This monitor is different than a Holter 24h ECG. The monitor is small enough for toy breeds and cats and can be worn for one to four weeks. There are two electrodes secured to the chest and hidden under a chest wrap.
  - A constant single lead ECG is recorded on a digital memory chip that is continually updated (erasing "old data").
  - When a "spell" is witnessed, the client promptly presses the large button on the monitor recorder. This stores the ECG for subsequent playback. The time stored is programmable, but is usually set to record 30 to 60 seconds before and 30 to 60 seconds after the button push.
  - Once the patient is stable, the owner calls a toll-free number. After speaking to the recording technician, the owner places the telephone mouthpiece (not the earpiece) over the circle on the recording box, presses another button, and transmits the stored ECG to the service.
  - This ECG is then printed and faxed to the veterinarian's office by the monitor service.
  - Once the ECG is obtained, the cardiac rhythm that occurred during the observed collapse or syncopal attack is known and can be interpreted in light of the clinical findings.
  - Rapid or polymorphic ventricular tachycardia (Fig. 148-1) suggests the likely cause of syncope is ventricular ectopy and unstable rhythm. Periods of protracted sinus bradycardia with sinus arrest are suggestive of sick sinus syndrome. In general, sick sinus syndrome affects typical breeds (miniature schnauzers, West Highland white terriers, cocker spaniels, dachshunds) and the periods of sinus arrest will exceed 7 to 8 seconds before signs are observed.
  - When sinus rhythm or sinus tachycardia is abruptly followed by vagal-mediated arrhythmias such as sinus pause, sinus arrest, AV block, or asystole, the

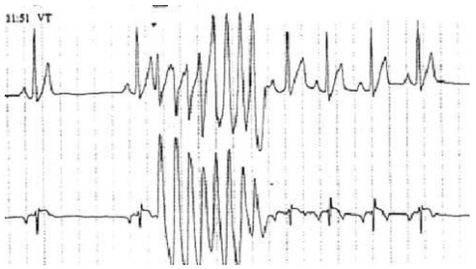

Figure 148-1. Ambulatory (Holter) ECG from a dog (two simultaneous chest leads) showing a period of polymorphic ventricular tachycardia.

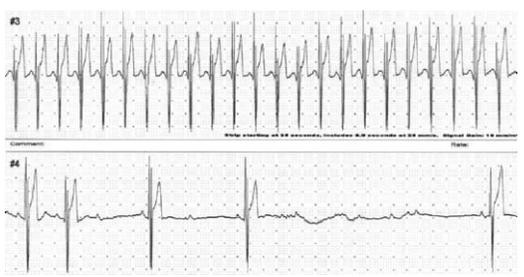

Figure 148-2. Single lead event monitor recording from a dog with fainting believed to be caused by reflex-mediated syncope. The heart rate is initially fast (sympathetic stimulation; strip #3 on top). Suddenly, the heart rate slows (lower strip, #4) leading to sinus bradycardia, some blocked P-waves, and a brief period of sinus arrest. The rhythm is typical of a vagal surge post-sympathetic stimulation. Presumably, the arterioles are also dilating at this time—this is a potent combination for hypotension (paper speed is 25 mm/sec).

diagnosis of reflex-mediated syncope should be considered (Fig. 148-2). This is a more difficult diagnosis because there may be a number of rhythm disturbances as well as artifacts. Typically the heart rate will recover before the dog.
  - Complete AV block with inadequate escape rhythm may be observed as a cause of syncope. In most cases, there will be evidence of conduction disturbance on the routine ECG as well. Transient complete or high-grade, second-degree AV block with ventricular asystole is more common in cats than in dogs but may occur in either species.
- A surgically implantable *loop recorder* is available for patients with very infrequent syncope, but these devices have been used rarely in veterinary practice.
- See Chapter 145 for more information on disorders of cardiac rhythm.

Tests of Baroreceptor Reflexes

- Baroreceptor testing (tilt table) is a common procedure in people with suspected reflex-mediated syncope; this study is not yet developed for routine clinical use in dogs or cats.
- Carotid sinus massage can be attempted in dogs in an attempt to induce sudden sinus node depression, but hypersensitive carotid sinus syndrome is not believed to be important in animals.

TREATMENT

Therapy of the syncopal patient depends entirely on the underlying cause.

- Dogs in CHF should be treated medically with systolic ABP maintained between 90 to 120 mm Hg (see Chapter 147).
- Pacemakers are used for bradyarrhythmias that are severe and persistent (as in sick sinus syndrome or with complete or high-grade, second-degree AV block) (see Chapter 145).
- Anti-arrhythmic drugs are used for tachyarrhythmias (for example, sotalol or mexiletine and atenolol for dogs with malignant ventricular tachycardia) (see Chapter 145).
- For reflex-mediated syncope in dogs, therapy is less certain.
  - In human patients, beta-blockers are used (to prevent sympathetic-induced hypercontractility of the myocardium and stimulation of the C-fibers); however, we have not had particularly good results with beta-blockers in dogs. Paradoxically, drugs that increase SNS tone (theophylline or terbutaline) or reduce vagal efferent effect (hyoscyamine, disopyramide) have worked better and can be tested for clinical benefit.
  - For patients not in CHF, consider supplementation of the diet with table salt to encourage drinking.
  - A pacemaker can be helpful if the major component of syncope is cardioinhibitory, but these devices will be of little value if vasodilation is a prominent component of the events.
- Syncope related to severe pulmonary hypertension is very difficult to manage; consult a cardiologist. Potential treatments include sildenafil (Viagra) to reduce pulmonary vascular resistance (see Chapter 146).

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Chapter

149 Valvular Heart Disease

John E. Rush / John D. Bonagura

VALVE FUNCTION AND DYSFUNCTION

Cardiac Valve Structure

The aortic and pulmonic valves separate the left and right ventricles from their respective great vessels. The semilunar valves consist of three individual leaflets that are closed during ventricular diastole and open during ventricular systole. Atrioventricular (AV) valves positioned between the atria and ventricles of the left and right heart are respectively called mitral and tricuspid valves. The left and right AV valves consist of two major leaflets ("tricuspid" is a misnomer in dogs and cats). The AV leaflets are attached via the chordae tendineae to the papillary muscles, which attach to the ventricular wall. The base of each AV valve is supported by a valve annulus. The AV valves open during ventricular diastole and close during ventricular systole.

Normal Function

The heart valves serve as one-way passages for blood and prevent retrograde (regurgitant) blood flow. The cardiac valves open and close in a cyclical pattern, and valve motion is dictated by changes in pressure within the cardiac chambers and great vessels. Competent AV valves permit the development of high ventricular pressures during systole. In a similar fashion, normally functioning semilunar valves prevent retrograde diastolic flow into the ventricles allowing for low ventricular diastolic pressures. Vibration of the heart, blood, and major vascular structures attending closure of the AV valves results in the first heart sound (S1) at the beginning of systole, and oscillation of these structures at the time of closure of the semilunar valves results in the second heart sound (S2) at the onset of ventricular diastole.

Valve Dysfunction

Cardiac valves may be dysfunctional as a consequence of congenital or acquired heart disease. General patterns of disease include:

- Obstruction to flow, termed valvular stenosis.
- Incompetent closure allowing valvular regurgitation (also called valvular insufficiency).

Valvular stenosis is almost always a congenital abnormality in animals. Valvular regurgitation may develop from congenital malformation or acquired diseases. Common anatomic and functional causes of AV valvular regurgitation are listed in Table 149-1.

▼ ***Key Point*** Because the AV valve consists of multiple anatomic components, disease of any portion of the apparatus or geometric changes in the ventricle can lead to AV valvular regurgitation.

Cardiac Murmurs

A hallmark clinical finding in valvular heart disease is a cardiac murmur. Murmurs are produced by high velocity and turbulent blood flow across the valve as the blood moves from a higher to a lower pressure chamber or vessel. With few exceptions, the absence of a cardiac murmur usually excludes the presence of clinically significant valvular disease (see Chapter 142).

- Semilunar valve stenosis or AV valve insufficiency leads to systolic murmurs.
- Semilunar valve insufficiency and AV valve stenosis leads to diastolic murmurs. In general, diastolic murmurs are softer than systolic murmurs of similar hemodynamic consequence.
- Cardiac murmurs may *not* be evident in the following situations:
  - Trivial valve regurgitation or stenosis. (Note: trivial stenosis or insufficiency may be relevant in breeding soundness examinations.)
  - Dynamic ventricular outflow tract obstruction in cats with hypertrophic cardiomyopathy or in dogs with subtle mitral valve malformation. Murmurs are often labile in these situations.
  - Massive, "wide-open" AV valve regurgitation in which the atrium and ventricle act as a common chamber and there is minimal pressure difference across the valve.

Table 149-1. CAUSES OF ATRIOVENTRICULAR VALVULAR REGURGITATION*

Congenital mitral valve dysplasia (MR)
Congenital tricuspid valve dysplasia (TR)
Chronic degenerative (myxomatous) valvular disease (endocardiosis causing MR, TR)
Bacterial endocarditis (MR)
Ruptured chordae tendineae (MR, TR)
Avulsion of the papillary muscle (MR, TR)
Transmural myocardial infarction (MR)
Causes of ventricular or atrial dilation leading to AV valve regurgitation
Patent ductus arteriosus (MR)
Ventricular septal defect/endocardial cushion defect (MR, TR)†
Atrial septal defect (TR)
Aortic regurgitation (MR)
Pulmonary regurgitation (must be severe to cause TR)
Myocarditis—for example, parvovirus, Chagas' disease (MR, TR)
Dilated cardiomyopathy (MR, TR)
Intermediate/restrictive cardiomyopathy (MR, TR)
Atrial muscular dystrophy—"silent atrium" (MR, TR)
Right ventricular cardiomyopathy—RV dysplasia (TR)
Hyperdynamic circulation—AV fistula, anemia, hyperthyroidism (MR, TR)
Chronic bradyarrhythmia—for example, complete AV block (MR, TR)
Pulmonary hypertension, including heartworm disease and chronic left-sided congestive heart failure (TR)
Causes of left ventricular hypertrophy (causing MR)
Subaortic stenosis
Hypertrophic cardiomyopathy
Systemic hypertension—for example, chronic renal disease
Hyperthyroidism
Acromegaly
Causes of right ventricular hypertrophy (causing TR)
Pulmonic stenosis
Pulmonary hypertension
Arrhythmic causes (MR and TR)
Cardiac arrhythmias preventing synchronous closure of AV valves—for example, ventricular premature beats

MR, mitral regurgitation; TR, tricuspid regurgitation.
*While this list is extensive, note that the most common causes of atrioventricular (AV) regurgitation are AV dysplasia, myxomatous degeneration, cardiomyopathy (any form), endocarditis, and hyperthyroidism (cats).
†May include mitral cleft or other AV valve malformation.

- Animals with very low cardiac outputs.
- Heart sounds muffled by lung sounds, pleural or pericardial fluid, or pneumothorax.

VALVULAR DISEASES OF CLINICAL IMPORTANCE

Chronic Valvular Disease

Chronic valvular disease occurs primarily in dogs. This progressive, degenerative disease is also referred to as endocardiosis, chronic degenerative valvular heart disease, chronic "myxomatous" valvular heart disease, or chronic mitral and tricuspid valvular fibrosis.

▼ ***Key Point*** Chronic valvular disease, or endocardiosis, a degenerative disorder of the cardiac valves, is the most important cause of heart disease in dogs.

Congenital Aortic Stenosis

This lesion usually is a *subvalvular* fibrous obstruction, although the lesion may extend to the valve proper (see Chapter 154 for a discussion of congenital valvular disorders).

Congenital Pulmonic Stenosis

A variety of anatomic lesions may contribute to narrowing of the right ventricular outflow tract, pulmonic valve, or pulmonary artery (see Chapter 154).

Congenital Mitral and Tricuspid Valve Dysplasia

Anomalies of the chordae tendineae, papillary muscles, valve cusps, or valve annulus can lead to incompetency or, less commonly, to stenosis of the valves (see Chapter 154).

Infective (Bacterial) Endocarditis

This condition almost always involves the left-sided heart valves in dogs and cats. Destruction of valve tissue commonly results in valvular insufficiency, although large vegetation(s) or valvular fusion may obstruct blood flow and create stenosis.

AV Valvular Regurgitation Due to Cardiomegaly or Cardiomyopathy

Valvular regurgitation may develop secondary to *ventricular or atrial dilation* or *ventricular hypertrophy* related to a variety of causes (see Table 149-1). For example, acquired mitral regurgitation in cats is typically caused by a form of cardiomyopathy.

CHRONIC VALVULAR DISEASE (ENDOCARDIOSIS) IN DOGS

Chronic valvular heart disease is a degenerative disorder of unknown cause affecting the endocardial and subendocardial portions of the valve leaflets, primarily in middle-aged and older dogs. It is not a consequence of endocarditis, although there is good evidence for a genetic predisposition to develop the disease in a number of canine breeds. The AV valves are principally involved, with the mitral valve affected in nearly 100% of cases, the tricuspid in 34%, and the aortic valve in a smaller proportion of cases based on pathology studies.

Pathology

- The valve leaflets in advanced disease are thickened and distorted by nodular changes in the free edge

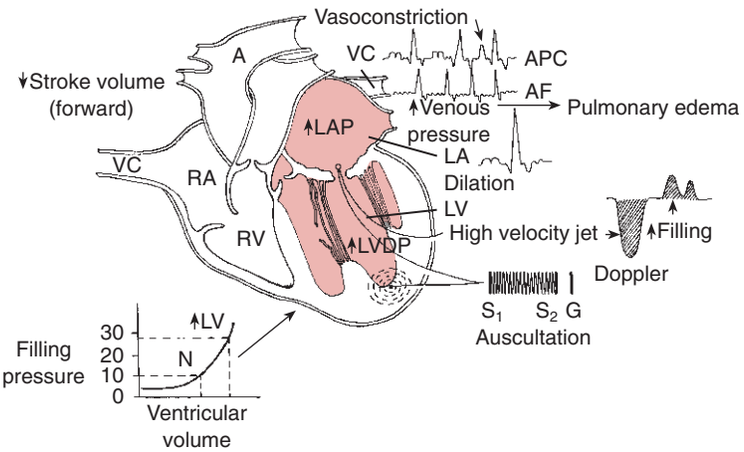

Figure 149-1. Diagrammatic representation of mitral regurgitation. Consult the text for an explanation of abbreviations and symbols.

and base of the valve. The valve surface glistens and the endocardium is grossly intact, distinguishing this degenerative change from endocarditis. In some dogs the valve surface may be increased with redundant connective tissue and billowing of a portion of the leaflets towards the atrium. Histological lesions are myxomatous in nature, characterized by deposition of acid-staining glucosaminoglycans within the valve leaflet and cusp. Collectively these lesions predispose to valvular regurgitation, which is typically slowly progressive in nature.

- The chordae tendineae are thickened near the valve attachment, and *chordal stretch* or *rupture* may be observed. Stretch predisposes to valve prolapse. Sudden rupture of a chord may lead to a flail leaflet and peracute congestive heart failure.
- Secondary *dilation of the left atrium and ventricle* develops in dogs with mitral valvular endocardiosis. Ventricular hypertrophy is of the eccentric type (with dilation of the ventricle) in isolated chronic valvular disease. The mitral valve annulus dilates as the ventricular dimensions increase, leading to further regurgitation and left atrial enlargement. In cases complicated by intercurrent systemic hypertension, there may be inappropriate thickening of the left ventricular wall.
- Focal subendocardial *myocardial fibrosis* may be evident, especially involving the papillary muscles. These fibrotic lesions may be related to narrowing of small, intramural coronary arteries.
- Endocardial sclerosis develops in the left atrium secondary to mechanical irritation from high velocity, regurgitant streams of blood. These "jet lesions" consist mainly of fibrous tissue. Fresh or healed linear left atrial tears commonly are found at necropsy, but rupture of the left atrium with pericardial tamponade rarely is encountered.
- The right ventricle and right atrium can become dilated because of concomitant tricuspid regurgitation, often complicated by pulmonary hypertension from left ventricular failure or intercurrent lung disease.

Pathophysiology

Endocardiosis represents a progressive process and does not cause detectable signs during the earliest period of structural changes. Progressive valvular distortion leads to detectable valvular insufficiency with accompanying cardiac enlargement. Mitral regurgitation (MR) causes left ventricular volume overload, left heart failure, pulmonary hypertension, and predisposes to cardiac arrhythmias (Fig. 149-1). However, heart failure does not develop in all dogs. The entire process usually requires many years, although some breeds (e.g., Cavalier King Charles spaniel) are affected relatively early in life and may have a rapid progression to heart failure.

▼ ***Key Point*** Mitral valve disease is the most important cause of heart murmurs and left-sided congestive heart failure (CHF) in mature dogs.

Mitral Regurgitant Volume

Total left ventricular (LV) stroke volume often is greatly increased, but a large proportion of LV output can be regurgitated into the left atrium. Forward stroke volume, the blood pumped into the aorta, is often maintained at near normal levels until CHF is present or advanced.

Left-Sided Cardiomegaly

Chronic mitral insufficiency increases LV and left atrial (LA) volume. Increases in LA pressure and volume cause progressive LA dilatation. Eccentric hypertrophy with dilatation of the left ventricular chamber results from the volume overload.

Increased Pulmonary Venous Pressure

LA and pulmonary venous (PV) pressures increase for a number of reasons:

- Progressive MR increases LA pressure, initially during systole. If the regurgitant volume increases gradually, LA compliance increases, and the condition is well tolerated. This explains why many dogs have severe cardiomegaly but minimal clinical signs. If the regurgitant volume is very large, or if regurgitation develops suddenly (e.g., chordal rupture), the limits of atrial distensibility are exceeded and mean LA and PV pressures increase, leading to pulmonary edema.
- The left ventricle may develop fibrosis or with progressive myocardial failure demonstrate reduced diastolic compliance and increased resistance to filling. The resulting higher LV diastolic pressure is transmitted to the left atrium and pulmonary veins.

Pulmonary Edema

Elevation of PV pressures increases pulmonary capillary pressure and may lead to pulmonary edema. Reduced forward output may promote retention of sodium and water by the kidneys and contribute to fluid overload. Clinical consequences include tachypnea, hypoxemia, coughing, and exercise intolerance.

Bronchial Compression

The left main-stem bronchus can become trapped between the pulsating aorta and the enlarging atrium. During systole, the bronchus is compressed by combined expansion of the aorta and the left atrium, triggering pressure receptors in the bronchus. As a result, exertional coughing and wheezing may occur even in the absence of lung edema.

Pulmonary Dysfunction

Chronic passive congestion of the lung causes ventilation perfusion inequalities (leading to hypoxemia) and, with chronicity, also might induce pulmonary fibrosis, which increases lung stiffness and the work of breathing.

Myocardial Failure

Chronic volume work by the left ventricle, combined with recurrent neurohormonal activation (renin-angiotensin-aldosterone; sympathetic nervous system; pro-inflammatory cytokines) can cause structural remodeling of the myocardium. Eventually reduced LV contractility and cardiac muscle failure occur ("cardiomyopathy of overload"). LV dysfunction is especially likely in larger dogs with primary mitral valve disease. However, in most cases, CHF often is manifest before substantial myocardial failure can be appreciated by clinical testing.

Low Cardiac Output

If forward stroke volume is inadequate, signs of low output (weakness, exertional or cough-related syncope, and prerenal azotemia) may develop. Low output signs are often associated with the development of pulmonary hypertension and right-sided CHF, although syncope can be the result of arrhythmias or of altered baroreceptor function leading to vasodilation and bradycardia.

Right Ventricular (RV) Failure

Left heart failure with secondary pulmonary hypertension, often combined with tricuspid regurgitation due to endocardiosis, causes progressive RV dilation. RV failure may ensue, as evidenced by hepatomegaly and ascites.

Cardiac Arrhythmias

Arrhythmias are common and can further decrease cardiac output (see Chapter 145).

- Atrial arrhythmias are triggered by dilation of the atria. Atrial premature complexes (APCs) frequently are recorded on the electrocardiogram (ECG). Atrial tachycardia and atrial fibrillation are evident in some cases.
- Ventricular premature complexes (VPCs) develop in some dogs, especially those with myocardial failure, but sustained ventricular tachycardia appears to be less common than in dogs with dilated cardiomyopathy.
- Iatrogenic arrhythmias (e.g., sinus bradycardia, AV block, APCs, and VPCs) may be precipitated by digitalis intoxication or diuretic-induced hypokalemia.

Ruptured Chordae Tendineae

This condition commonly is observed during echocardiographic examination of dogs with advanced MR. Catastrophic CHF may develop acutely; however, depending on the location of the chordal rupture, the added hemodynamic burden may be reasonably well tolerated.

Left Atrial Rupture

Rupture of the left atrium, although uncommon, can cause acute cardiac tamponade, cardiogenic shock, and sudden death. Rarely, splitting of the atrial septum produces an acquired left-to-right shunting atrial septal defect.

▼ ***Key Point*** Rupture of the mitral valve chordae tendineae, the development of sustained atrial tachyarrhythmias, and LA rupture are important diagnostic considerations when rapid hemodynamic deterioration occurs in dogs with chronic MR. Appropriate therapeutic intervention can

stabilize many of these patients, allowing sufficient time for further compensation.

Clinical Signs and Diagnosis

Signalment

Chronic valvular disease is most common in toy and small breeds of dogs (e.g., poodle, Yorkshire terrier, Cavalier King Charles spaniel, schnauzer, cocker spaniel, and dachshund). Some breeds, particularly the spaniels, German shepherds, and Afghan hounds, are prone to both valvular degeneration and dilated cardiomyopathy. Endocardiosis is an incidental finding in many aged dogs. Male dogs are predisposed to the development of CHF with chronic valvular disease.

▼ ***Key Point*** Occasionally, CHF from primary mitral valve disease develops in large-breed dogs, but dilated cardiomyopathy is a more important cause of CHF in these larger dogs.

History

The presenting complaints typically are those attributable to bronchial compression, pulmonary congestion, or low cardiac output and include cough, tachypnea, tiring on exercise, and syncope. Weight loss is a frequent but subtle finding until biventricular or right-sided heart failure develops. Unless there are other metabolic problems, such as hyperadrenocorticism, few dogs with overt CHF are obese. The opposite is often true in dogs with chronic respiratory disease. In general, the clinical signs gradually become more severe, reflecting the progressive nature of the disease. Syncope may be related to one or more of the following problems:

- Cough-syncope—fainting after vigorous coughing caused by decreased venous return, transient bradyarrhythmias, or inappropriate baroreceptor reflex-mediated activation.
- Paroxysmal atrial or ventricular tachyarrhythmias.
- Orthostatic hypotension—sudden weakness after rising may be related to abnormal baroreceptor activity, particularly in volume-depleted dogs.
- Insufficient forward flow from severe MR or from pulmonary hypertension, typically observed at the onset of exercise or with excitement.
- Reflex-mediated (neurocardiogenic) syncope. This may be the most common cause of excitement-induced syncope.
- Iatrogenic issues—hypotension secondary to diuretics, vasodilators, or angiotensin-converting enzyme inhibitors (ACEIs).

Physical Examination

Auscultation

As the disease progresses, the left apical systolic murmur of mitral insufficiency generally increases in intensity, and the duration increases from early systole to midsystole until it extends throughout systole (holosystolic). The murmur of MR radiates in the direction of the regurgitant jet, typically dorsal to the mitral valve on the left hemithorax, but very often to the right hemithorax as well.

▼ ***Key Point*** A systolic murmur heard best over the (palpable) left apex almost always is caused by MR. The murmur may radiate widely.

- A systolic click or short systolic murmur usually indicates early disease. The murmur of MR usually evolves from a soft decrescendo to a loud holosystolic murmur over a period of months to years. In some dogs with peracute CHF or in dogs with systemic hypotension from drug therapy or due to ruptured left atrium, the murmur can become softer and shorter.
- Left apical midsystolic clicks often are detected in asymptomatic dogs and may be confused with a ventricular gallop. These clicks probably indicate chordal laxity and valve prolapse.
- A ventricular gallop (third heart sound) may be heard at the left apex in some dogs with CHF. This sound often resolves after successful therapy.
- Cardiac arrhythmias and pulse deficits may be detected in patients with rhythm disturbances.

Precordial Palpation

The point of the left apical impulse shifts caudoventrally as the left ventricle enlarges. A precordial thrill develops in many dogs with advanced valvular incompetency and is palpable over the left apex or tricuspid valve area. A right-sided thrill is most often identified in dogs with the combination of TR and pulmonary hypertension.

Arterial Pulse

The arterial pulse is variable and depends on forward stroke volume, cardiac rhythm, and current therapy. A good arterial pulse is usually present in dogs with compensated disease. Heart rate typically is increased when CHF is evident.

▼ ***Key Point*** Pronounced sinus arrhythmia is atypical in dogs with untreated CHF caused by mitral valve disease but is common in patients with primary respiratory disease.

Pulmonary Auscultation

As lung congestion develops, ventilatory effort and lung sounds become abnormal. Inspiratory crackles and cyanosis may be detectable. Wheezes, representing "cardiac asthma" from peribronchial edema (cuffing) or left main-stem bronchial compression, may be noted. Pleural effusion may cause muffling of lung or heart sounds on the ventral thorax.

Right-Sided CHF

If the right heart fails, jugular venous pressure and liver size increase. Ascites is typical of advanced right-sided CHF, often with pulmonary hypertension. Pleural effusion usually indicates biventricular CHF, and is particularly common in dogs with atrial fibrillation. Occasionally, a dog is presented with predominant signs of RV failure due to pulmonary hypertension and severe tricuspid regurgitation (TR). Heartworm disease, pericardial effusion, dilated cardiomyopathy, tricuspid valve malformation, and atrial muscular dystrophy/myocarditis should be differential diagnoses in dogs with right-sided CHF.

▼ ***Key Point*** When there is pleural effusion and no jugular venous distention, ascites, or atrial fibrillation, strongly consider non-cardiac causes for the effusion.

Imaging—Radiography and Echocardiography

Cardiac imaging is discussed in Chapter 143.

- Progressive cardiomegaly is detected with left-sided heart enlargement predominating. Cardiac widening and LA enlargement typically are the first abnormalities detected. A vertebral heart score (comparison of length and width of cardiac silhouette to vertebral length caudal from the fourth thoracic vertebra) greater than 10.8 is good evidence of volume overload in dogs with chronic valvular disease. As the disease progresses, LV elongation, left main-stem bronchial compression, and pulmonary venous distention are observed.
- Left-sided CHF causes radiographic abnormalities that include increased lung density (interstitial and alveolar infiltrates) in the perihilar lung zones. These infiltrates characteristically are dorsal and bilaterally symmetric. However, owing to differences in pulmonary lymphatic drainage, edema may be worse in the right caudal lobe, a finding best appreciated in the ventrodorsal or dorsoventral view. Pleural effusion and ascites are present with right-sided or biventricular failure.
- Echocardiographic findings include cardiomegaly, thickened AV valves, and variable changes in LV shortening fraction. Valvular thickening may not be symmetric and often appears to preferentially affect the anterior (septal) mitral leaflet. Valve prolapse of the mitral or the tricuspid valve may be observed. In many cases, ventricular contractility appears normal to increased because the LV ejects a large portion of the total stroke volume backward into the low-resistance left atrium. The shortening fraction is rarely below the lower limits of normal reference values, helping to distinguish this condition from dilated cardiomyopathy. Stretched or ruptured chordae tendineae can result in focal leaflet prolapse or complete loss of valvular support (flail). Doppler studies can demonstrate mitral and tricuspid regurgitant flow and Doppler studies can be used to document the presence of pulmonary hypertension. Often, mild aortic regurgitation (that is silent to auscultation) is evident as well.

Electrocardiography

- The ECG can be normal, and heart rate and rhythm usually are normal until significant cardiomegaly or CHF develops.
- Arrhythmias become common as the disease progresses. Sinus tachycardia, supraventricular premature beats, paroxysmal or sustained atrial or supraventricular tachycardia, atrial fibrillation, and VPCs may be recorded (see Chapter 145).
- Atrial enlargement often causes widening of the P wave (P mitrale) as well as increased P wave amplitude. LV enlargement is suggested by increased voltages in leads II, III, and aV_F, widening of the QRS complex, and slurring or coving of the ST segment (see Chapter 144). Left axis deviation is uncommon.
- A 24-hour ambulatory ECG (Holter) recording or an event monitor ECG is helpful for evaluating dogs with syncope and for determining the need for and response to anti-arrhythmic therapy (see Chapter 148).

Laboratory Tests

Laboratory changes that accompany advancing endocardiosis typically reflect the hemodynamic changes and renal responses that develop in dogs with CHF. Laboratory studies help to identify complications caused by extracardiac diseases (e.g., Cushing's disease, renal failure) and drug therapy (e.g., diuretics).

- Significant pulmonary edema or tissue hypoperfusion causes arterial hypoxemia (decreased PaO_2), and the associated increase in ventilatory effort can cause respiratory alkalosis.
- Mild to moderate increases in blood urea nitrogen (BUN), serum creatinine, and phosphorus are detected in many dogs with endocardiosis as a result of chronic renal disease, decreased cardiac output, or hypotensive drug therapy. Azotemia may improve or resolve following a reduction in diuretic or ACEI dosages, if these can be tolerated without worsening of clinical signs of CHF. Diuretic therapy prevents use of urine specific gravity as a measure of renal interstitial-tubular function.
- Poor hepatic perfusion and hepatic congestion may cause mild to moderate elevations of serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Persistently elevated liver enzymes usually indicate a non-cardiac disorder of the liver, particularly when such changes are marked.
- Serum electrolyte abnormalities are uncommon. Hyponatremia sometimes is detected in dogs with

severe biventricular heart failure, especially in those with marked ascites and polydipsia, and is a poor prognostic sign. Hypochloremia and hypokalemia are usually iatrogenic as a result of diuretic therapy and anorexia. Co-therapy with furosemide and thiazide diuretics is most likely to cause most serious reductions in sodium, potassium, and chloride.

- Assays for plasma brain natriuretic peptide and/or atrial natriuretic peptide may prove useful for establishing a diagnosis of CHF or to provide prognostic information. At present, these tests are only available as research tools however clinically useful tests may be available soon.

Differential Diagnosis

The differential diagnosis of valvular heart disease includes any cardiac disease that leads to a heart murmur (see Table 149-1). The leading differential diagnoses are usually dilated cardiomyopathy, congenital AV valve malformation, and bacterial endocarditis. In dogs with cough or respiratory distress, CHF due to chronic valvular disease must be distinguished from tracheal or bronchial collapse, chronic bronchitis, pulmonary fibrosis, and other primary pulmonary diseases (e.g., pneumonia, thoracic neoplasia, allergic pneumonitis, and non-cardiac cause of pleural effusion).

- The typical age, breed, and clinical presentation make the diagnosis of chronic valvular disease straightforward in most cases.
- The echocardiogram is useful for distinguishing endocardiosis from congenital valve malformation or dilated cardiomyopathy.
- Bacterial endocarditis is associated with clinical findings of a multisystemic disorder. Physical, radiographic, and echocardiographic features of healed mitral endocarditis may be difficult to distinguish from myxomatous changes.
- CHF is commonly misdiagnosed in patients with chronic respiratory disease because these dogs often have cough, shortness of breath, and pulmonary crackles (which can be misinterpreted as "wet lungs," as opposed to small airway dysfunction). Concurrent compensated chronic valvular disease, when present, creates a cardiac murmur and complicates clinical decision making.
  - Determine whether radiographic cardiac enlargement is more consistent with cor pulmonale (right heart enlargement secondary to chronic lung disease) or left heart enlargement with left atrial and ventricular enlargement on both radiographic views.
  - Seek to identify positive findings of heart disease, such as murmur, arrhythmias, abnormal ECG, cardiomegaly (vertebral heart score >10.8) with left atrial enlargement, and pulmonary venous distention. With the possible exception of catastrophic CHF, the diagnosis of endocardiosis should not be considered unless the definitive murmur of MR is evident.
  - If mild CHF is the likely cause of respiratory signs, consider a trial course of furosemide (2 mg/kg, q12h) for 5 to 7 days. Anticipate a good response in cases of left-sided CHF, with concurrent radiographic improvement. Some patients with chronic lung disease also respond partially to diuretics (mechanism uncertain).
  - Pulmonary crackles or a cough without a murmur, a history of untreated, chronic (>6 months) cough, a "honking" cough, right heart enlargement, and marked sinus arrhythmia or slow sinus rhythm are more typical of chronic respiratory disease than of chronic CHF. Dogs with respiratory disease are more likely to be somewhat overweight and have a bronchial pattern on thoracic radiographs. Thoracic radiography, airway cytology and culture, and bronchoscopy can usually establish the cause as respiratory. If required, refer the client to a cardiac specialist for a second opinion.

Treatment

Therapy of chronic valvular disease depends on the stage of disease and severity of clinical signs. Combination drug therapy and dietary management is indicated once CHF has developed. Surgical repair or replacement of a cardiac valve is rare in veterinary practice. The aims of medical therapy are to control clinical signs of CHF, mitigate neurohormonal activation, reduce mitral regurgitant fraction, and prolong life. Diuretics, ACEIs, direct vasodilators, digoxin, pimobendan, pulmonary medications, and dietary measures may be prescribed at various times during the course of the disease. Anti-arrhythmic drugs are required in selected dogs, especially those with atrial fibrillation and serious ventricular arrhythmias. Atrial fibrillation is usually managed with digoxin combined with either a beta-blocker or calcium channel blocker (see Chapter 145). The clinical pharmacology of these cardiac medications is reviewed in Chapter 146. Specific management strategies for the hospital and home treatment of heart failure are discussed in Chapter 147 and summarized in this section. The following is a summary of general therapeutic approaches.

The Asymptomatic Dog

- The ideal approach to the management of the asymptomatic dog has not been determined. While ACEI use is still a subject of some debate, the two published clinical trials examining their use in asymptomatic dogs have failed to demonstrate appreciable clinical benefit.
- Some clinicians withhold all therapy until there are objective signs of CHF. Others prefer to prescribe an ACEI, empirically, if there is concurrent systemic

hypertension or evidence of marked cardiomegaly or clearly progressive disease on radiographs or echocardiography.
- There is no evidence that early enforcement of a very low sodium-restricted diet is of benefit. Early diuretic use and/or severe salt restriction activate the renin-angiotensin-aldosterone system and may be counterproductive. Moderation of sodium intake is often recommended at this stage, especially limitation of high sodium treats.

Coughing in the Dog with Mitral Regurgitation

- A harsh cough is often the initial clinical sign of advanced MR. Coughing is a frequent complication of left bronchial compression, a condition that often precedes the onset of overt pulmonary edema. The lack of clear-cut clinical or radiographic evidence of pulmonary edema in the dog with a mitral murmur and cough complicates determination of the cause of cough. Many dogs exercise well (except for an exertional cough) and sleep comfortably without tachypnea. It is unlikely that these dogs have overt CHF unless transient bouts of pulmonary edema develop with exertion.
- The best therapeutic approach to bronchial compression is unresolved.
  - One approach is prescription of an ACEI, possibly combined with a once daily diuretic. Such therapy can decrease cardiac size and blood pressure, which in turn may decrease regurgitant fraction. This therapy also is likely to mitigate transient, exercise-induced pulmonary edema and to delay the onset of more overt signs of CHF.
  - If the cough continues, medications effective for primary airway disease may be helpful. This can include a cough suppressant (butorphanol 0.55 mg/kg, PO, q8–12h or hydrocodone 0.22 mg/kg, PO, q8–12h). An empiric course of a theophylline salt can be tried (10–20 mg/kg of a sustained release preparation, PO, q12h; beware of excitement as a side effect). This should be discontinued if a clear response is not evident within 2 weeks. In dogs with suspected concurrent respiratory disease, consider a brief course of prednisolone (0.5 mg/kg daily for 5–7 days) to reduce inflammation and break the coughing cycle.

Hospital Treatment of Left-Sided CHF

- Once CHF has developed, the initial course of management is based on the severity of clinical signs of pulmonary edema. Initial therapy generally includes cage rest, oxygen if required, and furosemide (2–4 mg/kg, q6–q12h, IV or IM). Some clinicians also add nitroglycerin paste ($\frac{1}{2}$ to 1-$\frac{1}{2}$ inches cutaneously q8–12h) as a venodilator. Others administer aminophylline (10 mg/kg, q8h) if there is a concern about bronchospasm. The efficacy of bronchodilators has not been established, and they may induce tachycardia, arrhythmia, or anxiety in some dogs.
- Moderate to large volume pleural effusion should be removed by thoracentesis. Dogs with concurrent respiratory distress and large volume ascites may benefit from abdominocentesis.
- Life-threatening pulmonary edema requires more aggressive treatment beyond oxygen and high-dose furosemide (also see Chapter 147). Consider a constant rate IV infusion of furosemide. Drugs that reduce left ventricular afterload should be administered unless the patient is hypotensive. The direct arterial vasodilator, hydralazine (1–2 mg/kg, PO), or IV administration of sodium nitroprusside (1–5 µg/kg/min) will promptly lower blood pressure and LV load. Administration of an ACEI such as enalapril (0.5 mg/kg, PO) also reduces load, but the onset of action is slower.
  - The dose of these vasodilators should be titrated to a systolic arterial blood pressure of 85–95 mmHg. Aggressive afterload reduction significantly decreases the mitral regurgitant fraction. Such therapy is especially important in cases of peracute regurgitation caused by ruptured mitral valve chordae tendineae.
- Some patients in severe CHF exhibit marked anxiety and air hunger. Treatment with morphine may be useful if it does not induce vomiting (0.1 mg/kg, administer 25% IM; administer the balance SC 15 minutes later). Alternatively, consider subcutaneous administration of acepromazine (0.025 mg/kg) mixed with buprenorphine (0.005 mg/kg). Some clinicians find that butorphanol (0.25 mg/kg, IM) is an effective sedative with the advantage of not inducing vomiting.

Home Therapy of Left-Sided CHF

- Chronic therapy of heart failure caused by mitral valvular disease includes a maintenance dose of furosemide (2–5 mg/kg, q8–24h), an ACEI such as enalapril or benazepril (0.5 mg/kg, PO, q12–24h), and dietary sodium restriction. Titrate the daily doses of furosemide and the ACEI to clinical signs, objective measures of fluid accumulation, arterial blood pressure (to maintain a systolic pressure of 90–120 mm Hg), and renal function. Reduce dosages if hypotension or progressive azotemia develops. Pimobendan, a potent inotropic drug with vasodilating properties (see Chapter 146), has not been approved in the United States at the time of writing; however, it is available in many countries and represents a valuable drug for management of dogs with CHF due to MR.
- Digoxin also is prescribed by many cardiologists. Use an initial conservative dose (0.005 mg/kg, q12h), and adjust based on serum digoxin concentrations (target is 0.8–1.2 ng/ml at a 10–12 hour trough).

- Atrial fibrillation or frequent atrial ectopic beats represent clear indications for digitalization. Once CHF is controlled and digoxin has been initiated, co-therapy with a beta-blocker or diltiazem may be required to attain better ventricular rate control.
- Digoxin also may be useful to reduce syncopal episodes in dogs where no clear clinical cause for syncope can be established. Digoxin is contraindicated in the setting of complicated ventricular rhythm disturbances or ventricular tachycardia.

▼ ***Key Point*** Combination therapy is preferred in the management of CHF. Monotherapy with a diuretic or a diuretic and sodium-restricted diet is no longer considered appropriate treatment for most dogs because volume depletion activates the renin-angiotensin-aldosterone system.

- Treat progressive or refractory pulmonary edema first by optimizing current therapy. Should q12h ACEI therapy, q8h doses of furosemide, and pimobendan (where available) fail to control this problem, consider adding another vasodilator, digoxin, or a second diuretic.
  - Combination therapy with an ACEI and hydralazine (0.5–1 mg/kg, PO, q12h) or amlodipine (0.05–0.2 mg/kg, PO, q24h daily) can more effectively reduce the mitral regurgitant fraction. Such treatments are best initiated in the hospital, where arterial blood pressure can be monitored frequently. Many dogs can tolerate a systolic blood pressure as low as 80–85 mm Hg initially without overt clinical signs of hypotension, allowing time for further adaptive responses. Blood pressure in this 80–85 mmHg range during chronic management of CHF is sometimes associated with lethargy or weakness. A second vasodilator is also critical in dogs with MR and concurrent systemic hypertension despite full ACEI and diuretic therapy. Amlodipine, hydralazine, carvedilol, or compounded prazosin may be effective for individual patients (Chapter 153).
  - An alternative approach to progressive CHF is the addition of another diuretic, which is described in a following section.

Treatment of Right-Sided Congestive Heart Failure

- Right-sided CHF with ascites or biventricular CHF with pleural effusion is more likely to occur in dogs in which pulmonary hypertension, tricuspid regurgitation, or atrial fibrillation. Pulmonary hypertension usually is a consequence to chronic elevation in left atrial pressure or pulmonary vascular narrowing secondary to chronic CHF or primary lung disease.
- When right-sided CHF dominates the clinical picture, it is not uncommon to notice a reduction of dyspnea and an increase in exercise intolerance. Radiography often demonstrates minimal pulmonary edema, whereas Doppler echocardiography may show signs of pulmonary hypertension, such as high-velocity tricuspid regurgitation.
- Management of dogs with a prominent component of right-sided CHF includes treatment with an ACEI (q12h), furosemide (q8h), pimobendan (if available), and a restricted sodium diet. Digoxin is also useful to control fluid accumulation in many dogs. Should these methods fail then a variety of other strategies can be attempted. Initially, the dog may be hospitalized, treated with subcutaneous furosemide (or other loop diuretic), and receive judicious paracentesis for tense ascites (removing between $\frac{1}{4}$ to $\frac{1}{2}$ of the fluid accumulation). Treat atrial fibrillation if present. Two or 3 days of enforced cage rest and parenteral diuretic therapy may alleviate most of the retained fluid. At that point, treatment strategies can include any (or all) or the following:
  - Markedly increasing the oral dose of furosemide to effect (because poor absorption of the medication may be partially responsible for the refractory ascites).
  - Using flexible subcutaneous diuretic dosing (having the client substitute a subcutaneous dose of furosemide for the usual oral dose).
  - Adding spironolactone (2 mg/kg, PO, q12 to 24h) or another potassium-sparing diuretic to the regimen.
  - Adding hydrochlorothiazide and spironolactone (2–4 mg/kg, PO, q12–24h of the combined product) to the regimen. This approach is especially aggressive because electrolyte reabsorption is blocked at sequential points along the nephron. Accordingly, the potential for volume depletion and electrolyte disturbances is very high and must be monitored carefully (reevaluate the patient, blood pressure, and serum biochemistries at 3 days, 7 days, and 14 days after starting this treatment).
- Pleural effusion in valvular heart disease is often a poor prognostic sign. A neoplastic cause for the effusion should be excluded, and treatment of pleural effusion due to CHF is as discussed previously for right-sided heart failure. Periodic thoracocentesis may be required.

Other Respiratory Complications in Advanced MR

- A persistent, nonresponsive cough in animals with otherwise well-controlled CHF can be a vexing problem. Bronchial compression or intercurrent airway disease may be the culprit in many of these cases. Provided there is no radiographic evidence of pulmonary edema, it is reasonable to continue the current cardiac medications and to add a cough suppressant, such as hydrocodone or butorphanol, or even a brief course of prednisolone, to control the cough.

- In other dogs, signs develop that suggest accelerated pulmonary fibrosis. These dogs have exercise intolerance, some may faint, and some are persistently tachypneic but generally sleep well without any resting dyspnea. Auscultation reveals diffuse inspiratory crackles that might be easily confused with those caused by pulmonary edema. Hypoxemia and pulmonary hypertension may be present, however radiography indicates "clear" lung fields or minimal interstitial density despite marked cardiomegaly. Escalation of diuretic or vasodilator therapy often does not improve the respiratory signs and may predispose the animal to syncope by reducing blood pressure.
- Other reasons for persistent respiratory signs in dogs with MR include tracheal collapse, chronic bronchitis, pulmonary neoplasia, pneumonia, and recurrent pulmonary thromboembolism.

Patient Follow-Up

Follow-up examinations and complications are described in Chapter 147. In general, a repeat examination should be performed 5 to 10 days after initiation of CHF therapy. Testing at the recheck should include historical and physical examination, blood pressure, evaluation of serum BUN, creatinine and electrolytes, and possibly thoracic radiographs. In dogs with stable CHF, follow-up examinations every 2 to 4 months are recommended to titrate therapy and insure owner compliance.

Prognosis

The prognosis for longevity is highly variable. Dogs with heart murmurs but without clinical signs of heart disease may survive for many years and often succumb from a non-cardiac disorder. Clinical signs associated with bronchial compression indicate that sufficient volume overload has developed to compress the airways, but this alone is not an indication of CHF. Once *overt* pulmonary edema or ascites develops, the prognosis for life becomes guarded. Assuming initial stabilization is successful, a survival range of between 3 months and 2 years should be discussed with the client. With good veterinary and home care and a dedicated client, many dogs live for 9 to 12 months or longer before spontaneous death or euthanasia.

BACTERIAL (INFECTIVE) ENDOCARDITIS

Bacterial endocarditis (BE) is a bacterial infection of the valvular or mural endocardium. The mitral and aortic valves are the most common sites of cardiac bacterial infection in dogs and cats. Establishment of a cardiac infection requires a portal of bacterial entry into the circulation, subsequent bacteremia, and colonization of the endocardium. In most cases, bacterial endocarditis is manifested as a multisystemic disorder, and cardiac disease might not be the leading differential diagnosis. In order to diagnose this disease the clinician must maintain a high index of suspicion in animals with multisystemic clinical signs, especially when the differential diagnoses include serious infection or immune mediated disease.

Etiology

- Pathogenic bacteria identified in dogs and cats with bacterial endocarditis include streptococci, staphylococci, corynebacteria, *Escherichia coli, Enterobacter aerogenes,* and *Pseudomonas, Pasteurella, Erysipelothrix,* and *Bartonella* spp. Many of these bacteria are normal inhabitants of the skin, oral cavity, and respiratory and intestinal tracts. Bartonellosis is discussed in Chapter 19.
- Bacteria can gain access to the circulation via external wounds, established infections, and a variety of surgical procedures and invasive medical interventions; however, in many cases, there is no evidence of these sources. Endocarditis may be a sequela to septic arthritis, osteomyelitis, prostatitis, infected catheters, and other infections.
- Immunosuppressive drugs (e.g., corticosteroids, anticancer chemotherapy) also predispose to infection.
- Injudicious use of antibiotics may predispose to infection by resistant or virulent organisms.

Pathogenesis

- The pathogenesis of infective endocarditis involves entry of bacteria into the circulation and invasion of the valve endocardium by direct extension from the bloodstream.
  - Virulent bacteria may attach themselves to the valve surface, ulcerate the endocardium, and invade the valve stroma.
  - Previously diseased valves are believed to be more susceptible, particularly when the endocardium is disrupted. Dogs with subaortic stenosis are at increased risk for endocarditis, presumably because of jet lesions on the aortic valve. Conversely, for uncertain reasons, dogs with endocardiosis are rarely affected with BE.
  - High titers of agglutinating antibodies that cause clumping of bacteria, thereby increasing the size of the infectious inoculum, are thought to play a role in some cases.
- Collagen is exposed once micro-organisms colonize and ulcerate the endocardium, causing platelet aggregation and the local accumulation of fibrin.
  - Vegetations resembling thrombi form on the valve surface. These vary in color from yellowish red to gray and are covered by a thin layer of clotted blood.
  - Lesions usually are localized to the valve but can extend to the mural endocardium, chordae tendineae (causing rupture), or sinuses of Valsalva

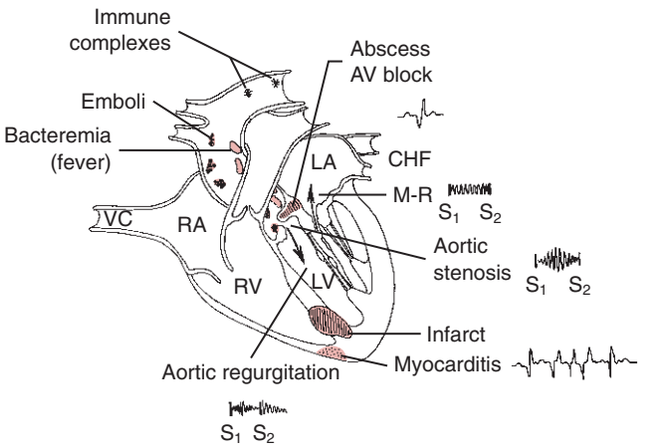

Figure 149-2. Diagrammatic representation of endocarditis. Consult the text for an explanation of abbreviations and symbols.

(this may hasten the spread of septic foci via the coronary arteries to the myocardium).

- Chronic valvular infections are established when layers of fibrin are deposited repeatedly at the site of infection, "protecting" the bacterial colonies from host responses and from many antibacterial agents.
- Deformation of the valve usually results in *valvular insufficiency*. Exuberant vegetation or fibrotic healing may form in such a way as to produce valve stenosis, but this is less common.
- Parts of the vegetation may break off, seeding the various tributaries of the systemic circulation, including the coronary arteries.
  - Intermittent bacteremia causes persistent or recurrent fever.
  - Thromboemboli, which can be septic or "bland" (aseptic), can also be shed from the infected valve.
- Formation of immune complexes is an important host response; these may be filtered into the joints, kidneys, or other tissues; attract complement and leukocytes; and cause inflammation in these tissues.

Pathophysiology

The clinical signs of infective endocarditis result from cardiac injury, bacteremia and sepsis, thromboembolic complications, and immune-mediated processes (Fig. 149-2).

Cardiac Injury

A variety of cardiac manifestations are possible, including

- Mitral and aortic valvular regurgitation.
- Valvular stenosis (less common).
- Coronary occlusion with myocardial infarction.
- Secondary myocardial invasion, causing myocarditis or myocardial abscessation.
- Pericarditis.
- Left-sided CHF (from advanced valvular injury).
- Arrhythmia.
  - Ventricular and supraventricular arrhythmias may be related to endomyocarditis, myocardial infarction from bland thrombi, cardiac dilation, or "toxemia." Extension of aortic root abscesses into the conduction system can cause AV block.

Bacteremia and Metastatic Infection

- Bacteremia causes fever, shivering, malaise, and anorexia.
- Other tissues may be seeded, resulting in brain abscesses, splenitis, osteomyelitis, septic arthritis, pyelonephritis, myositis, or other remote infections.
- In advanced cases, it is difficult to distinguish a primary infection (portal of entry) from a metastatic infection.
- Bacteremia and sepsis may be associated with disseminated intravascular coagulopathy (DIC) and lead to death from septic shock or organ failure.

Immune-Mediated Disease

Immune complexes may form and be trapped in many organs or tissues, with the following effects:

- The kidneys, leading to glomerulonephritis
- The brain and meninges, causing meningoencephalitis
- The joints, causing polyarthritis
- The skeletal muscles, causing myositis and myalgia
- The small blood vessels, leading to vasculitis, thrombosis, or hemorrhage
- The eye, leading to chorioretinitis

▼ ***Key Point*** Do not confuse the clinical findings seen in endocarditis of recurrent fever, multisystemic involvement, polyarthritis, and DIC with those of primary immunologic or neoplastic diseases; such an assumption may prompt inappropriate therapy with corticosteroids.

Thromboembolic Complications

Septic or bland (sterile) thrombi derived from the vegetation may be carried to distant tissues. Consequences include

- Myocardial infarction and myocarditis.
- Renal infarcts, abscess, pyelonephritis, and glomerulonephritis.
- Stroke, meningitis, and encephalitis.
- Bone infarcts and osteomyelitis.
- Vascular obstruction including aortic-iliac occlusion.
- Splenic infarcts.
- Intestinal ischemia.

Because of the low incidence of right-sided endocarditis in small animals, pulmonary embolism and pneumonia are rare. The notable exceptions are BE secondary to infection from patent ductus arteriosus

surgery and infection of a central venous catheter, dialysis catheter, or transvenous pacing lead.

Clinical Signs and Diagnosis

Signalment

Endocarditis is more common in certain large-breed male dogs (e.g., German shepherds) and in dogs with congenital subaortic stenosis.

History

- The history may suggest previous or concurrent infection (especially of the skin, oral cavity, gut, bone, or urogenital tract).
- Certain diagnostic and therapeutic procedures predispose to BE by causing bacteremia (e.g., surgical implants, endoscopy, and dental extractions).
- Persistent use of corticosteroids or antineoplastic drugs or improper use of antibiotics may predispose to BE.

Physical Examination

Physical examination findings may include

- Fever which may or may not be antibiotic-responsive, depression, anorexia, and shaking "chills."
- Polyarthritis (shifting lameness) with or without joint effusion and myalgia.
- Signs of vasculitis with hemorrhages (skin, eye, mucous membranes).
- Multifocal neurological deficits from meningitis or encephalitis.
- Signs of cardiac injury:
  - A cardiac murmur, particularly a "new" or changing murmur.
  - BE destroys portions of the valve; therefore, regurgitant murmurs (MR, aortic regurgitation) usually are present in dogs and cats with BE. A systolic ejection murmur often accompanies the diastolic murmur of aortic insufficiency due to increased LV stroke volume. Large vegetation(s) on the valves also may contribute to valve stenosis murmurs.
  - The pulse pressure increases with aortic insufficiency, which causes hyperkinetic femoral pulses with rapid run-off of diastolic pressure. Always consider BE when aortic regurgitation, which is uncommon in dogs and cats, is present.
  - Signs of overt left-sided CHF or arrhythmias (especially ventricular premature complexes) may develop from cardiac injury.

Laboratory Tests

Complete Blood Count (CBC)

Mild anemia and leukocytosis with neutrophilia and monocytosis may be present. Thrombocytopenia is often present, and red blood cell (RBC) fragments may suggest vasculitis (see Chapter 153) or DIC.

Serum Biochemistries

Biochemical alterations may reflect organ injury from infection, thrombosis, infarction, or poor perfusion from heart failure. Azotemia or liver enzyme elevations are often present, and elevation of serum alkaline phosphatase is common in dogs with gram negative infections. Hyperglycemia or hypoglycemia, hypoalbuminemia, and elevated bilirubin can also be noted.

Tests for Autoimmune Disease

Rheumatoid factor test, Coombs' test, or antinuclear antibody (ANA) assays can be positive in patients with BE.

Blood Cultures

Two or more positive blood cultures, obtained from a patient with compatible clinical signs, strongly suggest BE.

- Cultures are most rewarding if taken near febrile bouts when the animal is not receiving antibiotics. Cultures may be positive before, during, or after bouts of fever.
- Serial positive blood samples, taken 1 to 2 hours apart from different sites, help to rule out the possibility of skin contamination. (Aseptically prepare the skin before obtaining the sample.)
- Transfer sufficient blood (5–10 ml) into special broth media tubes (usual blood:medium ratio of 1:10). Aerobic and anaerobic culture and sensitivity are indicated. Special antibiotic adsorbing media are available for patients who have received antibiotic therapy.
- Some microorganisms are difficult to culture (e.g., *Bartonella* spp.), leading to so-called "culture-negative" endocarditis. Serologic testing and/or PCR testing can help establish a diagnosis of *Bartonella* in these cases. Dogs with culture negative endocarditis, especially those with aortic valve disease, should be suspected of having *Bartonella* (see Chapter 19).
- If a primary source of infection is suspected then cultures should be obtained from this location (i.e., urine culture, bone culture in suspected osteomyelitis, etc.).

Urinalysis

Hematuria, proteinuria, pyuria, or casts may be shown if pyelonephritis or glomerulitis is present. Culture the urine if there are any abnormalities, but do not automatically assume that organisms cultured from urine are responsible for the cardiac infection.

Cardiac Studies

Cardiac studies may substantiate the diagnosis and indicate the degree of cardiac injury. Serial studies after successful antimicrobial therapy are useful,

although complete resolution of valvular pathology is uncommon.

- Radiographs may indicate cardiomegaly, valve calcification (from chronic BE), CHF, or (rarely) embolic pneumonia.
- Electrocardiograms can be normal, but they may indicate chamber enlargement or arrhythmias (most often ventricular premature contractions).
  - ST-T changes, indicating ischemia or infarction, may be present (check precordial leads for these).
  - AV block in endocarditis likely indicates aortic valve involvement with a perivalvular inflammation affecting the bundle of His.
- Echocardiography is useful, especially for diagnosis and prognosis.
  - Routine 2-D or M-mode echocardiography may demonstrate a recent vegetation (oscillating thrombus) or more chronic lesion (thick, hyperechoic valve). Echocardiography is also helpful for identifying hemodynamic overload (cardiomegaly). A negative examination of the valves does not rule out BE.
  - Echocardiography alone may not be sufficient to distinguish mitral BE from advanced mitral endocardiosis.
  - Doppler studies can document both abnormal valvular regurgitation and stenosis. Hemodynamically significant aortic regurgitation is associated with an adverse outcome.
- Progressive cardiomegaly demonstrated by echocardiography or radiography indicates clinically significant valvular injury and is a poor prognostic finding.

Other Studies

Other studies may be abnormal depending on the organ involved. *Cerebrospinal fluid (CSF)* and *joint fluid* cytology and culture may show evidence of septic or aseptic (immune complex) suppurative inflammation.

Treatment

Consider the following principles:

- Use bactericidal antibiotics. Because the bacteria are sequestered within the vegetation, normal defense and healing processes (e.g., granulation) are impeded.
- Because the drug must penetrate fibrin, do not use most sulfa drugs.
- Long-term (1–3 months) therapy is needed to ensure sterilization of the vegetation.
- Ideally, use IV therapy to obtain the highest possible plasma concentrations for the first 5 to 7 days. (This is sometimes impractical.)
- Guide antibiotic therapy by blood cultures. It is appropriate to delay antibiotic therapy for 2 to 4 hours while blood cultures are being obtained, unless the patient is demonstrating signs of septic shock.
- Empirical therapy for BE often includes the following drugs:
  - Penicillins (high doses) are safe and useful for streptococcal infections but have limited efficacy against many staph and other microorganisms.
  - Aminoglycosides, combined with a synthetic penicillin or cephalosporin, provide wider antimicrobial coverage. Use of these drugs requires good patient hydration and careful monitoring for nephrotoxicity. Aminoglycosides should be withheld from animals with concurrent CHF that require furosemide administration.
  - A patient with renal failure may be treated with a newer-generation cephalosporin in lieu of an aminoglycoside.
  - In cases of suspected *Bartonella*, a combination of gentamicin (for 15 days) and doxycycline is recommended, with careful monitoring for nephrotoxicity. Azithromycin, 5 to 10 mg/kg q24h for the first 7 days, then every other day for 6 to 12 weeks, represents another approach to treating patients with confirmed *Bartonella* infection.
- Treat for at least 4 weeks (at least 10–14 days when using an aminoglycoside, with continuation of the penicillin or cephalosporin for the full 4 weeks). Some cardiologists recommend treatment for 6 to 8 weeks. Repeat blood cultures following discontinuation of therapy or if fever should recur.
- If left-sided CHF develops, treat according to guidelines described above for valvular endocardiosis. Remember that vasodilator therapy is contraindicated for dogs with septic shock.
- Use prophylactic antibiotics if the patient undergoes any procedure that may cause bacteremia. (The general subject of prophylactic therapy of BE is unresolved, and no firm recommendations can be made.)

Prognosis

The prognosis for BE is guarded. Negative prognostic predictors include large vegetations with accompanying marked cardiomegaly, CHF, marked aortic regurgitation, gram-negative infections, elevation of serum alkaline phosphatase or hypoalbuminemia, treatment with corticosteroids, delayed diagnosis or treatment with bacteriostatic antibiotics, and premature termination of antibiotics.

- Acute, ulcerative BE may cause dramatic clinical signs but, if promptly treated, may leave only mild cardiac dysfunction.
- Chronic BE with severe valvular destruction is more difficult to treat because severe CHF may develop.
- Echocardiographic evidence of diffuse, large vegetative lesions and documentation of volume overload imply a poor prognosis. The likelihood of CHF is high in these instances.

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Chapter

150 Cardiomyopathy

John D. Bonagura / Linda B. Lehmkuhl

OVERVIEW

The left and right ventricles are capable of undergoing significant morphologic change in response to stresses and stimuli. Reaction to increased volume or pressure work frequently leads to chamber dilatation and hypertrophy, along with alterations in the cytoskeletal matrix of the ventricle. Myocardial and chamber responses develop with chronic valvular heart disease, cardiac shunts, systemic and pulmonary hypertension, thyrotoxicosis, and chronic anemia. These responses to stress are directed by various neural, hormonal, and genetic messages acting on the myocardium. These signals influence genetic expression in the cardiomyocyte and interstitial cells, and remodel the ventricle.

"Cardiomyopathy" refers to disease of the myocardium and, by extension, the cardiomyocyte and the supporting collagen and interstitial matrix. Idiopathic or primary cardiomyopathies are those that cannot be explained by a malformation, acquired cardiac lesion, dysrhythmia, or coronary artery disease. Many idiopathic cardiomyopathies are genetic diseases. A more expansive definition of cardiomyopathy accepts that some myocardial diseases can be explained by other disorders, and in such cases, the term *secondary cardiomyopathy* can be used. When myocardial failure develops from chronic volume or pressure overload of the ventricle, the term *cardiomyopathy of overload* has been proposed to explain the remodeling associated with increased ventricular work.

Although there are many known causes of cardiomyopathy, most cases in cats and dogs are idiopathic and thought to represent a genetic disorder. This is particularly true of dilated cardiomyopathy in dogs and hypertrophic cardiomyopathy in cats. What stimulates these genetic factors to cause heart muscle disease is poorly understood, and most cases of cardiomyopathy are irreversible and progressive. But there are special examples that demonstrate that some cardiomyopathic states can be postponed, arrested, or even reversed. For example:

- Chronic tachyarrhythmias cause a cardiomyopathy with loss of myocardial contractility that is reversible if the arrhythmia is resolved.
- Taurine deficiency in cats is a classic example of a reversible dilated cardiomyopathy.
- Regression of left ventricular hypertrophy may occur after successful treatment of systemic hypertension or hyperthyroidism.

Cardiomyopathies often are classified by the postmortem anatomic appearance of the left (or right) ventricle and by the correlative echocardiographic features of ventricular anatomy and function. The most important forms of cardiomyopathy can be classified as follows (see Table 150-1):

- ***Myocarditis*—**An inflammation of the heart muscle observed most often in cats. It may be responsible for premature ventricular complexes, sudden death, or progressive heart failure.
- ***Dilated cardiomyopathy (DCM)*—**A dilated, poorly contracting left ventricle (LV) usually associated with development of congestive heart failure (CHF), cardiac arrhythmias, and sudden death. DCM is a common disease of dogs but is very uncommon in cats.
- ***Hypertrophic cardiomyopathy (HCM)*—**A thickening of the LV walls of unknown or genetic cause and displaying considerable phenotypic heterogeneity. HCM is mainly a disorder of cats and often leads to cardiac murmurs, CHF, or thromboembolic disease.
- ***Restrictive cardiomyopathy (RCM)*—**A heterogeneous and poorly characterized disorder defined by extensive fibrosis in the LV. It is encountered mainly in mature or older cats and is a recognized cause of arrhythmias, CHF, and arterial thromboembolism.
- ***Right ventricular cardiomyopathy*—**A disorder that affects mainly (or initially) the right ventricle resulting in either CHF or ventricular arrhythmias.
- ***Unclassified cardiomyopathy*—**Primary LV diseases that are not easily classified as HCM, DCM, or RCM. Some cases are probably related to myocardial infarction.
- ***Cardiotoxicity*—**The heart also can be damaged by a number of cardiotoxins, some of which are listed in Table 150-1. The outcome of cardiotoxicity is often an arrhythmia, conduction disturbance, sudden death, or development of a secondary dilated cardiomyopathy.

Table 150-1. CAUSES OF CARDIOMYOPATHY (CM)

Disorder*	Feline	Canine
Myocarditis		
Noninfective	Idiopathic	Idiopathic
	Thymoma (immune-mediated)	Trauma
Infective	Toxoplasmosis	Bacterial
	Feline infectious peritonitis?	Parvovirus
		Distemper virus
		Systemic mycoses
		Lyme carditis (*Borrelia*)
		Chagas disease (*Trypanosoma cruzi*)
Dilated CM (DCM)‡	Taurine deficiency	Idiopathic†
	Idiopathic	Carnitine or Taurine deficiency
	Potassium iodide toxicity	Breed-"specific" DCM†
	Hyperthyroidism	Doberman pinscher
	Sustained ventricular or supraventricular tachycardia	Boxer dog
		Cocker spaniel
	Chronic hypokalemia (causes taurine deficiency?)	"Giant" purebred dogs
		Springer spaniel muscular dystrophy
		Sustained ventricular or supraventricular tachycardia
Hypertrophic CM	Idiopathic† (familial?)	Idiopathic
Left ventricular concentric hypertrophy	Acromegaly (rare)	Hypertension
	Hypertension†	Hyperthyroidism (iatrogenic)
	Hyperthyroidism†	
Restrictive-intermediate CM	Idiopathic*	
Arrhythmogenic right ventricular cardiomyopathy	Idiopathic	Boxer dog (genetic)†
		English bulldog (genetic?)†
Cardiotoxicity	Sodium iodide	Catecholamines including brain-heart syndrome and pheochromocytoma
		Doxorubicin
		Digitalis purpurea (foxglove) and *Strophanthus* spp.
		Toad (*Bufo*) toxicity
		Chocolate toxicity

*Both primary (idiopathic) and secondary causes of cardiomyopathy are considered here.
†Most important types.
‡Also see infective and noninfective myocarditis because DCM can develop secondary to severe inflammatory disease.

This chapter will next describe the clinical features of feline cardiomyopathies and the therapy of related complications. Following this is a consideration of canine DCM and arrhythmogenic cardiomyopathy.

FELINE HYPERTROPHIC CARDIOMYOPATHY

Overview and Pathophysiology of Feline HCM

- Feline idiopathic HCM is characterized by hypertrophy and thickening of the left ventricle unexplained by congenital heart disease, systemic hypertension, or an endocrinopathy.
- The condition is genetic in a number of feline breeds, including the Maine coon cat, Persian cat, and the Ragdoll. Thus far, one sarcomeric mutation has been identified.
- The pattern of ventricular hypertrophy in this disease is variable as demonstrated at necropsy or by 2D echocardiography.
  - Symmetrical concentric hypertrophy of the LV walls and papillary muscles is considered typical of feline HCM, but there is substantial variation in the location and severity of hypertrophy in this disease.
  - The main histologic finding is of myocardial cell hypertrophy with fiber disarray. Small, intramural coronary arteries are often narrowed. Microscopically, there is fibrosis between myocytes. Focal areas of infarction or inflammation may be observed.
  - The left atrium (LA) is usually dilated and the wall may be hypertrophied from increased pressures needed to fill the LV. Atrial or auricular clots are found attached to the chamber wall in some cases.
- The natural history of untreated feline HCM is quite variable following a benign or lethal course; a brief or protracted clinical disease; and sometimes remarkable recovery from life-threatening complications. Some cats remain asymptomatic for many years before succumbing (if ever) to the disease.
- Clinical signs in HCM are explained by left-sided CHF, complications of arterial thromboembolism (ATE), LV outflow tract obstruction, or arrhythmias capable of causing syncope or sudden cardiac death.
- The differential diagnosis for the clinical signs of HCM in cats is extensive (Tables 150-2 and 150-3),

Table 150-2. DIFFERENTIAL DIAGNOSIS OF FELINE CARDIOMYOPATHY AND HEART FAILURE*

Other Causes of Dyspnea/Tachypnea
Airway obstruction
Nasopharyngeal polyp
Laryngeal paresis
Tracheal or esophageal foreign body, neoplasm, granuloma, abscess
Mediastinal masses
Lymphoma or thymoma
Primary bronchopulmonary disease
Bronchial asthma/bronchitis
Lungworms and lung flukes
Pneumonia (viral, bacterial, fungal, toxoplasmic)
Neoplasia
Aspiration
Pulmonary vascular disease/embolism
Heartworms/spontaneous worm death
Noncardiogenic pulmonary edema
Electrocution
Trauma (shock lung)
Anaphylaxis
Trauma
Diaphragmatic hernia
Pulmonary hemorrhage/edema
Pneumothorax
Hemothorax
Pleural effusion
Pyothorax
Hemothorax
Feline infectious peritonitis (FIP)
Lymphoma-associated effusion
Chylothorax
Hyperthermia/fever
Anemia
Methemoglobinemia
Acetaminophen toxicity
Cetacaine
Abnormal ventilatory pattern
Metabolic acidosis
Central nervous system disease
Other Causes of Acute Lameness/Paresis/Gait Abnormality
Musculoskeletal pain or injury
Bite wounds
Hypokalemia (weakness)
Peripheral neuropathy
Related to diabetes mellitus
Spinal cord disease
Injury
Neoplasia
FIP infection
Extradural mass/granuloma
Urinary obstruction
Causing abdominal pain and reluctance to move
Other Causes of Cardiac Murmurs/Gallops/Arrhythmias/ Cardiomegaly
Congenital heart disease
Especially spetal defects and mitral valve dysplasia
Congenital peritoneopericardial-diaphragmatic hernia
Bacterial endocarditis
Pericarditis
FIP infection
Idiopathic
Bacterial
Neoplastic
Lymphoma
Mesothelioma
Cardiac neoplasia
Lymphoma
Cor pulmonale
Heartworms
Severe chronic respiratory disease
Chronic degenerative valvular disease (mitral, aortic)
Dilation of the aortic root with aortic regurgitation
Cardiac arrhythmias (primary electrical disturbances)
Chronic bradyarrhythmias
Atrioventricular block in aged cats
Tachyarrhythmias and premature complexes
Sedatives, tranquilizers, anesthetic drugs
Chronic or severe anemia
Hyperthyroidism
Acromegaly
Systemic hypertension
Chronic renal disease
Hyperthyroidism
Idiopathic
Electrolyte abnormalities
Hyperkalemia
Urinary obstruction
Hypokalemia
Renal disease

*The most common clinical presentations of feline cardiomyopathy are dyspnea from congestive heart failure, rear-limb paresis from aortic thromboembolism and inactivity. The veterinarian often detects a murmur, gallop rhythm, arrhythmia, or cardiomegaly during examination.

and includes congenital heart disease, myocarditis, and other forms of primary cardiomyopathy (RCM, DCM). When an echocardiogram demonstrates thickening of the LV, specific disorders causing LV hypertrophy must be excluded including

- Mitral valve malformation causing dynamic obstruction of the LV outflow tract with secondary hypertrophy.
- Congenital aortic or subaortic stenosis.
- Hyperthyroid heart disease (thyrotoxicosis).
- Hypertensive heart disease.
- Focal basilar septal hypertrophy associated with aortic dilatation (aortoannular ectasia).
- Acromegaly (growth hormone excess).

- The *pathophysiology* of feline HCM (Figure 150-1) is relevant to the diagnosis and drug therapy of this disease. The presumptive cause of CHF is ventricular diastolic dysfunction, because most cats with HCM have a normal to hyperdynamic LV ejection fraction.
  - Diastolic dysfunction is the inability to fill the left ventricle with normal LA pressures.
  - Early diastolic dysfunction is characterized by abnormal myocardial relaxation with a vigorous LA contraction to support late diastolic filling. This situation is associated with the atrial (S4) gallop so often detected in these cats.
  - Progressive ventricular disease is associated with reduced chamber compliance with loss of passive

Table 150-3. COMMON FELINE CARDIAC DISEASES

Disorder	Necropsy and Echo (Anatomic Diagnosis)	Typical Clinical Problems	Etiologic diagnosis
Pericardial effusion and pericardial disease	• Peritoneopericardial diaphragmatic hernia (PPDH) • Secondary to CHF • Infection (including FIP) secondary to infection • Neoplastic related (LSA) • Echo: echo-free space around heart; +/− mass lesions; often observe *left*-sided cardiomyopathy; Liver and fat in PPDH	• Unexplained cardiomegaly (PPDH) • CHF as a cause of PE • CHF as consequence of PE and cardiac tamponade • Systemic illness (infection, neoplasia)	• Congenital (?genetic)—PPDH • Infectious (coronavirus) • Lymphosarcoma • Immunosuppression (?)
Septal defects—VSD, ASD, ECD	• Ventricular or atrial septal defect • AV valve malformation (ECD) • Echo: above lesions with volume overload of affected chambers	• Systolic heart murmur • Cardiomegaly • CHF • Cyanosis (reversed shunt)	• Congenital • Genetic?
Dilated cardiomyopathy (DCM) *phenotype*	• Cardiac chamber dilatation (typically left sided chambers +/− right sided) • Echo: cardiac dilatation & loss of myocardial contractility	• CHF—left-sided; biventricular • Arterial thromboembolism • Arrhythmias • Sinus bradycardia • Hypotension • Soft heart sounds • Secondary AV valvular regurgitation	• Idiopathic DCM • Taurine deficiency DCM • Moderate to severe anemia • Fulminant myocarditis
Hypertrophic cardiomyopathy (HCM) *phenotype*	• Left ventricular hypertrophy that is concentric or regional • Focal septal LVH (aged cats; dilated aortic root) • Echo: LV hypertrophy; variable; possible LA dilation	• Abnormal auscultation: heart murmur, gallop, arrhythmia • Thyroid adenoma in cases of hyperthyroidism • Target organ injury: brain, eyes, kidneys, and heart in systemic hypertension	• *Primary* HCM: genetic or idiopathic cardiomyopathy
Restrictive cardiomyopathy *phenotype*	• Left ventricular endomyocardial fibrosis or myocardial fibrosis (multifocal or generalized) • LV wall infarction • Echo: Marked bi-atrial dilatation; variable LV anatomy, wall motion, and systolic function	• Abnormal auscultation: gallop, arrhythmia, heart murmur • CHF—biventricular • Chylothorax (from CHF) • Arterial thromboembolism • Arrhythmias • Sudden cardiac death	• Idiopathic RCM • Antecedent myocarditis • Chronic HCM with myocardial injury from coronary thromboembolism, coronary vascular disease, or neurohormonal injury
Unclassified or "Intergrade" cardiomyopathy	• Left ventricular myocardial disease with variable morphologic characteristics with Echo showing systolic and diastolic LV function	• CHF—left sided or biventricular • Arterial thromboembolism • Arrhythmias • Sudden cardiac death	• Prior HCM with progressive myocardial failure or infarction (?) • Myocarditis (?)
Congenital mitral valvular disease	• Mitral valve dysplasia (MV malformation; generally causes MR; rarely MS) • Echo: Mitral valve malformation; LA and LV dilatation	• Systolic heart murmur • Development of CHF	• Congenital • Genetic?
Heartworm disease	• Pulmonary vascular disease • Pulmonary thromboembolism, pneumonitis, and fibrosis • Aberrant infection • Echo: parasites in the PA	• Signs related to pulmonary disease (cough), vomiting • Dyspnea and lung infiltrates due to thromboembolism or spontaneous worm death • CHF—chylothorax (uncommon)	• Dirofilaria immitis—adult parasites found in the pulmonary arteries and heart
Arrhythmias: PACs, PVCs; AV block	Necropsy or Echo may demonstrate cardiac lesions but often there is no overt structural lesion	• Syncope • Sudden cardiac death • CHF	• Cardiomyopathy • Degeneration of conduction system • Metabolic disorders • Hypoxia

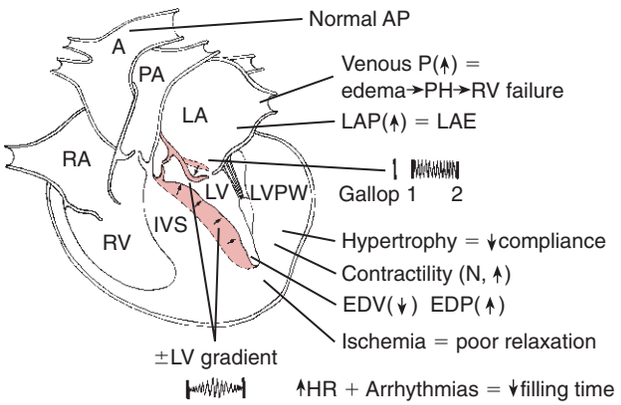

Figure 150-1. Diagrammatic representation of hypertrophic cardiomyopathy. Explanation of abbreviations can be found in text.

LV ventricular distensibility. Tissue injury and fibrosis increase myocardial and chamber stiffness, requiring elevated LA filling pressures. This creates a situation of rapid early diastolic filling that becomes restricted as the stiff ventricle is distended. This correlates to a ventricular (S3) or summation (S3+4) gallop.

- As the left atrium distends, a loss of atrial contractility may develop. This reduces filling effectiveness and also predisposes to stagnant flow, formation of atrial thrombi, and atrial fibrillation.
- The roles of myocardial ischemia, infarction, and neurohormonal activation in the pathogenesis of progressive tissue injury and cardiac dysfunction are possible therapeutic targets because β-blockers and angiotensin system inhibitors blunt these detrimental responses.
- Demand ischemia—the sudden increase in myocardial oxygen demand that outstrips coronary blood supply—may contribute to the sudden development of left-sided CHF (flash pulmonary edema) so often observed in stressed cats with HCM. Ischemia impairs myocardial filling and contraction. For this reason, drugs with anti-ischemic effects (atenolol, diltiazem) are often prescribed in this disease.
- Systolic abnormalities are identified in some cats with HCM. These include subtle abnormalities detected only by tissue Doppler echocardiography; identification of apical or free wall-infarcts; regional wall motion abnormalities; or rarely, a global loss of LV systolic function.
- Dynamic and labile pressure gradients between the LV and aorta are often identified during ejection across the LV outflow tract. In most cases, systolic gradients stem from either septal and papillary muscle hypertrophy (midventricular obstruction) or systolic anterior motion (SAM) of the mitral valve causing mitral septal contact. These abnormalities can be documented on high-quality echocardiographic studies. The presence of significant SAM is invariably associated with an eccentric jet of mitral regurgitation (MR), readily seen by color Doppler examination.
- Some chronic cases of HCM appear to evolve into a restrictive form of cardiomyopathy with either regional wall dysfunction (suggestive of myocardial infarction) or globally reduced LV systolic function (suggesting fibrosis or ischemia). Rarely, a cat will progress to a grossly dilated form of disease.

Clinical Findings in Feline HCM

The clinical presentation and examination findings in feline HCM are variable.

- Male cats are predisposed in some reports, and cats of any age, including young cats, may be affected. As previously noted, certain breeds are at genetic risk for this disease, and it is not uncommon to examine affected cats that are related.
- Most often, the idea of HCM is prompted by auscultation of a murmur or gallop sound in a cat that has no other signs of heart disease. Nonspecific signs such as lethargy or anorexia may be reported.

▼ ***Key Point*** Most cats with HCM are healthy and asymptomatic for the disease.

- When symptomatic for left-sided CHF, a cat will demonstrate tachypnea and dyspnea, signs attributable to pulmonary edema or pleural effusion. Cough can occur but is an inconsistent sign.
  - Stress, fever, moderate-to-severe anemia, thyrotoxicosis, anesthesia, surgical procedures, trauma, or fluid therapy may precipitate CHF in a previously stable cat.
  - Prior therapy with corticosteroids may be another risk factor, though cause and effect are not firmly established.
- Urgent presentation may follow ATE to the terminal aorta, a forelimb, or cerebrum.
- Syncope or sudden cardiac death can occur but are less common than in the human disease. Sudden death may be explained by a coronary embolus, a ventricular arrhythmia, or if signs of CHF are unrecognized and the cat succumbs to hypoxia.
- Typical physical examination features of HCM include various combinations of the following:
  - Gallop rhythm—This is related to ventricular diastolic dysfunction or heart failure.
  - Systolic murmur—Murmurs are commonly due to MR or dynamic LV outflow obstruction. These murmurs can vary, often increasing in intensity with higher heart rates (and higher sympathetic tone). This finding is not specific because functional ejection murmurs also become more intense with increasing sympathetic drive, and functional

murmurs are extremely common in cats of all ages.
  - Clinical signs of ATE—These are discussed below.
  - Auscultatory evidence of pulmonary edema or pleural effusion include increased bronchovesicular sounds, crackles or a fluid line, indicating CHF.
  - Prominent left apical impulse is a sign of possible LV hypertrophy.
  - Arrhythmias may be detected in some cats with HCM.
- ABP is usually normal in cats with HCM; however, some cats demonstrate profound hypotension associated with cardiogenic shock (along with hypothermia and bradycardia).
  - Low ABP also may be detected in the cat receiving diuretic and ACEI therapy for CHF.
  - Systemic hypertension may cause secondary LV hypertrophy; but HCM does not cause systemic hypertension.

Diagnostic Tests in HCM

A number of routine diagnostic tests are helpful in recognizing and staging HCM.

- The *electrocardiogram* may be abnormal, but results are very inconsistent. Increased amplitude R-waves in lead II (exceeding 0.7–1.0 mV.) or a left axis deviation compatible with concentric hypertrophy or left anterior fascicular block may be observed.

▼ ***Key Point*** A normal ECG does not exclude a diagnosis of cardiomyopathy.

- *Thoracic radiographs* can be normal, but in moderate to severe disease will demonstrate abnormalities.
  - Cardiomegaly (elongation), apex shifting (to the right or left), and LA enlargement (most evident as an auricular bulge on the DV view) are common findings.
  - In cats with CHF, the cardiac silhouette may be further enlarged by a small to moderate pericardial effusion caused by CHF. Cardiac silhouette size may be reduced considerably after diuretic therapy.
  - Prominent pulmonary vascular patterns may indicate pulmonary hypertension secondary to elevated LV diastolic pressure or fluid retention.
  - Increased lung densities are compatible with pulmonary edema and may be focal, patchy, diffuse, and often in more dependent areas than is typical for dogs with CHF.
  - Pleural effusion is common in acute CHF and in chronic, longstanding cases of heart failure. Evaluation of the effusion typically reveals a modified transudate and sometimes chylothorax.
- Routine *CBC and clinical chemistries* are unremarkable in most cases unless there is thromboembolism or intercurrent disease. The creatine kinase (CK), AST, and ALT all derived from skeletal muscle origin are markedly elevated in thromboembolism to the limb(s).
  - *Renal function* may become impaired in cats with concurrent renal disease or in those treated for heart failure with diuretics and ACEIs. In many cases of advanced, treated CHF there will be mild to moderate azotemia.
  - Serum *thyroxine* is normal in cats with idiopathic HCM (unless they are manifesting two diseases).
  - A number of recent reports indicate the potential value of measuring serum or plasma cardiac *troponin-I* (cTN-I) since this protein increases in cats with HCM. This may become a useful screening test for identifying cats with HCM.

▼ ***Key Point*** In a large percentage of cats with systolic murmurs, echocardiography demonstrates a normal heart or trivial cardiac pathology. Heart murmurs in these cases are considered functional, likely related to sympathetic stimulation of the heart.

- *Echocardiography*—Definitive diagnosis and staging of HCM relies on echocardiography and Doppler studies interpreted in light of clinical findings.
  - Typical HCM is characterized echocardiographically by papillary muscle thickening, generalized thickening of the LV walls (generally to 6 mm or more in diastole), normal to decreased intraluminal size, and normal or increased systolic shortening fraction.
  - There is a marked heterogeneity to the pattern of hypertrophy, and not all wall segments may be involved.
    There may be generalized involvement with greater involvement of the septal or free wall segments.
    Some cats demonstrate markedly asymmetric hypertrophy mainly affecting the LV free wall. This finding usually portends development of CHF.
    Conversely, focal midventricular hypertrophy, even with midventricular obstruction, is usually benign. In older cats, isolated, focal, dorsal septal hypertrophy is a common finding. Whether this represents true HCM, or a growth response to aortic dilation and altered subaortic blood flow, is uncertain, but the condition is generally benign.
  - Increased left atrial size is a strong indicator of risk for ATE or CHF.
  - Doppler studies may demonstrate MR, dynamic obstruction, or abnormal LV filling patterns. Early diastolic dysfunction is characterized by abnormal myocardial relaxation, shown on Doppler studies as delayed LV relaxation in early diastole with a vigorous LA contraction to support late diastolic filling.
  - Progressive ventricular disease is associated with reduced chamber compliance. Doppler studies

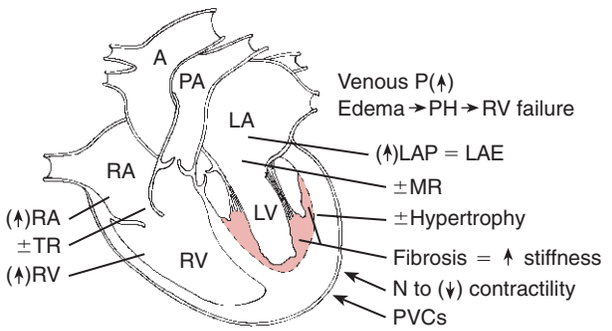

Figure 150-2. Diagrammatic representation of restrictive cardiomyopathy. Explanation of the abbreviations can be found in the text.

often show a prominent early filling (E-) wave with trivial atrial contraction (A-) wave. These findings generally precede development of CHF.

- The differential diagnosis of feline cardiomyopathy is extensive (Table 150-2), including other cardiovascular and noncardiac disorders.

FELINE RESTRICTIVE CARDIOMYOPATHY (RCM)

Feline RCM represents a heterogeneous disorder, and some latitude is used in placing cats within this category. The disorder described below might be interpreted by others as "intermediate cardiomyopathy" or as "unclassified cardiomyopathy."

Overview and Pathophysiology of Feline RCM

- The key pathologic feature is diffuse or multifocal endomyocardial or myocardial fibrosis.
- The pathogenesis of these lesions is undetermined. Antecedent myocarditis seems a likely, though unproven, initiating cause. In other cats, RCM clearly represents a late stage of HCM complicated by myocardial fibrosis or myocardial infarction.
- A variety of necropsy lesions have been observed in cats demonstrating clinical features of RCM.
  - LV endomyocardial fibrosis may be patchy, multifocal, or diffuse in distribution.
  - The left ventricle can exhibit regional hypertrophy, but overall the walls are not thickened. Often there is regional thinning or infarction of the LV free wall or apex interspersed with focal hypertrophy. Prominent papillary muscle hypertrophy or fibrosis is evident in some cats.
  - The LV cavity may be dilated but is usually normal to reduced in size.
  - Extreme endocardial fibrotic scarring can involve the mitral valve apparatus, lead to mid-ventricular stenosis, or obliterate the LV apex.
  - A common feature of RCM is striking biatrial dilation.
  - Systemic thromboemboli are common and LA and ventricular mural thrombi may be observed.
  - Histologic lesions include endocardial thickening, endomyocardial fibrosis, myocardial interstitial fibrosis, myocyte hypertrophy, and focal myocytolysis and necrosis. Arteriosclerosis of intramural coronary arteries may be recognized.
- The *pathophysiology* of RCM in the cat is unresolved but in many ways fits the "intermediate" label initially suggested by Harpster (Figure 150-2).
  - Echocardiography generally demonstrates mild systolic dysfunction, regional LV wall dysfunction, mild mitral or tricuspid valvular regurgitation, elevated LA pressures, and impaired LV distensibility with a "restrictive" filling pattern (tall but abbreviated E-wave; small A-wave).
  - Myocardial or endomyocardial fibrosis is the most likely explanation for these abnormalities.
  - Progressive increases of LA pressure develop, and the combination of ventricular dysfunction, atrial stiffness, and renal retention of sodium elevate pulmonary venous pressures and predispose to CHF and to pulmonary hypertension.
  - Pulmonary edema, pleural effusion, jugular venous distention, and hepatic congestion are typical manifestations of CHF in this disease. Clinically a diagnosis of "biventricular" CHF is often made.
  - Stasis of blood and the stretched LA places affected cats at risk for atrial thrombi and systemic thromboembolism.

Clinical Findings in Feline RCM

- The clinical findings and diagnostic studies of RCM are in many ways similar to those of HCM with a few notable differences.
  - Most cats with RCM are middle aged or older and present with signs of CHF or ATE.
  - Some have previously been diagnosed with HCM.
  - The most consistent physical auscultatory finding is a loud gallop sound; murmurs are variable and less common than in HCM.
  - Premature ventricular or atrial beats are common, leading to an irregular rhythm and arterial pulse.
  - Signs of elevated systemic venous pressure, including hepatomegaly, pleural effusion, and elevated jugular venous pressure, are common. This may indicate RV dysfunction from RV involvement, pulmonary hypertension, or simply the generalized response of fluid retention in compensation for chronic left heart failure.
- The *electrocardiogram* is frequently abnormal showing cardiomegaly patterns, axis deviations, or conduction disturbances along with atrial or ventricular ectopy.
- Thoracic *radiography* is often impressive and characterized by LA dilation and cardiac elongation that is typical of LV enlargement.

- The cardiac apex can be pointed or rounded.
- Some cats manifest astounding biatrial enlargement. Pericardial effusion may further enhance cardiac silhouette size.
- Pleural effusion is typical.

- *Echocardiography* demonstrates a number of possible abnormalities. The most characteristic feature of RCM viewed by echocardiography is marked LA or biatrial dilation, mildly reduced shortening fraction, and irregular or hyperechoic ventricular walls, +/− bands spanning the LV. Often there is marked wall thinning typical of myocardial infarction. Infarction or severe myocardial fibrosis often creates a segmental, hypocontractile wall.
- *Clinical laboratory tests* of cats with RCM are not specific and most abnormalities are attributable to CHF, diuretic therapy, or thromboembolism as described above for HCM. A plasma or whole blood taurine should be measured in cats with decreased LV ejection fraction. Analysis of pleural effusates indicates a transudate, modified transudate, or chyle. The predominant cells present are macrophages, mesothelial cells, and small lymphocytes unless there is chylothorax, in which case, well-preserved neutrophils may be more numerous in response to the irritation.

DILATED CARDIOMYOPATHY IN CATS

As shown by Pion and colleagues, dietary deficiency of taurine accounted for the vast majority of feline cases of dilated cardiomyopathy. Today DCM in cats is a relatively rare occurrence requiring echocardiographic evaluation for diagnosis. Taurine deficiency may still be observed in cats eating mostly "custom" diets or dog food, but most cases of DCM are idiopathic or a consequence of myocarditis.

- The primary post-mortem lesions of primary DCM are left-sided or four-chamber dilatation, accompanied by necropsy findings of CHF. There is no demonstrable congenital, coronary, or valvular heart disease. Histological findings include myocyte loss with prominent interstitial fibrosis and variable degrees of hypertrophy, myocytolysis, and inflammation (which is typically minimal).
- Left-sided or biventricular CHF, often complicated by systemic thromboembolism, are the typical consequences of this disorder. These conditions are readily identified by careful clinical examination and results of thoracic radiography.
- Certain breeds are historically at risk for DCM, notably the Burmese cat.
- Classic physical examination features of DCM include soft heart sounds (from reduced contractility or pleural effusion); gallop rhythm with or without a systolic murmur; hypokinetic arterial pulses; dull left apical impulse; and clinical signs of profound CHF. Exceptional cases are seen prior to onset of CHF.
- Cats with DCM are very likely to present in "cardiogenic shock" with sinus or junctional bradycardia, marked hypothermia, and severe hypotension (systolic ABP <70).
- Ophthalmic examination may indicate hyperreflective lesions of retinal degeneration adjacent to the optic disk (if the cause is taurine deficiency).
- The principle functional disturbance of DCM as shown by *echocardiography* is marked reduction of myocardial contractility as measured by shortening or ejection fractions. Morphologically, a dilated, thin-walled, hypokinetic left ventricle is observed often with dilatation of the other cardiac chambers. Ventricular filling also is impaired related to abnormal relaxation of the muscle and pronounced cardiac dilatation, which reduces diastolic compliance. There is often MR and TR by Doppler studies.

OTHER FELINE MYOCARDIAL DISEASES

A number of other diseases that affect the myocardium of the cat are briefly considered below.

- Myocarditis—Nonsuppurative myocarditis occurs sporadically in cats. The cause is unknown and definitive diagnosis requires microscopic examination of myocardium. Since myocardial biopsy is difficult in cats, and enzyme or plasma troponin-I elevations are nonspecific for inflammation, the diagnosis is usually tentative or reserved for the necropsy table. Some cats with myocarditis are presented for ventricular arrhythmias, while others develop fulminant heart failure, RCM (chronic myocarditis, healing phase), or thromboembolism.
- Right Ventricular Cardiomyopathy—A cardiomyopathy involving the RV has been reported in cats. The clinical findings can be explained by right-sided myocardial failure and severe right ventricular cardiac dilatation. There may be atrial standstill or apparent atrial fibrillation. A murmur of tricuspid regurgitation may be evident. Ventricular ectopic rhythms are common. Pleural effusion and ascites can develop from CHF and sudden death may occur. Diagnosis depends on echocardiography and exclusion of other predominately right-sided diseases such as atrial septal defect, tricuspid valve malformation, and pulmonary hypertension.
- Hyperthyroidism—Clinical findings of hyperthyroid heart disease are common in older cats with functional thyroid tumors. Thyrotoxicosis causes cardiac hypertrophy related to a hypermetabolic state, peripheral vasodilation, and increased demands for cardiac output. In addition, increased sympathetic activity and elevated thyroid hormone concentrations may stimulate myocardial hypertrophy.

- In chronic cases of hyperthyroidism, the left ventricle becomes hypertrophied. Concurrent systemic hypertension may contribute to this hypertrophy.
- Constitutional signs such as weight loss and abnormal behavior are typical. A thyroid "slip" is generally identified during physical examination.
- Cardiovascular findings can include sinus tachycardia (that can approach 300 per minute); premature atrial or ventricular complexes; hyperkinetic (bounding) arterial pulses; gallop sounds; and systolic murmurs (either functional ejection murmurs or murmurs stemming from mitral or tricuspid regurgitation).
- Isolated systolic hypertension or combined systolic/diastolic hypertension may be evident.
- In most situations, it is practical to obtain thoracic radiographs to evaluate cardiopulmonary status. Most examinations show only mild cardiomegaly characterized by cardiac elongation and mild LA prominence. In this group of cats, echocardiography is unlikely to contribute materially to the management of the patient.
  When done, typical echocardiographic findings include LV wall hypertrophy, mild LV dilation, normal to mildly increased left and right atrial dimensions, and hyperdynamic LV.
- ECG recordings often demonstrate sinus tachycardia (>240/min); cardiomegaly (increased QRS voltages); axis deviation (to the left or right); and premature atrial or ventricular complexes.
- In most cases, the cardiovascular complications of hyperthyroidism regress following successful treatment of the underlying condition.
  LV hypertrophy usually decreases *except* in the cat with concurrent diseases of uncontrolled hypertension or with primary (idiopathic) HCM.
  Hypertension may improve or resolve as cardiac output decreases with reduction of thyroid concentration; however, *other* causes of hypertension may endure (especially primary renal disease), requiring medical management with amlodipine.
  Sinus tachycardia and premature beats usually resolve with initiation of anti-thyroid medication (methimazole, Tapazole). Persistent tachycardia may indicate concurrent CHF or a need for low-doses of a beta-blocker (atenolol, $\frac{1}{4}$ of a 25-mg tablet PO, once or twice daily).
- In a small percentage of cats, the cardiac effects of hyperthyroidism are manifested in a more clinically significant manner. Thoracic radiographs will demonstrate that the heart is moderately to severely enlarged, and careful scrutiny may indicate a small (or even a large) pleural effusion. In these patients, a full cardiac workup is indicated.
  Re-examination of the patient may indicate prominent jugular pulses or overt jugular venous distension, compatible with plasma volume expansion and heart disease.
  In advanced hyperthyroidism, there can be sufficient cardiac dysfunction and volume expansion to cause more generalized cardiomegaly. Echocardiography often shows biatrial dilatation with normal or even reduced LV shortening fraction despite thickened LV wall measures.
  Affected cats should be evaluated for concurrent hypertension, anemia, or renal failure.
  Great care must be taken when administering fluid therapy as large pleural effusions may occur. Thoracocentesis may be needed.
  In cats with advanced cardiac disease, anti-thyroid medication should be initiated without delay; beta-blockers avoided to prevent cardiac depression; and an ACEI prescribed for cardiac protection, control of incipient (or overt) CHF, and for antihypertensive effects.
- Therapy of hyperthyroid heart disease is predicated on controlling the underlying disorder and is discussed in Chapter 31. Treatment of CHF as a complication of hyperthyroidism is discussed below.

- Systemic hypertension—Cats with systemic hypertension may develop progressive LV disease with concentric ventricular hypertrophy. The left ventricle and small coronary arteries represent one of the "target organs" of high blood pressure.
  - Most healthy cats have systolic ABP measurements of <150 to 160 mm Hg in the hospital setting. Persistent elevation of ABP, particularly values exceeding 160 to 170 mm Hg in the presence of target organ injury, is highly suggestive of hypertensive disease.
  - While systemic hypertension does increase the LV workload and stimulates myocardial hypertrophy, heart failure is not a common complication of this disease unless hypertension progresses unchecked or is superimposed on another form of heart disease.
  - Initial clinical signs more often are referable to the other target organs, namely the eyes (retinal hemorrhages, detachments), brain (depression, abnormal behavior, stroke), and kidneys (progressive azotemia).
  - Dissection of the aorta is a rare vascular complication of hypertension.
  - The cardiac changes of hypertension most often resemble mild HCM. Often there is a gallop sound or murmur (of uncertain origin), along with mild cardiac enlargement, evident by radiography or echocardiography. As many of these cats are older, there may be degenerative changes of the aorta observed such as aortoannular ectasia (dilatation) or aortic redundancy.
  - The diagnosis of hypertension is usually straightforward and is discussed in detail in the Chapter 153 in this section.

- Assessment of hypertension can be more complicated. For example, hypertension in a hyperthyroid cat may be related to
  High cardiac output from LV hypertrophy and a sympathetically-driven heart.
  Increased aortic impedance or stiffness, related to concurrent aortoannular ectasia.
  Abnormalities of plasma volume or renin-angiotensin regulation from concurrent (often masked) renal disease.
- Causes of systemic hypertension, including intrinsic renal disease, hyperthyroidism, and Conn's syndrome should be sought.
- LV hypertrophy may regress following successful control of blood pressure.
- The treatment of systemic hypertension in cats is discussed fully in Chapter 153.

SYSTEMIC ARTERIAL THROMBOEMBOLISM IN CATS

Acute arterial thromboembolism is most commonly associated with cardiomyopathy, though it may be encountered in multisystemic disorders including hematologic disease, endocarditis, and cancer.

- Thrombi generally arise in the LA/auricle. Many are large and traverse the aortic arch to lodge in the terminal aorta. This creates the classic "saddle thrombus" at the origin of the external and iliac arteries. The saddle thrombus also obstructs the internal iliac branches (serving the tail) and obstructs flow in the femoral arteries (as these extend directly from the external iliac system).
- Smaller clots may be diverted to other vascular beds, causing myocardial infarction (with arrhythmias, sudden death, or acute CHF); thrombotic stroke; forelimb monoparesis; renal infarcts; or rarely, mesenteric ischemia with severe colic.
- The pathogenesis of atrial thrombus formation is likely related to atrial dilation, stagnant blood flow, reduced atrial contractility, exposure of platelets to subendocardial collagen, and other ill-defined hemostatic factors particular to the cat. Impaired collateral blood flow is believed to be pivotal in the genesis of clinical signs of ATE, since simple ligation of the femoral arteries does not reproduce the syndrome in cats.
- Historical signs of ATE typically include the sudden inability to walk (or use a forelimb), severe pain with vocalization and obvious distress, and rapid or deep breathing patterns.
- Physical examination usually reveals a distressed, non-ambulatory patient, often assuming a sitting position with extended, firm, and painful rear limbs.
  - Respiratory rate is increased either from pain or concurrent CHF. Radiography is often needed to delineate the basis for dyspnea. Management of CHF is needed in some cats (see above).
  - Results of cardiac auscultation depend in part on the experience of the examiner, but often a murmur or gallop sound will be detected. In some cats, heart sounds are remarkably normal.
  - Shock-like signs are evident in some cats, probably related to systemic reaction and release of mediators from the thrombus. ABP must be measured in a forelimb.
  - Bradycardia is likely to be associated with hypotension and require additional treatments such as dobutamine.
  - Laboratory tests are variable and probably relate in part to any underlying disease. Stress-related hyperglycemia is typical, and a variety of electrolyte abnormalities may be seen.
- Diagnosis of aortoiliac ATE is straightforward and based on the usual history and results of physical examination demonstrating the triad of peripheral vascular disease, muscle injury, and peripheral neuropathy.
  - Loss of regional *vascular supply* leads to cold, pulseless, pale limbs. Doppler flow signals within the proximal femoral arterial system are absent indicating no flow. With reduced collateral blood flow, the superficial rectal temperature is often reduced, and the thermometer should be lubricated and very carefully advanced to obtain a more representative body temperature.
  - Severe *skeletal muscle injury* with extensive rhabdomyolysis occurs.
    This leads to ischemic contracture with severe muscle pain, as well as release of high levels of CK, AST, and ALT from damaged muscles into the blood.
    The limbs are typically very firm to palpation (especially the semitendinosus and gastrocnemius muscles).
    Since muscle contains very high concentrations of potassium that also leak out from the cell, there may be profound hyperkalemia following reperfusion of the damaged tissues.
    Some cats develop antibiotic-responsive fever within 2 to 7 days of the thrombotic event; we treat affected cats empirically with amoxicillin trihydrate + potassium clavulanate (Clavamox) for 10 days.
    Development of limb edema indicates severe tissue injury and portends a very poor prognosis for limb recovery. In some cases, tissue necrosis and limb contracture may require wound management or even limb amputation.
  - Peripheral (ischemic) *neuropathy* is identified.
    Motor function is absent in the rear limbs (or forelimb in the case of a brachial thrombus). Tail movement is lost in the typical saddle thrombus.

Neurological signs are usually bilateral, but there may be some asymmetry noted between the limbs; this often correlates with presence or return of pulse on the least-affected side.
After 24 to 48 hours, a relatively clear superficial sensory level can be detected in the proximal limb; with time, this descends toward the toes.
With revascularization, tail function returns first, and motor function is restored from proximal to distal.
Residual, distal proprioceptive deficits are common but do not prevent functional limb use.

- Recovery from the thrombus is *common,* and after 72 hours many cats have already begun to revascularize the limbs spontaneously. Mortality in the first 72 hours is generally due to one of three factors: (1) euthanasia; (2) reperfusion hyperkalemia; or (3) uncontrolled CHF, usually present at the time of admission.
  - Most studies report a worst-case scenario of about 35% recovery (release) rate because cats that are euthanatized without treatment or given sufficient time for recovery are included. Obviously, the client's and the veterinarian's perceptions and expectations weigh heavily into these figures. When euthanatized cats are not considered, at least 50% of cats are reported to be released from the hospital in most retrospective studies. More recent surveys, including the largest Minnesota study, demonstrate up to a 75% release rate for cats supported and managed aggressively for their disease.
  - Concurrent CHF worsens the prognosis. In the retrospective study of Smith and colleagues the difference in median survival for cats released from the hospital was 77 days for CHF cats compared to 223 days for those without CHF.
  - Despite the potential for short-term success, the complication of ATE creates difficult decisions for clients. The risk for future ATE is very high (probably exceeding 50% within 6 months); however, subsequent embolic events are often better tolerated, presumably related to development of collateral circulation. Clients also must be advised regarding the severity of the underlying heart disease (which should be evaluated by radiography, echocardiography, and an ECG).
- Management of ATE is discussed below.

THERAPY OF FELINE CARDIOMYOPATHY

A number of CV drugs are used in the management of myocardial and other feline CV disorders. While there some well-conducted studies of antihypertensive therapy in cats, there is little in the way of controlled and sufficiently powered clinical studies that address the treatment of asymptomatic HCM, therapy of heart failure, or management of ATE in cats with primary cardiomyopathies. Accordingly, treatment approaches to myocardial diseases remain largely empiric and are certainly guided by experience and clinical prejudice.

Major therapeutic end-points deal with survival, client observed symptoms, and the need for hospitalization related to clinical signs of disease. More theoretically based treatments (and the rationale for many current recommendations for therapy) consider drug effects on: (1) left ventricular function (diastolic filling; dynamic obstruction during systole); (2) protection of the myocardium from stress, catecholamines, or neurohormones; (3) prevention or control of CHF; (4) prevention or treatment of ATE; and (5) prevention of arrhythmias and sudden cardiac death.

The clinical pharmacology of specific drugs used in treatment of CHF in cats is detailed in "Cardiovascular Drugs" elsewhere in this section. The management of systemic hypertension in cats is discussed in detail in Chapter 153.

Management of the Asymptomatic Cat with HCM

In most practices, asymptomatic HCM is the most common form of idiopathic cardiomyopathy identified in cats. The main benefits of any therapy in this group would relate to: (1) improved ventricular diastolic function; (2) reduction of dynamic outflow tract gradients with decrease in MR; (3) reduced chance of sudden cardiac death; (4) prevention of ATE; or (5) regression of LVH. Currently, no data indicate a substantial benefit of therapy in asymptomatic cats with HCM, and it is well known that many cats live for years without apparent problems.

- Increasingly, cats with asymptomatic or mild HCM and normal LA size are left untreated. Many cats show little progression of disease at follow up. Thus, in the asymptomatic cat, the veterinarian could reasonably consider prescribing no therapy or, empirically, a β-adrenergic blocker or diltiazem. Some clients will indicate that their cat is more active when receiving treatment, but this may simply represent a placebo effect.
- Initially, cats with asymptomatic disease are examined by repeated echocardiography within 1 to 3 months of initiation of any stable therapy regimen and again 6 to 12 months later, depending on the level of concern for impending CHF or ATE. Echocardiography has the advantage of providing objective measures of wall thickness and LA size, and a Doppler study can be used to document a reduction in the dynamic obstruction and associated MR when these flow disturbances are identified at initial examination.
- The stable cat is seen every 6 to 12 months, with the intervals extending if follow up examinations show no disease progression. In many cases, the disease is unchanging, but in others, there is clear progression

and eventually signs of CHF or ATE occur, even years after initial diagnosis.

- Therapy with Atenolol–β-blockers are recommended in the management of HCM with moderate to severe LV outflow tract obstruction. Atenolol is most often prescribed for this purpose as it is a twice daily drug (compared to tid propranolol). The usual starting dose of atenolol is ¼ of a 25-mg tablet PO for 3 days and thereafter ¼ tablet PO q12h. Dosage is adjusted to achieve an examination heart rate of 120 to 160/min. Typically cats receive ½ tablet in the AM and either ¼ or ½ tablet in the PM.
  - Atenolol effectively reduces LVOT gradients and consistently slows the heart during times of stress (for example, a veterinary examination).
  - Cardiac benefits of beta–blockers in cats with HCM include preventing sinus tachycardia, reducing dynamic outflow obstruction, decreasing SAM and attendant mitral regurgitation, and prolonging diastole. Myocardial oxygen demand is reduced through decreases in heart rate, contractility, and blood pressure.
  - Unfortunately, the net effect of beta–blockade on diastolic function in cats with HCM is unknown (see "Cardiovascular Drugs" for a discussion).
  - Beta–blockade is especially helpful for reducing pressure gradients caused by dynamic LV outflow obstruction in cats with HCM. The murmur of mitral regurgitation generally becomes softer following beta-blockade, and the peak outflow tract velocity is substantially reduced in the majority of cats given an adequate dose of atenolol. In a small European study, another beta-blocker (propranolol), was associated with regression of LV hypertrophy, but this finding is inconsistent, and should not be expected.
  - Beta-blockers are contraindicated in cats with overt hypotension, bradycardia, uncontrolled pulmonary edema, AV block, or recent arterial thromboembolism (until collateral circulation has been restored); furthermore, their value in cats with recent-onset CHF appears to be unfavorable, based on a recent multicenter study, and should not be routinely prescribed for short-term management of the CHF patient.
  - Therapy with Diltiazem—When HCM is characterized by moderate to severe LV hypertrophy without obstruction, and especially when there is concurrent LA dilatation, diltiazem may be a therapeutic consideration. Dosing typically involves a long-acting preparation as standard diltiazem dosed at ¼ of a 30-mg tablet PO q8h is simply impractical for most cat owners. Dilacor XR (brand of diltiazem) can be administered at a dosage of 30 mg once or twice daily (open the 240 mg capsule and cut the four 60-mg pills in half). Others have used long-acting diltiazem capsules (Cardizem CD) compounded in a palatable syrup, starting at 30 mg of diltiazem once daily. The bioavailability and dosing regimens of these preparations have been issues. Diltiazem is thought to improve LV relaxation, but the precise mechanism for this benefit has not been elucidated (See "Cardiovascular Drugs" for a discussion).
  - Overall, diltiazem should reduce myocardial oxygen demand by decreasing contractility, blood pressure, and heart rate (though less effectively than atenolol).
  - While diltiazem is a negative inotrope, effects on reducing dynamic outflow tract gradients have been somewhat disappointing at the doses commonly used.
  - While the chronic administration of diltiazem has been reported to decrease LV hypertrophy in cats with very severe HCM, it is very uncommon to observe regression, even with prolonged therapy.
  - Thus, the main reason to choose diltiazem therapy in cats with HCM is for potential improvement of diastolic function and for prevention or treatment of CHF in HCM.
  - Contraindications to administration of diltiazem in cats are uncontrolled CHF, sinus bradycardia, hypotension, and AV block.
  - Bradycardia, hypotension, depression, and skin reactions (erythema/edema) have been observed in some cats receiving this drug. Anorexia is a relatively common client complaint. Adverse effects were reported in just over 20% of cats in one clinical report.
  - As with atenolol, diltiazem does not appear to have a role in the short-term management of CHF in cats.
  - ACEI Therapy—The potential of an angiotensin converting enzyme inhibitor (ACEI) to benefit HCM has not been demonstrated thus far, except in cats with overt CHF. Theoretically ACEI, especially with more 'tissue-sensitive' ACEI (such as ramipril) could prevent progressive myocardial injury or fibrosis in asymptomatic HCM. However, with no firm evidence of benefit, the authors' recommendations are to reserve an ACEI for cases of documented CHF or when moderate to severe LA dilatation is documented by echocardiography (especially in the setting of Doppler evidence of elevated LA pressure).

Hospital Management of the Cat with Acute CHF

Treatment of acute heart failure in cats is a challenge and may require aggressive initial treatment.

- Efforts are directed at improving tissue hypoxia, relieving stress, and reducing the venous and pulmonary capillary pressures.
- Many cats can be managed medically using the F–O–N–S approach (furosemide–oxygen–nitroglycerine–sedation). Thoracocentesis is performed if

there is a moderate or large pleural effusion. Intubation for 2 to 6 hours of artificial ventilation may be needed to manage impending respiratory arrest in cats expectorating edema fluid.

- Initial dosages of furosemide are typically 2 to 4 mg/kg IV/IM, followed by 1 to 2 mg/kg boluses IV or IM every 6 to 8 hours until the cat is stable.
- The cat should be placed at rest, administered oxygen (40–50%) by cage oxygenator, and sedated in most cases to relieve anxiety (butorphanol, 0.25 mg/kg, mixed with acepromazine, 0.05–0.1 mg/kg, with the cocktail administered subcutaneously. If rectal temperature is <99°F, or in the setting of bradycardia, avoid the acepromazine).
- Nitroglycerin (2%) ointment is also administered at a dose of ¼ inch, q12h for moderate to severe pulmonary edema.
- If an IV can be established without stress, a constant rate infusion of furosemide can be substituted for repeated boluses (calculate the daily dose and infuse continually for 24 hours). This treatment is continued for 24 to 48 hours. The CRI of lasix can be supplemented with additional IV boluses as needed.
- The cat with cardiogenic shock (hypothermia, bradycardia, systolic ABP <70 mm Hg) is treated with IV dobutamine infusion (2.5–10 mcg/kg/min titrated to an ABP of 90–100 mm Hg) for 24 to 48 hours. This is an effective therapy for cardiogenic shock regardless of the underlying form of cardiomyopathy.
- Once the cat has been diuresed and ventilation is stable, oxygen is withdrawn, nitrate ointment discontinued, and the dosage of furosemide reduced. The ultimate dose of furosemide should be titrated to the severity of pulmonary edema or pleural effusion.
- Many cats develop hypokalemia and pre-renal azotemia during intensive diuretic therapy. Fresh water and palatable food should be available shortly after diuresis has been initiated.
- Mild cases of renal failure need not be treated, but if the cat refuses to eat and drink after 24 to 36 hours of therapy, judicious fluid therapy of a balanced solution (e.g., 20–30 ml/kg/day) combined with potassium supplementation (IV or oral) will be needed.
- Liquid nutritional support given by an indwelling nasogastric tube may be considered if anorexia persists for more than 60 hours; however, most cats begin to eat following effective resolution of CHF.

Home Management of the Cat with Chronic CHF

- Therapy of chronic CHF in the cat with cardiomyopathy is based on two drugs: furosemide (1–2 mg/kg, PO, once or twice daily) and an ACEI, such as enalapril or benazepril (0.25–0.5 mg/kg, PO, once or twice daily, up-titrating the dose over a number of weeks). Spironolactone (6.25 mg, or ¼ of the 25-mg tablet, once daily) can be given for empiric cardioprotection and potassium-sparing effects.
- Since these cats also have LA dilation, a treatment to prevent thromboembolism is usually considered (see below). However, aspirin therapy when combined with an ACEI and diuretic may predispose to renal failure. When aspirin is prescribed for this purpose, ultra-low doses (5 mg per cat, q24–72h) may be a safer alternative.
- In general, neither atenolol nor diltiazem should be administered to cats with overt CHF, as such therapy has been shown to be either detrimental or not beneficial to short-term outcome.
- After at least 1 month of stable CHF control, atenolol can be considered for the cat with severe LVOT obstruction. Begin at ¼ of a 25-mg tablet once daily and cautiously up-titrate the dosage over several weeks to relieve obstruction. Excessive doses may worsen CHF, leading to pleural effusion or recurrent pulmonary edema.
- The benefits of diltiazem in cats with CHF from HCM have not been proven but might be considered once a cat is very stable on furosemide + ACEI +/− spironolactone.
- Cats with dilated cardiomyopathy are evaluated for taurine deficiency (particularly at-risk breeds including the Burmese, Abyssinian, and Siamese) and treated with taurine (250–500 mg twice daily for 12 weeks) pending results of a whole-blood taurine analysis.
- The bioflavonoid, Rutin (250 mg q12h), is prescribed when there is evidence of recurrent pleural effusion with chylothorax. Rutin improves macrophage function and may reduce reactive pleuritis by decreasing the accumulation of chylomicrons within the pleural space.
- Clinical trials with the inodilator pimobendan are underway in cats and may provide an additional treatment for cats with chronic CHF.
- The overall efficacy of heart failure therapy can be gauged by monitoring respiratory rate and depth at home and by regular re-examinations. Consideration of the affected cat's activity level, appetite, and interaction with family members offers a reasonable gauge of quality of life. Objective measures of CHF control can be obtained by a careful physical and cardiovascular examination and from inspection of serial thoracic radiographs. Morphologic or functional progression of heart disease can be assessed by echocardiography if desired.
- Clinical reevaluation should include a client interview; physical examination; ABP measurement; serum biochemical profile; thoracic radiographs (even one lateral view can provide objective evidence regarding fluid retention); and a focused, recheck echocardiogram.
- The timing of specific examinations depends on clinical circumstances and economic considerations but initially should occur within the first 7 to 10 days from initial diagnosis of CHF and continue every one to two weeks until the CHF is controlled and renal func-

tion stable. Thereafter, the interval may be extended to every one to three months, depending on the patient's progress.

- In general, progressive azotemia indicates the effects of diuretics plus an ACEI. If possible, the doses should be reduced.
- In some cats the heart may stabilize and allow drug diuretic therapy to cease.
- In other cases, there is a clear need to simply tolerate azotemia to prevent pleural effusion or pulmonary edema.
- Treatment of ventricular tachycardia (VT) in cats with CHF is very problematic. Propranolol (2.5–5 mg, PO, q8h), atenolol (6.25 mg, PO, once or twice daily), and procainamide ($^1/_4$ of a 250-mg capsule compounded or mixed in the food q8h) have been used. Sotalol has been used in cats, but it is hard to dose, and in research studies was effective mainly at the beta-blocking dosage. Negative inotropic effects of each of the mentioned drugs; poor client and patient compliance; and lack of efficacy studies limit the application of each of these treatments. In general, therapy of VT is reserved for symptomatic (i.e., syncopal) patients or those with dangerous ventricular arrhythmias documented by ECG.
- Diltiazem is a very effective blocker of AV nodal conduction and represents an excellent choice for heart rate control in cats with atrial fibrillation.
- The long-term prognosis of CHF in cats is guarded and quite variable.
- Although some reports indicate a survival time of six months or less, a 1-year survival is not uncommon following onset of heart failure, provided the client can medicate the cat at home and is willing to obtain consistent veterinary care. Some cats have been successfully managed for CHF for over 2 years.
- Remarkably, some cats with CHF can be weaned from medications (the reason is unknown); whereas, others have a relentless downhill course requiring higher and higher doses of diuretics or regular thoracocentesis.
- Progressive CHF, refractory pleural effusion, or ATE each present formidable obstacles to long-term survival in some cats.

Treatment and Prevention of Systemic Arterial Thromboembolism (ATE)

Management of thromboembolic complications in feline cardiomyopathies remains a serious challenge. Beyond the anticipated spontaneous revascularization of the limbs (once sufficient time elapses), there is no established medical, surgical, or interventional catheter treatment available for resolving acute ATE in cats. Unfortunately, there are no prospective studies demonstrating efficacy of any preventative treatment.

- Acute thromboembolic event—Treatment requires high-quality critical care, good nursing, and "tincture of time." There remains a propensity to euthanize cats with ATE within the veterinary community though published data suggest at least a >50% chance for good functional recovery and a median survival time of over 7 months for cats without CHF. Prognosis has been discussed previously in this chapter.
- For clients requesting care, sufficient time (at least 7 days) should be allowed for improvement. In most cases, a 2 to 3 day hospital stay is needed. Most cats show improvement within 48 to 72 hours with conservative therapy, and pain is markedly diminished within 36 hours of the event.

▼ ***Key Point*** Management of pain is the main therapeutic concern during the first 24 hours of treatment of cats with arterial thromboembolism.

- The initial treatment of cats with ATE involves analgesia with opioids. If the ABP is normal, acepromazine (0.05–0.1 mg/kg) is added to sedate the patient. Opioids for use in cats include:
  - Butorphanol—This drug is both an agonist and antagonist of the mu receptor, and can be dosed at 0.2–0.4 mg/kg IM/SQ q6–8h. While this drug is readily available in veterinary practices, it is a relatively weak analgesic for this magnitude of pain. Butorphanol should be considered only in the "step-down" of analgesic therapy (with potential to reverse some effects of other mu agonists).
  - Buprenorphine (Buprenix)—Dosed at 0.005 to 0.01 mg/kg, IM or SQ, q6h buprenorphine is a longer acting (partial) mu agonist and a better alternative to butorphanol.
  - Hydromorphone or Morphine—These opiates are full mu agonists and can be used in cats at 0.1 mg/kg IM q6–8h. Beware of respiratory depression, CNS excitation, or hyperthermia. If possible, combine with acepromazine.
  - Fentanyl—Fentanyl is a potent mu agonist and can be infused at 2 mcg/kg as an initial slow IV bolus and then maintained at 1 to 5 mcg/kg/hour. It also can be combined with acepromazine.
  - The opiate + acepromazine combination provides effective analgesia/sedation for many cats in moderate distress.
  - Epidural anesthesia is very effective in controlling rear limb pain in cats with ATE, but the injections require expertise in local analgesia and may increase the risk for epidural hemorrhage in cats receiving anticoagulation therapy.
  - Sodium bicarbonate (1 mEq/kg, IV, over 10–20 minutes) is sometimes administered to cats in shock with documented evidence of metabolic acidosis and/or hyperkalemia from muscle necrosis and reperfusion.
- Control of body temperature—Many cats with ATE are hypothermic, especially those with concurrent CHF. While a warm and preferably oxygen enriched

environment should be supplied, it is important to avoid over-heating cats with ATE.
  - Damaged limbs cannot dissipate heat normally and may burn.
  - Opiates used for analgesia may impact the thermoregulatory center. Sometimes cats on opiates will pant and this will abate once the external environmental temperature is lowered, a heating blanket removed, or a dose of acepromazine administered.
  - If elevated temperatures persist, true fever may be evident. Alternative causes of ATE should be considered, including bacterial endocarditis or disseminated neoplasia. However, in most cases the fever is related to the ATE and usually responds to IV cefazolin or oral Clavamox.
- Heparin is administered in ATE to prevent further thrombosis (initial dose is 200–300 U/kg intravenously, then subcutaneously at 100–200 U/kg every 8 hours for 48–72 hours).
- Some clinicians also administer one baby aspirin (81 mg) to cats that present within 2 to 3 hours of an ATE event.
- Beta-blockers, especially propranolol, should be avoided until the cat is walking without difficulty.
- If CHF is not an issue, an IV catheter is placed in a forelimb and *maintenance fluid therapy* is administered to maintain urinary output and reduce hyperkalemia following reperfusion.
- Excitement has waned for IV streptokinase (90,000 IU IV over 30 min followed by 45,000 I.U./hour for 3–6 hours) Streptokinase is no longer available. Excitement has waned for IV tissue plasminogen activator (0.25–1 mg/kg/hour to a total dose of 1–10 mg/kg). This expensive treatment is difficult to control and carries a very high mortality rate probably related to reperfusion hyperkalemia. The clinician must appreciate that limb reperfusion—whether spontaneous or induced by a thrombolytic drug—can lead to fatal hyperkalemia from rapid reperfusion of necrotic muscles.
  - Most cats are released from the hospital in about 3 days, provided there is evidence of revascularization (femoral pulses, improved motor function to the tail and proximal limbs). Clients should be counseled regarding home care, which includes
    Protecting the limbs from trauma or burning; daily inspection for edema.
    Maintaining a written log of progress relative to limb function and ambulation.
    Providing a low stress environment, comfortable bed, and an area for the cat to convalesce. It is likely that the bed will be soiled with urine or stool, so it may be helpful to use easily washable fabrics or apply appropriate protection to the bedding.
    Offering highly palatable food and fresh water that is readily available near the bed and supplemented with hand-feedings to encourage eating and drinking.
    Placing a litter pan relatively near the bed and assisting the cat in using the litter pan if necessary. If constipation becomes a problem, a small amount of soluble fiber ($^1/_4$ teaspoon of guar gum or Benefiber) or canned pumpkin mixed in the food may soften the stool.
    Administering any prescribed medications for CHF.
    Administering a drug to prevent further thrombotic episodes (see the following).
- Prevention of ATE—Drug prevention against thromboemboli is recommended when there is atrial enlargement (>17 mm on 2D echo) or a prior history of ATE. The aggressiveness of treatment is usually proportional to the risk. High risk cats include those with any of the following findings: prior documented thromboembolism; established thrombus in the LA or appendage; evidence of spontaneous LA echocardiographic contrast; a LA dimension exceeding 20 mm, especially with loss of an active auricular contraction (measured by PW Doppler echocardiography); or atrial fibrillation.

Three empirical approaches for prevention have developed:

- Aspirin to interfere with platelet function (81 mg coated, buffered aspirin given every third day or ultra-low dose aspirin given at 5 mg per cat, every 24–72 hours). This is the easiest to administer preventative but has the disadvantage of relatively poor efficacy.
- Daily warfarin to inhibit vitamin-K dependent clotting factors (starting at $^1/_2$ of a 1-mg tablet daily). This approach creates practical problems in terms of dosing and monitoring and creates some risk for iatrogenic hemorrhage.
- Low molecular weight heparin, subcutaneously injected, once or twice daily to inhibit thrombogenesis. Dalteparin or enoxaparin, each dosed at 100 U/kg SQ q12h, have been used (though once-daily dosing with dalteparin also might be successful). There has been empirical success with these drugs, but expense and the requirement for injection have limited widespread use.

These specific approaches, as well as additional details about preventing thromboembolism, are discussed more fully in Chapter 153, along with newer treatment approaches such as clopidogrel bisulfate (Plavix $^1/_2$ of a 75-mg tablet daily).

CANINE CARDIOMYOPATHY

Myocardial diseases are a common cause of heart failure, arrhythmia, and cardiovascular mortality in the dog, following chronic valvular heart disease in preva-

lence and clinical importance. Recognized forms of cardiomyopathy in dogs include the following conditions.

- *Dilated Cardiomyopathy* (DCM)—The most common canine myocardial disease is idiopathic (genetic) dilated cardiomyopathy. DCM is characterized by decreased left ventricular ejection fraction, cardiac remodeling with LV dilatation, and congestive heart failure. Arrhythmias—both atrial and ventricular—are common during all phases of the disease. Sudden cardiac death is relatively common in affected breeds.
- *Arrhythmogenic Right Ventricular Cardiomyopathy* (ARVC)—Aside from DCM, the most often recognized form of cardiomyopathy is arrhythmogenic right ventricular cardiomyopathy (ARVC), best characterized in the boxer dog, and associated with ventricular ectopy, syncope, heart failure, and sudden cardiac death. A less common variant of this disease is right ventricular dysplasia, characterized by severe replacement of myocardium with connective tissue and progressive right-sided CHF.
- *Persistent Atrial Standstill*—This disorder is caused by replacement of atrial myocardium with fibrous connective tissue. Consequences are chronic bradycardia and right-sided CHF, mainly affecting Springer spaniels.
- *Idiopathic Hypertrophic Cardiomyopathy* (HCM)—The condition of true HCM is rare in dogs but included in the differential diagnosis of left-sided CHF and sudden death. Hypertrophic cardiomyopathy must be distinguished from congenital subaortic stenosis, mitral malformation causing dynamic subvalvular aortic stenosis, hypertensive heart disease with secondary hypertrophy, and disease caused by iatrogenic thyrotoxicosis.
- *Secondary Cardiomyopathies*—Causes of canine myocardial disease include profound hypothyroidism, iatrogenic hyperthyroidism, doxorubicin (Adriamycin) administration, catecholamine injury (including pheochromocytoma), head trauma (brain-heart syndrome), systemic carnitine deficiency, severe taurine deficiency, protracted myocardial ischemia, and Duchenne's myopathy.
- *Cardiomyopathy of Overload*—Chronic volume or pressure overload (caused by congenital shunts, valvular diseases, and hypertension) can progress to the "cardiomyopathy of overload," wherein the ventricle is hypertrophied and systolic myocardial function impaired.
- *Tachycardia-induced Cardiomyopathy*—Relentless supraventricular or ventricular tachycardias are causes of reversible myocardial failure.
- *Inherited Arrhythmogenic Cardiomyopathy in German Shepherds*—This is a malignant ventricular tachycardia of young German shepherds that has been described in detail by Moise and colleagues.
- *Myocarditis*—Cardiac inflammation in dogs can be due to Chagas' disease (in endemic areas), septicemia, Lyme disease, and in newborn puppies by parvovirus.

Overview and Pathophysiology of Canine DCM

- Dilated cardiomyopathy is an idiopathic, genetic, or familial myocardial disease characterized by left ventricular or biventricular dilation, reduced myocardial contractility, and histologic abnormalities within the ventricle.
  - Necropsy studies and 2D echocardiography often demonstrate four-chamber dilatation with profound enlargement of the left ventricle and left atrium.
  - CHF is often identified in canine patients and at post-mortem examination.
  - Microscopic lesions include absence of inflammation, attenuated wavy fibers, or fibro-fatty replacement of myocytes; interstitial fibrosis; and other alterations in the cytoskeletal matrix.
  - Extramural coronary arteries are normal and the valves unremarkable, except in older dogs with concurrent mitral or tricuspid valve endocardiosis.
- The disease in most dogs is believed to be familial, and in Doberman pinschers is probably a dominant trait. The time-course of progression of DCM is reportedly great; however, some patients clearly develop LV dysfunction within a very short time interval.
- A deficiency of a myocardial metabolic substrate (such as L-carnitine or taurine) is identified in a very small percentage of affected dogs, often related to familial disease or gross dietary deficiencies. While supplementation with these micronutrients or other nutriceuticals (such as coenzyme Q_{10}) may be beneficial to the energetics of a failing cardiac muscle, such treatment does not reverse canine DCM except in rare cases of systemic substrate depletion.
- As systolic dysfunction progresses, there is a limited cardiac output which is compensated for by activation of neurohormones and cytokines released to support arterial blood pressure.
  - Neurohormonal assault causes further myocardial damage.
  - As the left ventricular ejection fraction continues to decrease, the heart dilates, and ventricular diastolic dysfunction can be recognized by detailed echocardiographic studies.
  - Secondary atrioventricular valvular regurgitation often develops leading to murmurs of mitral or tricuspid regurgitation.
  - Exercise capacity is reduced as an early sign of heart failure.
  - Arterial under-filling promotes renal sodium retention, which expands the plasma volume. Combined

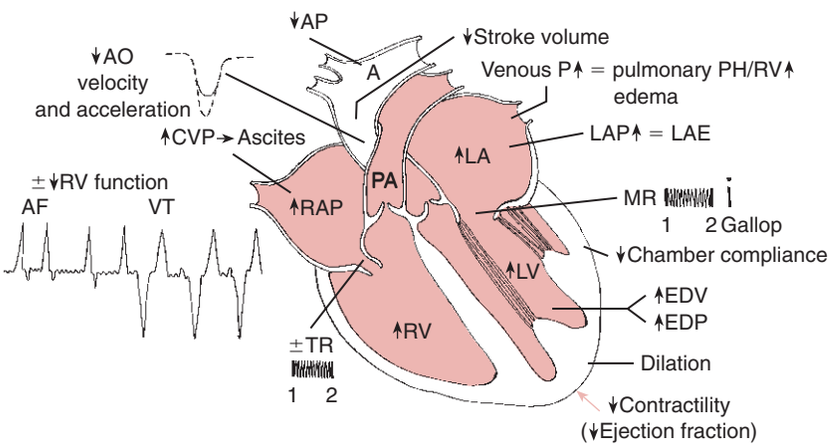

Figure 150-3. Diagrammatic representation of dilated cardiomyopathy. Explanation of the abbreviations can be found in the text.

with reduced left ventricular performance, venous pressures increase and CHF ensues.

- Arrhythmias can occur at any time during the course of DCM. Syncope, sudden cardiac death, or the onset of CHF are potential consequences of rhythm disturbances. Sudden death is especially common in Doberman pinschers with DCM. Frequently, biventricular CHF is precipitated by development of AF in a dog with previously "compensated" DCM (See Figure 150-3).
- Dilated cardiomyopathy occurs most often in middle-aged and older large and giant breed dogs, such as the Doberman pinscher, Great Dane, Irish wolfhound, Newfoundland, and boxer, but DCM can affect dogs of any age and many other breeds.
  - Often male dogs are predisposed or more likely to be affected at a young age. In breeds at risk, older dogs often tend to be females.
  - In addition to a high prevalence in the larger breeds, DCM is recognized regularly in a variety of spaniel and retriever breeds, in Dalmatians, and Portuguese water dogs. DCM occurs sporadically in small canine breeds.
  - The genetic and familial basis for DCM is obvious in many breeds, but the specific mutations or alleles responsible have not yet been demonstrated.
- The four most common clinical presentations of DCM are: (1) occult DCM; (2) CHF; (3) cardiac arrhythmia; and (4) sudden cardiac death. The first three of these conditions will be reviewed. The reader is also directed to the Chapter "Heart Failure in the Dog" for detailed descriptions of treatment plans for canine heart failure; "Cardiovascular Drugs" for discussions of the clinical pharmacology and use of drugs for heart failure and arrhythmias; and "Cardiac Rhythm Disturbances" for a review of electrocardiographic features of arrhythmias.

Occult Dilated Cardiomyopathy

- Occult DCM refers to the overtly *healthy* dog with evidence of *systolic dysfunction* by echocardiography. Some also consider the diagnosis of occult DCM viable when a breed-at-risk for DCM, such as a Doberman pinscher or Irish wolfhound, develops persistent or recurrent atrial or ventricular *arrhythmias* that can not be attributed to another recognized cause.
  - In this regard, there is some cross-over and reasonable debate between the designation of occult DCM with arrhythmia and a normal echocardiogram and that of *arrhythmogenic cardiomyopathy*, in which the principle disturbance is electrical and the echocardiogram is normal (see below). Myocardial dysfunction certainly develops in many, but not all dogs with persistent cardiac arrhythmias. But there is little doubt that many dogs with DCM spend time as "arrhythmogenic cardiomyopathy" before progressing to a more typical dilated form.
  - For the purpose of this discussion, we classify dogs with persistent arrhythmias and a normal echocardiogram as "arrhythmogenic cardiomyopathy" and those with LV dysfunction—with or without arrhythmias—as "occult DCM". While this distinction may seem academic, there is a clear trend to use cardioprotective drugs such as beta-blockers and ACEIs in dogs with occult DCM. Thus, one's perspective on the requirement to demonstrate systolic dysfunction before labeling a patient "occult" DCM may influence whether or not early intervention is prescribed.
  - Most diagnoses of occult DCM are made after a breeder requests that a cardiologist screen an important dog or following a veterinary examination that uncovers a murmur or arrhythmia.
- *Echocardiography*—The *diagnosis* of occult DCM is traditionally based on echocardiographic examina-

tion, with the minor axis estimate of LV systolic function (the shortening fraction) as the diagnostic criterion.
- LV shortening fraction = LV diastolic dimension minus the LV systolic dimension, divided by the LV diastolic dimension).
- Values below 25% are considered suspicious for occult DCM, but there is no unanimity about one specific figure that indicates myocardial failure. Some healthy dogs live for many years with shortening fractions <20%. A single linear approach to diagnosis also can be questioned because larger dogs shorten relatively more in the apical to basilar direction, and this motion is not assessed by shortening fraction.
- However, some data in Doberman pinschers indicate that specific ventricular measurements, such as an end-diastolic dimensions of >49 mm or end-systolic dimensions >42 mm, are highly predictive of DCM.
- Before accepting a diagnosis of occult DCM, the clinician should request more detailed echocardiographic measures of systolic function including LV short-axis shortening area (normally >48%), apical-to-basilar mitral annular motion, and volumetric estimates of LV ejection fraction (normally >45–50% in single plane models). Advanced Doppler methods of assessment are also available but require further definition.
- Serial echocardiographic examinations are very helpful in establishing a downward trend in LV function. One should accept however that a 5% to 8% day-to-day variation is not uncommon in measured or calculated echocardiographic variables, so that large differences and trends are more meaningful than tiny up or down movements.

- *Holter ECG*—The 24-hour ambulatory ECG is a useful adjunct in the diagnosis of occult DCM or arrhythmogenic cardiomyopathy. The Holter recording may help establish the diagnosis in breeds highly prone to DCM with cardiac arrhythmias, such as Doberman pinschers. Most cardiologists consider >50 VPCs per day clearly abnormal. Some consider even lower numbers of VPCs abnormal. In dogs in which ventricular ectopy is evident from auscultation and routine ECG, a Holter recording provides more objective information about the severity of the rhythm disturbance.
- *Other diagnostics*—Future directions are likely to lead to more dependence on *biomarkers* (troponins, natriuretic peptides) for identification of myocardial disease in breeds at risk or when screening echocardiograms return ambiguous results.
  - Breeders are always hoping for tests that will provide the earliest recognition of disease, but it is unrealistic to expect phenotype testing, no matter how sophisticated, to identify all genetically affected animals within a breeding line.
  - Many dogs that develop DCM do not demonstrate any signs until their later years, long after breeding has ceased.
  - In this regard, genetic testing will be a better answer for this particular group of clients and dogs.
- *Management* of occult DCM involves protection of the myocardium and management of serious arrhythmias.
  - An ACEI is prescribed for dogs with documented occult DCM based on echocardiography. Enalapril or benazepril at 0.5 mg/kg PO once or twice daily is appropriate. If LV function is very poor, b.i.d. dosing should be attained over a 2-week time. In the report of O'Grady and colleagues, in Doberman pinschers, treatment with enalapril roughly doubled the time duration between diagnosis of occult DCM and onset of overt signs of heart failure.
  - Beta-blockade with carvedilol or metoprolol also is cardioprotective and should be considered in dogs with occult DCM.
    In large breed dogs, long-acting metoprolol is usually well tolerated ($^1/_2$ of a 25-mg tablet, q12h).
    Carvedilol (Coreg) is relatively expensive, but dogs with occult DCM are more likely to tolerate it than dogs with overt CHF. Optimal target dosages are unknown, but initial dosing of 0.1 mg/kg PO q12h can be increased every 2 to 4 weeks to a target of 0.4 to 0.5 mg/kg q12h. If lethargy or exercise intolerance develops, insure that CHF has not been precipitated.
  - Blood pressure and renal function tests should be followed with these medications.
  - If cardiac arrhythmias are also present, a 24-hour Holter ECG should be done to assess arrhythmia severity (unless a routine ECG already shows that it is severe) and antiarrhythmic therapy considered. This is discussed more fully below under arrhythmogenic cardiomyopathy.
- *Prognosis*—Prediction of survival in occult DCM is difficult
  - One of the problems relates to that of precisely establishing a diagnosis of occult DCM.
  - Once unambiguous evidence of LV systolic dysfunction is identified (LVSF typically 15% or less in a dog with sinus rhythm and normal ventricular conduction), the development of CHF is likely within 6 to 12 months, even in the setting of cardioprotective drugs.
  - When less stringent criteria are set for diagnosis of occult DCM, many dogs will still be alive 2 to 4 years later.

DCM with Congestive Heart Failure

Advanced cases of DCM usually present with a history of exercise intolerance and clinical signs of CHF.

- Syncope related to ventricular arrhythmia or neural mediated syncope (inappropriate bradycardia and vasodilation) may be reported by the owner.
- Physical examination reveals signs typical of CHF:
  - There can be marked weight loss and cachexia.
  - The arterial blood pressure usually is normal owing to vasoconstriction and neurohormonal activation, but it will be decreased in profound DCM with cardiogenic shock.
  - Auscultation may reveal atrial and ventricular gallops, systolic murmurs, or arrhythmias.
  - The intensity of the first heart sound and strength of the arterial pulse is often diminished, indicating reduced LV contractility and stroke volume.
  - Crackles of pulmonary edema or a pleural fluid line may be evident.
  - Clinical signs of left-sided CHF include tachypnea, respiratory distress, abnormal breath sounds, and coughing related to pulmonary edema.
  - Right-sided CHF is characterized by jugular pulses and jugular venous distension, hepatomegaly, and ascites.
  - Pleural effusion is common in biventricular failure.
- Diagnostic studies in advanced cases of DCM.
  - The standard 6-lead ECG may demonstrate a number of abnormalities:
    Cardiomegaly (wide or tall P-waves; wide or increased amplitude QRS complexes).
    Myocardial disease (wide QRS, slurred R-wave descent with ST-segment coving, small complexes in boxers and English bulldogs; left bundle branch block).
    Atrial or ventricular premature complexes; atrial fibrillation; or ventricular tachycardia.
  - The signal averaged ECG may demonstrate late potentials indicating increased risk for ventricular fibrillation.
  - Thoracic radiography reveals cardiomegaly and typical vascular and pulmonary parenchymal features of heart failure. Pleural effusion is common.
  - The echocardiogram shows left ventricular dilation with reduced LV shortening fraction. Other common findings include:
    Increased mitral E-point to septal separation.
    Decreased LV or septal wall excursions.
    LA dilation.
    Variable right-sided cardiomegaly.
    Doppler evidence of mitral regurgitation and tricuspid regurgitation.
    Possible evidence for pulmonary hypertension.
    Diastolic ventricular dysfunction with a restrictive filling pattern.
- Routine chemistry laboratory tests are usually normal or reflect intercurrent disease, consequences of CHF, or complications of CHF therapy.
  - Specialized blood tests for taurine may be performed in selected cases (mainly in American cocker spaniels, golden retrievers, Newfoundlands, breeds atypical for DCM, and in dogs receiving all lamb and rice diets).
  - Cardiac troponin-I is usually elevated along with increased plasma ANP and BNP.
- Therapy of CHF associated with DCM is discussed in detail in Chapter 147.
- *Principles of Hospital Management of CHF include*
  - Administer *furosemide* (2–5 mg/kg IV); follow this with repeated IV or IM injections. Alternatively begin a constant rate infusion of furosemide.
  - Provide supplemental *oxygen* by nasal prongs or other method appropriate for the size of the dog. If oxygen is unavailable, direct a fan to the facial region to minimize dyspnea.
  - Administer *nitroglycerin* ointment topically (1–1.5 inches for a large breed dog q12h).
  - Treat life-threatening pulmonary edema with afterload reduction using an infusion of sodium *nitroprusside* (0.5–2.5 mcg/kg/min is the typical dosage range) with careful attention paid to arterial blood pressure. Titrate the infusion to a systolic value of 90 to 100 mm Hg. A less effective alternative for load reduction is enalapril at 0.25 to 0.5 mg/kg PO q12h.
  - Perform *thoracocentesis* if there is a moderate to large pleural effusion.
  - For CHF with systemic hypotension begin an infusion of *dobutamine* (2.5–10 mcg/kg/min) for 24 to 48 hours. Dobutamine can have benefits beyond the period of infusion.
- In the setting of hypotension, arterial vasodilators such as nitroprusside or an ACEI should be avoided until the pressure is stabilized by dobutamine.
- In dogs with AF, digoxin (0.01mg/kg PO q12h for the first two doses; 0.005 mg/kg PO q12h thereafter) is prescribed to control the ventricular rate response.
- Principles of long-term home management of CHF include
  - Furosemide (2–4 mg/kg PO q8-12h)
  - Spironolactone (1–2 mg/kg PO once or twice daily)
  - Enalapril or benazepril (0.25 mg/kg PO q12h; increase to 0.5 mg/kg PO q12h after the first reevaluation)
  - Digoxin (0.003–0.005 mg/kg PO q12h) unless there are contraindications for therapy such as ventricular ectopy or renal failure.
  - Pimobendan (Vetmedin, 0.2–0.3 mg/kg PO q12h) if available, generally supplants digoxin except in AF when both drugs are administered.
  - A sodium-restricted diet.
  - A β-blocker may be considered to blunt the cardiotoxic effects of the sympathetic nervous system; however, heart failure must be well controlled first. Consider carvedilol (Coreg), starting at 0.05 to 0.1 mg/kg PO q12h; up-titrate the dose every 2 to 4 weeks to a target of 0.2 to 0.4 mg/kg PO q12h.

Having pimobendan on-board facilitates up-titration of the beta-blocker.
Unfortunately, the prescription drug (Coreg) is expensive.
Dosing can be difficult in that dogs may not tolerate the negative inotropy of any β–blocker.

- When AF complicates CHF, diltiazem (up-titrate from 0.5–2.0 mg/kg PO q8h) is prescribed to control ventricular rate (see details in next section). Once heart rate is controlled, a long-acting form of diltiazem can be substituted (using the same total daily dose, but administered once or twice daily).
- Fish oil supplements containing omega-3 fatty acids may improve appetite and reduce cardiac cachexia (EPA—30–40 mg/kg PO daily; DHA—20–25 mg/kg PO daily).
- In dogs with a diagnosis of hypothyroidism, ensure that the plasma level is checked to prevent iatrogenic hyperthyroidism, a condition that increases the demand for cardiac output and is arrhythmogenic. In general, even a giant breed dog with hypothyroidism should not receive more than 0.6 to 0.8 mg of L-thyroxin daily.
- For serious ventricular arrhythmias in the setting of CHF: mexiletine (5–8 mg/kg tid) plus a low dose beta-blocker. Amiodarone or procainamide are alternatives, but results have not always been favorable. Optimally, a Holter ECG should be used to assess therapy.

Arrhythmogenic Cardiomyopathy

The term "arrhythmogenic cardiomyopathy" is a useful expression that refers to recurrent or persistent ventricular or atrial arrhythmias in the setting of a normal echocardiogram. The most commonly observed rhythm disturbances are PVCs and ventricular tachycardia (VT). However, atrial rhythm disturbances may be recognized including atrial fibrillation, paroxysmal or sustained atrial tachycardia, and atrial flutter.

- As discussed above, some dogs affected with arrhythmogenic cardiomyopathy clearly progress to classic DCM; however, many others do not. Thus, in some dogs, the key to clinical management of cardiomyopathy is control of the cardiac arrhythmia.
- ARVC—Arrhythmogenic cardiomyopathy with ventricular arrhythmias is particularly common in the boxer dog (and also in English bulldogs), where the term *arrhythmogenic right ventricular cardiomyopathy* (ARVC) is used to indicate the putative origin of arrhythmia. This term has largely replaced the "boxer cardiomyopathy" designation, but Harpster's original classification is still useful.
  - Many boxers demonstrate only isolated PVCs (upright or with a left bundle branch block morphology in leads I and II). Many boxers carry this Type I designation for years without incident.
  - Boxers often collapse or faint due to sustained VT; these were classified as Type II.
  - Some boxers will progress to develop more "classic" DCM as well, often with marked biventricular CHF. Ventricular and atrial arrhythmias are common in these Type III dogs.
- *Doberman Pinschers*—The Doberman pinscher is another breed that often manifests ventricular ectopics prior to the development of overt myocardial failure (DCM). Many of these dogs die suddenly, without premonitory bouts of syncope and before the onset of heart failure. Others progress to classic DCM with left-sided or biventricular CHF.
- *Lone AF*—The Irish wolfhound, Great Dane, and Newfoundland are giant breeds prone to AF without obvious impairment of LV contractility. Frequently, onset of AF is preceded by atrial premature complexes or paroxysmal atrial tachycardia or flutter.
  - This can be considered another form of arrhythmogenic cardiomyopathy, though it is more often designated as lone AF or occult DCM.
  - In one report, the average time interval between recognition of AF and CHF in Irish wolfhounds was about 2 years, but progressive DCM was a common feature of many dogs.
  - The results of other reports indicate that a relationship between AF and DCM is less clear.
- *Clinical Assessment*—A data base should be obtained from dogs with suspected arrhythmogenic cardiomyopathy, including
  - Careful review of clinical signs relevant to the arrhythmia.
  - Medication history.
  - Complete physical examination.
  - CBC and serum biochemical profile (including electrolytes).
  - Serum troponin-I (cTn-I).
  - Routine ECG with a long rhythm strip.
  - Ambulatory (Holter) ECG, especially when the rhythm is characterized by only isolated atrial or ventricular premature complexes and there are no related clinical signs. The Holter ECG is particularly important in the asymptomatic patient with a rhythm strip that does not indicate a clear need for therapy.
  - Echocardiogram.
  - Thoracic radiograph (optional).

From this information, the clinician should determine the most likely *etiology* of the rhythm disturbance and also attempt to judge the *overall clinical significance* of the arrhythmia. This assessment is pivotal to any therapeutic decisions.

- *Differential Diagnosis*—Arrhythmogenic cardiomyopathy must be distinguished from other causes of cardiac arrhythmias with normal left ventricular function.

- Other recognized disorders associated with cardiac arrhythmias should be excluded, for example:
  Cardiac tumors (hemangiosarcoma)
  Electrolyte imbalance (hypokalemia, calcium disturbances)
  Systemic hypertension
  Splenic tumor
  Postoperative or traumatic ventricular arrhythmia (caused by ischemia and reperfusion injury).
- A drug history should be obtained to ensure the arrhythmia is not caused by drugs or hormones that increase sympathetic tone (including excessive supplementation of L-thyroxin).
- In those cases where LV systolic function is reduced, a revised diagnosis of DCM with arrhythmia is appropriate, so long as a tachycardia-induced cardiomyopathy is eliminated.
  Sustained tachyarrhythmias can cause a reversible tachycardia-induced dilated cardiomyopathy; this is most likely when the tachycardia is relentless, with few intervals of sinus rhythm.
  In such cases, it is valuable to assess LV function before and 3 to 4 weeks after control of the tachyarrhythmia. Once the rhythm or heart rate response has been controlled, a more objective assessment of ventricular function can be obtained.

- *Management Approach*—Successful management of isolated arrhythmias in dogs is similar to that associated with treatment of arrhythmias in CHF, but with the advantage that normal ventricular function allows a wider selection and higher dosages of anti-arrhythmic drugs to be used. Most of the drugs used to control heart rhythm also depress cardiac function. This effect limits anti-arrhythmic drug use in heart failure. In this regard, the clinician should be vigilant, since an arrhythmia may be the first sign of progressive myocardial disease, and DCM and CHF may develop in the future.
  - The first question to address is whether the arrhythmias should even be treated. For example, isolated PVCs or atrial premature complexes probably should not be treated with potent anti-arrhythmic drugs unless there have been signs related to collapse or syncope.
  - The goals of therapy are three: prevent sudden death; prevent or reduce clinical signs; and protect the ventricle from tachycardia-induced cardiomyopathy.
  - When anti-arrhythmic therapy is prescribed, discuss the adverse drug effects with the owner, the importance of follow up ECGs (including Holter recordings), and discuss the potential for pro-arrhythmia (worsening of the rhythm).
  - Remember that the duration of therapy depends on the likely etiology of disease. In many cases of arrhythmogenic cardiomyopathy, treatment will be lifelong.
  - Have the client record any symptoms that might be related to the arrhythmias or possible adverse effects of the drugs.
  - Follow up with the patient at regular intervals. Begin with a client interview and routine auscultation. Follow with a standard ECG (if an arrhythmia is detected). Consider the use of a Holter ECG.
  - When a patient is stable on routine ECGs and is receiving a consistent dose of medication, perform another Holter ECG.

▼ ***Key Point*** Evaluate the response to therapy with both a routine ECG and a Holter ECG.

- *Lone Atrial Fibrillation*—In dogs with lone AF, Holter data provide insight about the daily heart rate and the exercise heart rate. Average daily heart rates that exceed 90 to 95/min or moderate-level exercise heart rates that exceed 200/min are reasonable grounds for slowing the heart rate response to AF or referring for cardioversion.
  - *Beta-blocker therapy* for heart rate control—Control of the ventricular rate response can be achieved with atenolol (0.5–1 mg/kg PO q12h) or metoprolol (12.5 mg PO twice daily in giant breeds). These drugs are also potentially cardioprotective if the AF is a premonitory sign of future DCM.
    For the first three days, the initial dose of the beta-blocker should be 50% of the prescribed dose, to prevent undue lethargy.
    Thereafter, the drug dose can be titrated up over 2 to 4 weeks to achieve an appropriate average daily heart rate (generally in the range of 70–80/min).
  - *Diltiazem therapy* for heart rate control—The use of this calcium channel blocker (dosed at 1–2.0 mg/kg PO q8h) is effective in controlling heart rate but does not confer the "cardioprotection" of beta-blockers should the arrhythmia represent early DCM. An initial dose of 0.6 mg/kg PO q8h for the first day is recommended before increasing the dose. Diltiazem can be used in combination with a beta-blocker. A long-acting preparation of diltiazem can also be used if q8h dosing is difficult (using the same total daily dosage, divided q12h).
  - *Digoxin therapy*—While digoxin can be prescribed for lone AF, cardiac glycosides are less effective for controlling excessive exercise-related rates and are not recommended by us when there is no evidence of heart failure.
  - *Cardioversion*—The conversion of AF back to sinus rhythm is definitely possible in dogs with lone AF. The use of procainamide, sotalol, or amiodarone for this purpose has met with mixed, and generally unfavorable, results. However, electrical DC biphasic cardioversion is highly successful in the setting of lone AF, especially in giant breeds, provided low-dose amiodarone is administered following the

procedure to maintain normal rhythm. This procedure requires referral to a cardiologist.

- *Ventricular arrhythmias and ventricular tachycardia*—Grading the severity of ventricular arrhythmias in terms of relative risk for sudden death is difficult but highly pertinent to management of these dogs. Once this had been done, and if a decision is made to treat the arrhythmia, a long-term plan for management should be established.
  - Relative Risk—Clearly the presence of clinical signs (collapse, syncope) is an indication to control ventricular tachycardia if the clinician is certain that a tachyarrhythmia is the basis for the episodes. In most cases, the situation is less clear cut, and the clinician must "grade" the arrhythmia in terms of severity.

    Isolated PVCs or runs of monomorphic, "slow" VT (usually <160/min) frequently are not treated. Couplets are not necessarily more dangerous than single PVCs, but closely timed couplets may indicate a higher "grade" of arrhythmia.

    Polymorphic VT (including torsade de pointe); non-sustained but flutter-like runs of VT; long runs of monomorphic, fast VT (exceeding 200/min); frequent multiform PVCs; and PVCs falling on the prior T-waves (R on T) suggest a higher grade or complexity of the arrhythmia. Anti-arrhythmic therapy is usually recommended.

    When serious arrhythmias are evident on a routine ECG, there is probably no need to perform a Holter ECG until after therapy has begun, especially in the dog with clinical signs. When a routine ECG shows "low-grade" arrhythmias such as isolated PVCs or runs of "slow" VT, it is reassuring to know if the results of a 24-hour Holter ECG support a low grade of complexity before deciding not to treat.

    When doubt remains, obtain consultation if possible.

▼ ***Key Point*** Decisions about initiating anti-arrhythmic therapy are imperfect, and dogs with recurrent PVCs or VT—whether on or off therapy—always carry a risk for sudden cardiac death. No anti-arrhythmic drug has been proven to prevent sudden death in dogs.

  - *Isolated PVCs*—Generally, it is better not to treat isolated PVCs. However, when they are frequent (such as >10,000 per day or about 7 PVCs per minute) they may be difficult to ignore. One well tolerated approach is to prescribe a beta-blocker such as atenolol (0.5–1 mg/kg PO q12h), which will likely reduce the total number of ectopics but not create a pro-arrhythmic situation.
  - *Ventricular Tachycardia*—When treatment is elected, the choice of drug depends largely on personal preference, but some recommendations can be advanced. The Chapter "Cardiovascular Drugs" describes the clinical pharmacology, use, and adverse effects of these drugs.

    Sotalol (1–2 mg/kg PO q12h) is generally well tolerated in dogs and clearly improves Holter ECG recordings in some breeds (such as boxers). This drug should not be used in German shepherds with inherited ventricular ectopy.

    Mexiletine—An oral drug related to lidocaine, mexiletine (Mexitil) is an effective ventricular anti-arrhythmic in many dogs (5–8 mg/kg PO q8h). We combine it with a β-blocker such as propranolol (0.5–1 mg/kg PO q8h) or atenolol (0.5–1 mg/kg PO q12h). Anorexia, tremors, and vomiting are adverse effects. For unresponsive patients, sotalol (1 mg/kg PO q12h) can be substituted for the other beta-blocker.

    Amiodarone (Cordarone) is an effective drug for VT, but may be more pro-arrhythmic and carries a higher incidence of adverse effects than sotalol. With a long elimination half-life, a loading dose is used initially (5–10 mg/kg PO q12h) followed by a lower maintenance dose (4–6 mg/kg PO once daily).

    Procainamide—The use of a long-acting procainamide preparation (15–20 mg/kg PO q8h) is recommended as procainamide HCl has a very short elimination half-life in dogs. As with mexiletine, it may be more effective when combined with a beta-blocker.

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Chapter

151 Pericardial Diseases

John D. Bonagura

The pericardium consists of two mesothelial-lined membranes: the visceral layer (epicardium) that is tightly adhered to the myocardium and the reflection of this membrane that forms the parietal pericardium. Between these is a space that contains the heart, origins of the major arteries, and terminations of the vena cava and pulmonary veins. The normal pericardial space also contains a very small amount of serous, lubricating pericardial fluid. The normal pericardium limits acute cardiac dilatation, maintains cardiac geometry, contributes to ventricular compliance and interdependence, reduces friction, and provides a barrier from inflammation. The pericardium is not essential to survival and can be removed surgically.

- The most important congenital forms of pericardial disease are congenital *peritoneopericardial diaphragmatic hernia* (PPDH) and the relatively rare congenital *pericardial cysts* (which will not be discussed in this chapter).
- The main acquired pericardial diseases in dogs and cats are pericardial effusion (PE), constrictive pericarditis, and constrictive-effusive pericardial disease. In many cases, PE is related to the presence of a cardiac or heart-base neoplasm.
- *PE* is the accumulation of excessive or abnormal fluid within the pericardial space.
- *Cardiac tamponade* refers to a state of cardiac compression and impaired filling from increased intrapericardial pressure. While mass lesions and cysts can compress the heart, the majority of cases are caused by a PE.
- The total volume within the pericardial space is finite. Pericardial fluid accumulation can occur only if the parietal pericardium stretches (increasing the volume of the pericardial space) or the volume within the cardiac chamber shrinks.
- Since the parietal pericardium contains few elastic fibers, it is not easily distended in the setting of acute fluid accumulation. For this reason, even small volumes of acute intra-pericardial hemorrhage can produce cardiac tamponade.
- When parietal effusion develops more gradually, the parietal pericardium and pericardial space expand substantially. Progressive pericardial stretching, combined with increases in venous pressure, permit a situation in which large volumes of PE may develop. Effusions exceeding one liter may accumulate in larger dogs.
- *Pericardial constriction* occurs secondary to pericardial inflammation or scarring. The normally strong pericardium becomes thicker and fluid within the space is reabsorbed. Eventually the pericardial membranes act as a "shrink wrap" about the heart.
- *Constrictive-effusive pericardial disease* is a condition that includes both pericardial restriction and a small volume of pericardial fluid.
- Pericardial diseases can eventually cause congestive heart failure (CHF).

▼ ***Key Point*** Pericardial disease is one of the most common causes of right-sided heart failure in the dog. In older dogs, cardiac or heart-base neoplasia is a common etiology.

PERITONEOPERICARDIAL DIAPHRAGMATIC HERNIA

PPDH is a defect in the embryologic septum transversum that separates the peritoneal from the pericardial space. Defects permit direct communication of abdominal organs or tissue with the heart. PPDH is relatively common in cats and also can develop in dogs. (Weimaraner dogs and schnauzers are predisposed.) Males may be predisposed. Himalayan and domesticated long-haired cats were more likely to be affected by PPDH in one study.

In cats, it is typical for the hernia to contain mainly fat with one or more lobes of liver. In the dog the hernia may be subtle, containing only falciform fat, or there may be liver or loops of intestine contained.

Clinical Signs

Many affected dogs and cats are without overt clinical signs, unless the hernia is large and there is a large volume of herniated abdominal content within the thorax. Infrequently, liver strangulation may lead to signs of discomfort.

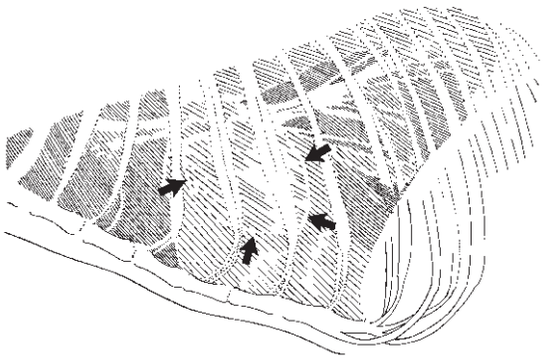

Figure 151-1. Representation of the enlarged cardiac silhouette and double-density cardiac shadow caused by omental fat in a patient with peritoneopericardial diaphragmatic hernia. Arrows indicate the edge of the heart.

Diagnosis

Physical Examination

- The diagnosis may first be suspected during routine examination as heart sounds may be muffled or displaced.
- Often there is a systolic murmur, which may be functional or represent a concurrent cardiac defect.
- Abdominal palpation may reveal a concurrent umbilical hernia.
- In a small percentage of patients, there are clear anomalies of the sternum; these may be palpable or evident by radiography.

Diagnostic Imaging

- Careful radiographic examination leads one to suspect the diagnosis (Fig. 151-1).
- One typically observes altered radiographic density in the caudoventral portion of the pericardial space. The heart and carina are usually displaced craniodorsally, as are pulmonary venous entries to the left atrium.
- Ventral to the caudal vena cava there may be a soft tissue shadow, the persistent mesothelial remnant that delineates the dorsal border of the hernia.
- Intestinal loops may create an unusual gas pattern within the mediastinum (pericardial space).
- Ultrasonography of the thorax, or a barium swallow (if intestinal loops are present) will be diagnostic.

Treatment

Treatment of PPDH is surgical and optimally accomplished at the time of spay/neuter. Surgical results have indicated a very favorable outcome. However, a PPDH often is an incidental finding in mature animals, and in these cases, surgical intervention may not be warranted unless intestines are contained within the thorax or the risk of herniation is deemed high. Consultation with an experienced surgeon can be helpful in these patients.

Cardiac tamponade is a rare complication of PPDH. Entrapment of a loop of bowel or strangulation of the liver requires prompt recognition and surgical management.

PERICARDIAL EFFUSION

Etiology

- Acquired PE is very common in dogs and is observed sporadically in cats.
- *Transudation* into the pericardial space occurs secondary to PPDH, right-sided CHF, cysts, hypoalbuminemia, infections/toxemia, and causes of increased vascular permeability. These fluid accumulations tend to be relatively small and are often incidental necropsy or ultrasound findings. Small effusions do not to impair heart function. There are two noteworthy clinical situations that do merit comment.
  - Mass lesions at the heart base, including chemodectomas, can obstruct lymphatic drainage leading to a large and compressive transudative PE.
  - In cats with severe CHF, a very large PE may develop which may resolve with successful medical therapy of heart failure.
- *Exudation* into the pericardial space is usually caused by infective or non-infective pericarditis; these conditions are relatively uncommon in small animals.
  - Nocardia infection and perforating foreign bodies are potential causes of septic pericarditis in dogs and cats.
  - Fungal involvement of the pericardium is recognized with coccidiomyocosis in the dog or with opportunistic fungi in immunosuppressed dogs (e.g., aspergillosis).
  - Idiopathic, sterile (inflammatory) pericarditis can develop occasionally in the dog and also may be a consequence of recurrent, idiopathic intrapericardial hemorrhage.
  - Pericarditis in cats has been associated infrequently with feline cardiomyopathy but does occur in the polyserositis form of infection with feline infectious peritonitis virus.
- *Idiopathic intrapericardial hemorrhage* (with or without secondary pericardial reaction) is relatively common in dogs. This is a disorder of dogs typically less than 7 or 8 years of age, though it can occur in older dogs. As the name suggests, the etiology is unknown. Recurrent bleeding evokes an inflammatory reaction with pericardial thickening that can be difficult to distinguish from mesothelioma. Constrictive or constrictive-effusive pericardial disease can develop.
- *Neoplasia* of the heart, heart base, or pericardium frequently leads to a hemorrhagic effusion in dogs.
  - *Hemangiosarcoma* of the right atrium is especially common in dogs >7 years of age. Tumors can be isolated to the heart or multicentric with splenic

involvement and pulmonary or distant metastasis. Metastatic disease is very common.
  - *Aortic body tumor* (or *chemodectoma*) originates from the base of the aorta and grows along the heart base, often along the path of least resistance. Metastatic disease is very unusual.
  - Ectopic (heart-base) *thyroid carcinoma* can cause a large heart base mass that is more likely to invade the myocardium.
  - *Mesothelioma* of the pericardium also occurs frequently, but the diagnosis is often difficult as discussed below. Progressive growth is typical and the pericardium may scar or constrict.
  - *Lymphosarcoma* of the right atrium and ventricles is an important cardiac neoplasm in the cat but is considered a rare cause of PE in dogs. It is frequently multicentric.
  - *Metastatic carcinoma* to the heart or pericardium is rare in dogs or cats.
  - Other cardiac tumor types (e.g., fibrosarcoma) have been reported but are rare.
- *Left atrial rupture* can occur in dogs with mitral regurgitation from chronic valvular endocardiosis. Linear tears develop within the stretched left atrial wall and occasionally transmural separation occurs leading to sudden cardiac tamponade.
- *Uncommon causes* of pericardial hemorrhage include blunt chest trauma; puncture of the heart (knife, bullet, and missile); coagulopathy, and as a complication of thoracocentesis.
- *Chyle* is a very rare fluid type in the pericardial space.

Pathophysiology

- The cause and underlying pathophysiology of a pericardial disorder influences the clinical presentation. An understanding of these processes (Fig. 151-2) is instructive relative to diagnostic studies and therapy.

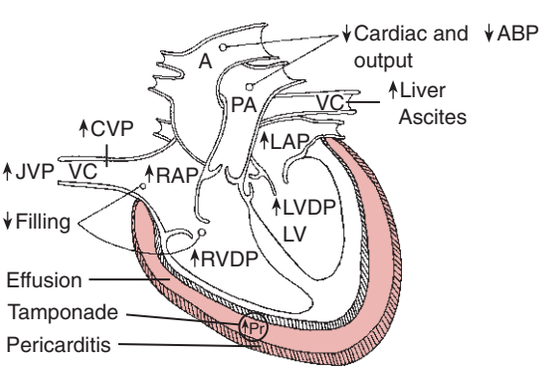

Figure 151-2. Diagrammatic representation of pericardial effusion. See text for explanation. A, aorta; ABP, arterial blood pressure; CVP, central venous pressure; JVP, jugular venous pressure; LAP, left atrial pressure; LV, left ventricle; LVDP, left ventricular diastolic pressure; PA, pulmonary artery; Pr, pressure; RAP, right atrial pressure; RVDP, right ventricular diastolic pressure; VC, vena cava.

- Inflammatory disease within the pericardial space may create clinical signs related to localized chest discomfort or constitutional signs of systemic inflammation. This is especially true in cases of septic pericarditis.
- *Cardiac tamponade* is the major pathophysiologic event in PE and represents the state of cardiac compression caused by increased intrapericardial fluid pressure. The normally negative inspiratory pericardial pressure becomes positive. This can be documented in clinical cases by a simple fluid manometer attached to a drainage catheter that has entered the pericardial space.
  - Tamponade is the mechanism by which low cardiac output and congestive heart failure (CHF) develop with PE.
  - Intrapericardial pressures can rise rapidly as the elastic limits of the membrane are exceeded (a steep pressure to volume relationship).
  - Increased (positive) intrapericardial pressure develops leading to diastolic collapse of the right atrium and the right ventricle along with compression of the vena cava.
  - Reduced right ventricular filling decreases preload and cardiac output; systemic hypotension occurs if sympathetic and fluid-retaining compensatory mechanisms are insufficient.
  - Syncope, collapse, or sudden death may occur if systemic hypotension is severe.
  - However, given sufficient time ABP is reestablished by combinations of heightened sympathetic discharge, systemic vasoconstriction, renal retention of sodium and water, and elevated venous pressures.
  - Extremely high venous pressures are characteristic of chronic pericardial diseases. Congestive heart failure, with a predominately right-sided component (ascites, pleural effusion, subcutaneous edema) is the consequence of *chronic* cardiac tamponade or constriction.
  - Additional hemodynamic features include equilibration of diastolic pressures in the ventricles, atria and great veins, and accentuated respiratory variation in ABP (pulsus paradoxicus).
- Diastolic equilibration of pressures requires cardiac catheterization for documentation.
- Pulsus paradoxicus is readily identified by palpation or ABP measurement with a Doppler flow system and is defined as an exaggerated fall in the ABP and pulse pressure during inspiration (see "Physical Examination").
- Pulsus paradoxicus is explained by exaggeration of the normal respiratory-induced variation in right and left-sided cardiac filling. Left ventricular filling and systemic arterial pressure fall as right ventricular filling is augmented by negative inspiratory pleural pressures. Since the total volume with the pericardial space is finite, the increased venous return shifts the ventricular septum into the left

ventricle during inspiration, reducing LV preload and stroke volume. As a result, palpable pulse pressure and measured systolic ABP decline during inspiration and increase with expiration as the process is reversed.

Diagnosis

The clinical diagnosis of PE follows a logical course from history and physical examination to selection of diagnostic tests. These studies should establish the diagnosis, etiology, and clinical significance of a PE. The electrocardiogram, thoracic radiography, fluoroscopy, abdominal ultrasonography, and echocardiography offer complementary information.

▼ ***Key Point*** Echocardiography is the clinical gold standard for diagnosis of PE.

Pericardiocentesis can be both diagnostic and therapeutic in this disorder. Diagnosis in some patients requires surgical exploration with biopsy of the pericardium or surrounding tissues.

Signalment

PPDH is more common in young dogs and cats but may be an incidental finding in older animals. Dogs >7 years of age are more likely to develop cardiac or heart base neoplasia. Golden retrievers and St. Bernard dogs are predisposed to idiopathic pericardial hemorrhage; brachycephalic breeds to chemodectoma; golden retrievers, Labrador retrievers, German shepherds, and many other breeds to hemangiosarcoma; golden retrievers to mesothelioma.

History

Collapse or syncope are particularly common signs with acute cardiac tamponade (e.g., sudden hemorrhage). Dogs with a history of sudden collapse are more likely to have an underlying neoplastic cause. Syncope also can occur after diuretic therapy of right-sided congestive heart failure (because elevated venous pressures are needed to maintain cardiac filling and cardiac output and this compensation is lost with volume depletion).

- Clients may note abdominal distension from CHF.
- Signs of illness may be present when there is underlying multicentric or metastatic neoplasia, septic pericarditis, or abdominal disease.

Physical Examination

- Patients with acute cardiac tamponade may be hypotensive with palpable distention of the jugular vein. A systolic ABP <90 mm Hg should be treated as an emergency with consideration for prompt pericardiocentesis.
- Elevated jugular venous pressure, distant heart sounds, and respiratory variation in blood pressure (pulsus paradoxicus) constitute the classic "triad" of physical findings in cardiac tamponade.
- The central venous pressure is generally quite high in PE, often exceeding 12 cm H_2O [normal <5 cm H_2O].
- The recognition of pulsus paradoxicus is not difficult and, in some cases, is obvious from simple palpation of the femoral arteries.
- When using a Doppler flow method for diagnosis, the pressure cuff should be slowly deflated to identify a consistent inspiratory fall and expiratory rise in systolic blood pressure. The intensity of the Doppler flow sound also changes, becoming fainter during inspiration (indicated reduced stroke volume).
- Pulsus paradoxicus is highly suggestive, though not specific for cardiac tamponade. Respiratory distress with marked variation in intrathoracic pressure can also lead to respiratory variation in the pulse. Panting can make it difficult to recognize pulsus paradoxicus.

▼ ***Key Point*** Pulsus paradoxicus is an often-overlooked physical examination finding of cardiac tamponade.

- Right-sided CHF is more typical of PE and is associated with elevated jugular venous pressure, hepatomegaly, ascites, and possibly pleural effusion. In one study, CHF was more commonly associated with idiopathic pericardial hemorrhage. Experimental PE in dogs leads to interstitial lung edema, but in clinical cases, it is rare to diagnosis overt left-sided CHF.
- Fever or thoracic pain may indicate infection or inflammation within the pericardial space.
- Cardiac auscultation of PE is characterized by muffled heart sounds. A pericardial friction rub may indicate pericarditis, but this is atypical of dogs and cats with PE.
- Breath sounds are muffled and there will be tachypnea or respiratory distress when pleural effusion complicates pericardial disease.
- Evidence of systemic disease, such as lymphosarcoma or hemangiosarcoma of the spleen might be noted during a complete physical examination.

Laboratory Tests

- Routine blood tests in pericardial disease may simply reflect the consequences of heart failure or prior diuretic therapy.
- The CBC may indicate inflammation, infection, or hemorrhage. Increased numbers of circulating nucleated RBCs are suggestive of hemangiosarcoma of the spleen (and heart). In cases of severe hemopericardium, the patients may be anemic due to blood loss or exhibit the nonregenerative anemia of chronic illness. Evidence of disseminated intravascular coagulopathy is evident with disseminated hemangiosarcoma.

- Serum troponins (cTnI) may increase with PE and are higher in the setting of cardiac neoplasia, especially in cases of hemangiosarcoma.
- Analysis of pleural or peritoneal effusions generally indicates fluid of an obstructive origin (transudate, modified transudate, or infrequently chyle). Bacterial cultures of the effusate, serum fungal titer (coccidiomycosis), or ELISA tests for FeLV or FIP (cats) may be positive when pericarditis is related to these infections.

Electrocardiogram

An **electrocardiogram** may show any of the following:

- Decreased amplitude QRS complexes (<1mV in all frontal plane leads in dogs). This finding is common but inconsistent.
- Electrical alternans (with large effusates and swinging of the heart). This is a relatively specific but insensitive finding in PE.
- ST segment elevation indicating a current of epicardial injury. This abnormality should be evident in >1 frontal plane lead and is observed most often with pericarditis.
- ST segment depression is more typical of subendocardial ischemia, which may indicate reduced blood pressure or coronary perfusion.
- Cardiac rhythms are variable.
- Sinus tachycardia is typical of cardiac tamponade, and the heart rate generally declines following pericardiocentesis.
- Vagal mediated reflexes can be invoked from stimulation of receptors within the pericardium, promoting a sinus arrhythmia with wandering pacemaker or even a "relative" bradycardia (in terms of blood pressure).
- In PE without tamponade, normal sinus rhythm or sinus arrhythmia may be observed.
- Atrial and ventricular arrhythmias are not uncommon and may develop secondary to myocardial cardiac tumors, ischemia, or concurrent primary heart disease.

Diagnostic Imaging

Radiographic techniques are valuable for identifying cardiomegaly, vascular abnormalities, pulmonary lesions, and pleural effusion.

- With moderate to severe PE, the cardiac silhouette enlarges, loses its angles and waists, and eventually becomes globular in shape ("basketball or soccer ball heart").
- The contour of the heart may become particularly sharp, related to diminished motion of the distended membrane.
- The region over the left atrium often appears more rounded as opposed to the more square appearance of true cardiomegaly.
- Should a metallic foreign body be observed over the heart on two views, constrictive or constrictive-effusive disease is likely.
- Pulmonary vascularity is often reduced from low cardiac output. This finding is in contrast to CHF from cardiomyopathy or valvular disease, wherein vascular prominence is more common.
- If CHF has developed, there may be increased pulmonary interstitial densities, distension of the caudal vena cava, hepatomegaly, or pleural effusion.
- Heart base tumors may deviate the trachea (generally to the right and dorsally), producing a mass effect. Occasionally, it may be difficult to distinguish another mediastinal tumor or a large lung tumor from a heart base tumor.
- In cases of isolated intracardiac tumor without pericardial effusion, there may be a distinct, rounded bulge in the region of the right atrium (DV projection) or right auricle (lateral projection).
- Fluoroscopy, if available, may demonstrate increased heart size with reduced cardiac motion.
- Pneumopericardiography can identify intrapericardial mass lesions, but this examination is rarely done today as echocardiography is safer and more accurate.
- Advanced imaging examinations such as computerized tomography and MRI angiography are referral examinations that require rapid acquisition systems and gating of the cardiac cycle. These methods may be useful in evaluation of mass lesions.
- Radiopharmaceutical studies may be helpful to identifying tumors of neural crest origin (chemodectoma).

Abdominal Ultrasonography

- Examination of the spleen, liver, and peritoneal space is indicated in older dogs or cats with PE.
- Hepatic venous distention and enlargement of the caudal vena cava are suggestive of right-sided CHF.
- The presence of free abdominal fluid may indicate CHF or hemorrhage of an abdominal tumor.
- The spleen and liver may demonstrate mass lesions suggesting hemangiosarcoma or metastatic disease.

Echocardiography and Doppler Studies

The echocardiogram is a highly sensitive test for detecting PE and cardiac tamponade and, in some cases, may demonstrate the etiology of disease. The distinction between idiopathic, hemorrhagic PE, and bleeding from a tumor may not be possible unless a high resolution, technically proficient echocardiogram is recorded from each side of the thorax and using multiple angled views. If the patient is stable (with ABP >90 mm Hg), and echocardiography is readily available, a brief delay is acceptable to obtain detailed imaging prior to pericardiocentesis. Cardiac and heart base tumors are more readily seen when surrounded by fluid.

- Bilateral pleural effusion is a common finding in pericardial diseases complicated by CHF. Fibrin stands and pulmonary atelectesis may be observed in some cases.
- Accumulation of fluid is evident as a sonolucent (generally black) space between the epicardium and normally hyperechoic pericardial/mediastinal interface. The fluid space typically extends from apex to base. In the most subtle effusions, the space is evident only during systole.
- Fluid with a mixed intrapericardial echogenic pattern is suggestive of an exudate or recent hemorrhage into the pericardial space.
- Acute hemorrhage may lead to a minimal effusion; for example, rupture of the left atrium may be associated with a small (<25 cc) effusion but with severe hemodynamic consequences. Conversely, in chronic cases, the PE can be great (exceeding one liter in larger breed dogs).
- Recognition of prolonged diastolic collapse (inversion) of the right atrial wall or early diastolic collapse of the right ventricular wall is supportive of increased intrapericardial pressure and is usually diagnostic of cardiac tamponade. Ventricular collapse may vary during the respiratory cycle. There can be false positives (large pleural effusion alone can cause this in dogs) and false negatives (as elevated CVP can distend the right heart chambers opposing obvious diastolic collapse).
- Cardiac mass lesions are often found in mature dogs with PE. These may be observed by transthoracic or transesophageal echocardiographic techniques. The chemodectoma (aortic body tumor) originates from the aortic root and surrounds the base of the heart; these tumors can become very large. The major differential diagnosis is the normal hyperechoic fat pad between the aorta and pulmonary artery.
- Hemangiosarcoma is usually identified within the right auricle or the right atrium (where it may resemble a smooth thrombus with focal attachment). The tumor may also invade and grow along the right atrioventricular groove.
- Mesothelioma is difficult to diagnose. The pericardium may appear thicker and one may identify roughly circular or oral tumors attached on the inner surface of the pericardium (blood clots may appear similar).
- Lymphoma in cats usually infiltrates the right atrium and the cardiac septa and is typically multifocal.
- Doppler studies can be useful in diagnosing the elusive constrictive pericardial disease. One characteristic feature is *marked* variation in cardiac filling profiles with ventilation.
- Extremely large mass lesions will impair right atrial filling, tricuspid inflow, or right ventricular outflow. These obstructions are usually accompanied by abnormal Doppler filling or ejection velocities.

Pericardiocentesis

- Fluid samples can be collected for analysis in cases of PE by the technique of pericardiocentesis. Drainage of the pericardium is also therapeutic (see "Therapy" for more details).
- Measurement of "static" intrapericardial fluid pressure prior to removing any PE can be accomplished by attaching one end of a saline-filled extension tube to the intrapericardial catheter and the other end to a central venous pressure manometer (prior to any drainage). While somewhat crude, the results can be instructive. Cases of tamponade demonstrate a high (positive) pressure, usually >12 cm to 15 H_2O above the midsternal line, with the patient resting in lateral recumbency. The pressure becomes subatmospheric following pericardiocentesis and rises and falls with ventilation. With constrictive-effusive pericardial disease, PE without tamponade, or isolated pleural effusion, the intrapericardial pressure may be near normal (i.e., near zero cm H_2O).

Fluid Analysis

- A sample of fluid can be collected anaerobically for measurement of pH. However, the pH of pericardial fluid is usually not diagnostic, unless it is very low (<7.0), a finding suggestive of pericardial inflammation. Values of 7.3 to 7.4 or greater are more typical of neoplasia or recent hemorrhage.
- Collected fluid eventually should be evaluated by a clinical pathologist. A Diff-quick stain can be used to screen a slide for obvious septic pericarditis while awaiting results from the laboratory.
- Fluid can be classified simply as a transudate, exudate, hemorrhage, or chyle.
- Except in cases of lymphosarcoma or septic inflammation, cytologic examination may not be especially helpful.
- It can be difficult to conclusively identify neoplastic cells within pericardial effusates. The problems include poor exfoliation of hemangiosarcoma and chemodectoma and the tendency to over-interpret reactive mesothelial cells as diagnostic of mesothelioma.

Confirming the Etiology and Establishing Prognosis in Pericardial Effusion

Knowledge of the underlying cause of pericardial disease has a great impact on disease management, prognosis, and client decisions. The prognosis of pericardial disease depends on the cause. Unfortunately, even with a high quality transthoracic echocardiographic examination and expert interpretation of pericardial fluid cytology, the underlying etiology for PE may be inconclusive.

▼ ***Key Point*** Establishing an etiology of pericardial effusion is pivotal as survival time in idiopathic pericardial effusion is very long when compared to neoplastic causes.

Idiopathic Pericardial Hemorrhage

In young dogs with PE, the diagnosis of *idiopathic pericardial hemorrhage* is one of exclusion. Such a diagnosis is tenable in the absence of a cardiac mass and with cytological findings of intrapericardial hemorrhage and mesothelial reaction without signs of infection or inflammation. Many dogs with idiopathic hemorrhagic PE recover completely following repeated pericardiocentesis or subtotal pericardiectomy. In one study, dogs undergoing pericardiectomy for idiopathic PE had a median survival of 1,218 days compared with 532 days for those not undergoing surgery.

Pericarditis

If cytology demonstrates an *infective* or *inflammatory pericarditis* in a dog or a cat, consider the condition a surgical disease. The prognosis with infective or inflammatory pericarditis is always guarded, but with prompt recognition a good outcome may be realized. The best long-term results will be obtained with subtotal pericardiectomy prior to the onset of constrictive pericarditis.

Neoplasia

Once dogs have achieved the age of 6 to 8 years, idiopathic hemorrhagic effusion or pericarditis remain viable diagnoses; however, *cardiac* or *related neoplasia* is the main etiologic consideration for PE. This conclusion impacts the prognosis considerably, and clients should be so advised. The clinician's and the client's expectations, resources, and perspective will influence management options in this group of canine patients. Nearly all published studies detailing prognosis with pericardial disease are retrospective, making it impossible to compare different treatment approaches or determine true prognosis.

Chemodectoma

Chemodectomas (aortic body tumors) often grow slowly, and in many cases, the PE can be palliated for more than one year with a pericardial window or subtotal pericardiectomy (with or without surgical removal or reduction of the primary tumor). In one small study of dogs with PE due to chemodectoma, median survival was 730 days with surgery. The prognosis is grave when the tumor is very large and the mass compresses vital structures or pulmonary venous drainage.

Right Atrial Hemangiosarcoma

The prognosis for *right atrial hemangiosarcoma* based on my experience and published information is very poor overall (although there are always exceptional cases). Some studies suggest benefit of partial pericardiectomy and others report no benefit. Even with chemotherapy (with or without surgical resection and pericardiectomy), most dogs do not survive for six months. Many dogs have multicentric disease or metastasis by the time of diagnosis (also see Chapter 28).

Ectopic Thyroid Carcinoma

Ectopic thyroid carcinomas can be particularly invasive and have a grave prognosis unless the tumor responds dramatically to chemotherapy.

Mesothelioma

Mesothelioma is a very difficult cancer to manage and chronic disease can be associated with pericardial constriction. The long-term survival reported for mesothelioma in the literature has been totally incongruous (ranging from weeks to years), and this confusion simply verifies the difficulty of establishing the diagnosis with certainty in many dogs. Clients should be given a poor prognosis but hope that the biopsy may not predict the actual biological behavior of the disease. Most dogs that are treated undergo a pericardiectomy during the collection of biopsy samples. Chemotherapy (see below) has not been very beneficial.

Idiopathic Pericardial Effusion

PE without an obvious cause is a common clinical dilemma is the older dog with PE but without a clearly delineated cardiac or heart base tumor. Following pericardiocentesis, one of two general courses can be followed to establish the etiology, prognosis, and treatment options: 1) regular surveillance with follow-up imaging; or 2) surgical exploration of the thorax and pericardium, especially with recurrent effusion.

Monitoring and Reevaluation

When the risk of neoplastic-associated PE is high, recommend repeated echocardiographic and ultrasound examinations of the heart and spleen (for example, at 2 weeks, 3 months, and 6 months after initial presentation), along with routine chest radiographs (for metastatic disease). Not only does this allow detection and management of recurring PE, but negative findings help to exclude neoplasia as a cause of disease.

- Hemangiosarcoma sufficient to cause PE should be relatively aggressive in behavior and demonstrable on repeated evaluation.

- While chemodectomas are slow growing tumors, regular reevaluation with echocardiography at the intervals noted above should reveal in time a heart base mass.
- Where available, referral for transesophageal echocardiography should be considered for identification of occult cardiac mass lesions. This technique has a higher sensitivity than for transthoracic examination. However, anesthesia is needed and the patient first must be stabilized.
- Referral for advanced imaging (high speed, gated, CT or MRI) may be useful for identifying a cardiac mass lesion, a predisposing abdominal tumor (usually hemangiosarcoma), or pulmonary metastasis.

Diagnostic Surgical Exploration

- Exploration of the thorax is a viable option for the older dog with PE of unknown etiology. Mesothelioma creates the greatest diagnostic problems, as even follow-up imaging studies may not be conclusive with this cancer.
- There are some who believe that time will separate cases of idiopathic hemorrhage with mesothelial reaction from true cases of mesothelioma. The latter is likely to have a progressive and more malignant course of unresponsive effusion. However, other reports indicate a potentially long survival time with this tumor.
- When definitive diagnosis is deemed important, consideration should be given to surgical examination of the thorax and pericardial space. Pericardiectomy should be done at the same time.
- Surgical exploration or a thoracoscopy procedure may be helpful in this type of patient. Exploratoration offers the chance to identify a cardiac or heart base mass, obtain a pericardial biopsy sample, and create a large pericardial window that may prevent recurrent cardiac tamponade. The last point is important because even with surgical examination and biopsy of the pericardium, an etiology may not be certain.
- Advise clients that even with a surgical approach to diagnosis, a definitive prognosis may not be possible, and consultation with the pathologist and an oncologist may be needed.
- Pericardial tissues can respond to hemorrhage or other insults with the formation of reactive tissue growth, including reactive pericardial fronds. Benign mesothelial cells have been reported to embolize to regional lymphatics (generally a sign of malignancy).
- Examination of these tissues and the cells that exfoliate from them can prompt an erroneous diagnosis of neoplastic disease. To complicate issues further, there are reported cases of long-term idiopathic hemorrhage transforming to mesothelioma.

Treatment

The treatment of PE involves consideration of the underlying etiology and initial stabilization with pericardiocentesis. Following this procedure, the potential for repeated pericardial taps or for various surgical and catheter-based methods must be considered on a case-by-case basis. Consultation with a cardiologist, oncologist, or surgical specialist may be helpful.

Pericardiocentesis

- Aspiration of PE is the treatment of choice for initial stabilization of the patient. Because of the steep pressure volume relationship of pericardial disease, removing even a modest amount of PE (25–50% of the total) is likely to relieve tamponade, improve ventricular filling, and increase cardiac output.
- The procedure can be performed using a long needle; a through-the-needle catheter; an over-the-needle intravascular catheter; a commercial thoracocentesis or pericardiocentesis drainage system; or a cardiac catheter inserted by a percutaneous, transthoracic approach. A long needle becomes relatively dangerous as the PE volume is reduced; a through-the-needle catheter tends to kink; and percutaneous catheterization of the pericardial space is only recommended if there is an intent to place a balloon dilation catheter (for balloon pericardiotomy).
- While commercial pericardiocentesis catheter drainage systems work well, for dogs >6 kg, I prefer a 14- to 16-gauge Angiocath or similar over-the-needle catheter.
- I use a 23- or 21-gauge butterfly infusion needle for cats or very small dogs.
- Place an intravenous catheter for administration of emergency drugs. ECG leads should be attached for rhythm monitoring. An ABP cuff is secured to monitor blood pressure.
- If ABP is stable, mild sedation is often tolerated and improves the procedure for all.
- In dogs, butorphanol at 0.2 to 0.4 mg/kg IM is generally safe.
- In cats butorphanol 0.25 mg/kg IM followed by 2 to 5 mg of ketamine, IV will provide about 5 minutes of restraint.
- Should symptomatic hypotension develop after sedation, infuse saline solution intravenously or administer dopamine (2–5 mcg/kg/min). Administer atropine (0.02–0.04 mg/kg, IV or IM) if symptomatic bradycardia occurs.

Technique

1. The tap can proceed from the right side (cardiac notch) or left hemithorax, depending on operator preference, the situation, and echocardiographic

findings. The author prefers the right-sided intercostal approach to avoid the larger left coronary vessels.

2. Place the patient in (left) lateral recumbency and the spine elevated slightly with a radiographic foam wedge. Starting in this oblique position and later rotating the animal as needed facilitates fluid withdrawal and patient restraint during the procedure. Others prefer to perform the procedure in dogs while the patient is standing.
3. The needed depth of penetration and the ideal puncture site can be guided by echocardiography. Alternatively, one can simply note the strongest palpable cardiac impulse as this is the location where the pericardium has been expanded closest to the chest wall.
4. An initial surgical preparation of the skin is made and a local skin circular infiltration of 2% lidocaine (about 1 ml) is made into the skin and subcutaneous tissues using a 25- or 23-gauge needle. Subsequently, inject another 1 to 1.5 ml of lidocaine within the intercostal space to infiltrate the intercostal muscles and pleura through which the needle will penetrate. Perform a second surgical preparation of the skin.
5. After gloving for the procedure, create a sterile working area using the opened glove envelope or a sterile towel placed on a Mayo stand or table. The over-the-needle catheter is dissembled and one or two small side holes are cut in the distal $^1/_3$ of the catheter using a sterile #11 scalpel blade (fold the catheter gently and shave a corner at the bend). Reinsert the puncture needle carefully into the catheter. Sterile tubing is connected at one end to a three-way stopcock and at the other to a drainage syringe (35 or 60 ml) and placed on the sterile tray. Prepare sterile vacuum tubes (one with EDTA) for sample submission. Use a bowl or large graduated cylinder to collect the bulk of drained fluid.
6. Next, advance the catheter through the skin. While some operators prefer to make a small stab incision with the #11 blade, this is not necessary for an Angiocath type catheter. The skin should be penetrated completely by pulling it outward with one hand while directing the catheter tip into the subcutaneous tissues.
7. Holding the catheter firmly with two hands, redirect the needle, and then advanced deliberately in a smooth motion through the subcutaneous tissue, intercostal muscles, pleura, pleural space, and finally into the pericardial space. Generally, there is no need to attach a syringe for aspiration. There is usually some drag as the catheter crosses the pericardium; in the case of thick pericardium it may be a substantial resistance.
8. Once fluid enters the catheter tip, advance the system 2 to 3 mm more and then the needle is held securely with one hand while advancing the outer catheter into the pericardial space.
9. Monitor the ECG for extrasystoles in case the heart is pricked with the needle or catheter. (Note: dorsal approaches may cause the catheter to perforate the atrium and this will not be associated with premature ventricular complexes.)
10. Once the pericardial space is entered, fluid (usually bloody) flows across the needle without the need for aspiration. Failure of fluid to well into the needle suggests an intrapleural location or pericardial effusion without tamponade.
11. Hold the catheter in place and withdraw the inner needle. Attach the male-end of the 3-way stopcock to the catheter.
12. If intrapericardial pressure will be measured, do it *immediately* with the CVP-manometer column attached to the 3-way stopcock. Intrapericardial pressure rapidly declines with evacuation of the fluid.
13. After measuring intrapericardial pressure, collect fluid samples for cytology (EDTA and plain tubes) and culture (with samples submitted pending results of cytology).
14. Observe the tube without anticoagulant for clotting. If immediate clotting develops, the sample is likely from the heart and the catheter should be withdrawn.
15. The position of the catheter tip can be determined by echocardiography during injection of saline (or some of the effusion) back into the catheter. The sudden appearance of microbubbles within the cardiac chambers indicates a perforation. In most cases of perforation, there will be PVCs evident on the ECG.
16. Drain the effusion with the syringe attached to the tubing. The sac should be emptied as completely as possible. Slight manipulation of the patient (gentle rolling, elevating the hindquarters) may help in fluid retrieval.
17. If negative pressure is obtained, inject $^1/_2$ cc of fluid back into the line to clear it; if negative pressure is again detected, it is likely the pericardial space has been emptied or the catheter tip has migrated into the pleural space (if there is pleural fluid, a different color fluid may be obtained, usually serosanguinous).
18. Owing to the relatively inelastic properties of the pericardium, the initial volume of fluid removed will often show immediate benefit with improvement in attitude, color, peripheral pulse pressure, and ABP.
19. Once completed, quantify the aspirated fluid volume. Repeated echocardiography can be used to verify the benefit of the procedure.
20. Evaluate a sample of the effusate by microscopy for cellular abnormalities and bacteria and is then cul-

tured (aerobic, anaerobic) if appropriate based on cytology.

21. If pH is to be measured, save a sample anaerobically.

Medical Therapy

- Intravenous saline, at shock doses, may be needed in cases of hypotension due to severe or sudden cardiac tamponade; however, in experimental tamponade volume infusion is not always beneficial.
- Thoracocentesis is a helpful adjunct in large pleural effusions.
- Ascitic effusions need not be tapped if pericardiocentesis is performed. The ascitic fluid usually resolves within 2 to 5 days.
- In patients with culture-negative, idiopathic, pericardial hemorrhage, conservative treatment with catheter drainage may be "curative," though diligent follow-up (for at least one year) is needed to assure that re-effusion or constrictive pericardial disease does not develop.

▼ ***Key Point*** While furosemide can decrease elevated venous pressures and reduce fluid retention, diuretic therapy is not a substitute for pericardiocentesis in the symptomatic patient. Furthermore, these drugs may reduce ventricular filling predisposing to hypotension, syncope, and renal failure.

- In general, diuretics are contraindicated except in recurrent, neoplastic-related right-sided CHF in which venous pressures can become exceptionally high and there is no other available treatment.
- Following successful pericardiocentesis, it is appropriate to administer one 1-mg/kg dose of furosemide SQ to enhance renal excretion of sodium (and overcome the sodium-retaining consequences of cardiac tamponade that may persist for a period following pericardiocentesis or pericardiectomy).
- Empirical use of antibiotics or of corticosteroids has offered no certain benefit and is not recommended. Drugs that prevent fibrosis might be considered, but these have not been suitably investigated in dogs and cats.
- When PE is due to coccidiomycosis, specific antifungal treatment should be administered.
- Aside from exceptional individual response, most cardiac and heart base tumors are either unresponsive to chemotherapy or develop drug resistance after periods of initial success.
- PE associated with hemangiosarcoma is best managed by pericardiocentesis and then by an established chemotherapy protocol for this neoplasm (see Chapter 28). Otherwise, the prognosis is dismal. Median survival was prolonged by chemotherapy to about 6 months, but as indicated above, a one year survival is very uncommon and other studies report median survivals of shorter duration.
- PE due to chemodectoma is poorly responsive to drug therapy. In cases of very large mass lesions, an oncologist should be consulted if clients wish to explore additional options.
- Mesothelioma is highly resistant to most chemotherapy protocols. Cisplatin and triethylenethiophosphoramide (thiotepa) have been used. An oncologist should be consulted.
- Balloon catheter dilation of the pericardium can be performed using percutaneous, transthoracic techniques to rip the pericardium and create a palliative window for cases of PE due to cardiac neoplasia. This approach requires special equipment and training.

Surgical Therapy

- Surgery (see Chapter 167 for principles of thoracic surgery) may be necessary for successful management of pericardial diseases, including recurrent idiopathic pericardial hemorrhage, septic pericarditis, chronic inflammatory pericarditis, and in treatment or palliation of PE related to tumors.
- Subtotal pericardiectomy (ventral to the phrenic nerves) may be needed in recurrent idiopathic hemorrhagic effusion, especially in younger dogs. Failure to perform surgical resection when there is recrudescence of PE predisposes the dog to development of constrictive pericarditis. In one small study, median survival in dogs treated by pericardiectomy was significantly longer. After two pericardiocentesis procedures, recommend surgery at the next recurrence of PE.
- The treatment for infective pericarditis includes broad spectrum antibiotics, followed by specific antibiotic therapy (based on aerobic and bacterial anaerobic culture), catheter drainage of the PE, and subsequent surgical removal of as much of the pericardium as possible. A pericardial window is inappropriate for these patients. A foreign body should be sought during exploration. Place chest drains and the postoperative management should follow that appropriate for pyothorax (see Chapter 164).
- As discussed in detail above, surgery is also indicated if there is a need to explore and biopsy the pericardium to rule out a tumor. The surgical approach depends on the case and the management goals.
- Palliative, subtotal pericardiectomy to create a pericardial "window" can be performed by thoracoscopy or mini-thoracotomy (with long instruments).
  - This approach provides reasonable access for direct examination and pericardial tissue biopsy in neoplasia-associated or suspected PE.
  - Morbidity is low and recovery fast with this approach.
  - Surgical access is more limited than with a standard thoracotomy.
  - Thoracoscopy requires special instruments and training.

Table 151-1. SURGICAL PROCEDURES FOR MANAGEMENT OF PERICARDIAL DISEASE

Subtotal Pericardiectomy

1. Perform either a right-sided or left-sided thoracotomy or a sternotomy (see Chapter 167).
2. Perform a subtotal pericardiectomy ventral to the phrenic nerve.
3. Identify the phrenic nerves on the dorsal right and left sides of the pericardial sac.
4. After placing pericardial stay sutures make a stab incision 1 cm ventral to the nerve.
5. Remove pericardial fluid via suction.
6. Incise the pericardium circumferentially using scissors. Avoid trauma to the myocardium and to the phrenic nerves.
7. Control hemorrhage via electrocautery (avoid touching the heart).
8. Place a thoracic drain tube.
9. Close the thoracotomy or sternotomy routinely.
10. Always perform histopathologic evaluation of the pericardium to rule out neoplasia (e.g., mesothelioma).

Excision of Heart Base Tumors

When heart base tumors have been determined by echocardiography or by MRI to be small and not invading major vessels, the tumor may be surgically removed. These tumors are slow-growing and rarely metastasize.

1. For better access to the tumor, perform a sternotomy.
2. Several hours of very delicate and intense surgery are necessary to remove these tumors.
3. Also perform a pericardiectomy.

In the rare situation in which the tumor is completely resectable, a good prognosis is warranted.
When heart base tumors are inoperable, continued pericardiocentesis or pericardiectomy is necessary.

Excision of Right Atrial Hemangiosarcoma

1. A small suspected hemangiosarcoma requires prompt attention. Perform a right-sided thoracotomy (see Chapter 167).
2. Examine the lungs for possible metastasis.
3. Remove the right atrial lesion if it is both small and easily isolated. Submit the tissue for histopathologic evaluation.
4. An alternative to open thoracotomy for pericardiectomy is thoracoscopy. However, specialized equipment and expertise are needed for this technique.
5. To remove atrial appendage tumors:
6. Double-clamp the atrial appendage with Satinsky clamps proximal to the tumor.
7. Incise the tissue between the clamps, and remove the tumor.
8. Oversew the appendage over the clamp using 4-0 polypropylene (Prolene, Ethicon; Summervilles, NJ) with simple continuous sutures.
9. Carefully remove the clamps, and place a second simple continuous suture layer.
10. Place additional sutures at areas of bleeding.
11. Alternatively, use surgical staples (TA, US Surgical; Norwalk, CT) to close the atrial tissue prior to tumor removal.
12. Place an indwelling chest tube, and close the incision routinely.

Once healing has occurred, initiate chemotherapy (see Chapter 26). In the majority of cases, by the time a suspected hemangiosarcoma lesion is evident, it has already metastasized.

- A full thoracotomy or a sternotomy is needed when the plan calls for a full exploration of the pericardial space and heart base, resection of a well-circumscribed neoplasm, or creation of a standard subtotal pericardiectomy (see Table 151-1). Surgical resection of some tumors is feasible, but it may be difficult to completely remove all neoplastic tissue.

CONSTRICTIVE PERICARDIAL DISEASE

Etiology

Pericardial constriction is relatively uncommon in dogs and cats and most often develops from chronic pericarditis, recurrent hemorrhage, intrapericardial foreign body, or as a consequence of diffuse mesothelioma. Most cases begin as an inflammatory PE. As the pericardium scars and contracts, fluid is reabsorbed. Eventually the heart is encased in a rigid, possibly calcified, compartment.

The fundamental pathophysiology of constrictive disease is restriction of ventricular filling. Cardiac filling is confined to early diastole, at which point further ventricular expansion is "checked" by the constrictive pericardium. Cardiac output becomes limited, and elevated venous pressures are required to compensate for the diastolic dysfunction. This leads to right-sided (or biventricular) CHF.

The term "constrictive-effusive" pericarditis refers to a state of constrictive physiology with concurrent PE (but without tamponade). It probably represents a transition from pericarditis with effusion to constrictive disease.

Diagnosis

- In most cases there are typical clinical findings of *advanced right-sided CHF*, often with remarkable jugular venous distension. Pulsus paradoxicus may be present.
- *Heart sounds* are normal to soft, but there may be a prominent diastolic sound (pericardial knock) associated with abrupt termination of ventricular filling. Some dogs have prominent tricuspid regurgitation.

Diagnostic Imaging

- *Radiography* often demonstrates a relatively normal heart size. There may be pleural effusion. The vena cava may be dilated from elevated venous pressures. A metallic foreign object in the pericardial space is of clinical significance and is probably tied to the disorder.
- *Electrocardiography* may show a normal ECG; atrial fibrillation; reduced voltage QRS complexes, or ST-segment elevation. If the rhythm is sinus, P-waves may be wide or enlarged.
- *Echocardiography*
  - 2D imaging—biatrial dilatation is typical, with more right atrial dilatation. The pericardium may appear thickened. In pure constrictive disease there is no PE, but a small to moderate PE is evident in constrictive-effusive disease. Systolic function is normal or mildly depressed.
  - Doppler echocardiographic recordings of the mitral and tricuspid inflow reveal marked early filling (E waves) with attenuated mid- to late diastolic filling. The early annular motion (Ea) of the mitral annulus is preserved or exaggerated. There may be prominent tricuspid regurgitation.
  - Disparate rates of ventricular filling are reflected by prominent and multiple diastolic movements of the ventricular septum on 2D and M-mode echocardiography; this is supported by marked variation in transvalvular inflow velocity signals related to the phase of ventilation.

Cardiac Catheterization

- *Right heart catheterization* may be needed to secure the diagnosis. The patient should be euvolemic prior to the intervention (or receive an IV fluid challenge during the catheterization).
- A prominent "y" descent occurs in the venous pressure tracing. This initial decline in ventricular diastolic pressure is quickly followed by a marked pressure increase and plateau, as the balance of ventricular filling requires very high venous/atrial/ventricular diastolic pressures.
- The right ventricular pressure curve typically shows an initial diastolic "dip" which is quickly followed by a "plateau" in the pressure tracing (square-root sign).

Treatment

- The treatment of choice for constriction is surgical removal of the parietal pericardium and decortication of the epicardium if that layer is involved. The surgery is difficult and carries a significant risk and is best done by an experienced thoracic surgeon.
- The operation is facilitated by residual fluid in the pericardial space (constrictive-effusive disease).
- Fibrosis of the epicardium prevents a definitive cure, and the long-term success of the procedure will require a "wait-and-see" attitude.
- Postoperative management includes pain management, monitoring for arrhythmias, treatments to prevent pulmonary thromboembolism (low dose heparin), and low dose furosemide for one or two days to facilitate diuresis in cases of right-sided CHF.

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Chapter

152 Heartworm Disease

Clay A. Calvert / Laura G. Ridge

Heartworm disease is a common problem in many areas of the world, particularly in tropical and subtropical regions. The disease has been endemic along the southeastern Atlantic and Gulf coasts of the United States as far west as Texas for more than 50 years. Heartworm infection has spread north and west to most areas of the United States, but the prevalence is still low at high elevations and in most northern states. Endemic foci frequently occur in regions with otherwise low prevalence. It is difficult to eliminate heartworms from a region once they have been established; therefore, all dogs should be tested regularly, and veterinarians should be alert for dogs that emigrate from endemic regions.

Wild animal reservoirs include wolves, coyotes, foxes, California gray seals, sea lions, and raccoons. Ferrets are also susceptible.

ETIOLOGY AND PATHOGENESIS

Heartworm infection is produced by the parasite *Dirofilaria immitis* and is transmitted to dogs mostly by 10 to 15 important species of mosquitoes, usually *Culex, Aedes,* and *Anopheles* spp. Mosquitoes can transmit infective larvae (L_3) 2 to 3 weeks after ingesting a blood meal. Infection rates vary among cats in endemic regions but are usually 10% to 20% of that of dogs within the same enzootic region. Being male, large, and outdoors increases the risk of canine infection, but hair coat length does not affect the risk.

Life Cycle in Dogs

- Female mosquitoes are the intermediate hosts and acquire the first-stage larvae (microfilaria) during feeding on infected dogs. Two molts then occur to produce the infective L_3 stage.
- Larvae development within the mosquito to the third stage usually requires 1 to 2.5 weeks, depending on the ambient temperatures.
- Mosquitoes can survive the development of only low numbers (<10) of larvae.
- Larvae development within the mosquito requires an average daily temperature of at least 57°F.
- The cooler the temperature, the longer the time required for L_3 to develop. The warmer the temperature, the shorter the time required for L_3 development.
- Mosquitoes have a maximum life span of about 30 days.
- Transmission is unlikely to occur during the dry, cold months of the year, even in most warmer climates within the United States. This is because when the temperatures are only modestly low, the time required for development for L_1 to L_3 may exceed the lifespan of the mosquito.
- Third-stage larvae (L_3) infect the dog via the bite wound created during the feeding of the mosquito. The next molt to the (L_4) stage occurs within 2 weeks.
- Larvae migrate through the subcutaneous tissues and vascular adventitial tissues for approximately 100 days. During this time, two molts occur.
- Young adults (fifth-stage, or L_5, larvae) enter the vascular system at 3 to 3.5 months post-infection.
- Young adult *Dirofilaria immitis* worms are in the small pulmonary arteries at 5 to 6 months post-infection.
- Adult worms are thought to have a natural lifespan of 3 to 5 years in the dog.
- Microfilaria are thought to have a natural lifespan of 1 to 2 years in the dog.

▼ ***Key Point*** Patent infection in dogs, as evidenced by microfilaremia, occurs approximately 6 months after transmission from the mosquito.

- Microfilaria, when present, increase in concentration for the next 6 months, plateau for several months, and then decrease if further infection does not occur.
- Microfilaremia does not occur in 10% to 67% of all heartworm infections and many of these are the result of an immune-mediated host reaction. Microfilaria-specific antibody-mediated, occult infections occur in the presence of persistent host antibody excess. Antibody-dependent leukocyte adhesion entraps microfilaria in the pulmonary microcirculation.
- In most endemic regions, the incidence of occult infections, other than drug induced, is approximately 20% to 25% of all heartworm infections.

- Microfilaria-leukocyte (neutrophils and eosinophils) complexes are engulfed by phagocyte cells of the mononuclear phagocyte system, resulting in granulomatous inflammation.
  - Predominately eosinophilic inflammation, with minimal granulomatous inflammation, produces allergic pneumonitis.
  - Progressive granulomatous inflammation occasionally leads to pulmonary eosinophilic granulomatosis.
- Other causes of occult mature infections include single sex infections and one high-dose (>200 mcg/kg) ivermectin administration.
- Dogs administered macrolide prophylaxis that are or become infected will not have microfilaremia.
- Serodiagnostic tests are negative in male-only infections and with infections less than 7 months post-L_3 inoculation.

Life Cycle in Cats

- The cat is relatively resistant to infection, requiring a greater L_3 inoculum. Some cats appear to be immune. Consequently, the infection rate in unprotected cats is likely to range from one-fifth to one-tenth that of unprotected dogs in an endemic area. Some mosquito species, as intermediate hosts, do not like to feed on cats. The numbers of infective larvae that mature are less than in dogs, and the pre-patent period is usually one to two months longer.
- The natural survival time of adult worms in the cat is thought to be no more than 2 years.

Epizootiology

Prevalence

- Heartworm infection is most common in tropical and subtropical climates.
- Infection rates in unprotected dogs approach 50% along the Atlantic and Gulf coasts as far inland as 150 miles.
- Most unprotected dogs in highly endemic regions eventually become infected.
- The prevalence in cats varies by geographic region:
  - Much lower than dogs in some areas.
  - Similar to dogs in some areas.
  - The incidence is probably higher than suspected.

Signalment

- Male dogs are infected more often probably because of increased outdoor exposure.

▼ ***Key Point*** Dogs housed outdoors have a four- to five-fold increased risk of heartworm infection when compared to indoor dogs.

- Infection is diagnosed most often in dogs 4 to 7 years of age. In highly endemic regions, infection is common in younger dogs.

Pathogenesis

Disease onset and severity largely reflect the number of adult heartworms, which can vary from 1 to more than 250 in a single dog. In infected cats, the average number of adult worms is 3 to 6, depending on the concentration of infected mosquitoes and the ambient temperature in any given region. Acute dyspnea and sudden death are more common in cats despite the low worm burden.

Worm Location

- Until the adult worm burden exceeds 50 in a 25-kg dog, nearly all worms are located in the pulmonary arteries.
- Worm burdens of approximately 75 are associated with worms located in the right atrium.
- The vena cava syndrome typically is associated with worm burdens of 100 or more.

Response to Live Worms in Dogs

- Pulmonary pathology is produced beginning with the young adults (L_5).
- Even if infection is identified 7 months post-infection with L_3, the L_5 have already been in the pulmonary arteries for a few months and some pathology has occurred.
- Pulmonary arterial endothelial damage and subsequent myointimal proliferation most often affects the caudal and intermediate lung lobes, that is, those receiving the highest blood flow.
- Pulmonary lobar arterial enlargement, tortuosity, and obstruction of smaller branches begin within a few weeks of worm arrival.
- Intrapulmonary blood flow is obstructed as the disease progresses, and blood is diverted to less severely affected lobes.
- Small downstream arterioles become damaged and leak plasma and inflammatory cells into the surrounding lung parenchyma. This causes interstitial and alveolar lung infiltrates and granulomatous inflammation.
- Pulmonary arterial obstruction and lung inflammation cause fever, coughing, dyspnea, hemoptysis, leukocytosis, and thrombocytopenia.
- Pathology is more severe and accelerated in active dogs, relative to inactive dogs, for any given worm burden.
- Small dogs do not tolerate heartworm infection as well as large dogs, presumably because of the small size of their pulmonary arteries.

Response to Live Worms in Cats

The response of cats and ferrets is similar to that of dogs. However, there is more arterial muscular hypertrophy. In cats, parenchymal pathology differs from that of dogs in that there is more alveolar Type II hyperpla-

sia. This creates a barrier to oxygen diffusion that is more severe than in the dog. Mortality in cats and ferrets is higher than in dogs.

Response to Dead Worms

- The most severe disease is seen in response to dead worm fragments that are swept into small arterioles.
- Worm death may be spontaneous or from melarsamine dihydrochloride (Immiticide, Merial) administration.
- Pulmonary vascular compliance and blood flow become impaired to varying degrees and severe arterial disease results in pulmonary hypertension, increased right ventricular afterload, and eventually right-sided CHF.
- Parenchymal lung disease (infarction and consolidation) occurs secondary to pulmonary arterial thromboembolism and increased vascular permeability.

CLINICAL SIGNS

The clinical signs associated with heartworm infection reflect the adult worm burden, duration of infection, and host-parasite interaction. Respiratory signs are most prominent.

Clinical Signs in Dogs

- Exercise intolerance, coughing, dyspnea, and respiratory crackles occur in dogs with moderate and advanced heartworm disease.
- Hemoptysis occurs in severe disease and is caused by pulmonary thromboembolism. It can be seen before, but occurs more often after adulticide treatment.
- Acute dyspnea and increased pulmonary alveolar densities may develop secondary to spontaneous worm death.

Syncope

Syncope is associated with severe pulmonary arterial disease and pulmonary hypertension.

Elevated Central Venous Pressure

Signs of elevated central venous pressure indicate severe pulmonary hypertension with incipient or overt right-sided CHF. Clinical signs include prominent jugular pulse, distended jugular veins, hepatomegaly, and ascites.

Hemoglobinuria

Hemoglobinuria commonly occurs in association with the vena cava syndrome (i.e., acute hemolytic crisis caused by obstruction of the vena cava with adult worms) and occasionally when severe pulmonary arterial disease results in fragmentation hemolysis due to fibrin-thrombus formation. Thrombocytopenia is usually a consequence of these complications.

Nephrotic Syndrome

This syndrome occasionally occurs as the result of severe glomerular disease manifested as amyloidosis or immune complex glomerulonephritis (see Chapter 77). Manifestations can include proteinuria, hypoalbuminemia, hypercholesterolemia, azotemia, ascites and occasionally peripheral edema.

Clinical Signs in Cats

Clinical signs of heartworm infection in cats are somewhat different than in dogs. The most common signs are vomiting, collapse or syncope, asthma-like syndrome, coughing, sudden death, and occasionally central nervous system signs. Signs occur most often several months after infection and again when young adult worms arrive in the pulmonary arteries. Severe pulmonary complications and death are most likely to occur whenever one or more adult worms dies, either spontaneously or as a result of Immiticide administration.

- Respiratory signs
  - Coughing in cats usually is associated with allergic or parasitic lung diseases; heartworm disease represents one cause.
  - Coughing is not a prominent feature of cardiomyopathies in cats.
  - Asthmatic signs are a common manifestation and often occur about 3 to 4 months post-infection. A strong antibody response at this time may destroy the developing larvae. If not, then a period of quiescence occurs only to have asthma-like signs reoccur in some cats 7 to 8 months post-infection.
  - Dyspnea.
- Vomiting (intermittent) is a common sign (approximately 20%) and occurs sporadically. It often is not associated with eating, but vomitus may include food. Mucus and bile are often the major components of the vomitus. Vomiting and coughing in the same cat should increase the index of suspicion.
- Sudden death related to spontaneous worm death and thromboembolism is more common in cats than in dogs.
- Neurologic signs, usually seizures, occur occasionally when aberrant worm migration to the brain occurs.

DIAGNOSIS

The diagnosis of heartworm infection is usually based on a positive immunodiagnostic test result. Microfilaria in the peripheral blood can be detected in some dogs by a direct smear or a concentration test (modified Knott test or milipore filter [Difil, Evsco]) in dogs with

or without clinical or radiographic findings consistent with the disease. Testing puppies younger than 6 months of age is not indicated.

Affected cats are usually negative for microfilaria but may have characteristic radiographic abnormalities. A positive enzyme-linked immunosorbent assay (ELISA) test for heartworm antigen, antibody, or both, may be present by 7 months following infection.

History in Dogs

- The history in dogs with heartworm infection varies considerably. Many infections are discovered in asymptomatic dogs by immunodiagnostic screening.
- Most heartworm-infected dogs have not received prophylactic therapy.
- Some dogs are totally without signs; others have unexplained tachypnea, exercise intolerance, or cough.
- Signs consistent with pulmonary hypertension with or without overt right-sided CHF are associated with severe heartworm disease.

History in Cats

- The history in cats varies considerably. Most infected cats have not been receiving prophylaxis. Lethargy and decreased appetite may be reported by the owners.
- Coughing, emesis, and sudden or episodic dyspnea are typical signs in cats.
- Sudden death may be the first sign of infection.
- Congestive heart failure is uncommon.

Physical Examination

- Findings vary from clinically normal to signs of right-sided CHF (see Chapter 147).
- Pulmonary crackles and loud bronchial sounds may be auscultated.
- Signs consistent with pulmonary hypertension, such as exercise intolerance, dyspnea, tachypnea, syncope, and splitting of the second heart sound, may be present.

Laboratory Studies

- Standard laboratory studies vary, depending on the patient's age, clinical signs, and preference of individual clinicians.
- The minimum pretreatment database for all dogs suspected of having heartworm infection includes packed cell volume (PCV), blood urea nitrogen (BUN), urine specific gravity, urine protein determination, and heartworm antigen test.
- We recommend thoracic radiographs because they reveal more about disease severity than any other single test.
- The minimum data base for cats should include thoracic radiographs.
- Cardiac ultrasound and fecal studies for lungworms are useful for the differential diagnosis of heartworm infection, feline asthma, cardiomyopathy, bronchitis, pulmonary fibrosis, and lung parasites.
- A tracheal or bronchial wash may be useful for detecting lung parasitic lesions such as those produced by *Filaroides* spp.
- Cardiac ultrasound is a sensitive test in experienced hands.

Screening in Dogs

Screening for heartworm infection usually is done in the late spring in cooler climates to maximize the likelihood of detecting infections acquired in the previous year. In hotter climates, where the transmission season is longer than 6 months, infections may be acquired as late as November and early December, and these infections are not detectable until May or June. Antigen testing is the preferred method. Test 7 months after the end of the transmission season in a given locale.

Screening in Cats

Combined antibody and antigen testing is recommended for cats. Although a positive antigen test confirms infection in cats, many infected cats are antigen-test negative. Most symptomatic infections in cats can be identified by cardiac ultrasound. A negative antibody test weighs heavily against the diagnosis.

Immunodiagnostic Tests

- These tests must be performed in strict compliance with the manufacturer's instructions. False-positive test results are usually the result of poor technique.
- Immunodiagnostic testing currently is the recommended screening procedure.
- The absence of circulating microfilaria in infected dogs is common (10–50%), and microfilaremia is rarely detected in infected cats.
- In some highly endemic regions, such as Hawaii, as many as 50% of infected dogs lack circulating microfilaria.

Heartworm Antigen Tests

Serodiagnosis of adult heartworm antigens in dogs is accomplished readily by membrane and microwell ELISA tests and membrane immunochromatographic tests. A number of very specific and sensitive tests are available. Test time duration is less than 30 minutes and for some tests is approximately 10 minutes. All of these tests can be performed with plasma or serum samples, and the majority can be run with whole blood.

- Positive antigen test results are the result of the presence of adult female worms. The antigen is associated with the worms' reproductive tracts.
- The particular test employed is influenced by the number of tests performed daily, the amount of

whole blood or serum required, and the speed of results.
- Some tests, such as Dirochek (Synbiotics), are very efficient for testing multiple samples simultaneously. Either serum or plasma is required.
- Weakly positive test results should be verified by repeat testing using a different antigen test.
- Most immunodiagnostic tests (ELISA based) are semiquantitative because rapid and strong positive test results are thought to be related to higher antigen concentrations.
  - Low antigenemia indicates a low adult heartworm burden and reduced risk of post-adulticide thromboembolic complications.
  - High antigenemia may be the result of a heavy worm burden and increased risk of thromboembolism.
  - Large quantities of antigen released from dead worms results in a quick, strong test reaction but does not necessarily mean that the worm burden is high.
  - Alternative adulticide treatment protocols for heavy worm burdens are recommended.
- Immunodiagnostic tests are the tests of choice in dogs receiving monthly macrolide prophylaxis.
- In cats, antigen tests are specific but are less sensitive, and false-negative results are common. False-negative test results are explained by low worm burden, male-only infections, and infection with young (<7 month old) female worms that have immature reproductive tracts. When adult worm infection is present in cats, the antigen test is usually positive if there are 3 or more mature female worms.

Heartworm Antibody Tests

Heartworm-associated antibody tests are useful to rule out infections in cats. Antibodies may appear by 2 to 3 months post-infection and are usually present by 5 months. A positive antibody test indicates exposure but not necessarily active infection; thus, use antibody tests in conjunction with antigen testing and other clinical information.

- Asthma-like signs due to developing larvae often occur months before the antigen test can become positive.
- Larvae-induced antibodies can persist after the larvae have been killed by a macrolide drug.
- A negative test result weighs heavily against the diagnosis.
- A strongly positive test result indicates preadult infection, live adult infection, or persistent (at least 6 months) antibodies after adult heartworm death. An antigen test and perhaps cardiac ultrasound are needed to confirm the diagnosis.
- Intermediate titers should be repeated in 1 month, if necessary. Also, other tests that may support a diagnosis should be evaluated—thoracic radiographs, echocardiography, serum globulins (hyperglobulinemia), CBC (eosinophilia, basophilia).

Microfilaria Detection

- In dogs, the incidence of occult (amicrofilaremic) infections is greater than the incidence of false-negative antigen test results.
- Annual microfilarial detection tests are required for dogs receiving diethylcarbamazine prophylaxis.
- Microfilarial detection tests are indicated for heartworm antigen-positive dogs if the intent is to kill the microfilaria rapidly using milbemycin oxime (Interceptor, Novartis).
- Evaluate a direct blood smear immediately after procurement of a blood sample. If the direct smear is negative, a concentration test is indicated.
- The Knott test (a centrifugal concentration test) or a filter test is at least 25% more sensitive for the detection of microfilaria. Each concentration test methodology has advantages and disadvantages, but efficacy is similar.
- Microfilarial testing is only performed if there is intent to rapidly kill microfilaria, when present.

Radiography

Pulmonary Arterial Disease

- A common finding in heartworm infected dogs is dilation of the main pulmonary artery segment at the one o'clock position on the ventrodorsal or dorsoventral projection. The main pulmonary artery segment is not visible in the cat because of its midline position.
- Tortuosity and abrupt pruning of the arteries (the latter due to thromboembolism) are best seen on the dorsoventral projection; the caudal lobar vessels are the most severely affected.
- The caudal lobar arteries, especially the right, are the first to enlarge and typically are the most severely diseased. The diameters of the caudal lobar arteries should not exceed that of the ninth rib at the point of their superimposition. If the lobar arteries are at least 1.5 times the diameter of the ninth ribs, then severe (Class 3) arterial pathology has occurred.
- The cranial lobar arteries are best evaluated on the lateral projection; their diameters should not exceed that of the proximal portions of the third or fourth ribs.

▼ ***Key Point*** Thoracic radiography is the most important diagnostic test for determining the severity of heartworm disease.

Parenchymal Lung Disease

- Parenchymal lung disease (patchy, ill-defined infiltrates) results from the pulmonary arteriolar thromboembolism with leakage of plasma and inflammatory cells into the adjacent tissues.

- Severity varies; disease is most prevalent in the caudal and intermediate lung lobes and is most concentrated surrounding the lobar arteries.

Allergic Pneumonitis

- It is associated with occult infections, eosinophilia, coughing, and dyspnea.
- This incidence is 10% to 20% of occult infections.
- This mixed diffuse interstitial-alveolar lung disease is best visualized in the caudal lobes.
- It often occurs with minimal pulmonary arterial enlargement.
- It may be mistaken, on radiographs, for left-sided CHF (pulmonary edema) or blastomycosis.
- It responds rapidly to anti-inflammatory dosages of corticosteroids continued for 3 to 7 days.
- Begin adulticide treatment soon after clinical and radiographic signs subside.

Feline Asthma-Like Syndrome

- Coughing, wheezing, and dyspnea are consistent with feline heartworm infection.
- Radiographic picture resembles feline asthma.
- It first occurs around 4 months post-inoculation of L_3.
- Can be episodic with mature infections.
- May be associated with eosinophilia or basophilia.

Clinical Pathology

No abnormal test results are pathognomonic for heartworm infection.

Complete Blood Count

- *Eosinophilia and basophilia* are the most common abnormalities in dogs.
  - Eosinophilia is more common; the highest eosinophil and basophil counts tend to occur in occult infections.
  - *Dipetalonema reconditum* infections produce eosinophilia equal to or greater than that associated with heartworm disease.
- *Neutrophilic leukocytosis,* often with a left shift, occurs with pulmonary thromboembolism.
- *Thrombocytopenia* commonly is associated with severe pulmonary arterial and parenchymal lung disease.
  - Activated clotting time is increased marginally to moderately in many cases.
  - DIC develops in some animals with severe thromboembolic disease.
- *Hemoglobinuria,* usually accompanied by thrombocytopenia, is seen with the vena cava syndrome and with severe pulmonary thromboembolic disease. Heparin, 75 to 200 U/kg q8hr SC, usually reduces hemoglobinuria and improves thrombocytopenia caused by severe lung disease.

Serum Biochemistries and Urinalysis

- *Azotemia* may occur in dogs with complicated infections.
  - Prerenal azotemia can be caused by dehydration or right-sided CHF.
  - Primary azotemia can result from glomerulopathies, including immune complex disease and amyloidosis.
- *Increased serum hepatic enzyme levels* may occur; however, increases up to 10-fold do not affect treatment, complications, or survival.
- *Hepatic insufficiency,* evidenced by increased serum bile acid levels, can occur, but mild to moderate increases do not alter the treatment protocol.
- *Proteinuria* is common and is most pronounced in patients with severe infections or renal amyloidosis. Proteinuria, when severe, produces hypoalbuminemia.
  - Nephrotic syndrome is a contraindication to treatment.
  - In the absence of hypoalbuminemia, proteinuria usually resolves after effective heartworm treatment.
- *Hypoalbuminemia* occurs in some dogs with severe infections; hyperglobulinemia is common in dogs and cats with chronic heartworm disease.
- Loss of albumin into the third space occurs with right-sided CHF and is complicated by hepatic insufficiency, intestinal congestion, and free-water retention.

Electrocardiography

Electrocardiography (ECG) is sometimes helpful for evaluation of arrhythmias in animals with severe heartworm disease. The ECG is not a component of the minimum data base. The ECG is not a sensitive test for identification of mild-to-moderate right ventricular hypertrophy. Even though the ECG will reflect severe hypertrophy, clinical signs and thoracic radiograph analysis provide much more clinical information.

- A right ventricular hypertrophy pattern is common in dogs with severe pulmonary hypertension and is found in 90% of dogs with overt right-sided CHF (ascites). However, significant pulmonary hypertension may exist in the absence of ECG abnormalities.
- Occasionally, cardiac rhythm disturbances occur in dogs with severe infections. Atrial fibrillation is the most common arrhythmia, especially in larger breeds.

Ultrasonography

- Evidence of right ventricular and pulmonary artery enlargement can be detected by two-dimensional (2-D) echocardiography in patients with moderate to severe pulmonary hypertension.

- Occasionally, worms may be detected in the right ventricle, main pulmonary artery segment, and main lobar arteries.
- Ultrasonography is particularly useful in antigen-negative cats.
- Echocardiography is the test of choice for diagnosis of caval syndrome (mass of worms is found in the tricuspid valve orifice).
- The echocardiographic features of severe heartworm disease include right ventricular eccentric hypertrophy, septal flattening, underfilling of the left ventricle and left atrium, dilation of the main pulmonary artery segment and main arteries, and high velocity tricuspid and pulmonic regurgitation, the latter two being indicative of pulmonary hypertension.

CLASSIFICATION OF HEARTWORM DISEASE SEVERITY

Severity of heartworm disease is determined by worm burden, duration of infection, and host responses to the worms. Most severe pulmonary complications are associated with occult infections. Three classes are defined that correlate to clinical signs and pulmonary arterial and lung parenchymal disease, though the classification does not clearly separate clinical signs related to lung parenchymal injury from that due to pulmonary vascular disease and pulmonary hypertension. Class assignment may assist in customizing Immiticide treatment.

- Class 1: Asymptomatic or mild clinical signs.
- Class 2: Moderate clinical and radiographic abnormalities.
- Class 3: Severe clinical and radiographic abnormalities, including right-sided CHF.
- Caval syndrome: This syndrome is sometimes referred to as Class 4. However, caval syndrome is not an indication that the severity of lung disease is worse than that of Class 3. Rather, it is a syndrome caused by obstruction of blood flow into and through the right heart. It is complicated by mechanically induced hemolysis and hepatic failure due to acute passive congestion.
- The outcome in Class 1 and 2 patients is excellent when proper treatment and restriction of activity are accomplished.
- The outcome for Class 3 patients is far less encouraging and treatment is labor intensive and expensive.

TREATMENT

The goal of treatment is to kill all adult heartworms and to accomplish this with minimal drug toxicity and a tolerable degree of pulmonary thromboembolism caused by the dying worms. Microfilaria should be eliminated, but rapid kill is not required. Gradual elimination of microfilaria over a period of 6 to 8 months with monthly macrolide administration is acceptable.

Patient Selection

Although most heartworm-infected dogs can be treated successfully, there are exceptions. Immiticide should not be administered to cats because a safe and effective treatment regimen has not been developed.

Contraindications to Adulticide Treatment

- In cats adulticide is not recommended.
- Hepatic failure
- Overt nephrotic syndrome
- Advanced renal failure
- Combination of right-sided CHF and severe renal azotemia
- Concomitant life-threatening disorders

Treatment of Old Dogs

- Experience is limited in the treatment of very old dogs. Heartworm disease pathology may be nonprogressive in old dogs that have chronic infections with low worm burdens.
- Low antigen level is seen.
- Class 1 patients do not require treatment.
- Monthly administration of ivermectin (Heartgard, Merial) at the standard prophylactic dosage (see "Prevention" section) will gradually kill adult worms over a period of 16 to 30 months.

Treatment of Cats

- Treat asthma-like signs with prednisolone (1.0–2.0 mg/kg, daily for 10 days; then taper the dose to 1.0 mg/kg every other morning.
- Do not use aspirin in cats.
- Immiticide should not be used until a safe and effective dosage and treatment schedule for cats has been determined, which is unlikely. Each worm will cause pulmonary thromboembolism when it dies. If multiple worms die over a short time period, lethal pulmonary thromboembolism is likely.
- It is generally believed that 30% to 50% of cats survive their infections.

Adulticide Therapy in Dogs

- The approved available adulticidal agent is Immiticide. The following regimens have proved effective in dogs (see "Aspirin," this chapter).
- Highly efficacious
- Reasonably good therapeutic index
- Easy to administer

Standard Immiticide Protocol

- The manufacturer recommends that Class 1 and Class 2 heartworm infections be treated by the standard Immiticide protocol.

- 2.5 mg/kg Immiticide injected IM twice, 24 hours apart.
- The two doses contain 0.75 mg/kg of total arsenic.
- Two injections (separated by approximately 24 hours) are given into the epaxial musculature at the level of the third to fifth lumbar vertebrae. One injection is given on each side of the dorsal midline.
- The appropriate volume of the reconstituted drug is aspirated into a syringe, and then a new needle is placed on the syringe.
- For dogs weighing more than 10 kg, use a $1^1/_2$-inch 22-gauge needle, and for smaller dogs, use a 1-inch 23-gauge needle.
- The injection should be completed before the needle is withdrawn, and finger pressure should be applied over the needle tract during and for a short time after withdrawal.

Alternate Immiticide Protocol

- Class 3 infections, pound dogs, and dogs with high antigen concentrations should be treated by the alternate Immiticide protocol. Many clinicians prefer to treat all infections, including Class 1 and Class 2, using the alternate protocol.
- There is concern that the high kill rate associated with the standard Immiticide protocol may provoke more frequent or more severe post-treatment pulmonary thromboembolism.
- A single, initial injection (2.5 mg/kg) is used. Approximately 50% (most males and some of the females) of adult worms are killed; therefore, post-adulticide thromboembolic complications are reduced.
- Two follow-up injections, each at the same dosage as the previously administered injection, at a 24-hour interval, are administered after 1 to 3 months. Post-treatment thromboembolism reoccurs, but the severity is reduced because fewer worms are present.
  - The extra 1 to 3 months required for maximum worm kill is seldom detrimental to the outcome.
  - Current data indicate that 100% of male and 98% of female worms are killed.

▼ ***Key Point*** Use the alternate Immiticide protocol to treat dogs with Class 3 infections, pound dogs, and those with high antigen concentrations.

Treatment of Class 3 Heartworm Disease

- Severe pulmonary arterial disease occurs in 10% of infected dogs in highly endemic regions. Infections are often occult. There are at least four treatment options.
- Option 1 is recommended for dogs that do not require continuous supplemental oxygen therapy, are eating, and have normal or pale pink mucosal color.
- Option 2, 3, or 4 is recommended for hemodynamically unstable dogs that require oxygen support; are anorectic; and have very pale, grey, or cyanotic mucosal color.

Option 1

Use the alternate Immiticide protocol (see the preceding section). Supportive therapy, such as judicious fluid administration, low-salt diet, and diuretics or short-term corticosteroids may be indicated.

Option 2

- Extraction of adult worms from the pulmonary arteries.
- Use only for patients with many worms in the right heart and pulmonary arteries.
  - High antigen concentration suggesting a high worm burden.
  - Ultrasound confirmation of high worm burden.
- Requires fluoroscopy and long, flexible, alligator forceps or a horsehair brush that is introduced into the right jugular vein via a surgical approach and manipulated through the heart into the pulmonary arteries. Numerous passages to grasp and remove worms are required and is accomplished with the aid of fluoroscopy.
- This procedure is highly effective in experienced hands.
- After the patient has been stabilized, treat with Immiticide to kill any remaining worms.
- Usually assume that some worms are not removed based on:
  - Persistent ultrasound detection of worms.
  - Positive antigen test result after 4 to 6 months.

Option 3 for Extremely Severe Class 3 Infections

- Cage confinement and aspirin in conjunction with the alternate Immiticide protocol (see the preceding section).
- Place patient in cage confinement for 1 week before, during, and for 3 weeks after adulticide therapy. Strict cage confinement may be the most important component of treatment.
- Begin Immiticide therapy after 1 week of cage confinement.
- Give aspirin (5 mg/kg daily) throughout the treatment period, beginning 1 week before adulticide therapy and continuing for 3 weeks after the second course of treatment.
  - Gastrointestinal (GI) bleeding is possible.
  - Monitor the hematocrit.

- Although efficacy is not proven and incomplete at best, consider GI protection with an H_2 blocker and/or sucralfate.
- Prescribe a diuretic and low-salt diet for patients with concomitant overt right-sided CHF.
- Low-dose (0.25 mg/kg once daily) enalapril (Enacard, Merial) is initiated after 48 hours of furosemide administration. Gradually increase the dosage to 0.25mg/kg q12h after one week, and then cautiously to 0.5 mg/kg q12h after one or two additional weeks. Hypotension is the primary adverse action of this treatment.
- If the patient lives long enough to complete the treatment, the survival rate can be 70% to 80%.
- This option is time consuming, labor intensive, and expensive.

Option 4 for Extremely Severe Class 3 Infections

- Cage confinement and heparin in conjunction with the alternate Immiticide protocol (see "Adulticide Therapy" section).
- Place patient in cage confinement for 1 week before, during, and for 3 weeks after the second adulticide treatment.
- Give heparin (50–100 units/kg, SC, q8hr) for 1 week before, during, and for 3 weeks after the second course of Immiticide treatment.
- Prescribe supportive therapy as above for overt right-sided CHF.
- Survival rate can be greater than 70% to 80% if the patient lives long enough to complete the treatment.
- This option is time consuming, labor intensive, and expensive.
- Prolonged hospitalization is usually required because of the SC injection of heparin.

Side Effects and Efficacy

- Mild myositis of 1 to 3 days duration often is observed after Immiticide injections. Approximately one-third of treated dogs experiences some swelling, and a sterile seroma occurs uncommonly.
- If an injection of Immiticide causes a local reaction, then consider administration of an antihistamine and rapid acting corticosteroid before subsequent injections.
- Hepatic and renal toxicity associated with Immiticide is uncommon; toxic doses produce non-cardiogenic pulmonary edema.
- Immiticide (2 doses) kills at least 90% of the adult worms.
- Confirmation of efficacy can be established at 4 months after Immiticide injection by antigen testing.
  - At least 80% seroconversion occurs.
  - Mean antigen concentration is reduced to 1% of pretreatment levels, indicating nearly complete elimination of worms.
  - Repeat the antigen test 4 months after the two injections of the standard protocol. If it is positive, wait 2 months and then retest.

Drug Storage

- Immiticide is purchased as a lyophilized powder that does not require refrigeration and has a shelf life of at least 2 years.
- Reconstituted drug must be kept refrigerated.

Post-Adulticide Complications

- Strict patient confinement is essential for 4 to 6 weeks post-treatment. Reduced blood flow demand through the pulmonary arteries is beneficial to diminish endothelial damage and to promote vascular repair.
- Thromboembolic complications may occur from several days to 4 or even 6 weeks post-adulticide.
- Most complications occur between 1 to 3 weeks post-adulticide.
- Most severe reactions occur in dogs with Class 3 infections and those associated with high antigen concentrations.
  - Coughing, gagging, lethargy, anorexia, tachypnea, dyspnea, syncope, hemoptysis, and fever are common.
  - Thrombocytopenia, inflammatory leukogram, and prolonged activated clotting time often are observed.
  - Radiographic evidence of parenchymal lung disease is usual.

Treatment of Vena Cava Syndrome

- Vena cava syndrome (Class 4) is uncommon except in highly endemic regions. It is associated with large numbers of worms in the right heart and vena cava. It is seen most often in the late spring and early summer in young dogs that have received a heavy L_3 inoculation over a short time period the previous year.
- Acute cardiovascular collapse and shock occur.
  - It is rapidly lethal unless surgical treatment is provided quickly.
  - Clinical signs variably include a systolic heart murmur, gallop heart rhythm, and hemoglobinuria.
  - Echocardiography is diagnostic.
- Surgical retrieval of the worms is the only recommended acute treatment.
  - Use minimal sedation.
  - Administer local anesthesia and perform surgical cutdown on the right jugular vein.
  - Introduce and advance long, flexible alligator forceps or a horsehair brush to the heart base and retrieve as many worms as possible from the vena cavae and right atrium during multiple passages. The procedure is finished when several passages fail to retrieve additional worms.

  - This is highly effective but experience is required for optimal results.
- Provide supportive care for 1 to 3 weeks.
- Immiticide treatment then is administered to eliminate remaining worms.

When to Initiate Macrolide Prophylaxis in Infected Dogs

- Macrolide prophylaxis can be initiated prior to, at the same time as, or within one month after Immiticide treatment.
- In microfilaremic infections, if acute microfilaricide treatment is not intended, Heartgard or Revolution can be initiated for prophylaxis. The sooner prophylaxis is begun, the sooner the microfilaria will disappear, and the shorter the reservoir time.

Rapid Microfilaricide Therapy

- Always complete adulticide treatment before initiating acute microfilaricide treatment. Attempts to eliminate microfilaria before completion of adulticide treatment are only partially effective.
- Adverse reactions to microfilaricide treatment can occur and are related to high microfilarial concentrations.
- Rapid death of high numbers (>40,000/ml) of microfilaria may produce adverse effects. Most dogs have much lower concentrations.
- Adverse reactions are more likely in small dogs.
  - Less than 10% incidence overall.
  - Usually mild and include mostly transient defecation and salivation.
  - Cardiovascular shock is uncommon and responds to fluids and corticosteroids, if detected early in its course.
  - Decreased appetite and lethargy may be observed for 1–2 days even when no acute reaction occurs.
  - Prediction of reactions is possible if microfilarial concentrations are determined, but this is not routinely performed.

▼ ***Key Point*** Interceptor is the most practical, effective microfilaricide. We recommend against the use of other drugs, such as ivermectin, for rapid microfilaricide action. Treatment recommendations are based on published research because Interceptor is not FDA-approved for use as a microfilaricide.

Milbemycin Oxime (Interceptor)

- Administer at 0.5 mg/kg.
- Administer the drug in the morning, and observe the patient throughout the day for signs of toxicity, such as vomiting, depression, diarrhea, and shock. If cardiovascular instability is suspected, give IV lactated Ringer's solution (20 ml/kg) with a soluble corticosteroid (dexamethasone SP, 2 mg/kg, IV).
- Further testing for microfilaria is not required. Persisting microfilaria levels will be low, the patient will not serve as a reservoir, and Heartgard, Interceptor, or Revolution monthly prophylaxis will eliminate any remaining microfilaria.

Therapy Variations

Occult Infections

Microfilaricide therapy is not indicated in the absence of microfilaremia.

Microfilaria: To Treat or Not to Treat

- Some veterinarians do not administer a microfilaricide with acute-kill capability. It is important to eliminate the reservoir, but slow kill with monthly prophylaxis is acceptable.
- There is an absence of proven pathologic changes associated with microfilaria.
- With the advent of highly sensitive antigen tests, it is no longer necessary to document the persistent elimination of microfilaria to confirm the elimination of adult worms.
- Macrolide prophylaxis eliminates microfilaria in 6 to 8 months.
- There is fear of adverse reaction in collies.
- There is no FDA-approved microfilaricidal drug.

When to Start Prophylaxis

- Prophylaxis usually is initiated within 4 weeks of the first Immiticide.
- Immiticide is larvacidal, which closes the window to re-infection.
- The "reach-back" effect of all macrolides also closes the window of re-infection.
- Prophylaxis can be initiated prior to adulticide therapy.

Confirmation of Adulticide Efficacy

- Four months after adulticide treatment, an antigen test should be performed.
  - After the first 2 doses of the standard protocol or after the third dose of the alternate protocol.
- A strongly positive test result indicates that live heartworms remain.
  - Uncommon.
  - Re-treatment is recommended.
- A weakly positive test result may be the result of a few persisting live worms.
  - Wait two additional months and retest.
  - Whether to retreat is controversial. Very few worms are likely to have survived. Retreatment may not be necessary.
- Retreatment is recommended for Class 3 infections, if clinical signs persist, and for performance dogs.

Adjunct to Adulticide Therapy

Aspirin

- Reduces pulmonary arterial lesions and improves intrapulmonary blood flow.
- For only the most severe cases of Class 3 disease, we recommend prescribing 5 mg/kg, q24h, PO, beginning 7 days before, during, and continuing for 21 days after the first part of the standard or alternate Immiticide protocols.
- Combine with strict cage confinement.
- Avoid the combination of aspirin and glucocorticoids (increased risk of serious gastrointestinal ulceration).

Heparin

- Can be used for the most severe cases of Class 3 infections instead of aspirin.
- Use approximately 75 units/kg, SC q8h, for 1 week before, during, and for 21 days after adulticide treatment.
- Combine with strict cage confinement.
- May be more effective than aspirin.
- Requires extended hospitalization unless the client can administer heparin at home.

Corticosteroids

- Reduces parenchymal disease in the lungs but promotes thrombosis and reduces pulmonary arterial blood flow if used for longer than 10 to 14 consecutive days.
- Do not use routinely but only as needed to control sequellae (see the following discussion).

Oxygen

- The only effective means of dilating the pulmonary arteries.
- For Class 3 infections associated with dyspnea, orthopnea, or congestive heart failure.
- Administer intranasally or by oxygen cage.

TREATMENT OF SEQUELLAE

Occult Heartworm Allergic Pneumonitis

- This complication occurs in 10% to 20% of patients with occult infections.
- Clinical signs include dyspnea, coughing, respiratory crackles, and exercise intolerance.
- Thoracic radiographs reveal diffuse interstitial-alveolar infiltrates.
- Eosinophilia is common, and in tracheal lavage cytology, eosinophils usually predominate.
- The syndrome responds well to oral prednisone (1–2 mg/kg, q24h for several days). Stop prednisone therapy after 3 to 7 days and begin Immiticide therapy.

Pulmonary Eosinophilic Granulomatosis

- This uncommon complication of occult heartworm disease probably results from the granulomatous inflammation known to be associated with occult infections. The reaction in many cases is progressive and assumes a neoplastic-like behavior.
- Clinical signs are coughing and dyspnea.
- Eosinophilia and basophilia are common findings, and hyperglobulinemia may occur.
- Pleural effusion (eosinophilic) occurs occasionally.
- Intrathoracic lymphadenopathy is always present.
- Peripheral lymphadenopathy is occasional.
- Multiple pulmonary nodules develop simultaneously and sequentially, grow at variable rates, and are 1–10 cm in diameter or larger.
- The trachea, liver, spleen, kidneys, abdominal lymph nodes, and intestines sometimes are infiltrated with eosinophils and eosinophilic granulomas.
- Combination chemotherapy is recommended:
  - Prednisone (50 mg/m^2 q24h) plus azathioprine (Imuran) (50 mg/m^2, q24h PO for 7–10 days; then alternate days).
  - Therapy usually results initially in partial or complete remission, but relapse is common even with continued aggressive therapy or when drug dosages are reduced.
  - The duration of therapy is indefinite, and the prognosis is poor.
- Consider lung lobectomy for focal lesions. However, small lesions in multiple lobes may not be detected.

Thromboembolic Lung Disease

This common sequellae of moderate to severe pulmonary arterial disease can occur before adulticide therapy but is most common 7 to 21 days after adulticide therapy. In dogs:

- Clinical signs include coughing, dyspnea, fever, and occasionally hemoptysis.
- A regenerative leukocytosis with thrombocytopenia usually is present.
- Thoracic radiographs reveal severe pulmonary arterial disease with periarterial parenchymal disease of variable severity.
- The following therapy usually is successful:
  - Initiate cage confinement for 5 to 10 days.
  - Administer prednisone (1.0 mg/kg, q24h for 3–10 days).
  - Use intranasal or cage-administered oxygen for dyspneic patients.

PREVENTION

- A microfilarial examination always is indicated before initiation of drugs that can be associated with an

acute adverse reaction. These drugs are Interceptor and diethylcarbamazine.

- Prevention should be in place whenever the average daily temperature exceeds approximately 57°F. Year-round prevention usually is practiced in hotter climates, even though transmission is less likely in December and January in the continental United States. With the advent of macrolide prophylaxis, a microfilarial examination prior to prophylaxis is necessary only if Interceptor is used.
  - Start as early as 6 to 8 weeks of age.
  - In cooler climates, start puppies on prophylaxis as soon after 6 to 8 weeks of age as dictated by seasonal risk.
  - Monthly prophylaxis should be started within 1 month of the transmission season. The monthly administered macrolide drugs kill migrating larvae during the first 6 to 8 weeks after L_3 inoculation.
- Interceptor is a potent microfilaricide at the preventative dosage.
  - Test for microfilaria before prescribing.
  - Adverse reactions can occur if the microfilarial count is high.
- Successful prophylaxis is confirmed by a negative antigen test result 1 year after initiation.
- Macrolides are safe for collies when prescribed according to the label.
- In infected dogs, prophylaxis with Heartgard or Revolution can be initiated prior to or within one month of the initiation of Immiticide. The only advantage of initiation of prophylaxis prior to or less than one month of initiating Immiticide is that microfilaria, if present, will be eliminated sooner, assuming that acute microfilaricide treatment with Interceptor is not planned.
- Macrolide prophylaxis interferes with larval embryogenesis, which reduces the circulating levels of microfilaria. Furthermore, these drugs gradually kill existing microfilaria over a period of 6 to 8 months.

▼ ***Key Point*** In all studies to date, owner administration compliance has been poor.

Ivermectin

- Heartgard (MSD-AgVet) at a dosage of 6 to 12 mcg/kg given monthly, is an effective preventive drug. A chewable formulation of ivermectin plus pyrantel pamoate is an effective heartworm preventive that also controls ascarid and hookworm infections.
- Drug reactions are rare at the recommended dosage.
- Chronic administration of ivermectin suppresses microfilaria in heartworm-positive dogs.
- The reach-back larvacidal action is 100% at one month and nearly 100% at two months.
- If initiated 4 months following L_3 inoculation and continued for at least 1 year, the likelihood of developing infection is reduced by at least 98%.
- When administration is begun 5.5 months post-L_3 inoculation, the subsequent adult worm burden is reduced by about 50%.
- When administration is begun 6.5 months post-L_3, the subsequent adult worm burden is reduced by about one third.
- Heartgard Plus kills adult heartworms slowly over a 16- to 30-month period.
- A dose of 24 µg/kg administered monthly is an effective heartworm prophylaxis in cats, and it removes and controls hookworms in this host.

Milbemycin Oxime

- Interceptor at a dosage of 0.5 to 0.99 mg/kg is an effective once-a-month preventive agent for heartworm disease in dogs and cats.
- It is not as effective as ivermectin at preventing the maturation of larvae when monthly administration is started 4 months post-L_3 inoculation.
- It also controls hookworm, roundworm, and whipworm infestations.
- One dose of Interceptor at the prophylactic dosage will kill most microfilariae within 24 hours. If the microfilaria concentration is high, an adverse reaction is likely.

Selamectin

- Selamectin (Revolution, Pfizer Animal Health) is a topical parasiticide and heartworm preventative drug. The recommended minimum monthly dosage is 6 mg/kg. It is recommended for use in dogs more than 6 weeks of age and is available in 6 separate dose strengths.

Moxidectin

- Moxidectin (ProHeart, Fort Dodge/American Cyanamid), 1 to 3 mcg/kg, is an effective once-a-month heartworm preventive. This drug has been carefully scrutinized because of reports of adverse effects. The incidence of adverse effects is low.

▼ ***Key Point*** All macrolide preventive drugs eliminate microfilaria, either quickly or slowly. For this reason, chronic dosing with Heartgard, Revolution, ProHeart, or Interceptor leads to "occult" status in infected dogs.

- In cats, all monthly prophylactic drugs can be administered without prior testing and without fear of adverse reactions.

Diethylcarbamazine

- Diethylcarbamazine (2.5–3.0 mg/kg, PO) given daily is an effective prophylactic drug. If the owner skips more than 2 days of treatment, do not reinstitute pre-

ventive treatment before performing a microfilarial concentration test. Diethylcarbamazine has been largely supplanted by the macrolide drugs.

▼ ***Key Point*** Never initiate diethylcarbamazine treatment in microfilaremic dogs because a severe reaction may develop.

- Duration of efficacy is short because the drug appears to affect the L_3 to L_4 (larval) molt 9 to 12 days postinfection.
- Begin therapy before the mosquito season and continue for 2 months after the first frost (or year-round in regions that have mosquitoes all year).
- All diethylcarbamazine products are equally effective.
- Combination diethylcarbamazine and oxibendazole (Filaribits Plus; Pfizer) controls intestinal helminths. An occasional side effect of oxibendazole is increased liver enzyme activity, icterus, and hepatic insufficiency, which are usually reversible after drug discontinuation.

Missed Doses of Macrolide Prophylactic Drugs

- One dose of any macrolide will kill all larvae that have infected a dog in the previous month.
- One dose of Heartgard, Interceptor, or Revolution will kill virtually all larvae that have infected a dog during the prior two months.
- Heartgard, Interceptor, and Revolution will prevent almost all infections from maturing after three consecutive doses are missed, providing that at least 12 consecutive monthly doses are subsequently administered.
- Heartgard will prevent over 95% of infections from reaching maturity after four consecutive doses are missed, providing that at least 12 consecutive subsequent doses are administered.
- Interceptor will prevent approximately 40% of infections from maturing if four consecutive doses are missed, providing that at least 12 consecutive subsequent doses are administered.

Macrolide Efficacy Against Adult Heartworms

- Heartgard will kill almost all adult heartworms if administered every month for 30 months.
- We rarely recommend Heartgard for adulticide treatment.
- Progressive pulmonary pathology will occur during at least the first 15 months.
- We recommend Immiticide for almost all infections.

Retesting Dogs Receiving Macrolide Prophylaxis

- Macrolide prophylactic drugs are highly efficacious, and therefore annual retesting often is not performed; however, we recommend annual retesting.
- Owner compliance has been proven to be poor in all regions examined.
- Inadequate dosing is likely in growing puppies.

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Chapter

153 Vascular Diseases

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Diseases of blood vessels are quite common in small animal patients. Hypertension represents a fundamental disorder of the vascular system with wide-ranging impact. The vascular endothelium or vessel wall can become a target tissue for a multisystemic disease. Vascular obstruction or disease also impairs organ function by limiting tissue perfusion or obstructing venous return.

This chapter considers some of the important disorders of the vascular system in small animals. Systemic hypertension is an emerging disorder of clinical importance to dogs and cats. Systemic arterial and systemic venous thrombosis can lead to sudden and devastating clinical deterioration of organ or tissue function. Systemic and pulmonary embolisms are recognized as complications of a number of diseases. Additional vascular disorders of clinical importance include vasculitis, arteriosclerosis, atherosclerosis, vascular neoplasia, and arteriovenous fistula.

SYSTEMIC HYPERTENSION

Overview of Blood Pressure

The blood pressure profile consists of a systolic (peak) pressure, a diastolic (minimal) pressure, and a mean pressure. The pulse pressure is the difference between systolic and diastolic pressures. The mean pressure represents the best estimate of tissue perfusion and is approximated as the diastolic pressure plus $^1/_3$ of the pulse pressure.

Blood pressure can be normal, low, or high. The precise limits of normal arterial blood pressure (ABP) in dogs and cats is still a subject of investigation and some debate. Low blood pressure or hypotension is discussed elsewhere, in the Chapters on Shock (Chapter 156) and Heart Failure (Chapter 147). Systemic arterial hypertension is an increase in systolic or diastolic ABP and is considered in this chapter.

Hypertension is identified by measurement of the ABP. Instantaneous blood pressure is usually measured noninvasively, using either a Doppler flow technique or an oscillometric method. The mechanisms and causes of hypertension vary and require some understanding of normal blood pressure and factors that influence these measures.

Systolic Blood Pressure

- Peak ABP depends on the prior diastolic pressure, the ventricular stroke volume, and the compliance of the arterial system (especially the aorta). Systolic pressure is most often used for the diagnosis of systemic hypertension because systolic blood pressure is easier to measure accurately than diastolic pressure, and because the majority of hypertensive dogs and cats have systolic or combined systolic/diastolic hypertension.
- The upper limit of normal for ABP depends on the species, the method of measurement, and the conditions of examination.
- In dogs, pressures >160 mm Hg (by the Doppler-flow method) are suspicious for hypertension. Values persistently greater than 180 mm Hg are diagnostic of hypertension, provided the dog is quiet, does not have tachycardia, and is not struggling.
- In cats, pressures >150 mm Hg are suspicious for hypertension, and values persistently greater than 160 mm Hg are considered diagnostic for hypertension (although some authors propose 170 mm Hg as the cutoff). Although "white-coat hypertension" related to the stress of examination has been reported in cats more frequently than dogs, both cats and dogs may have stress- or excitement-related elevations of blood pressure.
- In some animals, systolic pressures measured by oscillometric methods are about 10 to 20 mm Hg lower than those measured by Doppler-flow or direct arterial puncture methods. Thus, a systolic pressure of 170 mm Hg by an oscillometric method in a dogs is probably indicative of hypertension.

Diastolic Blood Pressure

- Diastolic ABP depends on systemic vascular resistance, heart rate, and cardiac output.
- Vasodilation associated with systemic diseases (anemia, hyperthyroidism) or arterial vasodilator therapy often lowers diastolic pressure. Conversely, spontaneous or

drug-induced vasoconstriction increases diastolic (as well as systolic) ABP.
- Diastolic pressure is detected with variable accuracy by oscillometric recording devices, but is more difficult to estimate with the Doppler flow method.
- Diastolic pressures exceeding 100 to 110 mm Hg are generally considered to be high, assuming that the animal is not excited during the recording. Values exceeding 120 mm Hg are generally treated for hypertension.

Mean Blood Pressure

- The mean arterial pressure is the geometric mean pressure during the cardiac cycle and is closer to the diastolic than the systolic reading.
- Oscillometric ABP devices measure this variable by detecting maximum oscillations in the blood vessel wall that correspond to the mean ABP. Provided the systolic and diastolic pressures can be recorded, the mean can be estimated as:

$$\text{MAP} = (\text{diastolic pressure}) + (\tfrac{1}{3}\,[\text{systolic pressure} - \text{diastolic pressure}])$$

Arterial Pulse Pressure

- The pulse pressure, or difference between systolic and diastolic ABP, is the basis for the palpable pulse identified during physical examination. The systolic and diastolic pressures are closely related in most circumstances so that each will increase or decrease proportionately. However, as indicated above, there are differences in the determinants of each pressure and situations are encountered where maximal and minimal pressures diverge.
- Aortic input impedance affects systolic ABP. For example, a potential reason for isolated systolic hypertension in older cats is the increase in aortic stiffness associated with idiopathic aortic dilation.
- Stroke volume has a marked effect on systolic ABP. Stroke volume is increased in cases of increased left ventricular filling (Frank-Starling effect) and increased sympathetic activity. Simply increasing stroke volume usually increases both systolic and diastolic pressures. But there are situations in which stroke volume increases but diastolic pressure decreases. This is especially likely in the setting of peripheral vasodilation, abnormal run-off of aortic blood flow, or when the heart rate is especially slow. Examples include:
  - Anemia
  - Thyrotoxicosis
  - Administration of arterial vasodilator drugs
  - Patent ductus arteriosus
  - Moderate to severe aortic regurgitation
  - Large arteriovenous fistula
  - Bradycardia (from drugs or chronic heart block)
- In these situations the arterial pulse is often bounding and measurement of systolic pressure does not provide a comprehensive picture of ABP or perfusion pressure.

Etiology

The precise mechanisms underlying hypertension in animals are not well understood except in experimental cases. Inability to regulate plasma volume (renal disease or hyperadrenocorticism), excessive adrenergic activity (pheochromocytoma), increased cardiac output (hyperthyroidism), and activation of the renin-angiotensin system (glomerular disease) are likely candidates. The clinical associations of systemic hypertension should be appreciated because some disorders are treatable and management may minimize the need for antihypertensive therapy. While systemic hypertension is considered idiopathic or "essential" in some dogs and cats, a number of well defined clinical disorders have been associated with increases in ABP.

- Renal disease (particularly glomerular disease)
- Hyperadrenocorticism—both Cushing's disease in dogs (with glucocorticoid excess) and Conn's disease in cats (associated with mineralocorticoid excess and hypokalemia) can lead to hypertension.
- Pheochromocytoma—a catecholamine-producing tumor of the adrenal medulla.
- Hyperthyroidism—both spontaneous disease in cats and iatrogenic disease in dogs
- Diabetes mellitus—in both dogs and cats
- Drugs—particularly the alpha-adrenergic agonists (such as phenylpropanolamine) that lead to vasoconstriction.
- Central nervous system (CNS) disorders—if associated with excessive sympathetic output.
- Idiopathic or "essential" hypertension—hypertension of undetermined cause.

▼ ***Key Point*** Systemic hypertension should be approached initially as a symptom or complication of another disease condition rather than a disease in itself. Only after underlying diseases have been excluded by appropriate testing can systemic hypertension be deemed "idiopathic."

Clinical Signs

Injury to arterioles or larger arteries or the direct transmission of pressure across the microcirculation is responsible for many of the clinical signs of hypertension. Additionally, the left ventricle must hypertrophy to maintain an increase in pressure work. Other clinical signs may be attributed to the underlying disease responsible for elevated ABP.

▼ ***Key Point*** The eyes, brain, heart, and kidneys are the main target organs of injury in cases of systemic hypertension.

Brain Abnormalities

- *Cerebral or brainstem injury* can result from hypertension owing to brain edema or hemorrhagic stroke. Clinical signs include signs of intracranial abnormalities, including abnormal mentation, neurologic deficits, head tilt, seizures, and coma. Presumably, as with human patients with hypertension, dogs and cats also develop "headaches" and this may account for some of the inactivity observed in affected small animals.

Ocular Abnormalities

- *Ocular abnormalities* include retinal edema, hemorrhage, and detachments. These lesions can progress to blindness. Sudden blindness also may develop due to intraocular hemorrhage and hyphema. Recognition requires careful ophthalmic examination. Acute lesions are often superimposed on chronic retinal changes.

Cardiac Abnormalities

- The *heart* generates the pressure in hypertension and may also be injured by work and the high pressures distributed across the coronary vascular system.
- A systolic cardiac murmur of uncertain cause or an atrial (S_4) gallop sound may indicate hypertensive heart disease. A systolic heart murmur may represent mitral regurgitation, flow into a dilated aorta, or dynamic ventricular outflow tract obstruction related to the hypertrophic disease.
- Concentric left ventricular hypertrophy and resultant cardiomegaly are the markers for chronic hypertension and can be identified by an echocardiogram (most sensitive), electrocardiogram (increased voltages or left-axis deviation), or thoracic radiograph (least sensitive).
- Coronary arteries also are injured from high arterial pressures.
- While congestive heart failure (CHF) stemming from hypertensive heart disease is relatively uncommon in dogs and cats, distinguishing left ventricular hypertrophy due to systemic hypertension from primary hypertrophic cardiomyopathy or hyperthyroid heart disease in cats can be a challenge. In dogs with chronic mitral valve disease, systemic hypertension increases the load on the left ventricle and increases the regurgitant volume. Persistent hypertension may prevent effective drug control of CHF in these dogs.

Kidney Abnormalities

- The *kidneys* are both a source and target of hypertension. Abnormal renal contour or size, proteinuria, and mild-to-moderate azotemia often are found in hypertensive animals. Hypertension injures glomerular vessels and damages renal tissues. In some cases it may be difficult to discern if hypertension is the cause or the consequence of renal disease and hypertension secondary to chronic renal disease promotes further glomerular damage.

Other Manifestations

- Other blood vessels can be injured in patients with hypertension.
- Epistaxis or bleeding from other sites also has been reported with hypertension, especially the labile hypertension of pheochromocytoma.
- Chronic systemic hypertension can lead to aortic dilatation even in relatively young animals. Rarely, the aorta can tear leading to a dissection of blood between layers.

Diagnosis

- When evaluating the hypertensive patient, search for an underlying cause, as treatment may reduce the need for antihypertensive drugs.
- Consider the history, and determine if any medications that might increase ABP have been prescribed (such as thyroid hormone; alpha-adrenergic agonists; antihistamine combinations with vasoconstricting properties).
- At a minimum, perform routine diagnostic studies that include a full serum biochemical profile; complete urinalysis; serum thyroxin; and either abdominal radiographs or optimally an abdominal ultrasound examination with particular attention to the kidneys and adrenal glands.
- Diagnosis of hypertension requires measurement of ABP using either an arterial puncture attached to a pressure transducer or an indirect determination that uses a reliable technology and consistent technique.
- Both oscillometric methods and Doppler flow methods have been used successfully for measuring ABP in dogs. Systolic ABP is slightly underestimated by the oscillometric technique.
- Systolic pressures can be readily determined in cats using Doppler flow meter and occlusion cuff on a fore or hind limb. Oscillometric measurements can be obtained from cats using an appropriately-sized cuff at the tailhead in the sternal animal. Oscillometric measurements using a tail cuff may underestimate Doppler-obtained blood pressure.
- Care must be taken to consider normal variation in excited animals. Slight differences (5–10 mm Hg) between front and back limbs are normal in many animals, and the cuff size (diameter) is critical to prevent overestimation (too small a cuff) or underestimation (too wide a cuff).

▼ ***Key Point*** Since the development of systemic hypertension is usually an indication for life-long therapy, the diagnosis should be as certain as pos-

sible. One or two high pressure readings in the setting of overt target-organ injury are sufficiently conclusive. However, in otherwise healthy animals, repeated measures—preferably over a number of days—should be obtained before establishing a diagnosis.

Technique for Measuring Blood Pressure

Because technical details are very important in establishing a correct diagnosis, consider the following *technical pointers for measuring blood pressure*:

- Understand your recording unit and how it works.
- Practice on numerous animals of different sizes. Practice improves skill and confidence. Train others to measure ABP and compare results. When using Doppler methods, learn to evenly decrease the pressure in the cuff and manometer.
- Measure ABP in calm animals that are comfortably restrained—in many clinical situations, it is advantageous to let the pet rest in its caretaker's arms or lap for the measurements. Avoid measuring ABP in sedated animals.
- Have a supply of different-sized pediatric cuffs (e.g., #1–#6 pediatric cuffs) available. Place nonelastic, self-adhesive tape (such as Vetwrap) around the cuff to prevent slippage.
- Do not allow the cuff tubing leading to the manometer to kink.
- Measure the limb and use an appropriate sized cuff. The cuff must compress the limb evenly and occlude the artery with the approximate pressure recorded by the manometer. Use the smallest cuff appropriate for the limb size. Cuff diameter should be 40% of the limb circumference in dogs and between 30% and 40% of the limb circumference in cats. There is often a 10- to 20-mm Hg difference between next sized cuffs; wider variations suggest a technical error in recording or a cuff problem.
- Place the cuff around the distal radius (antebrachium), metatarsus or tailhead, around a relatively cylindrical portion of the appendage. Secure the cuff with wrap and attach it to the manometer. The inflatable bladder of the cuff should be positioned directly over the underlying artery.
- Place the patient in either lateral or sternal recumbency on a *padded table*, in a *quiet room*, with *calm people*. Gently restrain the patient, and give the pet time to acclimatize to the environment.
- Measure heart rate (HR). If it is high (e.g., >160 in a dog; >240 in a cat), try to help the animal relax before proceeding.
- Consider the site of measurement relative to heart level. The cuff should be at the level of the heart during measurement. ABP should not be measured in a standing animal unless a tail cuff is used.
- Inflate the cuff one or two times, slowly and gently, and allow the animal to experience what will happen during measurement. Then record the pressure.
- With a Doppler method, place the crystal palmar (or plantar) and just distal to the large carpal (metatarsal) pad. Use subtle medial-lateral; anterior-posterior movements to detect the arterial signal. In cats and small dogs, or in patients with low blood pressure, use a light touch and copious ultrasound gel (not rectal jelly) to obtain an optimal acoustic signal. Clipping the hair can be helpful. Once a reading is obtained, repeat the measurement two more times noting the values and the concurrent HR.
- For Doppler flow systems, consider using earphones attached to the available output plug to reduce the loud, popping on/off sound of crystal movement, a noise that may startle the patient. At a minimum, do not place the audio speaker near the patient's head.
- If using an automated oscillometric device, attach the cuff at the tail base, the antebrachium, or the metatarsus. Place the two cuff lines on either side of the artery (which is generally ventral and slightly medial). Measure HR with a stethoscope. It should correspond almost exactly with the automated monitor. If it does not, do not accept the displayed values.
- If the ABP value is "low" (systolic pressure < 90 mm Hg) try the next *smaller* cuff. If it is still low, go to the hind limb to verify the value. If the animal is not symptomatic, interpret the clinical situation and determine the most likely cause (for example, volume depletion, sedatives, or cardiovascular drugs).
- If the ABP is high (systolic pressures of >180 mm Hg in dogs; >160 mm Hg in cats), try the next sized larger cuff, as this will more easily compress the artery. If ABP is still high (or <20 mm Hg lower than the last measurement), the initial measurement is probably accurate, but verify it by placing the cuff at an alternative site (e.g., from forelimb to metatarsus or tail).
- Labile hypertension may indicate a "white-coat" effect from examination stress or, in some patients, a true labile situation (as with pheochromocytoma in dogs).
- With either measurement method, obtain 3 to 5 measurements with approximately 30 seconds between measurements. Discard any obviously spurious readings and use the average of the repeated measurements to obtain a representative reading for that session.
- Interpret the findings of elevated ABP in conjunction with other clinical findings. In animals with ocular, renal, CNS, or cardiac disease, an elevated ABP measurement is more likely to represent a true finding of hypertension. If other clinical findings are negative, measure the pressure at another time or day.
- Be confident of the diagnosis of "hypertension" before initiating drug therapy.

Treatment: General Measures

- Treat the underlying problem (e.g., hyperthyroidism or hyperadrenocorticism) whenever possible; however, remember that in some cases there may be more than one reason for hypertension and that correction of one problem will not insure a normotensive state. For example, many older cats have preexisting renal disease as one risk factor and later develop hyperthyroidism, which can compound the hypertension.
- If pressure is very high (>200 mm Hg) or if target organ injury is evident (especially if there is ocular or cerebral disease), treat the hypertension before addressing the underlying disorder.
- Modest dietary sodium restriction is reasonable in treating hypertension, however, there is little evidence that severe sodium restriction will benefit most dogs and cats with hypertension. Attempting to control significant hypertension by diet alone is ill-advised, and diet should be viewed as simply an adjunct to antihypertensive drug therapy.
- Drug therapy is generally required to treat hypertension. ABP can be lowered pharmacologically by reducing cardiac output or reducing systemic vascular resistance by dilating systemic arterioles.
- Therapy of systemic hypertension usually involves a stepwise approach, starting with a moderate dosage of one drug, increasing the dose to the desired effect as needed, or adding other drugs if required.
- Consider possible drug interactions when prescribing multiple drugs.
- There are also some particular situations wherein a specific regimen of drugs is more desirable, for example, in glomerular disease or in hypertension associated with pheochromocytoma.
- A variety of drugs can be prescribed for treatment of hypertension. These and specific pointers for clinical use, are described below (also see Chapter 146 for more details).

Drug Therapy for Systemic Hypertension

Calcium Channel Blockers

- Most clinicians initiate treatment of systemic hypertension in cats with the calcium-channel antagonist/vasodilator amlodipine besylate (Norvasc). Dihydropyridines such as amlodipine and felodipine are more vascular selective than other calcium channel blockers such as diltiazem. Although diltiazem may slow heart rate, it is not recommended as a primary therapy for systemic hypertension.
- Amlodipine is an effective and well-tolerated therapy for hypertension in cats, based on a number of small, but convincing, clinical studies. Clinical experience indicates amlodipine at higher doses is effective for blood pressure control in dogs.
- The starting dose in cats is $^1/_4$ of a 2.5-mg tablet PO once daily. In some cases, higher doses, up to 1.25 mg PO q12h, may be needed.
- In hypertensive dogs, amlodipine is dosed initially at 0.1 to 0.2 mg/kg PO q12h. Response is variable in dogs, though it tends to be very good at higher dosage ranges of 0.2 to 0.5 mg/kg PO q12h.
- Amlodipine has a relatively slow onset in dogs, and a prolonged duration of action. Unless urgent control of ABP is needed, increase the dose gradually, over several weeks to target ABP levels (usually <140 mm Hg).
- Amlodipine monotherapy works better than an angiotensin-converting enzyme inhibitor (ACEI), beta-blocker, or diuretic in cats, and is the drug of choice for hypertension that is severe (>200 mm Hg systolic ABP) or associated with overt target organ injury (retinal or CNS signs).
- Comparison to ACEI: amlodipine is more effective than benazepril in lowering ABP, but is not considered directly renoprotective (aside from reducing ABP) in patients with significant proteinuria.
- The combination of amlodipine with benazepril or enalapril is reasonable in cats or in dogs with documented renal disease with proteinuria. Optimal ABP control may be facilitated by the amlodipine besylate, whereas benazepril may reduce proteinuria and delay progression of renal disease, especially in cats.
- Amlodipine is relatively expensive, compared to generic or veterinary enalapril or benazepril, and this may be an important issue in large dogs wherein combined therapy may allow for dose reduction of amlodipine.
- One approach to combination therapy is administration of amlodipine once daily in the morning and the ACEI once daily after noon. If higher doses of both drugs are needed, they can be administered together, twice daily. In addition, there is a combination capsule of 10 mg amlodipine/2.5 mg benazepril (Lotrel) that may be useful in some larger patients or might be compounded for individual use.

▼ ***Key Point*** In most feline patients, amlodipine besylate is the drug of choice for treatment of severe systemic hypertension and is generally effective as a single therapy when dosed appropriately.

Angiotensin-Converting Enzyme Inhibitors

- Hypertension in dogs or cats can be treated with an ACEI, typically *benazepril* (human Lotensin in the United States; veterinary Fortecor in many other countries) or *enalapril* (veterinary Enacard).
- The initial dose of an ACEI for cats is between 0.5 and 1 mg/kg PO once daily.
- Dogs are usually treated at 0.5 mg/kg PO q12h.

- An ACEI is particularly reasonable therapy in dogs and cats with mild hypertension and concurrent glomerular disease (see Chapter 77).
- As indicated above, in patients with moderate to severe hypertension, an ACEI is best added to the calcium channel blocker amlodipine besylate.

Diuretics

- In comparison to human patients, diuretic therapy of hypertension of dogs and cats is inferior and rarely undertaken.
- Diuretics decrease cardiac filling and cardiac output and lower ABP. However, diuretic monotherapy is rarely successful in controlling hypertension in small animals, and the resulting volume contraction can worsen azotemia and activate the renin-angiotensin system.
- Diuretics are more appropriate as adjunctive therapy in urgent hypertensive situations or in patients with where hypertension and congestive heart failure are both evident.
- A loop diuretic such as furosemide (1–2 mg/kg q12–24h) is most often used. This can be combined with spironolactone (0.5–1 mg/kg daily).
- If diuretics are used, they may be combined with an ACEI to limit further activation of the renin-angiotensin-aldosterone system.

Beta-Adrenergic Blockers

- Beta blockers decrease heart rate, cardiac output, and plasma renin activity. These and possibly other (central) effects are antihypertensive.
- Currently, these drugs are used mainly in co-therapy of four conditions:
- As an add-on drug to amlodipine and an ACEI in the rare case of unresponsive hypertension that requires "triple therapy" for control. Atenolol is chosen in cats; atenolol or carvedilol in dogs.
- In cats, as an initial management for mild hypertension associated with protracted sinus tachycardia and high cardiac output due to hyperthyroidism, *atenolol* (1–2 mg/kg PO q12–24h) is typically chosen. The daily dose often requires down-adjustment (or drug discontinuation) to prevent bradycardia once the hyperthyroid state is controlled with methimazole. In hyperthyroid cats with severe hypertension, a combination of amlodipine and atenolol can be used.
- In dogs with degenerative valvular heart disease and systemic hypertension caused by hyperadrenocorticism or chronic renal disease, the use of *carvedilol* (Coreg; dosed at 0.5–1 mg/kg PO q12h) may control hypertension and provide cardioprotection. Carvedilol is also an alpha-adrenergic blocker. The drug is expensive, and cost may limit its use. In dogs with concurrent CHF, first control the condition with diuretics and an ACEI before starting carvedilol.
- In dogs with functional pheochromocytoma to control heart rate, arrhythmias, and blood pressure, a beta blocker (*propranolol* starting at 0.25 mg/kg PO q8h) should be administered only *after* initial therapy with the nonselective alpha-blocker phenoxybenzamine or the alpha$_1$-adrenergic blocker prazosin (see below). If there is concern about beta-blockage, a brief infusion of the ultra–short-acting nonselective blocker esmolol (500 mcg/kg/minute infusion over 10 minutes) can be given as a test. In canine patients with concurrent non-cardiogenic pulmonary edema ("pheo-lung") or a catecholamine-induced dilated cardiomyopathy, beta-blockers must be used with great care if at all to prevent further impairment of pulmonary or cardiac function.

Other Vasodilators

- *Sodium nitroprusside*—an infusion of nitroprusside represents aggressive antihypertensive therapy in the setting of severe target organ injury, hemorrhagic stroke, and uncontrolled CHF.
- This drug is used mainly in dogs.
- Dosing in systemic hypertension is generally higher than that required for treatment of CHF (see Chapter 147).
- Initially begin at 2.5 mcg/kg/min; the infusion rate can be increased every 15 minutes by 1 mcg/kg/min to a maximum of 20 mcg/kg/min. Some dogs are highly resistant to even high-rate infusions.
- *Hydralazine*—The direct-acting arterial vasodilator hydralazine (1–3 mg/kg PO q12h) can be used in unresponsive systemic hypertension. In animals receiving other antihypertensive medications, hydralazine therapy should be initiated at the low end of the dosing range and titrated up slowly as needed to control ABP.
- *Prazosin*—the alpha-adrenergic blocker prazosin is an older medication that is not used very often today. While somewhat inconvenient to dose (coming in only 1-mg, 2-mg, and 5-mg capsules), it can be highly effective in dogs unresponsive to other medications, particularly in the case of pheochromocytoma (when *phenoxybenzamine* or Dibenzyline is unavailable).
- The initial dose of prazosin may result in profound drop in ABP. Blood pressure should be monitored carefully during therapy.
- An initial dose of 0.5 mg (discard $^1/_2$ of the capsule contents) can be given to most dogs. The usual dose in dogs is one 1-mg capsule, q8–12h; if higher doses are needed, the 2-mg capsule can be used.
- In cats, prazosin can be dosed at 0.5 mg PO, twice daily.

Follow-Up of Drug Therapy

- Reevaluate blood pressure regularly to ensure efficacy and prevent further organ injury.

- Be diligent in looking for signs of drug toxicity, including hypotension (weakness, depression, syncope, progressive renal failure).
- Follow serum biochemistries with particular attention to indicators of renal function.
- Continue to manage the underlying condition if known.
- As there are no large, prospective studies to guide therapy, treat each patient individually.

THROMBOSIS AND THROMBOEMBOLISM

General Concepts

- *Thrombosis* refers to the local formation of a blood clot within a blood vessel. Thrombi are potentially dangerous owing to obstruction of blood flow. Thrombi may develop in arteries or veins.
- *Embolism* is the sudden occlusion of an artery that occurs when an organized substance is carried from one point to another by the vascular system.
- A thrombus that is dislodged from the site of formation and is carried by the blood to another location is termed a *thromboembolus*.
- Systemic thromboembolism occurs when a thrombus is carried from a formation site in the left side of the heart to the termination of an artery within the systemic circulation.
- Pulmonary thromboembolism indicates that a thrombus formed within a systemic vein and dislodged, traveling with venous return across the right side of the heart and into the pulmonary arteries.
- Thrombosis may be initiated by different mechanisms (see Chapter 23).
- A systemic arterial thrombus typically starts with activation and aggregation of platelets (white thrombus). Arterial thrombosis frequently is initiated by injury to vascular endothelium or atrial endocardium.
- Stasis of blood and activation of clotting factors is thought to cause systemic venous thrombosis (red thrombus). Deficiencies of plasma antithrombin appear to predispose to venous thrombosis. Frequently venous thrombosis is associated with trauma, systemic inflammation, neoplasia, or other disorders favoring a pro-coagulant environment.
- A thrombus or embolus obstructs blood flow. Consequences of vascular obstruction include *ischemia* (lack of blood flow), *infarction* (*necrosis* of tissues nourished), and associated inflammatory reactions.
- *Systemic arterial thrombi* can be clinically silent or life-threatening, depending on the specific vessels, tissues, or organ injured.
- *Systemic venous thrombi* obstruct systemic venous return, typically leading to local edema from impaired venous drainage.
- *Pulmonary embolism* alters the normal relationship between lung perfusion and ventilation, impairs right ventricular function, and may produce considerable pulmonary parenchymal damage.

Etiology

A number of clinical disorders are associated with the development of thrombi or emboli in systemic arteries or veins (Table 153-1).

Pathophysiology

- The pathogenesis of clinical signs depends on the acuteness of injury, location of vascular obstruction, magnitude of thrombosis, collateral circulation, the tissue affected, and inflammatory mediators.
- The pathological consequences of ischemia or infarction of the *systemic circulation* include:
  Bone—Infarcts and zones of bone necrosis
  Brain—Ischemia-induced neuronal damage, edema, cell necrosis, hemorrhagic necrosis
  Limbs—Muscle ischemia, rhabdomyocytolysis, pain, peripheral neuropathy
  Myocardium—Myocardial ischemia or infarction, arrhythmias, abnormal ventricular wall motion, ventricular dysfunction, heart failure, sudden cardiac death
  Spinal cord—Neuronal degeneration, ischemic or hemorrhagic necrosis
  Kidney, adrenal gland, liver, spleen, or gut—Infarcts, hemorrhages, and parenchymal necrosis may occur with subsequent organ dysfunction
  Skin—Infarcts or cutaneous hemorrhages
- Pathological consequences of ischemia or infarction of the systemic venous or pulmonary arterial circulation include:
  - Lung—Pulmonary embolism and pulmonary parenchymal injury leading to ventilation-perfusion inequality in the lung.
  - A massive pulmonary embolus can obstruct the left or right pulmonary artery, severely limit cardiac output, and lead to hypotension, myocardial ischemia, and cardiac arrest.
  - Embolization of smaller pulmonary vessels can cause pulmonary infarction and also initiate the release of vasoactive chemicals that cause lung edema and inflammation.
  - Recurrent pulmonary thromboembolism reduces vascular cross-sectional area, increases pulmonary vascular resistance, and predisposes patients to chronic pulmonary hypertension. Acute or chronic pulmonary hypertension may result in signs of right-sided congestive heart failure (e.g., ascites, jugular distention).
  - Systemic veins—Obstruction of venous return, elevation of venous and capillary pressures, and edema of dependent tissues.

Table 153-1. CAUSES OF THROMBOSIS AND THROMBOEMBOLISM

Systemic Arterial Thrombosis/Thromboembolism	Systemic Venous or Pulmonary Arterial Thrombosis/Thromboembolism
Cardiac Disease/Origin	***Hypercoagulable states***
Feline cardiomyopathy (from the left atrium)	Deficiency of antithrombin III (protein-losing nephropathies)
Bacterial endocarditis (thrombi shed from the vegetation)	Venous stasis
Penetrating foreign body (needle, porcupine quill)	Systemic inflammatory reaction
Atrial fibrillation (rare, except in cats)	***Specific Disorders (Multiple Mechanisms)***
Missile—gun bullets or pellets that directly penetrate the vascular system	Cushing's disease
Aberrant filarial parasites within systemic arteries *(Dirofilaria immitis)*	Immune-mediated hemolytic anemia
Cartilaginous embolism of the spinal cord vessels	Pheochromocytoma
Inflammation of the blood vessel wall (arteritis or vasculitis)	Verminous pulmonary arteritis (Dirofilariasis; Angiostrongylosis)
Direct trauma or iatrogenic injury to arterial blood vessels	Heartworm embolus from adulticide therapy (dogs) or spontaneous worm death (cats)
Polycythemia	Invasive neoplasm
Disseminated intravascular coagulopathy	Diseases of veins
Torsion of a vascular pedicle (splenic torsion, mesenteric torsion)	Venous inflammation (phlebitis) from catheters, trauma, or drugs
Artificial heart valve	Thrombophlebitis—phlebitis with localized thrombus formation
	Fat emboli (from long bone fractures)
	Air emboli (from catheters or procedures such as cystography or cryosurgery)
	Retrograde venous embolus of the spinal cord
	Cardiac Disease/Origin
	Tricuspid valve thrombus
	Intracardiac tumor
	Intracardiac catheter
	Central line dialysis catheter
	Pacing lead

Diagnosis

- The clinical diagnosis of thrombosis or embolism requires a high level of suspicion. A sudden onset of clinical signs is typical of some conditions; other disorders are chronic in nature.
- The physical examination and laboratory signs of embolism depend on a number of factors, including the:
  - Vascular system involved and the tissues served by affected vessels.
  - Acuteness of the obstruction and magnitude of tissue injury.
  - Degree of collateral circulation available to support the affected region.
- Clinical abnormalities of thrombosis/thromboembolism range from subtle to obvious. Table 153-2 indicates some of the typical clinical and laboratory findings of various thrombotic or embolic diseases.
- Advanced *imaging studies* can be useful in confirming the diagnosis of arterial thrombosis or embolism. (see Chapter 4) The optimal examination varies with the suspected cause and tissues injured. In some cases the thrombus may be imaged directly; in others, perfusion deficits may be identified. Specialists should be consulted regarding specialized radiographic, ultrasonographic, echocardiographic, angiographic, and radionuclide studies.
- Clinical laboratory tests may demonstrate changes attributable to decreased blood flow, organ ischemia, or tissue necrosis.
- The diagnosis of cutaneous and appendicular thrombosis/embolism usually can be made from physical examination.
- Cutaneous vasculitis usually leads to hemorrhages and edema.
- Aortoiliac thrombosis (Chapter 150) causes typical clinical signs (see Table 153-2) along with marked elevations in skeletal muscle enzymes.
- A diagnosis of superficial venous thrombosis or thrombophlebitis is made from inspection and palpation of superficial veins and tissues.
- Duplex Doppler ultrasound can be used to examine the vessel lumen and interrogate blood flow patterns in ambiguous cases.
- Myocardial infarction is diagnosed by characteristic ECG changes, progressive elevations of cardiac troponin-I, and by echocardiographic wall motion studies.
- Diagnosis of abdominal thrombosis or embolism may be difficult and require surgical exploration in the case of an acute abdomen. In many cases, however, abdominal ultrasound with Doppler studies may show the presence of a thrombus and associated obstruction to flow from the aorta.

Table 153-2. CLINICAL FINDINGS IN THROMBOSIS AND THROMBOEMBOLISM

Organ or Tissue	Possible Clinical Findings	Laboratory Examination—Possible Findings
Brain	Ischemic neuropathy or "thrombotic stroke" Fainting, falling, persistent neurologic deficits, coma, or seizures	MRI or contrast CT can demonstrate imaging abnormalities Secondary changes in CSF
Spinal cord	Rapidly progressive segmental spinal cord disease Signs depend on the level and extent of cord injury	MRI or contrast CT can demonstrate imaging abnormalities Secondary changes in CSF Myelogram negative for extradural compression
Limbs	Sudden onset of limb weakness or paresis Affected limb(s) are pale, cold, and pulseless Absence of Doppler flow signals in affected arterial system Signs of ischemic lower motor neuron sensory and motor neuropathy Ischemic myopathy (pain, muscle contracture, possible late-onset edema) Bone infarcts may be associated with diffuse or shifting lameness or pain	Duplex Doppler studies show lack of blood flow in affected system Angiogram positive for obstruction (rarely necessary) Elevated muscle enzymes (CK > > > AST > > ALT) Increased blood lactate Hyperkalemia and hypermagnesemia (with reperfusion)
Myocardium	Discomfort, anxiety, tachypnea Premature ventricular complexes Hypotension Progressive heart failure Sudden cardiac death	ECG abnormalities (acute ST-T segment deviation, infarction patterns, ventricular arrhythmias) Elevated creatine kinase-MB Elevated serum troponin-I (cTn-I) Echocardiographic abnormalities (regional ventricular wall hypokinesis)
Mesenteric and splanchnic vessels*	Possible abdominal pain (colic) Severe abdominal pain if aortic thrombus or mesenteric ischemia Acute onset of hindlimb weakness or paralysis if thrombus is in caudal aorta Acute renal failure if thrombus is cranial to kidneys Shock	Serum biochemical abnormalities may reflect end-organ injury (azotemia or an Addisonian crisis) Abdominal ultrasound can frequently identify the presence and location of the thrombus Duplex Doppler studies of abdominal vessels may be revealing Arteriography positive for obstruction (rarely done) Exploratory surgery may indicate vascular obstruction Ancillary testing in dogs with aortic thrombi often reveals protein losing nephropathy or Cushing's disease
Skin	Cutaneous hemorrhages, petecchiae, or ecchymosis may be evident	Laboratory tests compatible with vasculitis
Pulmonary embolism	Sudden onset of tachypnea or dyspnea Possible mild pyrexia Variable heart rate, but may be increased Acute, severe: hypotension from impaired right-ventricular function sudden death Chronic: clinical signs of pulmonary hypertension; possible right-sided CHF Loud S_2; tricuspid regurgitation murmur in pulmonary hypertension	Thoracic radiographs may show nonspecific parenchymal changes, localized pleural effusion, or redistribution of blood flow (away from affected areas), but may be normal Radiographic signs of heartworm infection when due to dirofilariais Large proximal thrombi and heartworms may be identified by echocardiography with imaging of the pulmonary arteries in some cases Distal thrombi must be diagnosed from radionuclide scans (perfusion defects) or pulmonary arteriography Normal d-dimer test argues against pulmonary thromboembolism Positive heartworm tests when due to dirofilariasis
Systemic venous thrombosis	Cutaneous veins are swollen and may be "knobby" in appearance Superficial veins do not collapse, and may be warm and painful (thrombophlebitis) Subcutaneous edema in the tissues drained by the venous system Deep venous thrombosis involving the external iliac veins may lead to bilateral limb edema Bilateral jugular thrombosis can lead to intermandibular edema Thrombosis of the cranial vena cava causes intermandibular and pectoral edema, pleural effusion, or chylothorax There may be signs of pulmonary thromboembolism with any venous thrombus	Duplex Doppler echocardiography positive for thrombus or altered pattern of blood flow pattern of blood flow

*Thrombosis or volvulus of renal, adrenal gland, splenic, or splanchnic arteries

- Pulmonary thromboembolism is a difficult diagnosis. It may be suspected from the history and medical workup, but there are no readily available tests for definitive diagnosis (see Table 153-2). Radionuclide scans that show perfusion deficits may be highly suggestive in the absence of concurrent lung infiltration or a history of chronic respiratory disease (as parenchymal disease may affect perfusion). Doppler-echocardiographic studies documenting *acute*, high velocity tricuspid and pulmonic insufficiency is suggestive of pulmonary thromboembolism in a patient at risk for this complication.
- D-dimer assay may be positive in patients with pulmonary embolism; however, this result is not specific and may be positive in other disorders. A negative d-dimer test is more likely to be helpful in excluding pulmonary embolism.

Treatment

Principles of Therapy

- Principles of therapy for thrombosis and thromboembolism include prevention of further thrombosis, treatment of the underlying disorder, removal or disintegration of the clot when possible, and supportive care to damaged tissues.
- Thrombolytic therapy with tissue plasminogen activator has not been evaluated adequately in veterinary medicine. Although potentially effective in clot lysis, the high cost of the drug, the high incidence of adverse effects (including severe reperfusion hyperkalemia), the narrow window of time in which the medication must be delivered, and the high mortality associated with therapy of some conditions have limited the use of this medication in veterinary patients. A specialist with experience in thrombolysis should first be consulted.
- See Chapter 150 for details about treating thromboembolism associated with feline cardiomyopathies.

Heparin Therapy

Heparin is a heterogeneous anticoagulant that inhibits coagulation and is used in the prevention and management of systemic venous and arterial thrombosis and thromboembolism. Heparin is administered by injection, either subcutaneously or intravenously (as a bolus or constant rate infusion).

Formulations

- *Unfractionated sodium and calcium heparin* contain higher and lower molecular weight fractions. Unfractionated heparin binds with antithrombin (formerly AT-III) and inactivates a number of coagulation enzymes, most prominently activated thrombin (factor IIa) and activated factor X (Xa). This inactivation and the effects of the chosen doses can be measured using standard prothrombin and activated partial thromboplastin times; both values are prolonged with unfractionated heparins.
- *Low-molecular weight heparin* (LMWH), including *enoxaparin* (Lovenox) and *dalteparin* (Fragmin) preferentially inhibit factor Xa. These anticoagulants do not prolong the standard coagulation tests, and dosing must be assessed by less-available anti-Xa assays.

Indications

- Heparin therapy—either unfractionated or fractionated (LMWH)—is indicated in patients known to be at high risk for development of thrombosis. Heparin does not dissolve clots but reduces the expansion of existing clots and may prevent new thrombus formation.
- Common disorders managed by heparin include arterial thromboembolism in feline cardiomyopathy, pulmonary thromboembolism, catheter thrombosis of central lines, thrombophlebitis, thrombosis of the jugular vein, suspected deep venous thrombosis in the limb or abdomen, protein-losing nephropathy (provided plasma transfusion has been administered to replenish antithrombin), and some cases of acute bacterial endocarditis. In severe heartworm disease, the use of heparin during the post-adulticide period may reduce adverse effects and limit secondary thrombosis around dead worms.
- Heparin is also used for short-term prevention of thrombosis in patients at high risk for delayed thromboembolism after surgery, trauma, or during recovery from systemic inflammatory diseases.
- Low-dose heparin is often used in the management of disseminated intravascular coagulopathy (discussed more fully in Chapter 23)

Contraindications

- Heparin is contraindicated in overt bleeding, particularly in cases of CNS hemorrhage. Effects of heparin on platelets are complex and thrombocytopenia may occur. Heparin is teratogenic and long-term use may lead to other adverse effects such as bone loss. Overdoses can be reversed with protamine sulfate.

Administration

- Recommended doses of unfractionated heparin vary widely, ranging from 10–75 IU/kg SC q8h for "prevention" of thrombosis or treatment of disseminated intravascular coagulation to 200 to 300 IU/kg SC q8h or by constant rate IV infusion for cases of established thrombosis (e.g., aortoiliac thromboembolism in cats).
- In management of acute thromboembolism, an initial IV dose of 250 to 300 IU/kg IV can be administered, followed by 150 to 200 IU/kg SC q8h (do not administer IM).

- Obtain a baseline clotting profile and adjust the dose to maintain the activated partial thromboplastin time (APTT) or prothrombin time at approximately 2 to $2^1/_2$ times baseline; alternatively, the international normalization ratio (INR) prothrombin time can be prolonged to a value of 2.0 to 3.0.
- Doses of LMWH for veterinary medicine require further definition, but for dalteparin and for enoxaparin consider 100 IU/kg SC q12h, though once-daily dosing with dalteparin might be successful in some cases.
- In dogs dosages of 100 IU/kg to 200 IU/kg of enoxaparin have been used clinically.
- While LMWH can be used long term, drug expense and the need for one to two injections daily has limited the use of these drugs for long-term prevention of thromboembolism in dogs and cats.

Aspirin Therapy

- *Aspirin* inhibits cyclooxygenase and blocks the formation of thromboxane A_2 in platelets. Aspirin has been recommended for the prevention of arterial thromboembolism in a number of conditions including feline cardiomyopathy, canine heartworm disease, bacterial endocarditis, and after cardiac valve repair in dogs. However there is little objective published information regarding risk/benefit of therapy.
- Aspirin probably has little, if any, role in the therapy of established thrombotic disease aside from a single dose administered within 2 hours of an acute arterial thromboembolic event.
- Doses of aspirin are empirical, and there are doubts regarding efficacy in preventing clots.
- Commonly used doses in dogs with heartworm disease are 5 mg/kg PO q12–24h.
- In cats with cardiomyopathy, the traditional dose is one coated, adult, low-dose regimen aspirin of 81 mg per cat, PO every three days. However, ultra-low dosages of 5 mg per cat daily may be equally effective.
- Gastric ulceration is a concern with any dose of aspirin. Do not use aspirin with other anticoagulants or with corticosteroids because of the risk of fatal GI bleeding. Concurrent gastric protection with famotidine may be helpful in animals with signs of gastric irritation on aspirin therapy. The use of buffered aspirin is preferred to limit gastrointestinal upset.

Warfarin Therapy

- *Warfarin* (Coumadin) inhibits vitamin K-dependent factors important in coagulation. Extra-label warfarin has been used in home care of dogs and cats to prevent recurrent pulmonary thromboembolism in dogs and to inhibit arterial thromboembolism in cats with cardiomyopathy.
- There is more experience using warfarin in the cardiomyopathic cat that either has survived an embolic episode or is at high risk for future thromboembolism.
- Tablets can be crushed and $^1/_2$ of a 1-mg tablet PO daily is recommended. The second $^1/_2$ of the same tablet should be used on the subsequent day (as the tablet formulation may not be uniform). Ideally, when initiating warfarin therapy the cat should first receive heparin at 100 IU/kg q8h for 24 to 48 hours because warfarin initially creates a hypercoagulable state.
- Dosing is difficult in cats because $^1/_2$ of a tablet is often insufficient and $^3/_4$ of a tablet may be too much! The use of split dosing (alternating $^1/_2$ and $^3/_4$ tablet dosages) may be useful; alternatively, it is reasonable to ask a compounding pharmacy to dissolve a number of tablets into a solution so long as the drug remains stable.
- The initial dosage for dogs is approximately 0.1 to 0.2 mg/kg, PO daily. As in cats, split dosing may be needed to obtain benefit while limiting risk of hemorrhage.
- The optimal dose of warfarin should prolong the prothrombin time; for example, the INR should be prolonged to a value of 2.0 to 3.0 when a standard value is available for cats in the testing laboratory. Otherwise, a 2x to 3x prolongation over the baseline time may be used. The urine and stool should be carefully evaluated for fresh blood, a finding that indicates a need for downward dosage adjustment.
- Because of difficulties in dosing, numerous drug and food interactions, and the need to frequently test the clotting times, the overall use of warfarin in small animals is very low.
- Animals receiving warfarin therapy should not be allowed outside exercise without supervision.

Other Drugs to Prevent Coagulation

- *Clopidogrel bisulfate* (Plavix) has been studied in healthy cats. The drug inhibits ADP receptors on platelets. Based on studies in healthy cats, a possible dose of $^1/_2$ of the human Plavix 75 mg tablet (containing 97.8 mg of clopidogrel bisulfate = 75 mg of clopidogrel base) may be a reasonable daily dose for a cat. There are no published studies of efficacy in cardiomyopathic cats or long-term studies of toxicity. Use is strictly extra-label.
- *Abciximab* is a glycoprotein IIb/IIIa receptor antagonist that inhibits aggregation of platelets. There are limited feline data regarding this drug and no published studies of clinical use.

Surgery or Catheter Intervention

- *Surgical intervention* is recommended infrequently in the management of vascular thrombosis. Some blood vessels are simply inaccessible.
- Surgery in cats with iliac thrombosis due to cardiomyopathy is complicated by the risk of anesthesia,

development of disseminated intravascular coagulation, and the severe reperfusion hyperkalemia that can develop following revascularization.
- When suprarenal aortic thrombosis is suspected, abdominal ultrasound should be performed to evaluate the aorta and renal vessels. A positive study is an indication for surgery. Monitor ECG and serum potassium carefully intra-operatively and postoperatively.
- Other indications for surgery of arterial thrombosis include multiple splenic thromboses, suspected bowel infarction or volvulus, and bleeding/thrombosis with associated mechanical compression (e.g., extradural bleeding).
- *Catheter-based interventions* for the management of systemic or pulmonary arterial thrombosis/thromboembolism have not advanced in veterinary medicine. The use of embolectomy (Fogarty) catheters has not been evaluated satisfactorily in animals, but this technique often is limited by the small size of many veterinary patients. Similarly, the cost and risks of localized thrombolytic therapy delivered via an intracardiac catheter has deterred advancement of this area.

VASCULITIS

Etiology

- There are a number of causes of arteritis (inflammation involving arterioles or arteries) and phlebitis (inflammation of veins).
- *Arteritis* may develop as a component of multisystemic infections, including infectious canine hepatitis, (see Chapter 16), feline infectious peritonitis (see Chapter 10), and Rocky Mountain spotted fever (see Chapter 17). Immune-mediated arteritis is believed to be important in feline infectious peritonitis, systemic lupus erythematosus, idiopathic vasculitis in Akita, spitz, and Doberman pinscher dogs, and following some drug reactions. Cutaneous manifestations of vasculitis are discussed in other chapters in this text.
- *Phlebitis* is generally related to injection of irritating drugs or chemicals or physical trauma caused by indwelling catheters, often with secondary infections. Thrombophlebitis indicates a situation of vein inflammation with accompanying thrombosis.

Clinical Signs

- Clinical signs of vasculitis are related to local and systemic release of inflammatory mediators, increased vascular permeability, and interruption of the vascular endothelial lining; potential signs include:
  - Fever
  - Subcutaneous edema
  - Cutaneous hemorrhages
  - Coagulation disorders including thrombocytopenia and disseminated intravascular coagulopathy
  - Thrombosis and ischemic injury (see previous discussion of thrombosis)
  - Thrombocytopenia
- Vasculitis syndromes—Specific clinical vasculitis syndromes commonly seen in cats and dogs include:
  - Feline infectious peritonitis (see Chapter 10)
  - Verminous arteritis associated with dirofilariasis and *Angiostrongylus vasorum* infection (uncommon in the United States)
  - Rocky Mountain spotted fever, a tick-borne infection caused by *Rickettsia rickettsii* that affects dogs and human beings. Invasion of vascular endothelial cells causes vasculitis with mononuclear inflammation, microscopic thrombosis, and microinfarction. The condition is a multisystemic disorder that can affect the heart (myocarditis and arrhythmias), brain, blood (thrombocytopenia, neutropenia), and skin (edema, rash). Fever is common, and death may occur (see Chapter 17 for details).

Treatment

- Treatment of vasculitis depends on the underlying cause.
- Management of FIP (see Chapter 10), systemic lupus erythematosus (see Chapter 24), immune-mediated vasculitis (see Chapter 24), and Rocky Mountain spotted fever (see Chapter 17) are discussed elsewhere in this text.
- Antimicrobials such as doxycycline are often administered empirically while awaiting results of serologic tests.
- Immunosuppressive doses of glucocorticoids are indicated for the management of some vasculitides.
- Thrombotic complications may require prophylactic heparin to prevent disseminated intravascular coagulation (see under “Heparin Therapy”).
- Treatment of thrombophlebitis of superficial veins is supportive.
  - Remove any catheters from the affected vein or limb.
  - Hot-pack the area and gently wrap the limb to reduce edema and self-trauma.
  - If there is risk of infection, select a broad-spectrum antibiotic.
  - If there is a concern about extension of the thrombus centrally, examine the vessel using duplex Doppler ultrasound.
  - Therapy with unfractionated heparin or LMWH should be instituted, especially if there is a likelihood of pulmonary embolism (see above).
- For home therapy either long-term LMWH or warfarin should be considered until the problem has resolved.

- Chemical phlebitis can be treated with topical dimethyl sulfoxide (DMSO) and a corticosteroid ointment (q8–12h) with concurrent administration of prednisolone (0.5 mg/kg PO q12h).

ARTERIOSCLEROSIS AND ATHEROSCLEROSIS

Etiology

Arteriosclerosis

- *Arteriosclerosis* is a chronic arterial metamorphosis characterized by loss of elasticity, luminal narrowing, and proliferative and degenerative lesions of the intima and media.
- Coronary arteriosclerosis, prominent in older dogs with endocardiosis, has been related to small and microscopic areas of myocardial fibrosis. Presumably this is due to ischemic necrosis and infarction of myocytes secondary to reduced perfusion.
- Similar lesions also have been observed in dogs with congenital subaortic stenosis, in dogs with diabetes mellitus, and in cats with hypertrophic cardiomyopathy.
- Small-vessel (intramural) arteriosclerosis may contribute to the morbidity of other cardiac disorders by causing ischemia-induced arrhythmias (e.g., premature ventricular contractions) or increased myocardial stiffness (e.g., hypertrophic cardiomyopathy, subaortic stenosis).

Atherosclerosis

- *Atherosclerosis* pertains to the arteriosclerotic state that also includes fatty degenerative changes in the arterial wall. This is the typical underlying lesion of coronary artery disease in human patients, but is quite rare in small animals.
- Naturally occurring atherosclerosis occurs in severe canine hypothyroidism (see Chapter 31) when serum cholesterol concentrations are very high (generally >750 mg/dl).

▼ ***Key Point*** In canine and feline patients, clinically important hyaline arteriosclerosis is primarily related to the intramural coronary vasculature. The overall clinical significance of arterial degenerative changes in animals is relatively small compared with that in human beings.

Diagnosis

- The diagnosis of arteriosclerosis and atherosclerosis in clinical patients is difficult. Suspect this condition in patients with severe hypercholesterolemia and in association with the aforementioned cardiac disorders.
- Suspect acute myocardial infarction due to extramural coronary thrombosis with respiratory distress, ventricular arrhythmias, and severe ST-T segment changes on the ECG (particularly ST-T segment elevation). Echocardiography may reveal regional hypokinesis of the left ventricular free wall. Diagnosis is presumptive because coronary angiography is rarely performed in animals, but any of the above findings in conjunction with an elevated cardiac troponin-I (cTnI) concentration is suggestive of acute myocardial infarction. In some animals, acute myocardial infarction, superimposed on other heart disease, may lead to acute congestive heart failure.
- In the differential diagnosis of extramural coronary artery obstruction or thrombosis, rule out embolic complications of bacterial endocarditis.

Treatment

- Treatment of arteriosclerosis includes treatment of the underlying disease and the complications of ischemia. There are no published studies regarding management of acute coronary syndromes in dogs or cats. Drugs used in management of cardiovascular disease are discussed in Chapter 146.
- In cases of presumed myocardial infarction, administer oxygen and nitroglycerin ointment.
- Beta blockers such as carvedilol or atenolol decrease myocardial oxygen consumption and may be cardioprotective in animals with multifocal small vessel coronary arteriosclerosis. Their use in acute myocardial infarction is appropriate provided the patient does not demonstrate bradycardia, hypotension or signs of congestive heart failure.
- Calcium channel blockers (e.g., diltiazem, 0.5–2.0 mg/kg, q8h PO) may act as a coronary vasodilator and prevent coronary vascular spasm.

VASCULAR NEOPLASIA

Etiology

- Vascular tumors can be primary or metastatic. The endocardium and vascular elements of the heart also may become neoplastic. Primary arterial and venous tumors are uncommon:
- Carotid and aortic body tumors (chemodectomas) can act as space-occupying lesions in the neck, cranial thorax, or in the area of the ascending aorta and base of the main pulmonary artery.
- Aortic body tumors are an important cause of pericardial effusion in older dogs. These tumors also may be an incidental finding at necropsy (see Chapter 151).
- Tumors from vascular elements (e.g., hemangiosarcoma) and malignancies metastatic to blood vessels are described in detail in Chapter 28. Hemangiosarcoma is the most common intracardiac tumor. Multicentric involvement (e.g., liver, spleen, heart) is common. Pulmonary metastasis is frequent.

- Tumor-related hemorrhage into the pericardial space can cause cardiac tamponade.
- Intraluminal obstruction to venous return (usually of the caudal vena cava) causes ascites. This is most common with intracardiac hemangiosarcoma; however, other primary intracardiac tumors, such as myxoma and fibrosarcoma, can cause similar problems. When neoplastic lesions impinge on the cranial vena cava, jugular distention and subcutaneous edema of the head and neck may be seen.
- Extravascular neoplasms may invade blood vessels; for example, obstruction of the caudal vena cava can develop secondary to ingrowth of a pheochromocytoma from the adrenal medulla (see Chapter 33).

Clinical Signs

- Clinical signs depend on the type and location of the tumor
- Signs of cardiac or vena caval neoplasia are usually those of right-sided CHF (hepatomegaly, ascites, pleural effusion) or acute cardiac tamponade (hypotension and collapse).
- Compression of the cranial vena cava (e.g., from mediastinal lymphoma) can cause intermandibular and ventrocervical subcutaneous edema.

Diagnosis

- The differential diagnosis of caudal vena cava obstruction includes idiopathic sclerosis, neoplasia, kinking, or trauma of the caudal vena cava.
- Imaging studies are very useful in diagnosis. (see Chapter 4)
- Radiographic studies may demonstrate mass lesions; however, the cardiac silhouette may be radiographically normal when the obstruction is intraluminal.
- Nonselective angiography (peripheral venous injection) or selective angiography may demonstrate vascular obstruction or interruption.
- Ultrasound studies may demonstrate dilated hepatic veins typical of obstructed hepatic venous drainage or solid tissue mass lesions around blood vessels.
- Echocardiography can reveal intracardiac mass lesions.
- Computerized tomography and magnetic resonance imaging angiography are advanced methods to evaluate vascular mass lesions.
- Radiopharmaceutical studies may be helpful to identify tumors of neural crest origin (chemodectoma, pheochromocytoma).
- Although blood tests are not diagnostic for vascular tumors, an elevated cTnI concentration in an animal with pericardial effusion is supportive of the presence of hemangiosarcoma. Patients may be anemic due to blood loss in cases of severe hemopericardium, or exhibit the nonregenerative anemia of chronic illness. Evidence of disseminated intravascular coagulopathy may be noted.

Treatment

- Treatment of vascular neoplasia is complicated and requires surgery, and possibly chemotherapy (see Chapter 26). Most patients should be transferred to a referral hospital for advanced imaging, staging, and management.

ARTERIOVENOUS FISTULA

Etiology

- An arteriovenous (AV) fistula is a congenital or acquired communication between artery and vein.
- Congenital lesions tend to be multiple and involve the limbs or the thorax.
- A post-traumatic fistula is usually a single direct connection associated with abnormal healing of the injured blood vessels; a limb, an ear, or even the tail may be affected.
- Rarely, declawing operations and tumors have been associated with AV fistula formation in the feline paw.
- Thyroid carcinoma may lead to a cervical AV communication in dogs. AV fistulas also have been reported secondary to other tumors.
- An hepatic AV fistula is a special type of congenital vascular malformation. This condition usually is associated with portal hypertension and ascites (see Chapter 71).
- Multiple congenital aortic to pulmonary fistulas may create a pathophysiology similar to patent ductus arteriosus.

Clinical Signs

- Clinical signs of an AV fistula include local vascular changes (due to venous hypertension) and cardiac manifestations (due to increased cardiac output required to perfuse the shunt). Any combination of the following signs may be observed:
- AV fistulas are most common in a limb; associated signs may include: subcutaneous edema, pain, inability to use the limb, a warm or cool extremity, distended and tortuous superficial veins, and abnormal tissue growth.
- A continuous murmur (bruit) may be detected by auscultation over the affected area as blood shunts continuously through the fistula.

▼ ***Key Point*** A positive Branham sign may be present in large AV shunts; slowing of the heart rate follows digital occlusion of the artery as the result of a sudden increase in arterial resistance and pressure.

- Multiple aortic-to-pulmonary AV fistulas usually lead to left heart enlargement from increased venous return. Pulmonary overcirculation may be evident.

However, due to the low resistance of multiple shunts (that eventually enter the pulmonary veins), a heart murmur may be absent making the initial diagnosis very difficult.
- A large AV fistula will increase cardiac output (equal to the shunt flow). Compensation may be manifested by tachycardia, cardiomegaly, and increased pulmonary vascularity
- Increased cardiac work, cardiac dilation, renal retention of sodium and water, elevation of venous filling pressures, and eventually congestive heart failure (in the case of large shunts).

Diagnosis

- Diagnosis of AV fistula is made by clinical signs, ultrasonography (including Doppler studies), and selective angiography if necessary. These studies may generally require transfer of the patient to a referral hospital.

Treatment

- Ligation or removal of the shunt is the treatment of choice.
- The surgical approach usually is guided by imaging and vascular contrast studies.
- Other methods of vessel occlusion (e.g., catheter-delivered "umbrellas" or "coils") have not been used routinely in veterinary practice but can be useful in single fistulas that are clearly demarcated by angiography.
- The prognosis is good for animals with acquired AV fistulas that are not associated with malignancy.
- Congenital AV fistulas may be problematic and involve difficult surgical procedures.
- Limb amputation may be necessary if the exact location of the shunt cannot be isolated and ligated or if the limb becomes devitalized (see Chapter 116).
- Management of hepatic AV fistulas may require partial hepatectomy of the involved lobe.

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Chapter

154 Congenital Heart Disease

Henry W. Green / John D. Bonagura

ETIOLOGY

- Congenital heart disease (CHD) is a general term indicating malformation of the heart or great vessels. CHD is present at birth and represents the most common cause of cardiovascular disease in animals younger than 1 year of age.
- Diagnosis, staging, and management of CHD can be complicated, and the purpose of this chapter is to offer a framework for recognition and understanding of common cardiac malformations in dogs and cats.
- Common defects based on prevalence in referral centers include:
  - In dogs: patent ductus arteriosus (PDA), subvalvular aortic stenosis (SAS), pulmonic stenosis (PS), atrial and ventricular septal defects (ASD, VSD), mitral and tricuspid valvular dysplasia (malformation), persistent right aortic arch, tetralogy of Fallot, and cor triatriatum dexter.
  - In cats: atrial and ventricular septal defects, mitral and tricuspid valve dysplasia, patent ductus arteriosus, tetralogy of Fallot, and aortic stenosis.
  - Congenital peritoneopericardial diaphragmatic hernia is a common defect of the diaphragm and pericardium (see Chapter 151).

▼ ***Key Point*** Most congenital heart defects are considered to have a genetic basis, but the mode of inheritance is most often unknown or impacted by multiple genes.

- Even in cases of suspected autosomal dominant inheritance, the penetrance of the lesion may be incomplete, making clinical recognition difficult or impossible. Furthermore, there are no genetic tests available for detection of carriers. This situation makes genetic counseling difficult.
  - Animals with even mild CHD should not be bred.
  - Dogs or bitches with normal cardiac phenotype that produce CHD-affected puppies in more than one litter should be removed from breeding programs.
  - Breeding dogs with equivocal cardiac status based on echocardiography and Doppler studies should be bred only if other important characteristics are considered strong or outstanding.
- Other factors—including environmental, chromosomal, infectious, toxicologic, nutritional, and drug-related—may result in CHD; however, little is known concerning the direct cause and effect relationships in dogs and cats.

CLINICAL APPROACH

The vast majority of CHD cases are recognized initially by cardiac auscultation. A routine 6-lead electrocardiogram (ECG) and thoracic radiographs will also provide diagnostic information in cases of moderate to severe CHD; however, these studies are likely to be negative in mild disease. Definitive diagnosis requires advanced echocardiography with Doppler studies. The general approach to diagnosis based on initial auscultation findings is summarized in Figure 154-1 along with typical ECG and radiographic features. The following are some pointers regarding diagnosis and assessment of CHD in dogs and cats.

- As a general rule, soft ejection type murmurs in otherwise healthy puppies or kittens can be followed through the vaccine sequence. Increasing murmur intensity, other physical abnormalities (stunted growth, cyanosis), or any suggestion of clinical signs (exercise intolerance, dyspnea) should prompt immediate evaluation by a veterinarian with experience in congenital heart disease. A loud systolic murmur, a diastolic murmur, or a continuous murmur is not likely to be innocent and should be evaluated promptly.
- The signalment, physical examination findings, 6- or 9-lead ECG, and thoracic radiographs may provide a provisional diagnosis and help to guide any initial treatment plans.
  - PDA, VSD, SAS, and mitral valve malformation are more likely to lead to left-sided cardiomegaly, a finding that may be evident on ECG or thoracic radiographs. With ASD, PS, and tricuspid valve malformation, right-sided cardiomegaly might be identified.

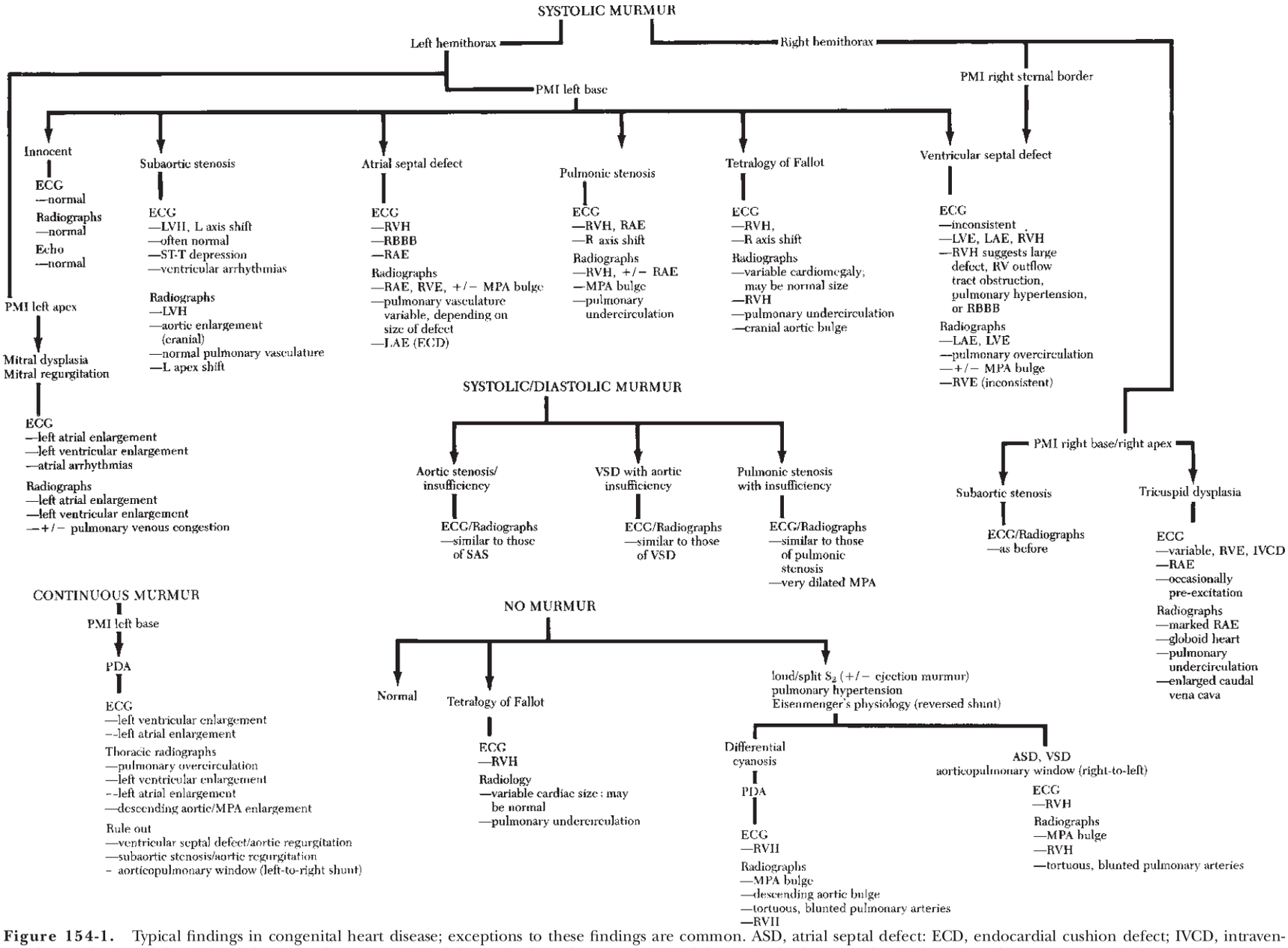

Figure 154-1. Typical findings in congenital heart disease; exceptions to these findings are common. ASD, atrial septal defect: ECD, endocardial cushion defect; IVCD, intraventricular conduction defect; LAE, left atrial enlargement; LVE, left ventricular enlargement; LVH, left ventricular hypertrophy; MPA, main pulmonary artery; PDA, patent ductus arteriosus; PMI point of maximal intensity; RAE, right atrial enlargement; RBBB, right bundle branch block; RV, right ventricle; RVE, right ventricular enlargement; RVH, right ventricular hypertrophy; SAS, subaortic stenosis; VSD, ventricular septal defect.

- Radiographs are particularly helpful for recognizing pulmonary vascular changes and congestive heart failure (CHF). However, such examinations are not definitive in terms of diagnosis, and do not substitute for expert evaluation using echocardiographic techniques.

▼ ***Key Point*** Definitive diagnosis and staging of CHD requires advanced imaging with echocardiography and Doppler studies. In ambiguous cases, cardiac catheterization and angiocardiography are necessary. Advanced cardiac evaluations are best obtained by referral to a cardiologist.

- When a dog or cat is suspected of having CHD consider the following points:
  - Animals presenting with one defect may have concurrent or complicating cardiac issues. For example, combinations of outflow tract obstruction and atrioventricular valvular dysplasia generate a less favorable prognosis. In chronic volume overload, as with uncorrected PDA, progressive myocardial failure or development of atrial fibrillation can impact prognosis negatively.
  - Young animals with relatively severe lesions often appear totally normal to the client and may remain compensated for months to years. The presence of exertional symptoms is generally an indication of serious CHD. Delaying cardiac evaluation until the onset of clinical signs is a serious clinical error, as by that time therapeutic options may be limited or less effective.
  - Early therapeutic intervention may slow or eliminate irreversible myocardial damage and prevent heart failure. For example, after successful closure of a PDA, most dogs will live a normal life without need for cardiac follow-up.
  - CHF or arrhythmic death may occur suddenly and unexpectedly in dogs or cats with CHD.
- Progressive pulmonary vascular disease develops in some patients with left-to-right shunts (PDA, VSD, ASD, aorticopulmonary window) or congenital mitral stenosis. Elevated vascular resistance can cause severe pulmonary hypertension (PH) in these patients.
  - PH due to vascular injury and high resistance increases pulmonary artery, right ventricular (RV), and right atrial pressures; reduces left-to-right shunting; and limits venous return to the left atrium.
  - This development usually improves symptoms (and facilitates growth), but the benefit is temporary. Severe pulmonary vascular disease eventually limits cardiac output, causes progressive exercise intolerance, and often leads to arterial desaturation (a reduced oxygen content due to low partial pressure of oxygen). Desaturation is related to either right-to-left shunting of blood across a defect (Eisenmenger's physiology) or development of bronchoesophageal collateral vessels that mix low-oxygen venous return with pulmonary venous blood.
  - A typical consequence of shunt reversal is progressive secondary polycythemia, a complication that can lead to a markedly elevated hematocrit and hyperviscosity syndrome.
  - Advanced pulmonary vascular disease changes the examination findings to that of marked RV hypertrophy, pulmonary artery dilation, and reduced size of the left heart chambers. In the case of shunt lesions, the right-to-left shunt serves as a needed pressure-relief valve for the right side, but predisposes to arterial desaturation and polycythemia. This situation is generally irreversible and explains why a "reversed" PDA cannot be corrected surgically without fatal consequences.

DIAGNOSIS

The balance of this chapter discusses the general approach to recognition of cardiac malformations from the perspective of the first examiner. Key points about prevalence, physical examination, and interpretation of diagnostic studies is presented along with an overview of management options for common defects. The reader is referred to the supplemental reading for a more complete review of specific defects and various complications of CHD.

Despite the technical advances in cardiology, a thorough history and physical examination is an essential part of the diagnostic process. In the evaluation of CHD, cardiac auscultation is especially important (Fig. 154-1), and experienced examiners can often establish a tentative diagnosis based on auscultation and breed predisposition (Table 154-1).

Signalment and History

Age, breed, and sex should be considered when evaluating animals for suspected CHD. As many specific breed predilections are identified—especially in dogs—a predisposition can be useful in formulating the differential diagnoses. Table 154-1 is a guide to breed for the most commonly recognized disorders, but is not a comprehensive listing.

- CHD is most often an incidental finding, discovered at the time of initial immunization.
- Most animals with CHD are asymptomatic when first examined, often in the face of hemodynamically severe defects. Thus do not conclude that the defect is mild in a patient with an unremarkable history.
- *Stunted growth* often indicates a patient with CHF or a right-to-left shunt (cyanotic heart disease). Signs of CHF may include coughing, exercise intolerance, orthopnea, tachypnea, respiratory distress, or abdominal distension.

Table 154-1. BREED AND SEX PREDILECTIONS FOR CERTAIN CONGENITAL CARDIAC DEFECTS*

Defect	Predilection
Patent ductus arteriosus (PDA)	Poodle, Bichon friese, collie, Pomeranian, German shepherd, Shetland sheepdog, and many other breeds (female : male, 2.2 : 1)
Pulmonic stenosis (PS)	Beagle, bulldog, fox terrier, miniature schnauzer, Chihuahua, Samoyed, Labrador retriever
Subaortic stenosis (SAS)	Newfoundland, boxer, German shepherd, German shorthaired pointer, golden retriever, rottweiler, bull terrier
Ventricular septal defect (VSD)	English bulldog, springer spaniel
Atrial septal defect (ASD)	Samoyed, boxer, Doberman pinscher
Mitral dysplasia	Great Dane, German shepherd, bull terrier (male > female)
Tricuspid dysplasia	Great Dane, German shepherd, Weimaraner, Labrador retriever (male > female)
Tetralogy of Fallot	Keeshond, English bulldog

**Note:* SAS, PDA, and PS are the most common defects in dogs. ASD/VSD and atrioventricular valve dysplasias are the most common defects in cats.

- *Exercise intolerance* is usually a sign of advanced CHD.
- *Syncope and exertional collapse* are usually signs of severe CHD and may be related to:
  - Right-to-left shunts (hypoxemia)
  - Ventricular outflow tract obstruction (e.g. aortic and pulmonic stenosis)
  - Intermittent ventricular arrhythmias
  - Inappropriate activation of cardiac baroreceptors following sympathetic stimulation (reflex-mediated syncope)
  - CHF

Physical Examination

Exam findings of particular importance in CHD include palpation of the precordium, auscultation of the heart, evaluation of the femoral arterial and jugular venous pulses, and inspection of mucous membranes. In addition, perform a careful respiratory and abdominal evaluation for signs of left- or right-sided CHF.

Precordial Palpation

The left and right apical impulses—the points of the strongest cardiac movements on each side of the thorax—identify the relative mitral valve area on the left and the tricuspid valve area on the right. Palpation is useful in localizing normal and abnormal cardiac sounds.

- A precordial heave is an apical impulse that is stronger than normal and often indicates hypertrophy or enlargement of the underlying ventricle. RV hypertrophy is suggested by a right-sided impulse of greater intensity than that on the left. Caudal displacement of the left apical impulse beyond the 6th intercostal space (ICS) may indicate cardiac dilatation.
- A precordial thrill is a palpable vibration, a manifestation of a loud heart murmur that identifies the point of maximum intensity (PMI).

Cardiac Murmurs

- Murmur characteristics may be suggestive of a particular cardiac defect (see Fig. 154-1 and Chapter 142). Most murmurs associated with CHD are systolic. A continuous murmur is due to PDA or, rarely, from an aorticopulmonary window. A diastolic murmur is most likely due to aortic regurgitation, a condition that may coexist with VSD, aortic valvular malformation, or SAS complicated by aortic valvular endocarditis. Atrioventricular valvular stenosis (or supravalvular stenotic ring) is a rare cause of diastolic heart murmurs.
- Distinguishing an innocent (functional) murmur from one caused by CHD, especially in the case of mild aortic stenosis or trivial mitral malformation, may be difficult if not impossible.
  - Murmurs caused by clinically-significant CHD are typically louder and of longer duration than innocent murmurs.
  - Innocent murmurs are often intermittent, may be musical, and usually diminish or resolve by 16 to 24 weeks of age. Murmurs that persist are more likely to suggest cardiac malformation.
  - A particularly difficult issue for breeders is the persistence of a soft ejection murmur in the absence of an echocardiographic imaging lesion. It may be impossible to determine if CHD is present or not.
- With the exception of ventricular outlet obstruction (SAS or PS), murmur intensity or duration does not correlate reliably with the severity of the cardiac lesion. For example, dogs with severe tricuspid valve dysplasia may have soft murmurs, whereas a small and restrictive VSD can create a very loud murmur.
- A murmur may be soft or absent in the following serious situations: right-to-left shunting defects with polycythemia, pulmonary or aortic atresia, large unrestrictive VSD, tricuspid dysplasia, or severe PH.

Pulse Evaluation

Inspect the jugular venous pulse and palpate the femoral arterial pulse. The arterial pulse character depends on the pulse pressure (systolic minus diastolic pressure), the stroke volume of the left ventricle (LV), and the rate of pressure rise during LV ejection.

- *Jugular venous distension* or pulsations suggest right-sided heart disease, for example, PS, tricuspid regurgitation, or right-sided CHF.
- Weak, hypokinetic, or late-rising arterial pulses suggest outflow obstruction as in significant subaortic stenosis, LV dysfunction, volume depletion, or heart failure. Conversely, bounding (hyperkinetic or waterhammer) pulses are most commonly associated with PDA or aortic regurgitation, as these situations create a wide pulse pressure.

Mucous Membranes

- Normal membranes are pink with a capillary refill time of <2 seconds. Membrane pallor suggests poor perfusion or anemia (evaluate for intestinal parasitism, especially hookworm infection). Pallor and prolonged refill time suggest heart failure or reduced blood pressure with reactive vasoconstriction.
- *Cyanosis* (blue-colored mucous membranes) develops from a low arterial oxygen tension with >5g/dl of desaturated hemoglobin. Pulmonary dysfunction due to left-sided CHF or concurrent bronchopneumonia is the most common cause of cyanosis in CHD. Lesions that allow right-to-left shunting, such as tetralogy of Fallot, can lead to persistent or exercise-induced cyanosis in the absence of pulmonary dysfunction.
  - *Right-to-left shunting* requires a source of high right-sided resistance, and a communication or shunt proximal to the obstruction. With this combination, desaturated right-sided blood may enter the left side of the circulation.
  - Reasons for high resistance include PH from high vascular resistance, PS, mid-RV obstruction, and tricuspid valve disease (either stenosis or severe regurgitation that raises right atrial pressure).
  - The lesion allowing shunting can be a patent foramen ovale, ASD, VSD, or PDA. Additionally, in certain complex defects, there may be only a single great vessel exiting the heart; one ventricle that serves each great vessel; or transposition of the great vessels. Each of these situations allows mixing of pulmonary venous and systemic venous blood and may lead to cyanosis.
  - The term "*differential cyanosis*" generally refers to the condition of pink oral membranes and cyanotic caudal membranes (best seen in the vulva or prepuce). This is most typical of reversed PDA caused by a large ductus and severe PH.

Electrocardiography

The ECG is of little value in recognition of mild CHD. Diagnostic yield increases when evaluating rhythm disturbances or identifying cardiac chamber enlargement in the presence of moderate to severe cardiomegaly (see Chapter 144). Common chamber enlargement patterns are summarized below.

- Left-Ventricular Hypertrophy—Tall R waves >2.5 to 3.0 mV in lead II in dogs or >0.9 mV in cats usually indicate eccentric hypertrophy of the LV. A left axis deviation is also compatible with concentric LV hypertrophy, though septal defects may lead to a similar axis shift. Common causes of LV enlargement include PDA, SAS, VSD, and mitral valve dysplasia.
- Right-Ventricular Hypertrophy—Right axis deviation with S waves in leads I, II, III, aVF, and V2 to V6 suggest RV hypertrophy. Common causes include PS, tetralogy of Fallot, ASD, tricuspid dysplasia, and PH. Splintered R-waves also may be observed with tricuspid valve malformation.
- Atrial Enlargement—a P wave duration of >0.04 seconds is suggestive of left or right atrial dilation; a P wave >0.4mV in dogs indicates right atrial dilation.

Thoracic Radiography

Routine thoracic radiography is used for evaluation of cardiac size and chamber enlargement; assessment of the great vessels; and evaluation of pulmonary circulatory dynamics (see Chapter 143).

- Determination of left-sided vs. right-sided cardiomegaly is informative in the differential diagnosis of CHD. While echocardiography is a more accurate method for assessing chamber size and wall thicknesses, the radiograph may be helpful. In particular, marked elongation of the heart is suggestive of LV dilatation, as with PDA. Conversely, concentric hypertrophy of a ventricle secondary to outflow obstruction may be underestimated by radiography.
- Remember that young puppies have a relatively dominant RV shadow until approximately 8 to 12 weeks of age.
- Dilation of the main pulmonary artery is suggestive of PS, a left-to-right shunt, or PH.
- Dilatation of the ascending aorta is typical of subaortic stenosis and pulmonary atresia; dilation in the descending aorta is typical of PDA (ductus bump).
- Radiographs are especially helpful for observing pulmonary vascular changes as with left-to-right shunts (overcirculation) or right-to-left shunts or severe PS (undercirculation).
- Radiographs also provide objective proof for the presence or absence of CHF.
- Radiographic changes associated with common malformations are summarized in Figure 154-1.

Echocardiography

Echocardiography represents a noninvasive method for obtaining detailed images of cardiac anatomy and assessment of cardiac function. Supplemented with Doppler studies of blood flow, the echocardiographic examination has largely replaced invasive cardiac

catheterization and angiocardiography for definitive diagnosis of CHD. Echocardiography provides information that is not only diagnostic but also supportive of surgical and catheter-based therapeutic interventions.

- Two-dimensional (2D) echocardiography allows identification of the anatomical defect(s). Among lesions that can be imaged are patent foramen ovale, ASD, VSD, PS, SAS, mitral valvular malformation, tricuspid valvular malformation, and the internal structure of a PDA. An estimate of the size and severity of a defect can also be obtained with high quality 2D images.

▼ ***Key Point*** Trivial or mild lesions of CHD may not be evident by 2D imaging.

- With 2D and M-mode imaging, the degree of myocardial hypertrophy or chamber dilation can be assessed as well as subsequent functional changes in heart function. This allows evaluation of overall significance of the cardiac lesion. Mild disease usually causes few anatomic or functional changes in the heart.
- Color and spectral Doppler echocardiography are used to detect normal and abnormal blood flow and measure the direction and velocity of blood flow in the heart and great vessels. Doppler studies can be used to provide estimates of intracardiac pressures. Combined with 2D imaging, these modalities provide highly accurate, noninvasive quantitation of the severity of a cardiac lesion. Doppler methods also may allow estimation of pulmonary arterial pressure, shunt ratio, magnitude of stenosis, and regurgitant fraction.
- Contrast echocardiography can be performed by injecting agitated saline or other gas-containing microbubbles into a peripheral vein to improve detection of cardiac shunting defects (particularly right-to-left shunts). These studies can be performed when Doppler technology isn't available or to improve Doppler echocardiographic studies.
- A summary of common echocardiographic findings in CHD is found in Table 154-2.

Cardiac Catheterization

Cardiac catheterization is an invasive procedure useful for diagnosing structural malformation and assessing physiologic abnormalities when echocardiographic Doppler studies are equivocal or when therapeutic, catheter-based intervention is beneficial. Because of its relatively invasive nature and the necessity for general anesthesia, catheterization has limited applications. These include:

Table 154-2. ECHOCARDIOGRAPHIC AND DOPPLER FEATURES OF SELECT CONGENITAL HEART DEFECTS

Defects	Echocardiographic and Doppler Features
Patent ductus arteriosus (PDA)	Dilated left atrium, left ventricle, and pulmonary trunk; possible identification of PDA; turbulent flow in main pulmonary artery, with retrograde diastolic flow and increased transmitral and aortic flow velocities, reduced LV systolic myocardial function
Pulmonic stenosis (PS)	Right ventricular hypertrophy, right atrial and pulmonary artery enlargement, outflow tract obstruction, thickened valve leaflets, septal flattening and/or paradoxical septal motion, high-velocity flow (>1.5 m/sec) across the pulmonic valve
Subaortic stenosis (SAS)	Left ventricular (LV) hypertrophy, dilated aorta, subvalvular narrowing, high-velocity flow (>2.0 m/sec) across the aortic valve
Ventricular septal defect (VSD)	Variable chamber enlargement, most commonly left atrial and ventricular, possible identification of defect, right ventricular hypertrophy if pulmonary hypertension (PH) or very large defect, visualization of flow across defect, may be bidirectional; increased transmitral and PA flow velocity, right-to-left shunt in the case of PH (Doppler or bubble study)
Atrial septal defect (ASD)	Right atrial and ventricular enlargement, possible identification of defect, main pulmonary artery enlargement, flow across defect, increased velocity flow across tricuspid (diastole) and pulmonic (systole) valves
Mitral valve dysplasia	Left atrial and left ventricular enlargement, abnormal mitral valve anatomy, increased transmitral diastolic flow velocity, turbulent retrograde systolic transmitral flow
Tricuspid valve dysplasia	Right atrial and ventricular enlargement, abnormal tricuspid valve anatomy, increased transtricuspid diastolic flow velocity, turbulent retrograde systolic transtricuspid flow
Tetralogy of Fallot	Right ventricular hypertrophy, right ventricular outflow tract obstruction, identification of VSD, overriding aorta, small left heart, contrast study indicating right-to-left shunting, septal flattening and flattening and/or paradoxical septal motion, right-to-left flow across VSD (Doppler or bubble study), decreased diastolic transmitral flow, possibly increased transaortic systolic flow, increased flow velocity across the pulmonic valve
Pulmonary hypertension (PH)	Right ventricular hypertrophy, right atrial enlargement, dilated main pulmonary artery, visualization of associated shunt, right-to-left shunt by Doppler or bubble study, increased flow *acceleration* across pulmonary valve

- Delineating ambiguous anatomic lesions.
- Identifying vascular abnormalities that evade ultrasound studies, such as some systemic to pulmonary shunts or multiple arteriovenous fistulas.
- Facilitating interventions such as balloon valvuloplasty for PS, balloon dilation for severe SAS, or transcatheter occlusion of shunts.

These procedures require referral to a cardiologist or a clinical specialist with advanced training, equipment, and expertise in the diagnosis and management of CHD.

TREATMENT OF COMPLICATIONS OF CONGENITAL HEART DISEASE

Definitive or palliative therapy for CHD often requires surgery or a catheter-based intervention. Prior to such treatments, establish a definitive diagnosis. Symptomatic medical therapy can be directed for complications of severe CHD such as CHF or arrhythmias. PH is a problematic complication to address. Severe polycythemia also requires management.

Congestive Heart Failure

- Most forms of CHD lead to progressive volume or pressure overload of the affected ventricle. With time, diastolic and systolic ventricular function decline and cardiac output becomes limited. This situation is worsened by development of mitral or tricuspid valvular regurgitation or atrial fibrillation. The end-result is development of left- or right-sided CHF.
- An important differential diagnostic consideration for right-sided CHF in a puppy or a young dog is cor triatriatum dexter. This disorder is characterized by the partitioning of the right atrium by an obstructive membrane that impairs venous return from the caudal vena cava.
- When CHD progresses to CHF, the medical therapy is very similar to that used for acquired heart disease (detailed in Chapter 147).
- Initial management of left-sided CHF involves treatment with furosemide (2–4 mg/kg IV, IM, or SC), oxygen, and 2% nitroglycerine ointment. Sedation with butorphanol (0.25 mg/kg IM or SC) may be added if necessary.
  - If this approach fails to control the CHF, and the cause is a left-to-right shunt, sodium nitroprusside (0.5–2.5 mcg/kg/min infusion) can be used to reduce the arterial pressure and magnitude of shunting.
  - Alternatively, enalapril or another angiotensin-converting enzyme inhibitor (ACEI) can be initiated to reduce afterload and reduce left-to-right shunting (see Chapter 147).
  - Maintain systolic blood pressure in the 80 to 120 mm Hg range, particularly in cases of aortic stenosis where hypotension can reduce coronary perfusion.
- Chronic medical therapy of CHF in dogs with CHD is identical to that described in Chapter 147 and includes furosemide, an ACEI, spironolactone, and often digoxin or (where available) pimobendan. In cats, the initial use of furosemide and an ACEI is appropriate.
- The use of beta-blockers in treatment of dogs with CHF is unresolved, and care must be used to avoid bradycardia, especially in dogs with fixed obstructions such as SAS and PS, as cardiac output in these conditions is relatively heart-rate dependent. For dogs already taking beta-blockers as cardioprotection, once CHF develops, the beta-blocker should be continued, the dosage reduced if needed to obtain a target examination heart rate in the 100 to 140/min range.
- In some cases, medical therapy for CHF may be discontinued if definitive repair of the defect can be successfully performed. This is particularly true in young dogs or cats with PDA.

Arrhythmias

- Controlling arrhythmias in the setting of severe CHD may help to maintain a compensated state and to prevent sudden death.
- Atrial fibrillation is particularly destabilizing to dogs with CHF; treat to achieve heart rate control with digoxin, diltiazem, and a beta-blocker. Electrical cardioversion is another option to restore sinus rhythm. Specific therapy of arrhythmias is discussed in Chapter 145.
- Re-entrant supraventricular tachycardia due to an accessory pathway may be encountered in some dogs with tricuspid dysplasia, particularly Labrador retrievers.
- Ventricular arrhythmias have been particularly associated with SAS and PS. Holter ECG monitoring may be indicated to screen for rhythm disturbances, especially in dogs with exertional symptoms. Chronic therapy of clinically significant ventricular tachycardia may include sotalol, mexiletine plus a beta-blocker, amiodarone, or procainamide.

Pulmonary Hypertension

- The presence of PH due to high vascular resistance is difficult to manage, as the vascular changes responsible are typically irreversible. The evaluation of PH usually requires referral to a specialist experienced in CHD.
- PH usually develops rapidly in dogs with large left-to-right shunts. In cats it is more gradual and, if caught, can be arrested by closure of a left-to-right shunt. Drugs that reduce pulmonary vascular resistance such as sildenafil (Viagra) at initial doses of 0.5 to 2 mg/kg q12h PO may be beneficial in cases of

advanced PH. Currently this therapy is very expensive. Arterial blood pressure must be monitored, as reduced systemic resistance will lead to greater right-to-left shunting.
- Controlled exercise is important to prevent exertional collapse or dyspnea. This may be difficult to achieve in puppies or kittens.

Polycythemia

- In cases of right-to-left shunting due to obstructive lesions of the right heart (PS, tricuspid stenosis), balloon valvuloplasty or surgery may decrease right-sided pressures and control the cause of shunting. Care must be exercised with a large ventricular septal defect, since florid left-to-right shunting may develop across the VSD.
- Phlebotomy may be required in patients with right-to-left shunting and secondary polycythemia. A packed cell volume (PCV) of 62% to 65% is often well tolerated, but values exceeding 68% to 70% are likely to cause exercise difficulties or stroke-like signs.
- Usual treatment measures for polycythemia include periodic phlebotomy with replacement by IV or subcutaneous crystalloid fluid (see Chapter 22 for a discussion of management of polycythemia).
- When the need for phlebotomy becomes too frequent, bone marrow suppression can be attempted using hydroxyurea. Treatment may not work, and anorexia, gastrointestinal disturbances, and skin rash may limit tolerability of the drug. A regular complete blood count and platelet count should be performed.

TREATMENT AND PROGNOSIS OF SPECIFIC DEFECTS

In addition to management of complications of CHD discussed above, the potential to more definitely treat the specific malformation is inviting. Unfortunately, many of these conditions require an operation during cardiopulmonary bypass by a highly skilled cardiothoracic surgeon. Even extracardiac procedures such as PDA ligation or catheter-based treatments for PDA or PS can end badly if the clinician is inexperienced.

▼ ***Key Point*** Surgical or interventional management of cardiac defects should be performed only by properly trained and experienced clinicians in a fully equipped and staffed hospital.

Patent Ductus Arteriosus

- Closure is strongly recommended in left-to-right shunting defects as the 1-year mortality for untreated dogs exceeds 60%. In the reversed (right-to-left) shunting PDA, closure of the defect is contraindicated and therapy is focused on reducing complications of PH and polycythemia by periodic phlebotomy (see above).
- Thoracotomy and surgical ligation of the ductus is very successful with perioperative mortality that should be <5% at experienced surgical centers (see Chapter 155). Closure generally results in complete resolution of signs. A postoperative murmur of mitral regurgitation is common, due to LV stretch, but is generally gone by the time of suture removal.
- Less invasive transcatheter techniques for closure of PDA have gained significant popularity and have superseded surgery at some institutions. As with surgery, success is greatest in the hands of experienced operators. Embolization coils are best suited for small to medium diameter defects; the Amplatzer occluding device has been used for larger diameter (>4mm) defects.
- The prognosis following isolated closure of a PDA is excellent. A normal lifespan can be anticipated, and most cases do not require any cardiac follow-up. Exceptions to this rule include dogs with marked LV systolic dysfunction (determined by echocardiography), dogs with prior CHF, or dogs with atrial fibrillation. Refer these patients to a cardiologist for evaluation.
- Reversed PDA has a poor prognosis, though with vigilant therapy some patients live beyond 5 years of age, affected mainly by rear limb weakness during exercise.

Ventricular and Atrial Septal Defects

- Surgical closure of septal defects is the definitive treatment but requires cardiopulmonary bypass and open heart surgery. While this has been successfully performed, it is not commonly practiced in veterinary medicine.
- Palliative pulmonary arterial banding, creating a supravalvular PS, has been used successfully to reduce the left-to-right shunt of a VSD. This procedure is recommended only for those animals with rapidly progressive cardiomegaly and overt or impending CHF. Simple cardiomegaly is not an indication for banding, as very few of these patients ever develop CHF.
- Transcatheter occlusion devices have been developed for closure of septal defects, but are still experimental.
- Right-to-left shunting may develop in dogs or cats with VSD due to PH, valvular or subvalvular PS, or progressive, mid-ventricular fibromuscular obstruction (so-called double-chambered RV). Exercise intolerance and polycythemia may develop. Treatment is as described above for polycythemia.
- The prognosis for septal defects is variable.
  - CHF associated with ASD is rare in dogs, but may develop in cats, especially in those with endocardial cushion defects and large communications.

- A small, restrictive VSD carries an excellent prognosis for longevity. CHF associated with VSD is actually quite rare because most patients are "naturally-selected" for smaller defects and rarely require any intervention. Thus, the prognosis for dogs that attain 16 weeks of age without signs of CHF is good.
- The exception is the dog with a VSD and aortic root prolapse or aortic malalignment defects because severe (audible) aortic regurgitation may occur, and CHF can develop in middle age from LV volume overload.
- Cats with VSD are more likely to develop CHF, especially if the detect is large (50% of aortic diameter).

Tetralogy of Fallot

- Definitive surgical treatment for tetralogy of Fallot includes closure of the VSD and removal or bypass of the stenosis under cardiopulmonary bypass.
- Palliative surgery involves creation of an extra-cardiac shunt between the systemic and pulmonary circulations (e.g., Blalock-Tausig shunt). Such shunts increase pulmonary flow, improve arterial saturation, and may produce significant clinical improvement. The major limitation is the extent to which these shunts will remain patent.
- Animals with a sedentary lifestyle will often tolerate this disease well, especially if the PS is not too severe. Some will live for 5 or more years. Exercise creates vasodilation in skeletal muscle and increases tissue oxygen demands; accordingly, most tetralogy of Fallot patients have signs of tachypnea and exercise intolerance with exertion.
- Sudden death is common consequent to progressive hypoxemia, polycythemia and cardiac arrhythmias.
- Avoid drugs that cause systemic vasodilation in these patients, as right-to-left shunting may be exacerbated.
- Beta-blockage with the nonspecific beta-blocker propranolol (start at 0.25 mg/kg PO q8h and up-titrate over 4 weeks to 1 mg/kg PO q8h) may be beneficial by reducing exercise-induced RV hyper-contractility, an event that can add a dynamic component to RV outflow obstruction. The $beta_2$ blocking effect should theoretically benefit by preventing some exercise-induced peripheral vasodilation.
- Manage polycythemia as described above (see Chapter 22).

Pulmonic Stenosis

- Transcatheter balloon valvuloplasty is the treatment of choice for PS when the lesion is characterized by valvular thickening with commissural fusion. In experienced hands the procedure mortality is <5% and the dilation results in a 50% or greater reduction of RV systolic pressures. If the cases are chosen carefully, almost all treated dogs will benefit. Therapy should not be delayed as gradients and muscular hypertrophy can progress with time and growth.
- When PS is complicated by severe muscular hypertrophy and subvalvular fibromuscular obstruction, balloon valvuloplasty combined with atenolol therapy (1–2 mg/kg PO, q12h) is the initial treatment of choice. In some cases the dynamic muscular obstruction resolves over time; otherwise, atenolol can be continued for life.
- Surgical techniques such as patch grafting, pulmonary valve repair or resection, or surgical dilation have been used and are still indicated in cases with severe (fibro-) muscular RV obstruction, a broad subvalvular fibrous ring, or in dogs where PS is complicated by marked pulmonary valvular hypoplasia.
- In cases that cannot be treated more definitively, atenolol provides cardiac protection and is well tolerated.
- PS with patent foramen ovale, ASD, or VSD may progress to right-to-left shunting with polycythemia, and is treated accordingly.
- Mild to moderate PS (peak pressure gradients measured by Doppler studies of <50 and 100 mm Hg, respectively) generally carry a good prognosis (survival of 8 years or more). Some dogs in the 75 to 100 mm Hg range do benefit from valvuloplasty in terms of exercise capacity and reduction of RV hypertrophy. Comparatively, severe disease (Doppler echocardiographic gradient >100 mmHg) increases the likelihood of sudden death or CHF.

Subaortic stenosis

- Aortic stenosis is rare in cats. In dogs, subvalvular obstructions are common and prognosis and management recommendations depend mainly on the magnitude of the peak pressure gradient as measured by Doppler echocardiography. As a general rule, gradients <50 mm Hg indicate mild SAS; peak Doppler-derived pressure gradients of >80 to 100 mm Hg indicate severe SAS.
- Transcatheter balloon dilation of the stenotic orifice has been performed and successfully reduces LV pressure gradients by approximately 50%. This benefit, however, becomes attenuated over time, and the procedure has largely been abandoned, though it may be a consideration for severe cases of SAS.
- Open surgical resection of the stenotic lesion provides the best long-term success in terms of reduction of gradients, but it requires cardiopulmonary bypass, and long-term survival has been disappointing.
- Beta-blockade with atenolol (1–2 mg/kg PO q12h) improves survival over historical controls and median survival of >4 years has been reported in dogs with even very severe SAS (>120 mm Hg). Atenolol is recommended for all dogs with a gradient >50 mm Hg.

Beta-blockade is particularly helpful in the specific situation of dynamic SAS caused by mitral valve malformation wherein beta-blockade may completely alleviate the obstruction and allow regression of LV hypertrophy.

- Unfortunately, severe SAS carries a discouraging prognosis owing to premature death. Sudden arrhythmic cardiac death and progressive LV dysfunction with development of CHF are typical outcomes. Mature dogs with mild SAS are more likely to live normal lives, though some still experience sudden death.
- Dogs with even mild disease are at higher risk for development of bacterial endocarditis. Therefore, administer prophylactic antibiotics during elective surgical procedures or whenever wound contamination is an issue.

Atrioventricular Valve Dysplasia (Stenosis)

- Balloon valvuloplasty has been performed with variable success in dogs with tricuspid and mitral valvular or supravalvular stenosis.
- Surgical repair of affected valves can be attempted. Replacement of dysplastic valves has been performed successfully with cardiopulmonary bypass.
- Most cases are treated medically when signs of CHF or atrial fibrillation develop. Consideration should be given to ACEI (enalapril) and to beta-blocker (carvedilol or metoprolol) therapy for establishing cardioprotection in dogs with severe mitral regurgitation and associated cardiomegaly.
- Tricuspid malformation, associated with an ASD, may lead to right-to-left shunting; secondary polycythemia should be managed (see under "Polycythemia").
- Mild mitral or tricuspid valvular dysplasia is often well tolerated; however, severe lesions lead to CHF and arrhythmias such as atrial fibrillation. Dogs with severe mitral disease usually develop CHF in early to middle age, particularly when the valve is both stenotic and incompetent. Many dogs with relatively severe tricuspid regurgitation survive for 7 or 8 years before CHF ensues.
- Tricuspid stenosis is typically associated with an ASD or patent foramen ovale, leading to secondary polycythemia.

SUPPLEMENTAL READING

Bonagura JD, Lehmkuhl LB: Congenital heart disease. In Fox PR, Sisson DD, Moise NS (eds): Textbook of Canine and Feline Cardiology: principles and clinical practice, 2nd ed. Philadelphia: WB Saunders, 1999.

Oyama MA, Sisson DD, Thomas WP, Bonagura JD: Congenital heart disease. In: Ettinger SJ, Feldman EC (eds): Textbook of Veterinary Internal Medicine, 6th ed. St Louis: WB Saunders, 2005.

Chapter

155 Surgical Correction of Patent Ductus Arteriosus

Eric R. Schertel

Ligation of the patent ductus arteriosus (PDA) in dogs and cats is a rewarding surgical procedure. When performed by an experienced surgeon, the combined operative/postoperative mortality rate is relatively low (8–10%) compared with surgery of other forms of congenital heart disease. The long-term prognosis after correction is excellent. However, like any thoracic or cardiovascular procedure, special attention to the details of anesthetic and surgical techniques is necessary for success. An accurate diagnosis is important, as is a thorough knowledge of the anatomy and physiology of the cardiovascular system.

ANATOMY AND PHYSIOLOGY

- The ductus arteriosus is a remnant of the left sixth aortic arch and connects the pulmonary artery and the descending aorta in the fetus and newborn. Its continued patency after birth results in left-to-right shunting of blood causing volume overload of the left atrium and ventricle. In severe cases, left ventricular failure may be present.
- The relationship of the descending aorta, main pulmonary artery, and right and left pulmonary arteries with the PDA must be appreciated (Fig. 155-1).
- The PDA may vary in size and shape but generally is approximately one-fifth to one-fourth the diameter of the aorta, or slightly smaller than the left main pulmonary artery. The PDA is usually short (0.5–1.0 cm), bridging the small distance between the aorta and pulmonary artery.
- The left vagus nerve lies over the ductus and is immediately underneath the visceral pleura. The recurrent laryngeal nerve arises from the vagus and courses caudal and medial to the PDA.
- Rarely, a persistent left cranial vena cava may be found coursing over the pulmonary artery. This does not pose a surgical problem in PDA ligation.

PREOPERATIVE AND PERIOPERATIVE CONSIDERATIONS

- Consult the chapter on congenital heart disease (see Chapter 154) for details of diagnosis and medical management.
- Institute conservative medical management before surgery when there is evidence of heart failure. More aggressive medical management may not benefit the patient as much as surgery.
- Mortality with surgery is higher when congestive heart failure (CHF), atrial fibrillation, or substantial myocardial failure is present. The mortality of nonsurgically managed PDA patients also is high. Thus, if conservative therapy for heart failure is not effective in 24 to 48 hours, surgery combined with intensive medical management is the appropriate course of action in most patients.
- Administer IV fluids judiciously during anesthesia and surgery, especially in animals with heart failure.
- Perioperative mortality is 8% to 10% according to published reports.
- Perioperative complications occur in 10% to 15% of cases.

LIGATION OF THE PATENT DUCTUS ARTERIOSUS

Objectives

- Careful exposure and definition of the ductus arteriosus through a left fourth intercostal space thoracotomy. (The left fifth space may be indicated in cats.)
- Double ligation of the ductus without trauma to the vessels or other surrounding structures.

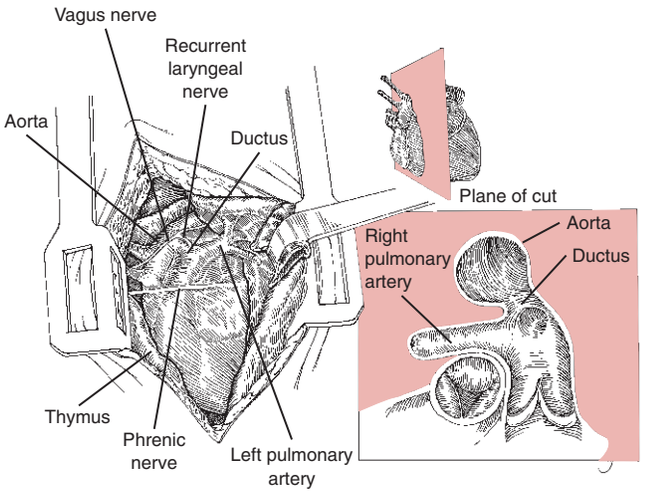

Figure 155-1. Retraction of the left cranial lobe of the lung allows exposure of the region of the ductus.

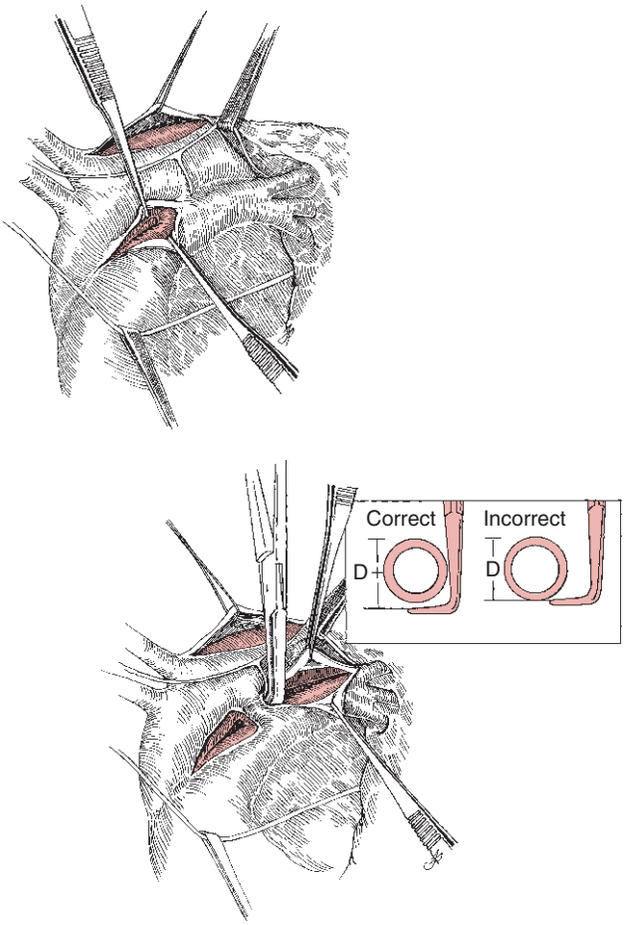

Figure 155-2. Exposure of the ductus. *Top,* Initial area of dissection. *Bottom,* Use of closed right-angle forceps to dissect the region behind the patent ductus arteriosus. See text for further details.

Equipment

- General surgery pack and standard suture, plus instruments required for thoracic surgery (see Chapter 167).
- Assorted sizes of right-angle forceps
- Vascular clamps, preferably pediatric/infant ductus clamps (three pairs)
- Multipurpose peripheral vascular clamps (two pairs)
- Suture; silk, sizes 3-0 up to 1-0, and non-absorbable, 5-0 or 6-0, on a cardiovascular needle

Technique

1. Use an appropriate anesthetic regimen based on the preoperative assessment of cardiac function (see Chapter 2 for discussion of anesthesia techniques). Positive pressure ventilation is required during the majority of the procedure.
2. Place the patient in right lateral recumbency. Clip and aseptically prepare the left thorax from the cranial border of the scapula to rib 13, and from the dorsal to the ventral midline. Include the left shoulder and axilla, and extend past the elbow.
3. Perform a standard left fourth intercostal space thoracotomy (see Chapter 167).
4. Identify the region of the ductus following caudal retraction of the left cranial lung lobe (see Fig. 155-1). Retract the lobe with a moist sponge or laparotomy pad.
5. Elevate the vagus nerve and encircle with silk suture or umbilical tape for retraction to expose the PDA. Identify the location of the recurrent laryngeal nerve as it courses from the vagus to the caudal aspect of the ductus.
6. Palpate the thrill in the main pulmonary artery for reference.
7. Begin blunt and sharp dissection cranial and caudal to the PDA. Extend the dissection caudally between the aorta and left main pulmonary artery for a distance of at least 1.5–2 times the diameter of the ductus (Fig. 155-2, *top*). Extend the dissection cranioventrally between the aorta and main pulmonary artery a similar distance. The depth of the dissection should be at least equal to the width of the ductus (Fig. 155-2, *inset*). Dissect adjacent to the relatively thick-walled aorta.
8. Consider preparing the craniodorsal aspect of the aorta just distal to the left subclavian artery by reflecting the pleura and adjacent mediastinal tissues. This requires a small amount of time and ensures a clear path for clamp placement if hemorrhage control is necessary (see below).
9. The pericardium has a variable insertion at the level of the ductus. It may be inserted on the aortic side or on the main pulmonary artery side of the ductus. Thus, the ductus occasionally is within the pericardium. In these circumstances, incise the pericardium at its insertion on the ductus or aorta.

10. Once the cranial and caudal aspects of the ductus are exposed, initiate blunt dissection behind the PDA using right-angle forceps (Fig. 155-2, *bottom*). Take care to identify the depth of the ductus. Accomplish dissection behind the ductus by inserting closed forceps, spreading gently, and removing the forceps. Carry out dissection *adjacent* and *parallel* to the surface of the aorta.
11. I prefer caudal to cranial dissection to avoid repeated work in the cranial aspect of the ductus. The vascular structures of the cranial region are more readily damaged and are most prone to hemorrhage. However, minor medial dissection in this area often is necessary.
12. When the majority of the medial dissection is complete, gently separate the aorta and main pulmonary artery cranial to the ductus to allow identification of the tips of the right-angle forceps as they are passed from caudal to cranial. When the tips are visible, carefully incise the remaining *fascia* over the tips of the forceps with a #15 blade. This is preferable to repeated efforts at pressing through this fascia.

▼ ***Key Point*** Do not cut any tissue unless you are certain that it is fascia and not vessel wall.

13. Individually pass two strands of 1-0, 2-0, or 3-0 silk or polyester suture, depending on the size of the dog or cat, and the size of the ductus (Fig. 155-3, *top*).
14. Attenuate the ductus prior to ligation to observe the hemodynamic effects. If bradycardia is observed, atropine may be given. Double-ligate the ductus, aortic side first. Palpate the pulmonary artery again for ductal-related thrill or turbulence.
15. If hemorrhage is encountered from perivascular structures, control with pressure, ligation, or cautery. If the ductus ruptures and aggressive hemorrhage is encountered, first use digital pressure to control blood loss. Next, place vascular clamps on the aorta in the previously prepared region just caudal to the left subclavian artery and cranial to the ductus (Fig. 155-3, *bottom*). Also place clamps caudal to the ductus on the aorta and across the base of the ductal origin from the pulmonary artery. Identify the region of hemorrhage and suture with 5-0 or 6-0 nonabsorbable suture on a cardiovascular needle. A recent study evaluated the use of deliberate hypotension for dogs with hemorrhage during PDA dissection. Intravenous nitroprusside was used to lower blood pressure and reduce bleeding, allowing continued dissection and ligation of the ductus. See Supplemental Reading for more information.
16. Subcutaneously tunnel a #5 or 8 Fr. red rubber tube from a small wound made caudal to the skin incision. Place the tube in the thorax through the thoracotomy. Close the thorax in a routine manner, incorporating the temporary thoracic tube (see Chapter 167).
17. After evacuating air and fluid from the thorax, remove the temporary thoracic tube. If hemorrhage or inadvertent lung injury occurs, place a standard indwelling thoracic tube (see Chapter 3).

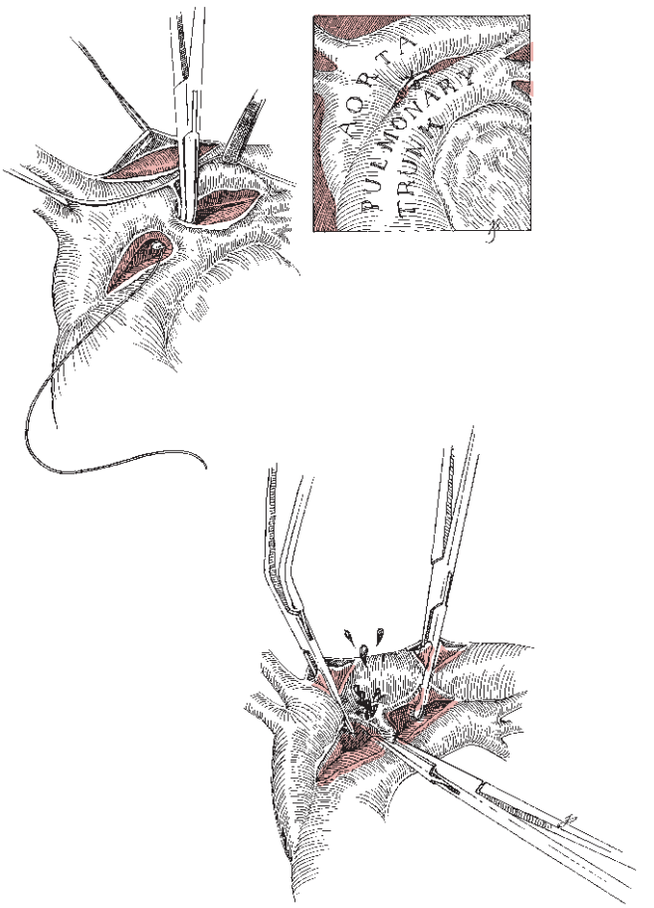

Figure 155-3. *Top,* Suture placement for double ligation of the ductus. *Bottom,* Procedure for controlling hemorrhage after ductus rupture.

POSTOPERATIVE CARE AND COMPLICATIONS

Short Term

▼ ***Key Point*** Close postoperative monitoring in an intensive care setting is of the utmost importance.

- Monitor the following parameters/signs:
  - Mucous membrane color, capillary refill time, respiratory rate, blood pressure
  - Dyspnea, urine output
  - Recovery of body temperature, pulse, thoracic auscultation

- Analgesic therapy is indicated in animals with pain (see Chapter 6 for discussion of postoperative analgesia).
- Some surgeons treat routinely with furosemide (1–2 mg/kg) during the preoperative and immediate postoperative periods. This may be guided by the preoperative status, course of surgery, patient size, and operative fluid balance. If preoperative medical management was instituted, continue it postoperatively until clinical signs resolve.
- Perform frequent intermittent evacuation of the thorax (e.g., q2h) if a tube was left in place. Remove the thoracic tube when negative pressure is achieved or fluid or air production has subsided.
- Limit fluid therapy but maintain a sterile intravenous catheter for 24 hours.
- Auscultate the heart postoperatively for persistent murmur. A systolic murmur of mitral insufficiency, caused by left ventricular dilation, may be present. This murmur generally abates within 10 days. There should be no diastolic murmur if ligation was successful.

Long Term

- Reevaluate heart sounds at 2 weeks when sutures are removed, at 6 months, and then yearly thereafter to detect the uncommon occurrence of recanalization.
- Recanalization of the PDA occurs rarely (1–2% of cases) and is treated by relegation or division of the ductus and oversewing of the cut ends.
- PDA ligation has excellent long-term results if ligation is complete.

SUPPLEMENTAL READING

Hunter SL, Culp LB, Muir WW 3rd, et al. Sodium nitroprusside-induced deliberate hypotension to facilitate patent ductus arteriosus ligation in dogs. Vet Surg. 2003, 32(4):336–340.

Chapter

156 Shock

Eric R. Schertel

▼ ***Key Point*** Shock is the clinical state resulting from an inadequate supply of oxygen to the tissues or an inability of the tissues to utilize oxygen properly.

Shock involves numerous physiologic disturbances and pathologic changes that affect multiple organ systems in different ways. Veterinarians often are alerted to the presence of shock in their patients by the physical findings of depressed mentation, pale mucous membranes, tachycardia, and weak pulse pressure. These clinical signs are the manifestations of a complex process and do not represent the full extent of the problem. The objective of this chapter is to provide a simplified approach to the diagnosis, monitoring, and treatment of shock. Information on the various manifestations, mechanisms, and temporal patterns of shock is beyond the scope of this book, but nonetheless is considered important to appropriate and successful therapy. Therapy for shock caused by acute heart failure is discussed in Chapter 147. See appropriate chapters for discussion of specific diseases that can cause shock.

ETIOLOGY AND CLASSIFICATION

Shock generally is classified by etiology because each cause of shock may produce distinct primary and secondary pathophysiologic changes and temporal patterns. Shock etiologies can be organized into those forms that result from:

- An abnormality or inadequacy of the vehicle of oxygen transport (blood)
- An abnormality of the transport system (cardiovascular system)

Hypovolemia and hypoxemia (anemic, hypoxic) are examples of the first category (Table 156-1). Diseases that disrupt the cardiovascular system and its control mechanisms (circulatory control mechanisms) also cause shock. The three important circulatory control mechanisms regulate:

- Blood pressure and blood flow distribution
- Blood volume distribution
- Cardiac function

Shock may also develop from the presence of one or more of these conditions.

- Sepsis is an example of a condition in which shock is caused by a loss of control of blood flow distribution.
- Endotoxemia and gastric dilatation-volvulus also cause shock by interfering with the distribution of blood volume, but via different mechanisms.
- Heart failure creates shock due to inadequate cardiac function (see Table 156-1).

CLINICAL SIGNS

Mental Attitude

Depressed mentation often is the most apparent physical finding in a patient with shock. This parameter is subjective and may be complicated by head injury.

- *Causes:* Decreased cerebral blood flow and oxygen delivery, circulating toxins, or head injury.

Arterial Pulse Pressure

A weak pulse is common but not necessary for shock to exist. The pulse feels weak at mean arterial pressures <60 to 70 mm Hg. Below 40 mm Hg, the pulse may not be palpable.

- *Causes:* Low cardiac output or low peripheral vascular resistance.

Mucous Membrane Color

The color may be pale, gray (muddy), cyanotic, brick-red, or normal.

- *Causes:* Pale mucous membranes reflect hypovolemia or anemia. Gray or cyanotic mucous membranes generally indicate severe cardiovascular compromise or arterial hypoxemia. Brick-red mucous membranes are common in septic shock. Mucous membrane color may be normal.

Table 156-1. CLASSIFICATION AND COMMON ETIOLOGIES OF SHOCK

Shock Involving Normal Circulatory Control Mechanisms
Hypovolemia
Hypoxemia
Anemia
Hypoxia
Shock Involving Abnormal Circulatory Control Mechanisms
Blood flow maldistribution
Sepsis
Trauma—surgical and accidental
Blood volume maldistribution
Endotoxemia
Anesthesia
Neurogenic shock
Anaphylactic shock
Gastric dilatation-volvulus
Impaired cardiac function
Systolic functional failure
Cardiomyopathy
Valvular heart disease
Myocardial ischemia
Myocardial contusion
Arrhythmias
Diastolic functional failure
Pericardial disease—tamponade
Myocardial disease—decreased diastolic compliance

Body/Extremity Temperature

Hypothermia (<99°F) and cold extremities are common. Patients that are septic may be hyperthermic (>103°F) with warm extremities.

- *Causes:* Decreased cardiac output, oxygen delivery, and ambient temperature. Cold extremities result from severe vasoconstriction. Hyperthermia results from the increased metabolic rate that commonly accompanies sepsis. Warm extremities reflect peripheral vasodilatation.

Capillary Refill Time

Capillary refill time typically is prolonged (>2 seconds), but may be normal.

- *Causes:* Prolonged capillary refill time reflects hypovolemia and poor peripheral blood flow.

Heart Rate

Heart rate is commonly elevated: >140 beats per minute (bpm) in large-breed dogs, >160 bpm in small-breed dogs, and >180 bpm in cats. Begin monitoring with electrocardiography (ECG) if an irregular rhythm is detected.

- *Causes:* Hypotension, hypovolemia, pain, stress, and fever may cause tachycardia. Irregular rapid heart rhythms result from ventricular tachycardia and atrial tachyarrhythmias, including atrial fibrillation (see Chapter 145).

Respiratory Rate

Increased respiratory rate (tachypnea) is common, but may be due to excitement or fever.

- *Causes:* Hypoxemia, metabolic acidosis, pain, fever, and excitement.

Urine Output

Urine output is decreased (normal range is 1 to 2 ml/kg/hr).

- *Causes:* Urine formation virtually ceases when mean arterial pressure is <60 mm Hg. Blood pressure may be normal in mild to moderate hypovolemia.

MONITORING AND TREATMENT

Goals

The goal for managing the shock patient is to optimize the functions of the cardiovascular system. Employ monitoring techniques that provide accurate information about functional parameters, such as blood volume, cardiac output, arterial blood pressure, and oxygen delivery.

Cardiac output, arterial blood pressure, and oxygen delivery are dependent on blood volume. When blood volume is expanded these other parameters commonly return to normal.

▼ ***Key Point*** Blood volume is the most important parameter to optimize and monitor in shock patients.

Monitoring

Blood Volume

- Physical signs and findings do not accurately reflect blood volume.
- Central venous pressure (CVP) is the simplest measurement that reflects blood volume. It may be obtained via a jugular catheter positioned so that its tip is within the thorax (see Chapter 3). CVP is approximately equivalent to the right atrial pressure and reflects the function of the systemic circulation and the right heart (Fig. 156-1).
- CVP is easily measured by a water manometer attached to the jugular catheter (see Chapter 3).
- Normal CVP ranges from 0 to 5 cm H_2O. In shock, CVP usually is −3 to 2 cm H_2O but may be as low as −5 cm H_2O. The goal of fluid therapy in shock is to optimize blood volume by administering fluid in an amount that increases CVP to between 5 and 12 cm H_2O.
- Plasma proteins, particularly albumin, maintain plasma volume. Assess total plasma proteins prior to fluid therapy and frequently during treatment to ensure that values remain above 4.0 g/dl (albumin >1.5 g/dl).

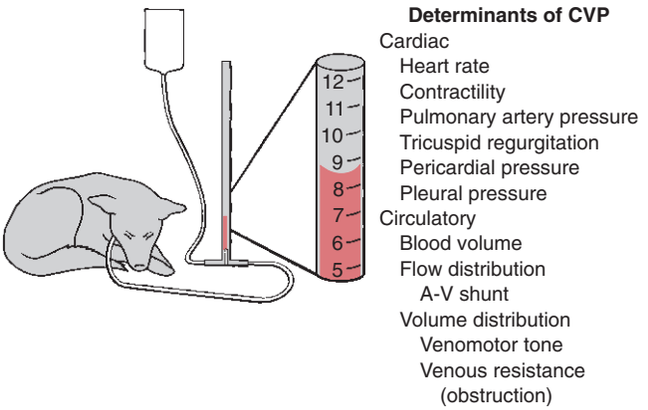

Figure 156-1. Determinants of central venous pressure (CVP).

Arterial Pressure

- Digital palpation may be used to assess mean arterial pressure (MAP). Strong pulse pressure usually reflects a MAP of >70 mm Hg. A weak pulse is detected when MAP is <70 mm Hg. When MAP is <40 mm Hg, the pulse is difficult or impossible to palpate.
- Arterial pressure also may be assessed using Doppler or oscillometric methods. These techniques are noninvasive and are generally accurate, except when arterial pressure is low.

Cardiac Output

- Capillary refill time, body temperature, and mentation are the physical findings that best reflect cardiac output. However, these are not always accurate.
- Urine output is a good indicator of cardiac output. When cardiac output is reduced, sympathetic nervous system activity may maintain blood pressure within normal limits but may decrease renal blood flow. Consequently, urine output will be decreased (<1 ml/kg/hr). However, other causes of reduced urine formation must be considered.
- Cardiac rhythm influences cardiac output and can be monitored by ECG.

Oxygen Delivery

- Oxygen delivery is determined by cardiac output as assessed above; pulmonary function is assessed by arterial oxygen pressure (Pao_2) or oximetry; and hemoglobin is assessed by hematocrit.
- Mucous membrane color, mentation, body temperature, and respiratory rate are the physical findings that best reflect oxygen delivery.
- Obtain blood samples for hematocrit measurement prior to treatment for shock. Repeat measurements frequently during aggressive fluid therapy (e.g., q1–2h). Maintain hematocrit >20%; in severe shock, it should be >30%.

Treatment

Preliminary Measures

- Establish an airway and ventilate if necessary. Administer 100% oxygen via an endotracheal tube, mask, nasal tube, or tracheal catheter.
- To evaluate the patient for the cause of shock, obtain a history and perform a physical examination. The time allotted for these efforts depends on the condition of the patient.
- Place and secure a large-gauge intravenous (IV) catheter, preferably jugular. The jugular catheter should be long enough to reach the thoracic cavity.
  - Jugular catheterization has the advantages of allowing the use of a large-gauge catheter even in small patients, ease of placement, access for blood sampling, rapid fluid administration, CVP measurement, and catheter security. The major disadvantage is that jugular catheters are slightly more expensive.
- Obtain blood for storage in ethylenediaminetetraacetic acid (EDTA) and clot tubes. Measure hematocrit and total protein, serum electrolytes, serum creatinine, blood glucose, and a complete blood count.

Optimize Blood Volume

- Initially, administer sodium-rich isotonic crystalloid fluids (e.g., 0.9% NaCl, lactated Ringer's solution) at a rate of 60 to 90 ml/kg/hr (Table 156-2). To ensure effective plasma volume expansion, maintain the sodium concentration of the isotonic fluid at >130 mEq/L.
- Administration of 7% NaCl (hypertonic saline) is an alternative resuscitation regimen in patients that are not hydrated. Deliver the initial dosage of 4 to 6 ml/kg over 5–10 minutes (Table 156-3). The hypertonic saline may be combined with 6% dextran 70 or hetastarch and given at the same dosage. Supplement this form of initial treatment by giving isotonic crystalloid fluids at a minimum rate of 20 ml/kg/hr.
- The goal of the initial rapid rate of fluid administration is to establish a normal arterial pressure and optimize blood volume. An adequate arterial pressure is easily determined by palpation of pulse pressure. Physical signs, including pulse pressure, may be normal despite continuing tissue hypoxia and less than optimal or unstable blood volume.
- Blood volume is optimized when CVP is 5 to 12 cm H_2O.
- To treat hypoproteinemia, fresh or frozen plasma may be administered at a dosage of 10 to 20 ml/kg/day IV.
- Alternatively, synthetic colloids may be used to treat hypoproteinemia. Those useful in small animal patients include 6% dextran 70 and 6% hetastarch. The dosages are similar to those for plasma

Table 156-2. TREATMENT OF SHOCK

Therapeutic Goal	Therapy	Specific Objectives	Dosage Recommendations
Optimize blood volume	Crystalloids Isotonic Hypertonic Colloids Whole blood	CVP 5–12 cm H_2O Wedge pressure 7–20 mm Hg Total protein >4.0 g/dl Albumin >1.5 g/dl Normal skin turgor	Isotonic fluids: 0.9% NaCl or LRS; 60–90 ml/kg/hr to effect IV Hypertonic saline/dextran: 7% NaCl or 7% NaCl in 6% dextran 70, 4–6 ml/kg slowly IV Plasma: 10–20 ml/kg IV 6% Dextran 70: 10–20 ml/kg/day IV 6% Hetastarch: 10–20 ml/kg/day IV Whole blood: 20–30 ml/kg IV
Optimize blood flow	Fluids Inotropic agents	Urine output >1 ml/kg/hr CRT <2 sec P_{VO_2} >35 torr Cardiac index 150–200 ml/min/kg	See Optimize Blood Volume in text Dopamine: 2–10 µg/kg/min IV Dobutamine: 2–15 µg/kg/min IV
Optimize oxygen delivery and consumption	Fluids Whole blood Packed red cells O_2 supplementation Mechanical ventilation Respiratory care	P_{aO_2} >70 torr P_{VO_2} >35 torr Hct >25 Pink mucous membranes Patient bright, alert, responsive	See Optimize Blood Volume in text Packed red cells: 10–20 µl/kg IV F_{IO_2}: 40–100%
Optimize blood pressure	Fluids Vasopressors	Arterial pressure: Systolic, 100–160 mm Hg Mean, 70–120 mm Hg Diastolic, 50–100 mm Hg Strong pulse	See Optimize Blood Volume in text Dopamine: 5–10 µg/kg/min IV Epinephrine: 0.1–0.3 µg/kg/min IV Phenylephrine: 0.01–0.1 µg/kg/min IV Methoxamine: 0.2 µg/kg IV
Optimize heart rate/rhythm	Fluids Antiarrhythmics	70–160 bpm Sinus rhythm	See Optimize Blood Volume in text Lidocaine: 1–2 mg/kg bolus IV, 25–75 µg/kg/min IV Procainamide: 15–20 mg/kg IM
Correct acid-base imbalance	$NaHCO_3$	pH >7.3 and <7.5	Sodium bicarbonate: 0.5–5.0 mEq/kg IV or mEq = 0.3 × base deficit × kg
Optimize urine output	Fluids	1–2 ml/kg/hr urine production	Furosemide: 2–4 mg/kg IV Mannitol (20%): 1–2 g/kg IV
Control sepsis	Antibiotics Surgery Culture and sensitivity	Negative culture Wound/infection management	Cephalothin: 20 mg/kg IV q6h Ampicillin: 20 mg/kg IV q6h Gentamicin: 2 mg/kg IV q8h
Optimize blood glucose	Glucose Insulin	Blood glucose 60–120 mg/dl	Dextrose 5% in maintenance fluids Dextrose 50%: 0.5–2.0 g/kg/hr Insulin (regular): 0.5–2 units/kg q2–6h IV (if hyperglycemic)
Immune/inflammatory modulation	Corticosteroids	Same as Therapeutic Goal	Dexamethasone sodium phosphate: 1–2 mg/kg IV Prednisolone sodium succinate: 10–20 mg/kg IV

CRT, capillary refill time; CVP, central ventral venous pressure; F_{IO_2}, inspired oxygen fraction; Hct, hematocrit; LRS, lactated Ringer's solution; P_{aO_2}, arterial oxygen partial pressure; P_{VO_2}, venous oxygen partial pressure.

Table 156-3. HYPERTONIC SALINE AND SYNTHETIC COLLOID THERAPY*

	Sodium Chloride Solutions			Synthetic Colloids	
	3% NaCl	5% NaCl	7% NaCl	6% Dextran 70	6% Hetastarch
Approximate osmolality (mOsm/kg)	1000	1800	2400	N/A†	N/A
Maximum dosage range (ml/kg IV)	20	6–10	4–8	10–20	10–20
Maximum infusion rate (ml/kg/min IV)	2	1	1	1	1
Available products	3% NaCl	5% NaCl	7% NaCl	Gentran 70	Hespan
Manufacturers	Baxter, Kendall McGaw	Baxter, Abbott, Kendall McGaw	Butler	Baxter	DuPont

*Indications: hypovolemia, traumatic shock, endotoxemia, septicemia, gastric dilatation-volvulus. Contraindications: dehydration, hypernatremia, hyperosmolality, heart/renal failure.
†N/A: not applicable.

(10–20 ml/kg/day) and commonly are divided into 5 to 10 ml/kg slow IV infusions (over 10–20 minutes).

- Fresh or stored blood may be given to optimize blood volume if the hematocrit and total protein are decreased below acceptable levels. Blood collected from the abdominal or thoracic cavity may be autotransfused if other, more acceptable sources are unavailable. This blood must be free of bacterial and neoplastic contamination; administer via a blood administration set (including filter). Autotransfused blood will have decreased platelets, clotting factors, and fibrinogen concentration.

Optimize Blood Flow

- Cardiac output increases and is often optimized as a result of aggressive volume expansion.
- If volume expansion has increased the CVP to 5 to 12 cm H_2O but urine output and other physical signs reflecting cardiac output are not normalized, evaluate cardiac function with ECG.
- If the ECG is normal, administer a positive inotropic agent. Dobutamine (Dobutrex, Lilly) and dopamine (Intropin, DuPont) are inotropic drugs (see Chapter 146) that are commonly used to enhance cardiac function in shock patients.
  - Dobutamine produces dose-dependent increases in contractility when administered at a dosage of 2 to 15 µg/kg/min IV (Fig. 156-2).
  - Epinephrine administered at dosages of 0.05 to 0.2 µg/kg/min IV improves contractility and increases cardiac output and peripheral vascular resistance, causing renal and mesenteric arterial vasoconstriction.
- Cardiac arrhythmias may contribute to low cardiac output. Consider causes of arrhythmias (myocardial hypoxia, myocardial contusion, and electrolyte disturbances) and correct them if possible (see Chapter 145). Ventricular arrhythmias are the most common and may be treated with lidocaine administered IV at 1 to 2 mg/kg or as a continuous infusion of 25 to 75 µg/kg/min (see Chapter 146) (Fig. 156-2).

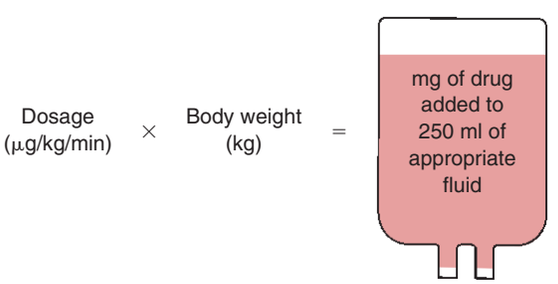

Figure 156-2. Simplified method of dosage formulation for continuous-infusion drugs. Once formulated, administer at 15 ml/hr or 1 drop/4 sec from a 60-drop/ml administration set to achieve desired dosage.

Optimize Blood Pressure

- Arterial blood pressure often is returned to normal by fluid therapy.

▼ ***Key Point*** When arterial blood pressure is <40 mm Hg (pulse weak or not palpable), increase blood pressure immediately.

- In cases of severe shock, epinephrine may be needed to increase peripheral vascular resistance and cardiac output until fluid therapy can be initiated and blood volume expanded.
  - The IV dosage of epinephrine for cardiac arrest is 0.02 to 0.2 mg/kg (0.02–0.2 ml/kg of 1:1000 dilution).
  - When the primary problem is severe hypotension, not cardiac arrest, administer epinephrine continuously at a dosage of 0.1 to 0.3 µg/kg/min IV (see Table 156–2).
  - Once blood volume is expanded and cardiac output and mean arterial pressure are restored, discontinue epinephrine.
- Use of an abdominal wrap or "belly band" to augment arterial blood pressure and to tamponade abdominal bleeding may be dangerous and is not recommended. Any increase in arterial resistance (arterial pressure) created by an abdominal wrap may be counteracted by obstruction of the vena cava and portal vein and by decreased venous return. Furthermore, the abdominal wrap may compromise respiratory function, exacerbate diaphragmatic hernia, and lead to hypotension when it is removed.
  - Manage uncontrolled intra-abdominal hemorrhage by aggressive fluid replacement, and perform surgical exploration if the condition fails to stabilize.

Optimize Oxygen Delivery

- Optimal oxygen delivery is often attained by aggressive volume replacement.
- Hemodilution or pre-existing anemia may limit oxygen delivery. Red blood cell (RBC) replacement (whole blood, packed red cells) is necessary when hematocrit is <20%. Administer whole blood at a dosage of 20 to 30 ml/kg and packed RBCs at 10 to 20 ml/kg (see Chapter 22).
- Administration of corticosteroids (e.g., prednisolone sodium succinate, 10–20 mg/kg) before transfusion minimizes the risk of severe transfusion reaction and improves the RBC function of stored blood.
- Oxygen supplementation improves arterial blood oxygen content and may be administered via mask, nasal catheter, oxygen cage, or transtracheal catheter and is particularly crucial when the patient is anemic (see Chapter 3).
- In cases of severe lung injury, provide ventilatory assistance. This requires anesthetizing the patient

and placing an endotracheal tube. Alternatively, a tracheostomy may be performed (see Chapter 3).

Correction of Acid-Base and Electrolyte Disturbances

- The metabolic acidosis that results from shock that is mild or of short duration often can be managed effectively by fluid replacement therapy.
- The degree of metabolic acidosis that develops in shock depends on the severity and duration of the oxygen delivery deficit. If blood gas analysis can be performed, the milliequivalent (mEq) dosage of $NaHCO_3$ required to correct the acidosis may be calculated by the following formula:
- $NaHCO_3$ (mEq) = 0.3 × body weight (kg) × base deficit
- If blood gas analysis is not available, an estimate of the base deficit may be made based on the severity of the shock state and its duration. Mild, moderate, and severe shock may be treated with $NaHCO_3$ dosages of 1.0, 3.0, and 5.0 mEq/kg of body weight, respectively (see Chapter 5 for more information on treatment of acidosis).
- Hyperkalemia is the most common serum electrolyte concentration abnormality observed in shock. Hyperkalemia generally responds to aggressive volume replacement, increased urine output, and improvement of metabolic status. Glucose and $NaHCO_3$ infusions facilitate reduction of serum potassium concentration (see Chapter 5).
- Hypokalemia often occurs after aggressive volume replacement. Once maintenance fluids are started, they should contain 15 to 20 mEq/L of KCl (see Chapter 5).

Corticosteroid Therapy

- Corticosteroids may be of benefit for most forms of shock, but are not recommended for septic shock. Administer early in the course of therapy to derive maximum benefits.
- Use water-soluble drugs, including dexamethasone sodium phosphate (Azium-SP, Schering), 1 to 2 mg/kg IV, and prednisolone sodium succinate (Solu-Delta-Cortef, Upjohn), 10 to 20 mg/kg IV.

Miscellaneous Treatments

- Broad-spectrum antibiotics are indicated in most forms of severe shock, particularly septic shock.
- Surgical management of a septic focus should be performed as soon as cardiorespiratory stability is established.
- IV glucose can provide some of the caloric requirements of the shock patient. Maintenance fluids should contain 5% dextrose. This treatment is helpful over the short term, but supplies only a fraction of the caloric requirements. More complete caloric supplementation may be achieved by administration of 50% dextrose at an hourly dosage of 0.5 to 2.0 g/kg.

SUPPLEMENTAL READING

Schertel ER, Tobias TA: Hypertonic fluid therapy. In DiBartola SP (ed): Fluid Therapy in Small Animal Practice. Philadelphia: WB Saunders, 1992, p 471.

Tobias TA, Schertel ER: Shock: Concepts and management. In DiBartola SP (ed): Fluid Therapy in Small Animal Practice. Philadelphia: WB Saunders, 1992, p 436.

Chapter

157 Cardiopulmonary Cerebral Resuscitation

William W. Muir III

Resuscitation is the restoration of life after apparent death. Cardiopulmonary resuscitation (CPR) includes therapy to restore heart and lung function to normal. Most resuscitative techniques incorporate methods to maximize and maintain cerebral blood flow and clinicians have redefined CPR as cardiopulmonary cerebral resuscitation (CPCR). Preparedness and early recognition of the signs of sudden death are the major factors that determine long-term outcome (Tables 157-1 and 157-2).

CPCR is divided into three phases:

- *Phase 1,* basic life support (BLS), consists of establishing an airway (A), breathing (B), and circulatory support (C).
- *Phase 2,* advanced life support (ALS), incorporates the use of drugs (D), electrocardiography (E), and methods to convert ventricular fibrillation or asystole (F) to sinus rhythm.
- *Phase 3,* prolonged life support (PLS), includes measures that focus on treating the causes of cardiac arrest and deciding whether to continue resuscitative efforts. Gauging (G) (monitoring of patient trends), hypnogenesis (H) (use of sedation, anesthesia, and pain control), utilization of methods to restore cerebral function, and intensive care (I) oriented toward preventing multiorgan failure are also elements of PLS.

BASIC LIFE SUPPORT: AIRWAY, BREATHING, AND CIRCULATORY SUPPORT

Airway

▼ ***Key Point*** Establishing a patent functional airway should be accomplished as soon as possible.

Establishing an Airway

Mouth to Endotracheal Tube

To pass a cuffed endotracheal tube of appropriate size place the patient on the sternum, open the mouth widely, and maximally extend the head and neck. Expose the larynx (using a laryngoscope if necessary) and proceed with intubation.

Tracheotomy

A tracheotomy may be necessary in animals with upper airway obstruction, brachycephalic animals, or in dogs and cats that are successfully resuscitated, regain consciousness, and object to oral-tracheal intubation. (Tracheotomy is described in Chapter 3.)

Mouth to Muzzle

Tightly cup hands around the muzzle of small dogs and cats, or place mouth directly over the patient's muzzle. Blow exhaled air into the animal's lungs.

Mouth to Mask

A variety of masks have been developed for use in dogs and cats for the delivery of oxygen or inhaled anesthetics.

▼ ***Key Point*** Mouth-to-muzzle and mouth-to-mask methods do not secure the airway but may be useful when equipment is limited. Distention of the stomach with air may limit lung expansion and predisposes to regurgitation.

Proper Endotracheal Tube Placement

Correct placement of the endotracheal tube can be verified by:

- Clearing and securing an airway.
- Direct observation of the tube positioned through the larynx (most reliable technique).
- Palpation of the endotracheal tube in the trachea.
- The appearance of water vapor on clear endotracheal tubes.
- The inability of the animal to vocalize.
- Gas exiting the endotracheal tube during exhalation. This sign, which frequently is used clinically, should not be the only method used to ensure proper endotracheal tube placement.

Table 157-1. SIGNS OF CARDIOPULMONARY ARREST

Evaluations	Clinical Signs and Observations
Effort, rate, and rhythm of breathing	Dyspnea (abdominal breathing) Gasps (gurgling sounds) Tachypnea Bradypnea Altered patterns of breathing: Cheyne-Stokes Agonal
Heart rate and rhythm	Tachycardia Bradycardia Irregular rhythm
Pulse	Peripheral arterial pulse is difficult or impossible to palpate at systolic BPs < 40–50 mm Hg
Heart sounds	Heart sounds are inaudible at BPs < 40–50 mm Hg
Bleeding	Absence of bleeding Change in color of blood from red to blue during surgical procedure
Peripheral perfusion	Change in mucous membrane color: Pale or white Blue or cyanotic—5 g/dl of reduced Hb imparts bluish discoloration to mucous membranes; anemic animals (<5 g/dl Hb) do not demonstrate cyanosis
Pupils	Pupils dilate within 1–2 min after cardiac arrest
Mental state	Altered consciousness Coma

BPs = arterial blood pressures; Hb = hemoglobin.

Air or Oxygen Delivery Systems (Fig. 157-1, *top*)

- *Self-refilling bags* connected to oxygen (Ambu bag) can be used to provide an air or oxygen source during controlled breathing.
- *Demand valves*, which are oxygen-powered, manually triggered ventilatory devices, permit both the initiation and termination of ventilation.
- *Anesthetic machines* are the most readily available source of oxygen in most hospitals.
- *Automatic pressure- or volume-cycled ventilators* can be used to assist (control volume) or control (control rate and volume) breathing. Most ventilators do not function properly during thoracic compression.
- In *translaryngeal or tracheal insufflation* (see Fig. 157-1, *bottom*), place an over-the-needle catheter (Surflo, Terumo Medical Corp.) (17-14 gauge) in the trachea and attach to a three-way stopcock, venous extension tubing, and oxygen supply.

Breathing

A ventilator, delivering 50% to 100% oxygen, can be used to assist or control breathing. The resuscitator's exhaled air, which contains 16% to 18% oxygen, may be expelled into a properly placed endotracheal tube and is adequate for maintaining Pao_2 if large tidal volumes are used.

- Detect and immediately treat:
  - Tension pneumothorax
  - Hemothorax
  - Open chest wound
  - Flail chest
  - Cardiac tamponade

Maximal oxygenation of arterial blood with minimal hemodynamic impairment can be obtained by:

- Providing adequate oxygenation (inspired $O_2 > 50\%$)
- Proper placement of an endotracheal tube
- Slow (1–2 sec) inflation of the lungs
- Providing adequate (14–20 ml/kg) tidal volume
- Providing adequate (25–30 cm H_2O) but not excessive inspiratory pressure
- Inflation of the lung with an excessive volume of gas impairs venous return and cardiac output during closed-chest CPCR. Therefore, be careful not to overinflate the lung.
- Sedation and/or anesthesia may be necessary to control ventilation in conscious or semiconscious patients (see Chapter 2) that resist placement of an endotracheal tube.
  - Diazepam, 0.2 to 0.5 mg/kg IV
  - Propofol, to effect: 3 to 4 mg/kg IV; 0.1 to 0.4 mg/kg/min
  - Isoflurane, 1 to 2%
- Positive end-expiratory pressure (PEEP; 5 cm H_2O) helps to prevent small airway closure, thereby improving gas exchange.

Circulation: Closed Chest Compression

The early re-establishment of normal or near-normal hemodynamics, particularly cerebral blood flow, is vital to long-term survival. Closed chest compression should begin immediately when the pulse is lost or it is determined that the existing pulse is not providing adequate tissue perfusion and oxygenation. Closed chest compression should only be interrupted by the establishment of a patent airway.

▼ ***Key Point*** External chest compression is effective in restoring blood flow to the systemic circulation and brain if proper techniques are utilized.

One-Rescuer CPCR with Intermittent Positive Pressure Ventilation (IPPV)

Perform one-rescuer chest compression (80–100 compressions/min) by placing the animal in lateral recumbency and manually compressing the thorax from side to side, using the thumb and first two forefingers for animals less than 5 kg and the heels of the hands for larger animals (Fig. 157-2). Ventilate the lungs after each set of 15 chest compressions.

Table 157-2. ESSENTIAL EQUIPMENT TO PERFORM CPCR*

1. Assortment of cuffed endotracheal tubes with inside diameter of 2–15 mm
2. Oxygen supply source
   a. Ambu bag and oxygen source
   b. Small animal anesthetic machine
   c. Demand valve
   d. Oxygen hose to deliver nasal oxygen
   e. Respirator (pressure or volume cycled)
   f. Oxygen chamber
3. Fluid and drug administration equipment
   a. Assortment of intravenous needles and catheters
      (1) Needles—18–25 gauge
      (2) Over-the-needle or through-the-needle catheters—17–22 gauge
   b. Assortment of syringes—1, 3, 6, 12, and 60 ml
   c. Solution administration sets
      (1) Standard solution administration sets (10 drops/ml) for animals over 5 kg
      (2) Mini-drop solution administration sets (60 drops/ml) for animals <5 kg and to deliver drugs that must be administered by infusion
   d. Venous extension tubing to prolong the time until drug effect, by increasing distance between fluids and patient
   e. Three-way stopcocks and catheter injection plugs
4. Fluids
   a. Balanced electrolyte solutions to be administered IV in most emergency situations; rate of fluid administration is determined by circumstances (see text for dosages):
      (1) 20 ml/kg/hr during hypotension
      (2) 40 ml/kg/hr following acute cardiac arrest
      (3) 90 ml/kg/hr following circulatory collapse due to hemorrhage
   b. Other solutions
      (1) 5% dextrose in water to supply volume and additional calories and dilute plasma potassium concentration
      (2) Normal saline (0.9% NaCl) to supply volume and dilute plasma potassium concentration
      (3) Colloid solutions (6% dextran 70; hetastarch) to supply volume and oncotic value
      (4) Mannitol (20% Osmotrol) to be used as an osmotic diuretic and as an oxygen free radical scavenger
   c. Special solutions
      (1) Hypertonic saline solutions (usually 3 or 7%) to restore vascular volume; the appropriate quantity of NaCl may be mixed in 6% dextran 70; 7% NaCl in 6% dextran 70 can be administered IV, 4 ml/kg, over 1–2 min
      (2) Blood substitute (Oxyglobin, Biopure), 10–30 ml/kg/hr IV, to maintain tissue oxygenation following acute hemorrhage or in severe anemia
5. Drugs (see text for dosages)
   a. Anticholinergics (atropine or glycopyrrolate)
   b. Epinephrine (1:1000 and 1:10,000)
   c. Dopamine or dobutamine
   d. Calcium chloride
   e. Lidocaine (2%)
   f. Injectable procainamide
   g. Glucocorticosteroids (dexamethasone, prednisolone sodium succinate)
   h. Furosemide
   i. Mannitol
   j. Diazepam, thiobarbiturate (thiopental), phenytoin
   k. Oxymorphone, other opioids
   l. Doxapram
6. Surgical instruments
   a. Scalpel and several #10 blades
   b. Mosquito and Kelly hemostats
   c. Rib retractors
   d. Thumb forceps
   e. Metzenbaum and Mayo scissors, needle holders
7. Bandage material (1, 2, and 4 inch)
   a. Sterile 4-inch × 4-inch gauze sponges
   b. Cotton bandage
   c. Elastic bandage
   d. Tape
8. Other equipment
   a. Clippers
   b. Leg splints (tongue depressors can be used in animals under 10 kg)
   c. Water circulating heating pad
   d. Electrocardiographic machine
   e. Electrical defibrillator
   f. Aspiration or suction device and tubing
   g. Assortment of suture material

*This material should be kept in one place, preferably on an emergency cart or in a large tool chest.

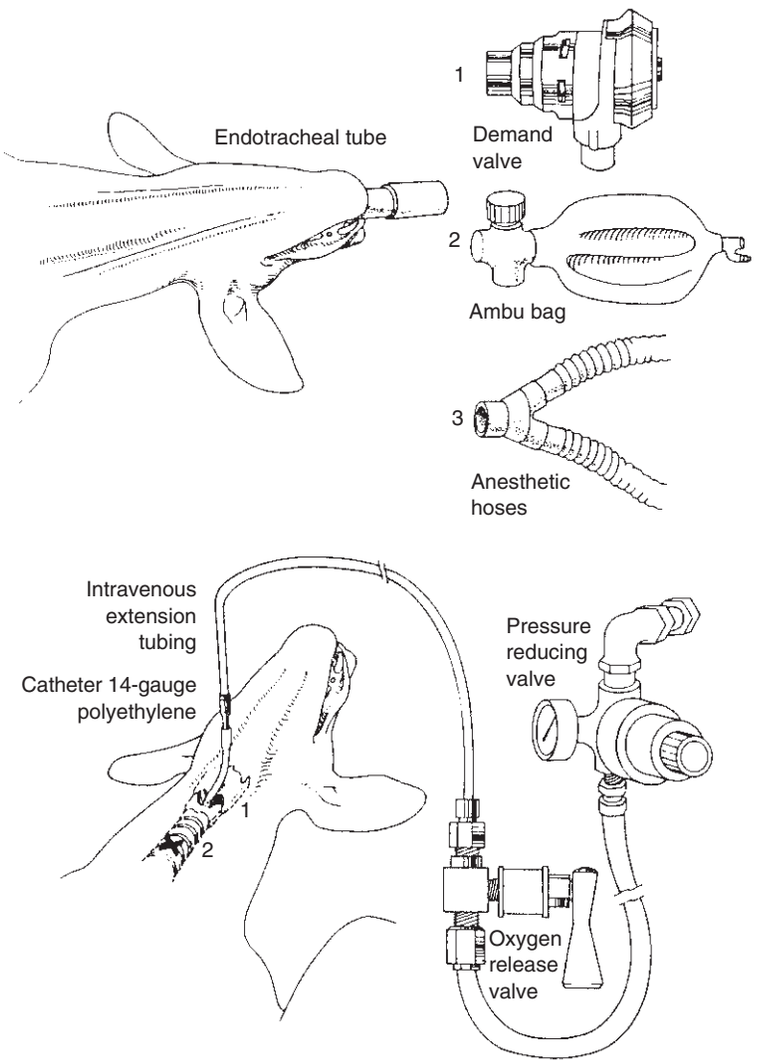

Figure 157-1. Methods of endotracheal oxygen administration *(top);* transtracheal oxygen administration *(bottom)* via catheter placement through the cricothyroid notch (1) or between tracheal rings (2). (Modified from Sherding RG: Medical Emergencies. New York: Churchill Livingstone, 1985.)

Figure 157-2. Chest compression in the dog *(left, middle);* chest compression in the cat *(right).*

Two-Rescuer CPCR with IPPV

The technique for compressing the chest is identical to that in one-rescuer CPCR (see above). Ventilate intermittently without slowing the rate of chest compression (1 breath for each set of 15 chest compressions) or simultaneously with chest compression (SVC or simultaneous compression ventilation–CPCR). Take care not to overinflate the lungs (use <30 cm H_2O), in order to prevent or minimize pulmonary barotrauma and pneumothorax.

Three-Rescuer CPCR with IPPV and Abdominal Pressure

Applying steady or intermittent abdominal pressure during CPCR or SVC-CPCR may augment carotid arterial pressures and cerebral and myocardial blood flow.

- The palm of the hand (third rescuer) may be used to compress the abdomen against the backbone for periods of 5 to 10 seconds. Repeat this procedure 2 to 3 times per minute.
- An elastic bandage can be tightly wrapped around the rear legs to prevent venous pooling and to promote venous return.

ADVANCED LIFE SUPPORT

The primary purpose of advanced life support techniques is to restore adequate spontaneous circulation. Open-chest CPCR is considered an advanced life support technique. Antiarrhythmic, inotropic, and antishock drugs (e.g., glucocorticosteroids, free radical scavengers) are used in conjunction with fluid therapy to restore supernormal hemodynamics.

Drug Therapy

Drugs and fluids are preferably administered intravenously (see Table 157-3 for dosages and side effects; also see Chapter 146 for additional details regarding the pharmacologic actions of cardiovascular and antiarrhythmic drugs). Place a large-bore catheter (18–14 gauge) in the cephalic or jugular vein. Placement of an IV catheter may require a "cutdown" or placement of an intraosseous needle (20 or 18 gauge), because the veins collapse shortly after cardiac arrest (see Chapter 3).

Epinephrine

▼ ***Key Point*** Epinephrine is the drug of choice for the treatment of cardiac arrest regardless of cause (Table 157-4).

- Large doses of epinephrine (0.2 mg/kg IV) produce dramatic increases in heart rate, arterial blood pressure, and cerebral blood flow in dogs and cats suffering from severe bradycardia (<30 beats/min) with hypotension, but may induce ventricular arrhythmias and ventricular fibrillation in animals that are in sinus or idioventricular rhythms.
- Initial doses of 0.01 mg/kg IV are adequate in most patients with hypotension or bradycardia and may be adjusted upward according to the patient's response (see Table 157-4).

Lidocaine

Lidocaine is the first choice antiarrhythmic for the treatment of ventricular arrhythmias in dogs and cats.

- It is the drug of choice for the treatment of cardiac arrhythmias induced by catecholamines and digitalis glycosides, and ventricular arrhythmias produced by myocardial contusion, inhalation anesthetics, and thiobarbiturates.
- Initial IV bolus dosages should not exceed 4 mg/kg in dogs and 1.0 mg/kg in cats. A lidocaine infusion (40–60 µg/kg/min) produces a sustained antiarrhythmic effect. A solution containing 1 mg (1000 µg) of lidocaine per ml is made by mixing 25 ml of 2% lidocaine in 500 ml of lactated Ringer's solution (infuse 0.5 ml/10 kg/min). Potassium (K^+) may be added to the fluid (15–20 mEq) to enhance lidocaine's effects (do not exceed 0.5 mEq/kg/hr). Occasionally procainamide may be effective (6–20 mg/kg; 40–60 µg/kg/min) when lidociane is ineffective.

▼ ***Key Point*** Lidocaine is relatively ineffective in hypokalemic patients and should never be administered to patients with complete (third-degree) AV block.

Sotalol

Sotalol is an antiarrhythmic drug used for long-term therapy of ventricular arrhythmias (see Chapter 146).

- Initial dosages range from 1 to 2 mg/kg PO and are titrated to effect.

Sodium Bicarbonate

Sodium bicarbonate administration helps to combat the development of metabolic acidosis and, more specifically, lactic acidosis produced by anaerobic metabolism secondary to circulatory arrest.

- The initial dose of sodium bicarbonate (1 mEq/kg IV) is not required until after 10 to 15 minutes of arrest and may be repeated (0.5 mEq/kg IV) every 10 to 15 minutes until resuscitative efforts are successful or terminated.

Anticholinergics

Atropine (0.01–0.02 mg/kg IV) or glycopyrrolate (0.005–0.01 mg/kg IV) is effective for the treatment of bradyarrhythmias (sinus bradycardia, high-grade

Table 157-3. THERAPEUTIC MANAGEMENT OF PROBLEMS ASSOCIATED WITH CARDIAC ARREST

Problem	Treatment	Trade Name or Device	Dosage	Side Effects or Contraindications
Hypovolemia	Crystalloid	Lactated Ringer's	50–90 ml/kg/hr IV	Hypervolemia, pulmonary edema, hypoproteinemia
Fluid loss	Hypertonic saline (7%)	Generic	5 ml/kg IV	Hypokalemia, hypernatremia, acidosis, arrhythmias
Plasma loss	Colloid expanders	Gentran 70	10–20 ml/kg IV	Hypervolemia, pulmonary edema, allergic reactions
		Hetastarch	10–20 ml/kg IV	
Blood loss	Whole blood		10–40 ml/kg IV	Hypervolemia, allergic reactions
	Blood substitute	Oxyglobin	15–30 ml/kg IV	Hypervolemia, pulmonary edema
Hypotension	See Hypovolemia			
	Phenylephrine	Neo-Synephrine	10–50 µg/kg IV	
	Epinephrine	Adrenalin	3–5 µg/kg IV	Hypertension, tachycardia, arrhythmias
	Dopamine	Intropin	3–10 µg/kg/min IV	
	Dobutamine	Dobutrex	3–10 µg/kg/min IV	
Cardiac arrhythmias				
Bradycardia	Atropine	Atropine	0.01–0.02 mg/kg IV	Tachycardia
	Glycopyrrolate	Robinul	0.005–0.01 mg/kg IV	Tachycardia
Tachycardia	Propranolol	Inderal	0.05–0.1 mg/kg IV	Bradycardia, cardiac failure
Atrial arrhythmias	Quinidine	Quinidine gluconate	4–8 mg/kg/10 min IV	Hypotension
	Diltiazem	Cardizem	0.5–2.0 mg/kg PO q8h; 5–10 µg/kg/min	Hypotension, AV block
Ventricular arrhythmias	Lidocaine	Xylocaine	2–4 mg/kg IV dogs; 1 mg/kg IV cats 40–60 µg/kg/min IV	CNS excitement
	Procainamide	Pronestyl	6–20 mg/kg/10 min IV	Hypotension
Acute heart failure	Calcium chloride		1 ml 10%/10 kg IV	
	Epinephrine	Adrenalin	3–5 µg/kg IV	Hypertension, tachycardia, cardiac arrhythmias
	Dopamine	Intropin	3–10 µg/kg/min IV	
	Dobutamine	Dobutrex	3–10 µg/kg/min IV	
Respiratory failure				
Hypoxia	O_2 nasal catheter; oxygen cage		2–4 L/min	
	Ventilation		Tidal volume = 14 ml/kg	Decreased venous return, respiratory alkalosis
Hypercarbia	Doxapram	Dopram V	1–2 mg/kg	CNS excitement
	Ventilation		Tidal volume = 14 ml/kg	Decreased venous return, respiratory alkalosis
Dyspnea	Tracheostomy			
	Chest tube			
	Ventilation		Tidal volume = 14 ml/kg	Decreased venous return, respiratory alkalosis

Sepsis	Surgery (if indicated)			
	Gentamicin	Gentocin	1–3 mg/kg q6–8h IM, IV	Muscle weakness, renal toxicity
	Kanamycin	Kantrim	10 mg/kg q6h IM	Muscle weakness, renal toxicity
	Ampicillin	Omnipen	10 mg/kg q6h IV	
	Cephalothin	Keflin	20–30 mg/kg IV q6h	Phlebitis, myositis
Metabolic acidosis	Sodium lactate*		Bicarbonate dose = base deficit × 0.3 × wt (kg) or 0.5 mEq/kg/ 10 min IV to effect	Metabolic alkalosis, hyperosmolarity, CSF acidosis hyperkalemia, hypocalcemia
	Sodium acetate*			
	Sodium bicarbonate			
Hyperkalemia	Sodium bicarbonate		0.5–2.0 mg/kg IV	As above
	NaCl 0.9% solution		10–40 ml/kg/hr IV	Hypervolemia, hypoproteinemia
	Calcium gluconate		0.5 ml/kg of 10% solution IV	Tachycardia
	Hyperventilation		Tidal volume = 14 ml/kg	Decreased venous return, respiratory alkalosis
Hypoglycemia	Dextrose 50%		1–2 ml/kg IV 0.5–1.0 g/kg/hr, 10% glucose	Hyperosmolarity
Renal ischemia	Fluids	Lactated Ringer's solution	10–40 ml/kg/hr IV	Hypervolemia, hypoproteinemia, pulmonary edema
	Mannitol 20%	Osmitrol	0.5–2.0 g/kg IV	Hyperosmolality
	Furosemide	Lasix	1.0–2.0 mg/kg IM, IV	Decreased cardiac output
Hypothermia (<36°C)	Fluids	Lactated Ringer's solution	10–40 ml/kg/hr, warmed to 37°C	Hypervolemia, hypoproteinemia, pulmonary edema
	H_2O-filled heating pad		Warmed slowly to 38°C	
Disseminated intravascular coagulation	Correct hypotension	Lactated Ringer's solution	10–40 ml/kg/hr, IV	Hypervolemia, hypoproteinemia, pulmonary edema
	Correct hypoxemia	Nasal catheter	2–4 L/min	Decreased venous return, respiratory alkalosis
		Ventilation	Tidal volume = 14 ml/kg	
	Correct acidosis	Sodium bicarbonate	0.5–1.0 mg/kg IV	
	Heparin		Dog: 500 U/kg SC q8h for 24 hr Cat: 250–400 U/kg Sc q8h for 24 hr	Bleeding
Cellular ischemia	Fluids	Lactated Ringer's solution	10–40 ml/kg/h IV	Hypervolemia, hypoproteinemia, pulmonary edema
	Mannitol	Osmitrol	0.5–2.0 g/kg IV	
	Oxygen	Nasal catheter	2–4 L/min	
	Dexamethasone sodium phosphate	Azium	4–6 mg/kg IV	
	Prednisolone sodium succinate	Solu-Delta-Cortef	>10 mg/kg IV	

Modified from Muir WW, Bonagura JD: Cardiovascular emergencies. *In* Sherding RG, ed.: Medical Emergencies. New York: Churchill Livingstone, 1985, p 52.
*Questionable efficacy during severe low-flow states.

Table 157-4. EMERGENCY DOSES OF EPINEPHRINE

Route	Dose	Comments
Intravenous		
Arrest/ventricular fibrillation	0.01–0.1 mg/kg	Dose determined by heart rate: begin at low dose
Bradycardia	0.01–0.1 mg/kg	
Intracardiac	0.01–0.02 mg/kg	Potentially arrhythmogenic
Intratracheal	0.1 mg/kg	Dilute with 0.9% NaCl (1 ml/5 kg body weight), ineffective during cardiac arrest/fibrillation

second-degree and third-degree AV block) produced by increases in vagal tone.

▼ ***Key Point*** Do not administer anticholinergics unless indicated. Anticholinergics can produce sinus tachycardia and predispose to cardiac arrhythmias and ventricular fibrillation in hypotensive patients.

Calcium Chloride

Calcium chloride and calcium gluconate have the potential to increase the force of myocardial contraction and thereby increase cardiac output and peripheral blood flow.

- IV administration of calcium chloride (1 ml/10 kg of a 10% solution) is indicated for the treatment of hyperkalemia, hypocalcemia, and inhalation anesthetic or calcium antagonist (e.g., verapamil, diltiazem) overdose.
- Do not use calcium routinely during the initial phases of CPCR because calcium-mediated cardiac injury (calcium overload) can occur.

Parenteral Fluids

Fluid therapy is mandatory during cardiac arrest in order to treat the hypovolemia and hypotension and to establish diuresis. The basic principles of IV administration of drugs described previously also apply to parenteral fluid administration. See Chapter 5 for a comprehensive discussion of fluid therapy.

▼ ***Key Point*** Administer fluids cautiously with close monitoring in traumatized patients when there is a suspicion of ongoing hemorrhage. Rapid fluid administration may facilitate uncontrolled hemorrhage and pulmonary edema, and increase mortality.

Crystalloids

- A minimum of 15 to 20 ml/kg of crystalloids to effect (e.g., lactated Ringer's solution) is needed to reverse the relative blood loss due to venous pooling and vasodilation caused by cardiac arrest.
- Replace blood loss by administering at least three times as much crystalloid as blood lost (3:1) and guide fluid therapy by changes in the packed cell volume (PCV), total protein concentration, and central venous pressure when appropriate.

▼ ***Key Point*** Do not dilute the PCV < 20% or the total plasma protein < 3.0 g/dl with crystalloids.

Colloids

Colloids (e.g., 6% hetastarch) provide colloid osmotic pressure and produce marked improvement in cardiac output and arterial blood pressure while helping to prevent blood sludging and capillary microembolization.

- Colloids are relatively confined to the intravascular fluid compartment and are used to replace blood loss in a ratio of 1:1 (thereby producing less hemodilution than crystalloids). Colloids are administered up to 5 ml/kg IV to a total volume of 20 ml/kg.

Hypertonic Saline

- Hypertonic sodium chloride solutions (3% and 7%) are extremely effective in drawing interstitial fluid into the vascular compartment, thereby increasing cardiac output and arterial blood pressure and restoring peripheral perfusion following hemorrhage in dogs and cats.
- The effects of hypertonic saline solutions can be prolonged by mixing 7% hypertonic saline with 6% hetastarch. A 7% solution of hypertonic saline in 6% hetastarch is produced by adding 70 mg of sodium chloride to each ml of 6% hetastarch. The dose of 7% sodium chloride mixed with either colloid is 5 ml/kg IV.

Blood

- Blood replacement therapy is indicated whenever hemorrhage is severe (>25 ml/kg), the PCV is <20%, or the total plasma protein is <2.5 g/dl.
- Like colloids, blood replacement therapy is administered in a ratio of 1:1 with blood loss.

Blood Substitute

- The blood substitute Oxyglobin (Biopure) is an oxygen-carrying oncotic solution and plasma expander that does not require cross-matching and has a 2-year shelf life.
- Administer 10 to 30 ml/kg/hr IV in dogs; 5 to 10 ml/kg/hr in cats, for tissue oxygenation that is equal to or better than that of blood.

Electrocardiography

Electrocardiography (ECG) can be used to detect changes in heart rate and rhythm, particularly

asystole and ventricular fibrillation (Fig. 157-3; Table 157-5).

Treatment of Bradycardia

▼ ***Key Point*** Bradycardia produced by hypoxemia or anesthetic overdose may be very difficult to treat and may require large doses of epinephrine (0.2 mg/kg IV).

- Isoproterenol (5 µg/kg IV; 1–3 ug/kg/min) may be temporarily effective in some cases of bradycardia (third-degree atrioventricular block).
- Long-term therapy is best accomplished by transvenous placement of a cardiac pacemaker.

Treatment of Ventricular Fibrillation

▼ ***Key Point*** The only consistently effective method for treating ventricular fibrillation is electrical defibrillation.

- Both external and internal techniques for converting ventricular fibrillation to sinus rhythm are successful in healthy patients that unexpectedly develop ventricular fibrillation (Table 157-6).
- The prior administration of epinephrine and lidocaine helps to reduce the energy required for defibrillation and the possibility of post-defibrillation ventricular arrhythmias, respectively.
- Use extreme care to avoid electrical injury to personnel.

Open-Chest Cardiac Massage

Open-chest direct cardiac massage may be the only way to provide adequate coronary and systemic blood flow, particularly in barrel-chested dogs and animals with penetrating chest trauma, broken ribs, pneumothorax, hemothorax, pericardial effusion, or thoracic masses.

- Consider open-chest direct cardiac compression within the first 5 minutes if closed chest compressions and IV epinephrine are ineffective.

Technique

1. After minimal skin preparation, make a skin incision at the fourth or fifth intercostal space on the left side.
2. Make a small hole in the pericardium near the apex of the heart and reflect the pericardium dorsally.
3. Compress the heart between the thumb and forefingers or in the heel of the hand, concentrating effort on the left ventricle. The usual compression rate is 60 to 80 per minute.
4. Administer epinephrine (5–10 µg/kg) into the apex of the heart (left ventricular chamber) to initiate or strengthen contractions. Much larger doses of epinephrine may be required to initiate an effective contraction in dogs and cats that have bradyarrhythmias and cardiovascular collapse produced by hypoxic arrest or anesthetic overdose. This technique can also be used during ventricular fibrillation prior to electrical defibrillation.

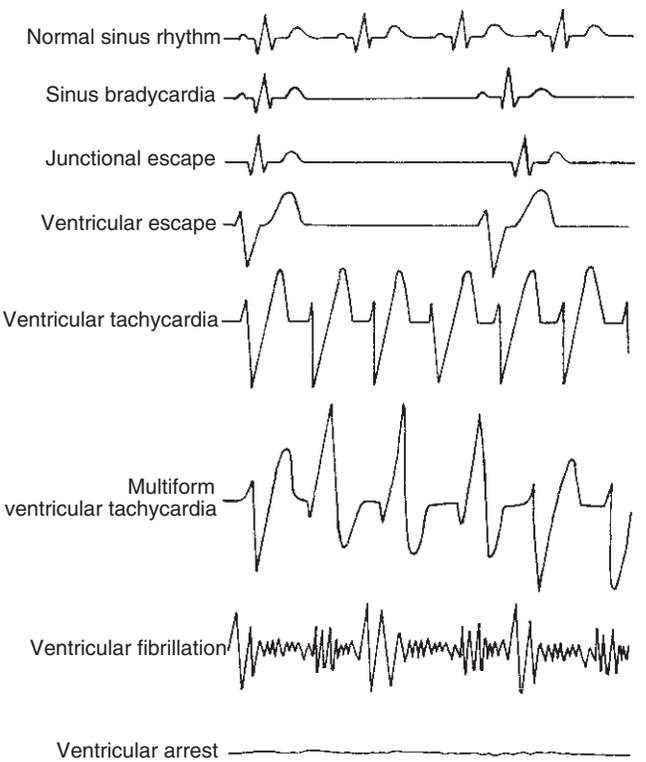

Figure 157-3. Significant cardiac rhythm patterns during cardiopulmonary cerebral resuscitation. (From Muir WW, Bonagura J: Cardiac emergencies. In Sherding R (ed): Medical Emergencies. New York: Churchill Livingstone, 1985, pp 37–93.)

PROLONGED LIFE SUPPORT

Prolonged life support incorporates all the medical and surgical methods necessary to prevent central nervous system and multiple organ failure following cardiac arrest (Table 157-7).

▼ ***Key Point*** Adequate tissue oxygenation is vital to long-term survival. Patients may require supplemental oxygen (nasal or tracheal O_2; O_2 cage) for several days following successful resuscitation. Maintain PCV <20%.

Drug Therapy

Catecholamines

Dopamine and Dobutamine

These produce dose-dependent increases in cardiac output and peripheral perfusion. Try to maintain

Table 157-5. DISTINGUISHING CHARACTERISTICS OF SEVERAL TYPES OF CARDIAC FAILURE AND ARREST

Cause	Peripheral Pulse	Auscultation of Heart Sounds	ECG	Visual Observation
Ventricular tachycardia	Weak, rapid, pulse deficit	Muffled; may be variable intensity	Wide QRS-T complexes; absence of P-QRS, large T wave relationship (see Fig. 157-3)	Disorganized, rapidly beating heart
Ventricular fibrillation	None	None	Absence of QRS-T complexes; fibrillation waves (see Fig. 157-3)	Fine to coarse rippling of ventricular myocardium
Bradycardia	Slow; may be irregular	Normal or muffled; infrequent	Infrequent or irregular P-QRS-T complexes; junctional or ventricular escape complexes (see Fig. 157-3)	Infrequent coordinated ventricular contractions
Ventricular asystole	None	None	Absence of QRS-T complexes; straight-line ECG	No cardiac improvement
Pulseless electrical activity	None or weak	None or muffled	Normal or near-normal P-QRS-T complexes	Feeble or absent cardiac contractions; systolic arterial BP < 50 mm Hg

Modified from Muir WW, Bonagura JD: Cardiovascular emergencies. *In* Sherding RG, ed.: Medical Emergencies. New York: Churchill Livingstone, 1985, p 80.

Table 157-6. DEFIBRILLATION TECHNIQUES

Ventricular Tachycardia with Severe Hypotension or Ventricular Fibrillation
Direct current fibrillators: 0.5–2.0 ws/kg internal; 5–10 ws/kg external
  Small patient (<7 kg):
    5–15 ws internal
    50–100 ws external
  Large patient (>10 kg):
    20–80 ws internal
    100–400 ws external
Alternating current defibrillators
  Small patient:
    30–50 V internal
    50–100 V external
  Large patient:
    50–100 V internal
    150–250 V external

Unresponsive Ventricular Fibrillation
Evaluate ventilation
Evaluate chest or cardiac compression
Repeat epinephrine 0.02 mg/kg (see Table 157-4)
Repeat sodium bicarbonate administration every 10 min
Administer lidocaine
Repeat electrical defibrillation (direct current; see above)

Modified from Muir WW, Bonagura JD: Cardiovascular emergencies. *In* Sherding RG, ed.: Medical Emergencies. New York: Churchill Livingstone, 1985, p 90.
ws = watt seconds; V = volts.

systolic arterial blood pressure (ABP) greater than 80 mm Hg.

- The IV infusion rate varies from 1 to 5 ug/kg/min but may be increased to 15 to 20 ug/kg/min, depending on the patient's response.
- Administer dopamine to produce heart rates ranging from 120 to 160 beats/min. Administer dobutamine or dopamine to sustain systolic blood pressure (by Doppler) >100 mm Hg.
- Dobutamine is less likely than dopamine to produce tachycardia and is preferred in patients with preexisting sinus tachycardia or supraventricular arrhythmias.
- Vasopressin has been recommended as an alternative to epinephrine, dopamine, and dobutamine to support arterial blood pressure in patients that remain hypotensive. The clinical efficacy of vasopressin in hypotensive dogs and cats with naturally occurring disease has not been validated.

Diuretics

Furosemide and Bumetanide

These highly potent loop diuretics are used to treat edema (e.g., pulmonary edema), promote diuresis, and mobilize fluids.

- The dosage of furosemide is 1 to 2 mg/kg IV.
- The dosage for bumetanide is 0.005 to 0.01 mg/kg IV.

Table 157-7. BRAIN-ORIENTED RESUSCITATION

Problem	Therapy/Drug	Dose
Hypotension	Lactated Ringer's solution	35–70 ml/kg IV
	6% Hetastarch	5 ml/kg IV
	7% NaCl	5 ml/kg IV
	7% NaCl in 6% Hetastarch	5 ml/kg IV
	Dopamine	2–5 µg/kg/min IV
	Dobutamine	1–3 µg/kg/min IV
Seizures	Pentobarbital	1–3 mg/kg IV
	Propofol	1–3 mg/kg IV
	Phenytoin	10–20 mg/kg IV
	Diazepam	0.1–0.2 mg/kg IV
Cerebral edema or increased intracranial pressure	Ventilation	$Paco_2$ 25–35 mm Hg
	Oxygenation	Pao_2 60 mm Hg
	Furosemide	1 mg/kg IV
	Mannitol	0.5–1.0 g/kg IV
	Methylprednisolone sodium succinate	5–10 mg/kg IV
Toxic cellular products*	Dimethyl sulfoxide	250–500 mg/kg IV
	Allopurinol	10 mg/kg PO

Modified from Muir WW: Brain hypoperfusion post-resuscitation. Vet Clin North Am [Small Anim Pract] 19:1151, 1989.
*These therapies await clinical verification of efficacy.

Mannitol

Mannitol (osmotherapy) produces an osmotic gradient that causes tissue dehydration and diuresis. Use mannitol (0.5–1.0 g/kg IV) if the period of cardiac arrest exceeds 3 minutes. This dose can be repeated at approximately 2 to 4 hours.

Glucocorticosteroids

Therapy with dexamethasone (Azium; 3–5 mg/kg IV) or prednisolone sodium succinate (Solu-Delta-Cortef; 10–20 mg/kg IV) has multiple benefits. These drugs can:

- Stabilize lysosomal membranes
- Reduce and prevent histamine release
- Protect against increases in capillary membrane permeability
- Cause vasodilation and inhibit phospholipase A_2 breakdown of arachidonic acid to prostaglandins and leukotrienes
- Impart a feeling of well-being

Calcium Entry Blockers

Calcium entry blockers, or calcium antagonists, are potentially beneficial in preventing reperfusion and reoxygenation injury, thereby limiting the detrimental effects of platelet aggregation and the vasoactive and membrane damaging effects of prostaglandins, leukotrienes, and other ischemia-induced (reperfusion injury) cascades.

- Diltiazem can be given at 0.5 to 2.0 mg/kg/q8h PO or 5 to 10 ug/kg/min IV for 10 minutes.
- Calcium solutions (chloride, gluconate) can be used to antagonize the negative inotropic actions of any of the calcium entry blockers.

Free Radical Scavengers

Dimethyl sulfoxide (DMSO) (250–500 mg/kg, IV) and allopurinol (10 mg/kg, PO), are experimental drugs potentially useful as oxygen–free radical scavengers. Mannitol (see previous discussion) is also an oxygen–free radical scavenger.

Heparinization

The administration of 100 IU/kg SC q6–8h of heparin is of questionable value in the post-arrest period (once hemorrhage has been controlled); it may limit the clotting cascade and microcirculatory plugging.

Sedation

- Dosages of pentobarbital (1–3 mg/kg IV) are adequate to reduce cerebral oxygen requirements and prevent seizures in most dogs and cats.
- Propofol, to effect: 3 to 4 mg/kg IV; 0.1 to 0.4 mg/kg/min.
- Phenytoin, 15 mg/kg IV, may be used for the same purpose.
- Diazepam or midazolam, 0.1 to 0.3 mg/kg IV, or an infusion, 2 to 10 µg/kg/min, is an excellent alternative to pentobarbital and produces less CNS depression.

Antibiotics

The choice of antibiotics is based on the potential for efficacy (see Table 157-3).

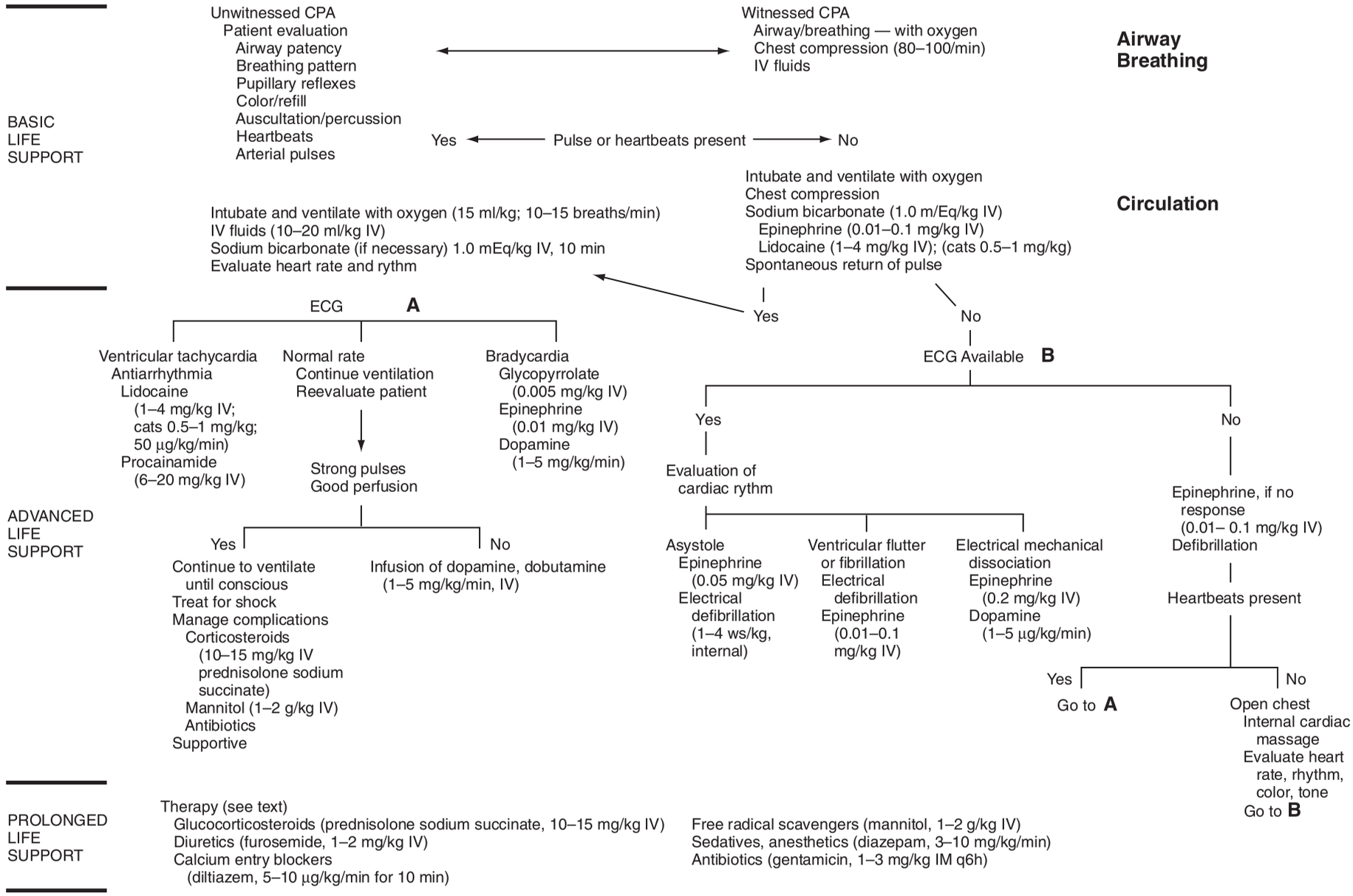

Figure 157-4. Flow chart for decision making during cardiopulmonary resuscitation. CPA: cardiopulmonary arrest.

PREDICTING OUTCOME

- Rapid recovery of eye (corneal) reflexes, upper airway reflexes including swallowing and sneezing, and spontaneous breathing are good prognostic signs.
- Continued unconsciousness, unresponsive pupils, persistent hypotension, hypothermia, and progressive deterioration of responses to physical stimulation after initial partial recovery are poor prognostic signs.

A simple algorithm for CPCR is illustrated in Figure 157-4.

Chapter

158 Diagnostic Methods in Respiratory Disease

Larry Berkwitt / James C. Prueter

This chapter briefly considers some of the more important diagnostic methods used in the recognition and assessment of respiratory disease with the goal of reminding the clinician of potential studies that may be of use in the diagnosis of upper and lower respiratory tract diseases.

UPPER RESPIRATORY TRACT

Nasal Cavity Diseases

Sneezing and nasal discharge are the principal clinical problems associated with nasal cavity and sinus diseases. A number of infectious diseases can be responsible (see Chapter 163 for additional information and diagnostic pointers). Inflammation, parasites, exudate, foreign bodies, or tumors may extend into the nasopharynx leading to gagging, reversed sneezing, or stertor. Diagnosis can be simple or highly challenging.

History

When taking the history, include:

- The chronology, progression, and duration of clinical signs, such as sneezing
- Type of nasal discharge
- Site of involvement (unilateral or bilateral)

Sneezing

- *Acute paroxysmal sneezing* typically is associated with viral rhinitis, nasal foreign body, allergic rhinitis, or trauma.
- *Chronic sneezing* suggests neoplasia, parasites, prolonged infection or inflammation (e.g., fungal rhinitis), chronic foreign body, or trauma with secondary infection or osteomyelitis.
- *Reversed sneezing* is a sign of disease or inflammation in the nasopharynx. Mites, post-nasal drip, foreign bodies, follicular rhinitis, and neoplasms are associated with this sign. When no lesions are evident, it is likely that (idiopathic) nasopharyngeal spasm is the cause.

Nasal Discharge

- Serous discharge typically is associated with acute foreign body, allergy, and viral infection.
- Mucopurulent and/or serosanguineous discharge typically is associated with viral infections (complicated by bacteria); bacterial, mycotic, and parasitic infections; long-term foreign body; neoplasia; and lymphocytic-plasmacytic inflammation.
- Hemorrhagic discharges suggest trauma, neoplasia, coagulopathy, and prolonged infection.
- Foodstuffs in the discharge suggest a communicating congenital defect (cleft palate) or acquired oro-nasal fistula.

Duration of Clinical Signs

- Sudden onset of signs suggests foreign body, viral infection, trauma, or coagulopathy.
- Chronic signs are associated with neoplasia, infection, foreign body, parasite infection, chronic inflammation, or congenital defect.

Site of Involvement

- Unilateral discharge suggests early neoplasia, foreign body, early infection, dental disease, or trauma.
- Bilateral discharge suggests chronic infection or inflammation, chronic foreign body with resulting infection/osteomyelitis, advanced neoplasia, coagulopathy, pneumonia, parasites, allergy, or trauma.

Physical Examination

A complete physical examination includes a thorough evaluation of the oral cavity, mucous membranes, tonsils, hard and soft palate, retropharyngeal area, regional lymph nodes, and teeth. Heavy sedation and/or anesthesia are generally required if the nasal cavity, nasopharynx, or larynx will be examined (see below).

- Identify swelling and asymmetry of the face, palate, or eyes (exophthalmos) that might suggest neoplasia, fungal infection, or trauma.

- Identify areas of pain that may localize the disorder.
- Evaluate for loss of patency of one or both nasal passages.
- Note ocular discharge that may be associated with nasolacrimal duct inflammation and/or obstruction secondary to inflammation or neoplasia.
- Identify cracked, loose, and infected teeth.

Complete Blood Count (CBC), Serum Chemical Profile, and Coagulation Screen

These evaluations are important when systemic diseases may be an underlying cause of signs. Although clotting disorders can cause epistaxis, it is far more commonly associated with platelet disorders such as immune-mediated thrombocytopenia, von Willebrand's disease, thrombocytopathia (drug-related or from hyperglobulinemia), or ehrlichiosis.

Serology

- Serologic tests such as immunodiffusion and enzyme-linked immunosorbent assay (ELISA) for aspergillosis and penicilliosis antibodies and for cryptococcal capsular antigen can be used for diagnosis of mycotic rhinitis. However, false-negative results are common, limiting the usefulness of serology. Molecular methods of diagnosis, confined to reference laboratories, are used for agents such as *Bartonella* spp.
- Direct observation, cytology, culture, and biopsy are more reliable than serology for identifying nasal fungi.

Radiography

- General anesthesia is essential for proper positioning and for prevention of motion artifacts.
- Include the following radiographic views (see Chapter 4):
  - Open-mouth ventrodorsal projection
  - Intraoral (occlusal)
  - Rostral-caudal frontal skyline
  - Lateral
  - Oblique skull views, particularly if dental arcade problems are suspected

Computed Tomography (CT) and Magnetic Resonance Imaging (MRI)

- Use CT of the nasal cavity and skull to delineate the extent of masses, loss of turbinates, bony lysis, midline shifts, or accumulation of fluid.
- Use MRI for better definition of brain involvement from invading nasal tumors (see Chapter 125).

Nasal Flushing for Cytology and Biopsy of Nasal Tissue

Nasal cytologic evaluation is often of little or no value unless it is performed with aggressive nasal flushing or by rhinoscopic visualization with the animal under anesthesia. Biopsy samples can be obtained under direct visualization, or by a blind method, guided by results of clinical examination and imaging. Retrograde rhinoscopy is needed to biopsy caudal masses or lesions extending into the nasopharynx.

- Perform aggressive nasal flushing with a polypropylene (rigid) male urinary catheter. Measure the length (nares to medial canthus) prior to insertion to avoid penetrating past the cribriform plate.
  - Perform intermittent flushing and suctioning via syringe to obtain as much nasal fluid and/or tissue fragments as possible.
  - Place gauze sponges in the nasal pharynx to catch any tissues that may be extracted during the flushing procedure.
  - Submit samples for culture, cytology, and histopathology.
- Small and medium-sized clamshell forceps can be used to obtain biopsy samples with or without benefit of rhinoscopy.

Rhinoscopy

Rhinoscopic examination under anesthesia allows visualization of mucosal lesions, masses, or foreign bodies. Biopsy and procurement of specimens for cytology, culture, and sensitivity can be guided by direct visualization. Different instruments are often used to evaluate the nostrils and cranial nasal cavity versus the posterior choane and nasopharynx (the passage located dorsal to the hard and soft palate). A flexible scope is superior for retrograde rhinoscopy, though it may be possible to evaluate the nasopharynx with a dental mirror, spay hook (to pull the soft palate cranioventrally), and a bright light. Polyps in cats are often visible simply by pulling the soft palate forward. Instrumentation for rhinoscopy can include any of the following:

- A flexible cytoscope or rhinoscope with an outer diameter of 2 mm is preferred.
- An otoscope with bright light source may be used for antegrade rhinoscopy.
- An arthroscope or cystoscope with an outer diameter of 1.9 to 5 mm will be useful in larger dogs.
- A bronchoscope with an outer diameter of 2.9 to 5 mm will be useful in larger dogs.
- Flexible pediatric bronchoscope.

Surgical Biopsy

- Exploratory rhinotomy with removal of a bone flap (see Chapter 160) provides complete exposure of the nasal cavity for biopsy, foreign body retrieval, culture, and debridement of diseased tissue.
- Drainage tubes can be placed at the time of surgery for treatment of bacterial and/or fungal infections.

Laryngeal Diseases

History

Clinical signs of laryngeal disease often are slowly progressive, and the owner may have noted them for an extended period of time. Laryngeal paralysis is common in a number of breeds (see Chapter 161).

- The owner may report hoarseness, progressive changes in voice, or complete loss of voice.
- Noisy respirations characterized by high-pitched inspiratory stridor or by mild, raspy, or fluid-sounding noise are common.
- Choking, gagging, and coughing may be observed, particularly while the animal is eating and/or drinking. This often worsens as the disease progresses or if there is concurrent pharyngeal disease.
- Exercise intolerance, cyanosis, and syncope may be observed in patients with laryngeal obstruction (e.g., laryngeal collapse, paralysis, foreign body, or neoplasia). Problems are exacerbated in high heat and humidity.

Physical Findings

- The most common physical findings in laryngeal disease are inspiratory dyspnea and stridor. Auscultation can detect upper respiratory inspiratory stridor ("wheeze") or lower-pitched obstructive sounds centered over the larynx.
- Palpation of the laryngeal area may detect the site of pain, fractures, and subcutaneous emphysema in cases of trauma and asymmetry due to neoplasia, granulomas, laryngitis, or unilateral muscle atrophy.
- The gag reflex may be decreased in some cases of laryngeal paralysis.

Laryngoscopy/Bronchoscopy

- Perform direct visualization under a *light* plane of anesthesia for evaluation of pharyngeal structures, soft palate, and laryngeal motor function. Tiletamine HCl/zolazepam HCl (Telazol) can cause laryngeal paralysis, so another form of sedation should be used. Propofol also depresses laryngeal motion. The use of doxapram has been advocated to stimulate the respiratory center to decrease the number of false positive examinations.
- Observe laryngeal (arytenoid) movement during both phases of respiration. Often asymmetry is observed between the left and right arytenoids and vocal folds. Be certain not to confuse passive abduction during expiration with active movements.
- A bronchoscope allows the best evaluation of the pharynx and the subglottic area for masses, infiltrates (areas of discoloration), granulomas, and polyps. In cats, laryngeal paralysis is often related to invasion by a neoplasm.
- Aspiration or brush cytology and endoscopic biopsy may be performed at the time of examination, if appropriate. Following laryngeal biopsy, the patient should be closely observed, as postsurgical edema or hemorrhage at the biopsy site may result in airway obstruction.

Radiography and Ultrasound

- A lateral radiograph of the larynx is rarely diagnostic but may demonstrate:
  - Dilated lateral saccules in cases of paralysis
  - Soft tissue swelling and/or asymmetry caused by neoplasia or trauma
  - Fractures, dislocations, or subcutaneous air caused by trauma
  - Elongated soft palate
  - Collapsed or ruptured trachea
- Thoracic radiographs may reveal chronic pulmonary or cardiac disease associated with upper respiratory diseases.
- Ultrasonography has been effective in the recognition of laryngeal disease and paralysis.

Electromyography

Abnormal electromyographic studies of the laryngeal muscles may be associated with neuromuscular, immune-mediated, and hypothyroid-related laryngeal disorders.

Thyroid Function Testing

Uncommonly patients with acquired laryngeal paralysis may have subnormal levels of triiodothyronine (T3), thyroxine (T4), and free T4 as well as abnormal results of TSH assay.

Histopathology

Histopathology of any abnormal growth or mass is important in order to differentiate chronic granulomatous disease and neoplasia and may also be useful in a generalized case of polyneuropathy.

Tracheal Diseases (see also Chapter 161)

History

- Usually there is a chronic, nonproductive, dry "honking" cough with intermittent attacks of dyspnea, particularly elicited with excitement, exercise, drinking, eating, or tracheal pressure (e.g., digital pressure or collar).
- Dyspnea and occasionally cyanosis may be demonstrated.
  - Inspiratory dyspnea and stridor develop if the cervical or extrathoracic trachea collapses.
  - Expiratory dyspnea is evident with intrathoracic tracheal collapse.

- Both phases of ventilation, especially expiration, are abnormal if the entire trachea is involved.

Physical Examination

- Tracheal palpation may demonstrate "sharp" edges or angles of the collapsible margins of the trachea.
- Cardiac examination is important to differentiate tracheal disease from primary cardiac disease and for evaluation of coexisting chronic cardiac disease (see Chapter 142).
- Auscultate the entire respiratory tract to localize primary abnormalities and to differentiate tracheal disease from lower respiratory tract disease (see Chapter 163).

Radiography

Radiographic examination (ventrodorsal and lateral views) is mandatory for routine evaluation of the cervical and thoracic trachea (see Chapter 159).

- Careful positioning avoids artifactual deviations of the trachea.
- Obtaining both inspiratory and expiratory films identifies an intermittently collapsing trachea or bronchus (this may be difficult or impossible in small-breed dogs).
- Survey radiography has limited sensitivity and specificity for diagnosis.
- Fluoroscopy may permit evaluation of dynamic tracheal functions and intermittent tracheal or principal bronchus collapse.

Transtracheal Wash

Perform an endotracheal wash (via a sterile endotracheal tube) for cytology, fluid analysis, and microbiologic evaluations to identify initiating or complicating factors that may be important in the treatment regimens. The procedure is discussed below.

Tracheoscopy

Tracheoscopy can be used to visualize anatomic lesions, tracheal collapse, hypertrophy of dorsal tracheal ligament, parasitic granulomas, foreign bodies, or neoplasia. Extreme care must be taken because of the potential of worsening airway collapse by trauma and iatrogenic irritation. In toy breeds with obvious tracheal collapse, the procedure is rarely needed except to guide surgery or stent placement. Tracheoscopy is very helpful for uncertain diagnoses or for those cases in which there is concern for a neoplastic or polypoid mass lesion, congenital defects, or concurrent mainstem bronchial collapse. As the patient must be extubated for diagnosis, supplemental oxygen should be supplied either through or around the endoscope proximally (with a small, flexible tube) during this examination. See "Bronchoscopy" in the bronchopulmonary section for further discussion of this procedure.

BRONCHOPULMONARY AND PLEURAL DISEASES

The diagnosis of diseases of the respiratory tract and pleural space depends on information obtained from a thorough history, a physical examination, and a series of ancillary tests that are well conceived and organized so as to limit the patient's discomfort and stress.

When evaluating the dyspneic patient, use sound clinical judgment in selecting tests that will aid in the diagnosis but will not place the patient in further respiratory distress. Often these patients must be stabilized, based on the physical examination, history, and dorsoventral thoracic radiograph, prior to performing other tests.

History

Coughing, tachypnea, dyspnea, and exercise intolerance are the principal signs associated with bronchopulmonary and pleural disease.

- Determine the patient's signalment, because certain breeds or age groups are more susceptible to particular diseases. For example, small and toy breed dogs are more susceptible than large breed dogs to lower respiratory disease secondary to a collapsing trachea. Cocker spaniels are prone to chronic bronchitis.
- Note the client's complaint. Determine if the patient's problem is acute or chronic and if it is improving, unchanging, or progressive.
- When evaluating a cough, determine the time of day of the cough. Cardiac coughs are usually nocturnal, whereas an infectious cough will occur throughout the day.
  - Determine the quality of the cough, such as dry hacking (nonproductive) or moist (productive).
- Note prior medical and travel history.
  - It is imperative to know what medications have been given previously and what medical response was obtained.
  - Consider geographically distributed diseases (e.g., systemic mycoses) in pets that travel or have lived in various locations.
  - Determine the patient's recent exposure to other pets that might be a source of infectious disease (e.g., in a kennel or grooming situation).
- Note the patient's current medical history. Do not overlook routine history questions about water consumption, appetite, and eliminations, because this information can give insight into the diagnosis of a systemic disease with pulmonary manifestations (e.g., hyperadrenocorticism leading to thromboembolism).

Physical Examination

Perform a complete physical examination.

- It is important to evaluate each body system, because key diagnostic physical findings may be present and pulmonary complications of heart disease may be evident. For example:
  - A remote lesion, such as a rectal carcinoma, may be the source of metastases that cause dyspnea and abnormal lung sounds.
  - In a coughing patient, skin lesions in endemic areas and lymphadenopathy suggest a diagnosis of blastomycosis.
  - A potbellied appearance, endocrine alopecia, and acute dyspnea may lead to a diagnosis of hyperadrenocorticism.
- Physical examination of the lower respiratory system and pleural space includes observation, auscultation, palpation, and percussion (see also Chapter 142).

Observation

Observe the patient's rate and pattern of breathing. Certain diseases cause inspiratory versus expiratory dyspnea.

- Note whether the patient is barrel-chested or overweight.
  - Barrel chest may indicate chronic obstructive pulmonary disease.
  - Pickwickian-type syndrome in obese animals may account for breathing problems.
- Slow, deep breathing with inspiratory difficulty can be due to large upper airway obstructive disease.
- Short, shallow breathing may be associated with restrictive disease.

Pulmonary Auscultation

Pulmonary sounds usually are classified as normal or vesicular, bronchial, or bronchovesicular (see Chapter 142). Adventitious sounds include crackles (rales), wheezes, stridor, rhonchi, and rubs.

- As air travels through the lung, it produces vesicular or bronchovesicular sounds. Depending on the medium through which the air travels (e.g., fluid or mucus) or if there are changes in diameter of diseased airways, the sound is modified (e.g., crackles, rhonchi, wheezes).
- Identification of crackles (small airway or parenchymal disease), rhonchi (airway disease or exudate), and wheezes (airway obstruction) indicates a need for additional diagnostic studies.

Percussion

The lungs and thoracic cavity emit a specific resonance when percussed by striking the second phalanx (p) of the middle finger positioned on the chest with the knuckle joint (p1–p2) fully extended (see Chapter 142).

- Dull resonance is associated with increased density (fluid or mass lesion) within the underlying pleural space or lung.
- Increased resonance (drum-like) is associated with increased air within the pleural space or lung.

As an example of incorporating all parts of the physical examination, consider the patient that has a mammary mass with louder or adventitious lung sounds on auscultation and dull percussion on the left side of the thoracic wall. This patient may have pleural effusion associated with metastatic disease. If dull percussion is present without lung sounds, suspect a consolidating mass lesion.

Thoracic Imaging—Radiograph, Ultrasound, and CT (see also Chapter 159)

Standard radiographic views include inspiratory lateral and ventrodorsal views.

- To evaluate for metastatic lung disease, right and left lateral projections with the ventrodorsal view may be helpful, and are strongly recommended.
- In a dyspneic, unstable patient, a single dorsoventral view is recommended to avoid unnecessary stress and to enable the clinician to initiate stabilizing therapy prior to further evaluation.

Evaluation of Radiographs

- Good-quality radiographs are important because excess motion or underexposure may result in false information regarding the pulmonary interstitium (see Chapter 4). Expiratory films may cause the pulmonary interstitium to have an increased density that can be mistaken as abnormal.
- To evaluate thoracic radiographs:
  - Determine the type of radiographic infiltrative pattern present, such as interstitial, alveolar, bronchial, vascular, or combinations of these.
  - Characterize the location of the infiltrate as localized or diffuse; cranial or caudal; and ventral, dorsal, or hilar.
  - Pleural effusion is indicated by blunted costophrenic angles, pleural fissure lines, and ventral scalloping of the lungs on the lateral projection.
- Thoracic ultrasound is valuable for detection of small amounts of fluid, for visualization of consolidated areas of lung and for larger mass lesions, and for identification of mediastinal mass lesions. This method, which requires advanced training for optimal use, can also guide tissue sampling.
- Computerized tomography is helpful for the detection of smaller pulmonary and pleural lesions, including metastatic lesions of the lung and pleural space, and of the presence or absence of hilar lymphadenopathy. The study may help to distinguish pulmonary mass lesions from mediastinal or esophageal

mass lesions. This is a referral examination in most cases.

Complete Blood Count

The CBC may be helpful in evaluation of respiratory disease. For example:

- Leukocytosis can indicate infection or inflammation.
- Polycythemia is associated with chronic hypoxemia.
- Eosinophilia may suggest a parasitic or allergic disease.
- Nucleated red blood cells may indicate acute hypoxemia.

Serum Chemistry Profile

No single segment of the standard automated serum chemistry profile is pathognomonic for respiratory system disease; however, this study is useful as a baseline to evaluate other organ systems. For example:

- If a patient has a localized anterior ventral alveolar infiltrate, calcification of the airways, neutrophilic leukocytosis, lymphopenia, and eosinopenia with elevated alkaline phosphatase and cholesterol levels, a tentative diagnosis of bacterial pneumonia secondary to hyperadrenocorticism might be made pending confirmatory tests.
- D-dimers may be elevated with pulmonary thromboembolic disease. The test is not specific, but a negative test argues against a diagnosis of thromboembolic disease.

Arterial Blood Gas (ABG) Analysis and Pulse Oximetry

The ABG specimen usually is drawn from the femoral artery, dorsal pedal artery, or an indwelling arterial catheter. ABG arterial analysis evaluates the patient's ability to oxygenate arterial blood. Pulse oximetry is a measure of the functional status of the patient in terms of hemoglobin saturation. Patients with saturations below 90% require immediate attention; this typically correlates to a partial pressure of oxygen of <70 mm Hg.

- In the normal patient breathing room air, the partial pressure of oxygen should be >95 mm Hg. In recumbent patients the values often are lower, but should still be >85 to 90 mm Hg.
- When the level is <60 mm Hg, respiratory failure is present.
- Elevations in CO_2 indicate ventilatory failure and contribute to respiratory acidosis. If a patient has decreased Pao_2 and increased Pco_2 the prognosis is guarded to poor.
- Alveolar-arterial oxygen difference ($A\text{-}aDO_2$; normal 4–17 mm Hg) is a parameter of gas exchange efficiency calculated as (150—$PaCO_2$)—PaO_2 when breathing room air at sea level, or using the standard full formula.

Serology and Molecular-based Tests

Specific serologic- and molecular-based evaluations aid in the diagnosis of fungal, rickettsial, and obligate intracellular microorganisms, as well as some immune-mediated diseases.

Fecal Examination

To establish the diagnosis of parasitic lung disease, evaluate fecal specimens by direct smear, flotation, and sedimentation techniques (available from commercial laboratories). Fecal sedimentation is an important tool for the detection of lungworm larvae (e.g., *Filaroides, Aelurostrongylus*) that otherwise could be overlooked if flotation is used.

Transtracheal Washing

Tracheal washing is a simple, inexpensive procedure in which warm sterile saline is instilled in the lower respiratory tract and then retrieved. Use this technique to obtain specimens for cytologic and microbiologic evaluation of the lower respiratory tract to aid in the diagnosis of bronchopulmonary disease.

Technique

1. In *dogs,* insert a long through-the-needle catheter (12 or 18 inches) percutaneously under local anesthesia between the tracheal rings or through the cricothyroid membrane and then advance it into the lower airway. Alternatively, an endotracheal wash can be performed under general anesthesia by placing a sterile urinary catheter through a sterile endotracheal tube. This approach is better for cats, small dogs, or animals with primary tracheal diseases.
2. In *cats,* use an open-end urinary catheter placed through a sterile endotracheal tube or adapt a 3-way stopcock or syringe adaptor directly to the endotracheal tube.
3. The catheters ideally should extend to the level of the tracheal bifurcation.
4. Inject warm sterile saline (6 ml in cats and small dogs; up to 20 ml in large dogs) through the catheter.
5. After instillation of the fluid, induce coughing by gently slapping the rib cage bilaterally (in awake patients).
6. Retrieve the fluid from the airway by aspiration with a syringe. In anesthetized patients, continual suction with a mucous trap provides the best results.
7. Prepare samples of the lavage fluid for cytology, culture, and sensitivity testing.
8. Any fluid remaining in the airways is harmless because it is rapidly absorbed by the pulmonary lymphatics.

Bronchoalveolar Lavage and Bronchoscopy

Bronchoalveolar Lavage

This is an effective method for retrieving diagnostic material from the lung and is particularly useful in alveolar-interstitial lung diseases and in tachypnea/dyspnea when prominent cough is absent. Proper performance of this study and bronchoscopy require advanced training.

Technique

1. Advance a flexible fiberoptic bronchoscope into the bronchial tree.
2. Visually locate the diseased area and wedge the bronchoscope within the bronchus.
3. Instill 20–30 ml of warm saline (for a 15 kg dog) through the bronchoscope channel and then retrieve it. Thoracic coupage may facilitate fluid retrieval.
4. Prepare samples for cytology, quantitative cell counts, culture, and sensitivity testing.

Bronchoscopy

Bronchoscopy allows direct visualization of the lower airway to the level of the third, fourth, or fifth bronchial divisions, depending on the size of the patient and the length and diameter of the bronchoscope.

- Bronchoscopy is a valuable alternative when no diagnostic material is obtained using the tracheal wash procedure. This can occur because there is not enough cellular material present within the airway, because the catheter is too short to retrieve any material, or because the disease is unilateral.
- Diseased areas can be directly visualized, and the exudate or tissue can be removed for cytology or histopathology.
- If there is no visible material present, bronchial brushing or bronchoalveolar lavage can retrieve cells that may aid in a diagnosis.
- Direct biopsy of visible lesions can be performed through the bronchoscope as well as through transbronchial lung biopsy, which is described in the following section.

Lung Biopsy

When the cause of diffuse lung disease cannot be determined using one of the methods described previously, consider a lung biopsy. The types of lung biopsy procedures performed in small animals include:

- Fine-needle aspiration
- Bronchoscopy
- Ultrasound- or CT-guided biopsy
- Mini-thoracotomy
- Thoracoscopy (referral centers)

Fine-Needle Aspiration

The simplest, most cost-effective procedure is fine-needle aspiration. This is usually performed on diffuse or large, superficial lesions within the parenchyma or pleural space. Peripheral lesions well visualized with ultrasound are best suited for this procedure.

Technique

1. Clip and surgically prepare the thoracic wall and instill a local anesthetic at the site. In a fractious patient, a light plane of anesthesia is preferable.
2. Attach a 22-gauge needle to a short extension set and 6cc. syringe. A spinal needle is preferred because of its length.
3. Visualize the lesion with ultrasound. Place the needle into the lesion, and with multiple short strokes take a sample each time.
4. Use the syringe to empty the sample onto a slide. This same procedure can be used to obtain samples from other organs with ultrasound guidance.

Bronchoscopic Biopsy

A lung biopsy can be obtained utilizing the bronchoscope. This method is used with deeper, more central lesions and ideally should be performed under fluoroscopy. The endoscopic biopsy forceps are passed through the bronchial wall into the pulmonary parenchyma.

Keyhole Lung Biopsy

The most invasive type of biopsy is performed via a mini-thoracotomy.

Technique

1. Make an incision 3 to 7 cm long between the ninth and tenth ribs.
2. Bring the lung tissue into the incision, place a ligature or staple around the affected area of lung, and remove the sample.
3. Inspect the stump for hemorrhage or air leak.
4. Thoracic tube should be placed, and the patient observed for 24 hours.
5. Remove the tube after obtaining negative aspirations.

Potential Risks of Biopsy

Because of the risk of hemorrhage and pneumothorax with each of these procedures, postbiopsy monitoring is essential.

- Open-lung biopsy decreases the risk of pneumothorax because the biopsy site is visualized and all leakage can be controlled.

- In fine-needle aspiration, withdrawal of infectious material can contaminate the pleural space and cause pyothorax.

Thoracocentesis

The diagnosis of pleural effusion generally depends upon analysis of pleural fluid obtained by thoracocentesis (see Chapter 3 and Chapter 164 in this section). Thoracocentesis can also be therapeutically beneficial. Perform the procedure with minimal stress to the patient.

Electrocardiography and Ultrasonography

Often, it is difficult to determine whether a patient's problem is respiratory or cardiovascular.

- With pulmonary hypertension secondary to thoracic disease, the electrocardiogram may show P-pulmonale evidenced by p waves >0.4 mV and deep s waves in leads I, II, III, and aVF.
- When pulmonary hypertension is suspected, pulmonary artery pressure and flow velocity should be measured with Doppler echocardiography.
- Ultrasonography can identify specific cardiac abnormalities and masses within the mediastinum, pleural space, and pulmonary parenchyma (see Chapters 4 and 159). Echocardiography can help to rule out cardiac disease as a cause of respiratory signs.

Other Specialized Diagnostic Tests

Other useful tests include thoracoscopy, bronchography, lymphangiographic studies for evaluation of chylothorax, computed tomography, magnetic resonance imaging, vascular and radioisotopic studies to identify pulmonary thromboembolism, and pulmonary function testing. These procedures, if necessary, are performed at referral centers.

Chapter

159 Diagnostic Imaging in Respiratory Disease

Valerie F. Samii

INDICATIONS FOR RADIOGRAPHIC EVALUATION

Radiography is commonly used for evaluating respiratory disease in small animals. Thoracic examinations can be performed rapidly and noninvasively, often without the need for patient sedation. Serial evaluations of the thoracic cavity are often performed to monitor resolution or the advancement of pathological processes. Although radiography is a sensitive method for detecting respiratory disease, changes are often nonspecific, and similar radiographic findings may be seen in different disease processes.

▼ ***Key Point*** Radiographic findings need to be assessed in light of the patient's clinical and physical examination findings.

RADIOGRAPHIC ANATOMY

- Radiographic evaluation of the nasal cavity and nasopharynx is best accomplished with the patient under general anesthesia. The open-mouth, ventrodorsal view of the maxilla is the best view for assessing disease within the nasal passages. Mirror image symmetry between the right and left nasal passages, on either side of the nasal septum, should be observed. Nasal turbinates appear as thin, lacy mineralized structures surrounded by air. Occasionally, deviation of the nasal septum is seen as a variation of normal. The frontal sinuses are typically underdeveloped in dogs with congenital hydrocephalus or with a domed cranium conformation (e.g., Chihuahua).
- Radiographic evaluation of the upper airways, to include the nasopharynx, oropharynx, larynx and trachea, is best accomplished with the patient in lateral recumbency. The soft palate and epiglottis are well outlined by air. The larynx is ventral to the first two cervical vertebrae. The bones of the hyoid are easily identified and should not be mistaken for foreign bodies. Mineralization of the laryngeal and tracheal cartilages is a common finding, particularly in older dogs and chondrodystrophic breeds. The normal larynx is slightly wider than the trachea.
- The trachea should be uniform in diameter throughout its length. The trachea is typically positioned to the right of midline in the cranial thorax. The cartilaginous tracheal rings are incomplete dorsally in the dog. Calculation of the ratio of tracheal diameter to thoracic inlet diameter is one way used to assess tracheal size. The normal ratio in non-brachycephalic breeds is 0.20 ± 0.03. The ratio is slightly smaller in brachycephalic breeds.

▼ ***Key Point*** The dorsal trachealis muscle may relax and protrude into the tracheal lumen at the level of the thoracic inlet in normal dogs.

- The following structures should be visible on a normal thoracic radiograph: the cardiac silhouette, pulmonary arteries and veins, caudal vena cava, descending aorta, trachea, primary bronchi, diaphragm, and (in young animals) the thymus.
- The following structures are often not seen on a normal thoracic radiograph: the cranial vena cava; aortic arch; brachycephalic trunk; esophagus; secondary and tertiary bronchi; and the mediastinal, tracheobronchial, and sternal lymph nodes. It is not uncommon to see small amounts of gas in the cranial to mid-thoracic esophagus, particularly in a sedated or aerophagic animal. It is also not uncommon to see a small amount of fluid (soft tissue opacity) in the caudal thoracic esophagus, particularly when the animal is in left lateral recumbency.
- Radiographically the pulmonary vessels account for the majority of the pulmonary patterns observed on normal films. The pulmonary arteries and veins should be matched in size.
  - On the lateral thoracic radiograph, the artery lies dorsal to its corresponding vein. On the dorsoventral (DV) or ventrodorsal (VD) radiograph, the artery lies abaxial to its corresponding vein. Hence,

*The author would like to acknowledge the contributions to this chapter made by Dr. C. Wendy Myer, Diplomate ACVR.

veins are central and ventral relative to their corresponding arteries.
  - On the lateral radiograph, the diameter of the cranial lobar vessels should be roughly the width of the fourth rib as it crosses that rib. The diameter of the caudal lobar vessels should be roughly the width of the ninth rib as it crosses that rib. Vessels should be linear, soft tissue opacities that taper toward the periphery of the lung.
- The bronchi are thin-walled structures that appear as paired, soft tissue opaque lines running parallel to vessels in the longitudinal plane, and as thin-walled doughnuts in the cross-sectional plane. Bronchial wall mineralization may be seen in older animals.

TECHNICAL CONSIDERATIONS

Two orthogonal radiographic views of the thorax should be obtained. Standard views include either a right or left lateral and VD or DV radiographs. The cross-bars of the collimator should be positioned just caudal to the scapula.

Thoracic radiographs should be made using a high kVp and a low mAs to increase image latitude. Exposure times should be fast, not longer than $^{1}/_{60}$ second, to diminish the effects of cardiac and respiratory motion. In tachypneic or panting animals, temporarily holding or blowing into the animal's nose may briefly cease respiratory motion.

▼ ***Key Point*** Thoracic radiographs should be exposed at peak inspiration using proper technique to evaluate the pulmonary parenchyma. Poorly aerated or underexposed lung will appear diffusely increased in opacity and may be misinterpreted as interstitial disease.

- Inspiratory and expiratory radiographs with the patient in lateral recumbency may be used to demonstrate dynamic tracheal or bronchial collapse if fluoroscopic imaging is unavailable.
- Inspiratory and expiratory radiographs with the patient in DV or VD positioning may be used to demonstrate diaphragmatic paralysis if fluoroscopic imaging is unavailable.
- For animals with moderate to severe pleural effusion, if a VD is tolerated, it is preferred to the DV radiograph to better assess the cardiac silhouette and pulmonary parenchyma. Pleural effusion will increase the overall opacity of the pulmonary structures due to summation. Also, pulmonary opacity will increase due to lung underinflation secondary to fluid in the pleural space.

Effect of Gravity on the Dependent Lung

When an animal is placed in lateral recumbency, the lung closest to the cassette becomes partially atelectatic and receives more blood volume and less air than the 'up' lung. This decreases contrast resolution in the dependent lung and the lung will have an increased soft tissue opacity. Therefore, pulmonary pathology that might be readily apparent on other radiographic views may be difficult to see when in the dependent lung. This is particularly apparent in portions of lung that are adjacent to or summate with the mediastinum, cardiac silhouette, or diaphragm. Thus, soft-tissue opaque pulmonary structures are best seen radiographically when they are in the better aerated, nondependent, 'up' lung. For this reason, both right and left lateral views of the thorax are commonly taken to screen for pulmonary metastatic disease.

Follow-Up Studies

▼ ***Key Point*** When performing recheck examinations, it is important to use similar radiographic techniques and positioning to facilitate the comparison of studies.

This is especially critical in animals with unilateral pulmonary disease (i.e., lobar pneumonia, primary pulmonary neoplasia) because pathological changes in the dependent lung may not be well appreciated on the lateral radiographic views. Accurate assessment of pleural fluid volume is also difficult when comparing DV and VD projections, even when the two radiographs are taken during the same examination. Depending on the initial thoracic pathology and the degree of resolution or advancement, additional radiographic exposures using modified techniques may be helpful.

RADIOGRAPHIC ABNORMALITIES OF THE NASAL CAVITY

- Rhinitis and neoplasia may cause focal or diffuse increases in radiographic opacity of the nasal passage. Turbinate destruction is often present in animals with neoplasia or erosive rhinitis. Most cases of bacterial or foreign body rhinitis involve the rostral and middle portions of one or both nasal passages. Most nasal neoplasms originate from one nasal passage but may extend into the other.
- Fungal rhinitis, such as aspergillosis, often causes osteomyelitis with a productive osseous component, most notably involving the frontal sinuses. There may be a diffuse *decrease* in radiographic opacity of the nasal passages due to the complete destruction of turbinates, which is followed by the animal sneezing them out. Fungal rhinitis often involves the entire nasal cavity.
- Neoplastic processes often appear more destructive than rhinitis. The mass effect caused by some neoplasms may result in displacement of normal nasal structures and distortion of anatomical structures.

Definitive diagnosis of nasal disease is generally not possible radiographically. Rhinoscopy with biopsy, cytology, and/or culture is necessary.

RADIOGRAPHIC ABNORMALITIES OF THE NASOPHARYNX, OROPHARYNX, AND LARYNX

- Upper airway diseases such as brachycephalic upper airway obstruction syndrome, laryngeal paralysis, and laryngospasm are best evaluated using visual examination externally or endoscopically.
- Masses, such as neoplasia, nasopharyngeal and oropharyngeal polyps, abscesses, and granulomas, may appear radiographically as soft tissue opacities within the airways. These masses may or may not have internal mineralization.
- Masses outside the larynx or pharynx are more difficult to identify because they are not surrounded by gas. These lesions may be identified based on their encroachment of air-tissue interfaces.

RADIOGRAPHIC ABNORMALITIES OF THE TRACHEA (Fig. 159-1)

- Tracheal hypoplasia is a congenital disorder seen most commonly in brachycephalic breeds, particularly English Bulldogs. The tracheal diameter is diffusely decreased and in severe cases, the ratio of tracheal diameter to thoracic inlet diameter may be reduced to less than 0.10.
- Tracheal displacement by regional soft tissues is a reliable sign of mass lesions once positioning artifacts and breed characteristics have been considered.
- Except for tracheobronchial and mediastinal lymphadenopathy and severe cardiomegaly, lesions causing significant attenuation of the tracheal lumen usually originate within the trachea.

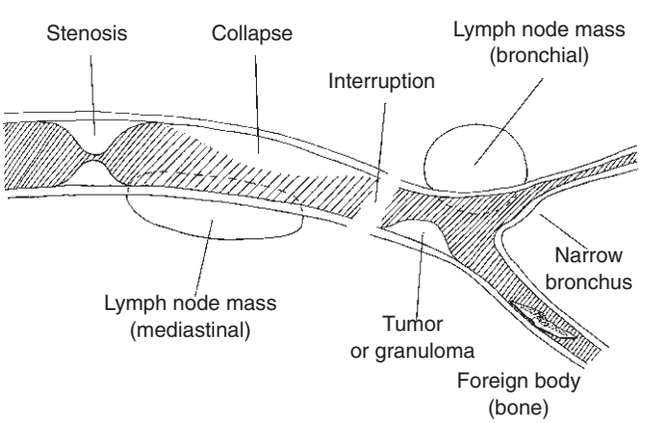

Figure 159-1. Schematic representation of various causes of tracheobronchial disease.

- Masses, such as neoplasia, polyps, abscesses, granulomas, and foreign bodies, may appear radiographically as soft tissue opacities within the airways. These masses may or may not have internal mineralization. Tracheal neoplasia is rare in small animal patients.
- Tracheitis, secondary to upper airway inflammation, may cause transient luminal narrowing due to tracheal mucosal swelling and must not be incorrectly diagnosed as tracheal hypoplasia.
- Tracheal perforation usually occurs in the thoracic inlet portion of the trachea and results in subcutaneous emphysema, pneumomediastinum, and often pneumoretroperitoneum. Occasionally, a pneumomediastinum may progress to a pneumothorax.
- Complete tracheal rupture is an uncommon, life-threatening event. In addition to severe peritracheal air accumulation, discontinuity of the tracheal wall is seen with separation of the tracheal rings. This is best assessed on the lateral radiographic view. This occurs most commonly in cats just cranial to the heart base.
- Focal tracheal stenosis is most commonly secondary to previous trauma (i.e., dog fight, prolonged overinflation of endotracheal tube cuff) with resultant stricture.
- Tracheal collapse is usually dynamic in nature, resulting in variation of tracheal diameter relative to the phase of the respiratory cycle. Tracheal collapse is often exacerbated during periods of excitement or during coughing. This is most commonly seen in toy breed dogs prone to loss of structural rigidity of the trachea and mainstem bronchi secondary to chondromalacia. To adequately assess tracheal dynamics, lateral thoracic radiographs are needed. These should be taken during peaks of inspiration and expiration, and should include the caudal neck. The cervical and thoracic inlet portions of the trachea collapse during inspiration, whereas the intrathoracic portion of the trachea and mainstem bronchi collapses during expiration.

▼ ***Key Point*** Superimposition of the esophagus over the dorsal aspect of the trachea is a common finding that may lead to the misdiagnosis of tracheal collapse in a normal dog. This appearance does not change during respiration unlike an animal with true tracheal collapse.

RADIOGRAPHIC ABNORMALITIES OF THE EXTRAPLEURAL SPACE

- The extrapleural space communicates with many of the fascial planes of the body via the thoracic inlet. It can be divided into two areas:
  - The potential space between the parietal pleura and the body wall
  - The potential space within the mediastinum

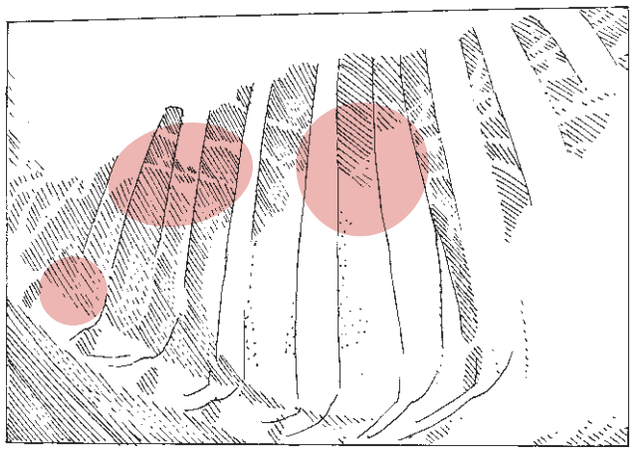

Figure 159-2. Location of thoracic lymph nodes.

- Conditions affecting the extrapleural space include abscesses, hematomas, granulomas, and neoplasms.
- Radiographically, most extrapleural diseases appear as relatively spherical, smoothly marginated masses that have a convex border facing the lung with tapering or concave cranial and caudal margins (the *extrapleural sign*).
- Thymic masses, mediastinal lymphadenopathy, and rib tumors with osteolysis are common extrapleural lesions.

Thoracic Lymph Nodes (Fig. 159-2)

The thoracic lymph nodes are located in three areas within the mediastinum:

- Dorsal to the second sternabra (sternal lymph nodes)
- Dorsal aspect of the cranial thorax (mediastinal lymph nodes)
- Hilar area of lung surrounding the bifurcation of the mainstem bronchi from the trachea (tracheobronchial lymph nodes)

▼ ***Key Point*** The thoracic lymph nodes are usually not visible in a healthy animal. When enlarged, they appear as soft-tissue opaque masses in these locations.

- Cranial mediastinal lymphadenomegaly may cause apparent widening of the cranial mediastinum on the DV or VD radiographic view, and dorsal displacement of the trachea on the lateral radiographic view.
- Enlargement of the tracheobronchial lymph nodes may compress the mainstem bronchi abaxially and ventrally. On the VD or DV radiographic view, this *splaying* of the mainstem bronchi can mimic the radiographic appearance of left atrial enlargement. However, on the lateral radiographic view, tracheobronchial lymphadenomegaly causes *ventral* displacement of the mainstem bronchi, whereas left atrial enlargement would cause dorsal deviation of the mainstem bronchi.
- The sternal lymph nodes receive afferent vessels from the abdominal wall and serosa as well as the thymus, thoracic wall, and mammary glands. Hence, abdominal disease should be suspected when sternal lymphadenomegaly is seen, particularly if thoracic disease is not identified.

Mediastinal Shift

A mediastinal shift occurs as a result of a unilateral decrease (ipsilateral shift) or increase (contralateral shift) in lung volume. Other intrathoracic masses may also cause a contralateral mediastinal shift.

▼ ***Key Point*** A mediastinal shift can only be identified on straight VD and DV radiographic views.

Cranial Mediastinal Masses

Thymoma and lymphoma are the most common neoplasms. In the cat, lymphoma frequently causes a large cranial thoracic mass that is non-compressible on physical examination. Other lesions that may cause a mass effect in the cranial mediastinum are branchial cysts, abscesses, and granulomas (most commonly the result of esophageal perforation).

▼ ***Key Point*** Obese animals and brachycephalic breeds may contain a large amount of fat in the cranial mediastinum, mimicking the appearance of a mass. Hence, it is important to recognize the radiographic differences between fat and soft tissue opacity to make this differentiation. Fat will be less opaque than soft tissue.

Concurrent pleural fluid may mask the presence of a cranial mediastinal mass. Thoracocentesis prior to radiography and/or horizontal-beam positional radiography (patient standing erect) is recommended.

Mediastinal Fluid

Mediastinal fluid is of soft-tissue radiographic opacity and may be difficult to distinguish from a mass. Horizontal-beam positional radiography may be helpful in differentiating a mediastinal mass from fluid.

Common causes of mediastinal fluid accumulation include hemorrhage (coagulopathy or trauma-induced), esophageal perforation, and feline infectious peritonitis (FIP).

Pneumomediastinum

Pneumomediastinum (i.e., air within the mediastinum) may result from a perforating injury of the esophagus, trachea, or bronchus near the hilus, usually in association with penetrating wounds of the cervical soft tissues or thoracic inlet.

This condition enables radiographic identification of the normally invisible mediastinal structures such as the esophagus, cranial vena cava, brachiocephalic artery, and other mediastinal vessels.

Because the cranial mediastinum communicates with the fascial planes of the body, extensive subcutaneous emphysema and/or pneumoretroperitoneum are common complications of this condition.

Pneumothorax may occur secondary to pneumomediastinum; however, the reverse does not occur.

RADIOGRAPHIC ABNORMALITIES OF THE PLEURAL SPACE

The normal pleural space is not visible radiographically. Filling of this space with air, fluid, or viscera (diaphragmatic hernia) will cause the space to enlarge and become apparent radiographically.

Pneumothorax

In animals with pneumothorax, the pleural space appears widened and radiolucent, the lung appears smaller than normal and increased in interstitial opacity (atelectatic), and the heart appears dorsally deviated from the sternum on the recumbent lateral radiographic view, due to shifting of the heart from midline. Pneumothorax may be classified as open or closed.

Open Pneumothorax

In an open pneumothorax, there is a defect in the body wall and air enters the thoracic cavity from the environment. Air will enter the thoracic cavity until the pleural pressure equals the atmospheric pressure.

Closed Pneumothorax

In a closed pneumothorax, there is a rent in the visceral pleura and the free pleural air comes from the lung. A closed pneumothorax may be further divided into simple and tension forms.

Simple Closed Pneumothorax

This is caused by a puncture wound or laceration of the lung that allows free movement of air through the defect during both inspiration and expiration. There is rapid equilibration between the lung and pleural cavity, and the severity of the condition depends on the dimensions of the injured area.

Tension Pneumothorax

This occurs when pleural space pressure exceeds atmospheric pressure during inspiration and expiration. Often, a flap-like defect, acting as a one-way valve, is the cause. Air can enter the pleural space during inspiration but closes and does not allow air to leave during expiration. Thus, pressure inside the pleural space may continue to increase, and progressive pulmonary atelectasis and cardiovascular compromise may develop. This condition is a medical emergency. Radiographically, tension pneumothorax is characterized by flattening of the diaphragm, severe progressive pulmonary atelectasis, and microcardia.

Pleural Effusion

- Pleural effusion is characterized by increased soft-tissue opacity within the pleural space that changes in distribution depending on patient positioning. It is not possible to radiographically determine the type of effusion within the pleural space; thus, thoracocentesis with fluid analysis is necessary to reach a definitive diagnosis.
- Radiographically, the pleural space appears widened and radiopaque and the lungs appear smaller and separated by the pleural soft-tissue opacity.
- The ease with which pleural effusion can be detected depends on the quantity and distribution of fluid. Pleural fluid gravitates to the dependent portions of the thorax. On the DV radiographic view, pleural fluid will result in an overall haziness to the internal thoracic structures, obscuring the outline of the ventrally positioned cardiac silhouette and the diaphragmatic cupula. On the VD radiographic view, pleural fluid will surround retracted lung lobe margins dorsally and the cardiac silhouette and diaphragmatic cupula are less obscured because they are adjacent to aerated lung
- Horizontal-beam positional radiography is helpful in distinguishing pleural effusion from an intrathoracic mass.

▼ ***Key Point*** If fluid accumulation is limited to one hemithorax or if peripheral lobar margins are excessively rounded, restrictive pleuritis secondary to chronic pyothorax or chylothorax should be considered.

Pleural Thickening

Pleural thickening is characterized by thin, soft-tissue opaque fissure lines between lung lobes and cannot be differentiated from small volumes of pleural effusion. Pleural fissure lines are often seen as an incidental finding in healthy dogs.

RADIOGRAPHIC ABNORMALITIES OF THE DIAPHRAGM

The normal diaphragm is a thin, soft tissue structure that silhouettes with the liver and is not distinctly visible radiographically. Radiographic evidence of diaphragm pathology is nonspecific and changes observed most frequently include general or focal outline loss of the tho-

racic diaphragmatic surface and changes in diaphragmatic shape and position.

- The position of the diaphragm changes during inspiration and expiration.
- Cranial displacement of the diaphragm is most commonly associated with abdominal disease or generalized diaphragmatic paralysis.
- Caudal displacement of the diaphragm is most commonly associated with respiratory disease (e.g., feline asthma), pneumothorax, or pleural effusion.
- During extreme inspiration, particularly for animals in respiratory distress, the thoracic surface of the diaphragm may have a scalloped appearance on the VD and DV radiographic views. This is often referred to as *tenting* of the diaphragm.
- An asymmetrical shape to the diaphragm may occur with hemiparalysis.
- Suspected diaphragmatic paralysis may be confirmed using fluoroscopy.

Diaphragmatic Hernia

Most diaphragmatic hernias are traumatic in origin, although congenital hiatal, peritoneal-pericardial, and true hernias also occur.

- The radiographic appearance of a diaphragmatic hernia varies, depending on the size and location of the defect and the amount and type of herniated viscera. The most obvious radiographic signs are discontinuity of the diaphragm and herniation of the gastrointestinal tract (gas filled viscus) or other abdominal viscera into the thorax. The lungs, heart, and mediastinum often will be shifted cranially and laterally. The heart and portions of the diaphragm may be obscured owing to their contact with herniated viscera or with pleural effusion (hemorrhage), which are almost always present in cases of trauma.
- Herniation of abdominal viscera through small diaphragmatic rents may result in strangulation and secondary serosanguineous pleural effusion.
- Although gas is often present within a herniated small intestine or stomach, administration of a small amount of barium (1.0 ml/kg orally), followed by repeat thoracic radiographs 30 minutes later, may be helpful to verify the herniation of a portion of the gastrointestinal tract.
- Herniation of the stomach may result in acute gastric dilation and become a potential source of life-threatening cardiovascular compromise.

Positive-Contrast Peritoneography

If the diagnosis of a diaphragmatic hernia is uncertain, positive-contrast peritoneography may be helpful to assess diaphragmatic integrity. Prior to peritoneography, pleural and peritoneal effusions should be removed. Effusions will dilute the positive contrast, making it less visible.

Procedure

Administer 1–2 ml/kg of a sterile aqueous tri-iodinated contrast agent such as that used for intravenous (IV) excretory urography. Warm the contrast agent to body temperature.

- Shave, surgically prepare, and locally anesthetize a small area just to the right of the umbilicus. Pass a needle-catheter combination into the abdomen, avoiding trauma to the spleen, urinary bladder, or intestine. Perform aspiration to verify that there has been no perforation of a hollow viscus or laceration of a blood vessel.
- Slowly introduce the warmed contrast medium into the peritoneal cavity, remove the needle, and gently roll the animal to facilitate distribution of contrast medium. If the animal is stable, positioning the animal with the hind end elevated for 5 to 10 minutes may promote cranial distribution of the contrast medium.
- Obtain radiographs immediately; if findings are inconclusive, repeat in 15 to 20 minutes.
- Optimally, obtain all four radiographic views centered on the diaphragm (right and left laterals, VD and DV). However, if the clinical state of the animal is compromised and only limited views can be taken, place the area of suspected rent dependently (i.e., left lateral and DV views for a suspected ventral, left-sided tear).
- In an animal with an intact diaphragm, the contrast medium will coat the abdominal surface of the diaphragm. Discontinuity of the diaphragmatic silhouette or extension of contrast medium into the thorax indicates a diaphragmatic tear.

RADIOGRAPHIC ABNORMALITIES IN PULMONARY DISEASE

Principles of Interpretation

A number of different methods have been used to describe the radiographic findings associated with pulmonary disease. One common technique uses a pattern approach that is based on the microscopic pathologic changes involved in the disease process.

▼ ***Key Point*** The radiographic patterns of pulmonary disease are alveolar, interstitial, bronchial, and vascular. Mixed pulmonary patterns may also be seen.

When making a radiographic differential diagnosis, evaluate the extent of the lesion (diffuse or focal), the location of the lesion within the lung, the opacity of the lesion, the size and shape of the lesion, and any associated abnormalities of other thoracic structures. Two radiographic signs important in the evaluation of pulmonary disease are the silhouette sign and summation.

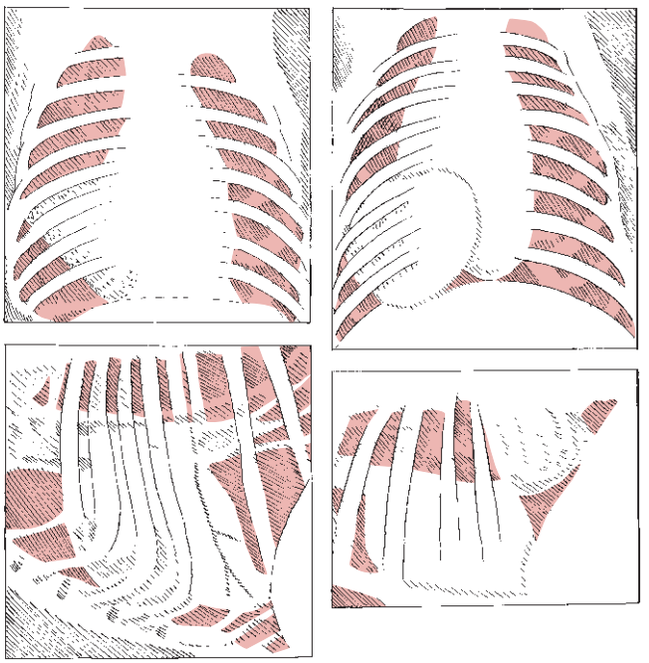

Figure 159-3. Representation of silhouette sign *(left, top and bottom)* and summation *(right, top and bottom).*

Silhouette Sign

The silhouette sign occurs when two objects of the same radiographic opacity contact one another and are oriented in such a way that there is a gradual, rather than abrupt, change in thickness at their borders (Fig. 159-3, *left, top and bottom*).

- Radiographically these objects appear to blend together and the borders between them are obscured. Therefore, it is not possible to perceive where one object ends and the other begins.
- This sign is most commonly seen in the thorax when abnormal fluid opacity within the lung or pleural space contacts the heart or diaphragm and the borders of these structures become indistinct.

Summation

Summation occurs when two objects are superimposed in such a way that there is an abrupt change in thickness at the border where these structures overlap or when they are separated by material of a different radiopacity (Fig. 159-3, *right, top and bottom*).

This occurs when a soft tissue opaque mass is within a well-aerated portion of lung and is superimposed over the heart or diaphragm. In this case the heart and mass are separated by air and the opacities of the mass and heart will be additive.

Thus, the margin where the two objects overlap is enhanced and the mass appears more opaque than it actually is.

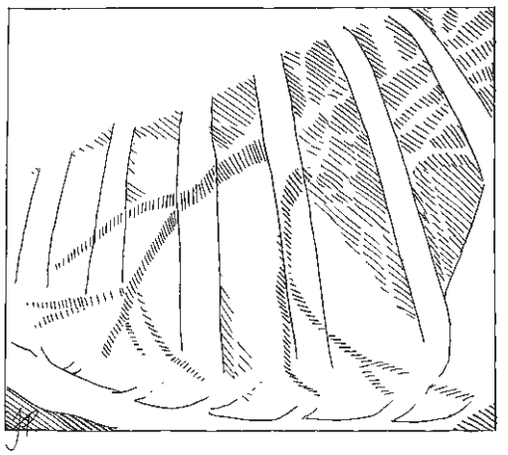

Figure 159-4. Alveolar lung consolidation with air bronchograms (shaded areas in ventral lung).

Alveolar Pattern

The alveolar pattern of pulmonary disease is seen when there is decreased air within the lung secondary to alveolar collapse or filling of the alveolar air spaces with fluid or cellular infiltrate. It is not possible to determine radiographically what type of fluid is present in the alveoli. Often there is a lag period, both at the beginning and at the end of the disease process, when radiographic signs do not correlate with the severity of clinical signs. Thus, the patient history, signalment, and other clinical information are extremely important in arriving at a definitive diagnosis.

Characteristics of Alveolar Disease

- Patchy, ill-defined areas of infiltration that fade into adjacent normal lung.
- The tendency for these lesions to coalesce, leading to lobar consolidation.
- Air bronchogram pattern and the silhouette sign (*lobar sign*).

Air Bronchogram

In an air Bronchogram, the air within the bronchus provides excellent contrast with the fluid-filled lung, and the bronchus appears as a tubular, branching, radiolucent structure within an abnormally soft tissue opaque lung lobe (Fig. 159-4). The normally seen soft tissue opaque pulmonary vessels and bronchial walls are not seen because of the silhouetting of these structures with the infiltrated lung (these signs distinguish the alveolar pattern from the bronchial pattern).

▼ ***Key Point*** The air bronchogram sign characterizes alveolar disease (the sign typically looks something like black, branching tree limbs in a snow storm).

Associated Disease Processes

Common disease processes that cause an alveolar pattern include bronchopneumonia, pulmonary edema (cardiogenic and non-cardiogenic), and pulmonary hemorrhage/contusion. The distribution of the alveolar pattern in the lung may be helpful in the differential diagnosis of these conditions.

Bronchopneumonia

- Bronchopneumonia can be divided into two categories: inhalation pneumonia (secondary to inhaled pathogens) and aspiration pneumonia (secondary to the aspiration of gastric contents). Both types typically result in focal or diffuse alveolar infiltration of the cranioventral *(dependent)* portion of the lung. The right middle lobe is one of the most commonly affected lobes. Air bronchograms and lobar consolidation are common findings in patients with bronchopneumonia.
- Soft tissue opaque inhaled foreign bodies, such as plant awns, are usually diagnosed by the infiltrate they stimulate around the bronchus rather than by direct visualization. The right caudal lung lobe is the most common site of bronchial foreign bodies in the dog.
- Hematogenous pneumonia refers to the systemic spread of bacteria, fungi, or other infectious agents. Unlike bronchopneumonia, hematogenous pneumonia often has a diffuse or caudodorsal pulmonary distribution.

Pulmonary Edema

- Pulmonary edema, whether cardiogenic or non-cardiogenic, usually has a dorsal or caudodorsal distribution.
- Edema due to anaphylaxis, left-sided congestive heart failure, or electrocution usually is most severe in the hilar area of the lung.
- Initially, pulmonary edema usually results in an increased interstitial pattern, secondary to fluid build-up in the pulmonary interstitium. Eventually, the excess fluid in the interstitium may spill over into the alveoli, leading to an alveolar pattern.
- Air bronchograms may not be a consistent feature of cardiogenic edema secondary to mitral insufficiency, possibly because of the slow onset and chronic nature of this type of heart failure. Animals with acute onset of pulmonary edema from any cause are more likely to have air bronchograms because of the rapid accumulation of pulmonary fluid. Alveolar infiltrate predominance in the right caudal lung lobe is observed in some cases of heart failure.
- Edema secondary to seizures or head trauma (neurogenic) tends to affect the more peripheral portions of the caudal lung lobes.
- Acute upper airway obstruction is a relatively uncommon cause of pulmonary edema. When it occurs, it is often similar in distribution to cardiogenic edema.

Interstitial Pattern

The interstitium surrounds and supports the pulmonary vessels, lymphatics, bronchi, and alveoli; therefore, diseases of these structures may be reflected in the interstitium. The interstitial pattern can be subdivided into structured (nodular) and unstructured patterns.

Nodular Interstitial Pattern

The nodular interstitial pattern is one of the most common pulmonary patterns. The ease of detection of pulmonary nodules depends on their size, number, parenchymal distribution, margination, and opacity. Soft tissue opaque nodules less than 0.5 cm in diameter are extremely difficult to detect unless they are numerous, mineralized, and located in the peripheral portions of the lung lobes where summation with other soft tissue structures of the thorax is at a minimum.

Smooth Versus Indistinct Nodules

- Nodules with smooth, well-defined borders suggest a slowly progressive process with minimal involvement of the surrounding alveoli. Examples include primary and metastatic neoplasia and chronic (inactive) pulmonary granulomas and abscesses.
- An indistinct nodular margin suggests a more active process that extends into the adjacent alveoli or is causing associated edema, inflammation, or hemorrhage. Highly aggressive neoplasms, active granulomas, and pulmonary abscesses often appear irregular or indistinct in margination.

Differentiating Nodules from Vessels

- On-end pulmonary vessels can be differentiated from nodules because they are:
  - More numerous in the hilar area.
  - Consistently more radiopaque than the adjacent vasculature.
  - Associated with a longitudinal vessel of which they are a branch.
  - Progressively less numerous and smaller in the periphery of the lung.
- In contrast, pulmonary nodules are:
  - Randomly distributed throughout the lung (i.e., small nodules may be seen centrally and large nodules peripherally.
  - Often less radiopaque or have the same opacity as the pulmonary vasculature.
  - Frequently *not* associated with a vessel of similar or greater size.

▼ ***Key Point*** Pulmonary osteomas (benign osseous metaplasia) are small, irregularly margined mineral opacities seen as an incidental finding in some dogs, particularly the collie breeds. These should not be confused with pulmonary nodules.

Granulomas

- Granulomas, such as those secondary to *Paragonimus kellicotti*, may be solitary or multiple, cavitated, and may occur anywhere in the lung.
  - Radiographic appearance varies from lesions that are almost entirely cystic to those that are primarily granulomatous with only a small cystic cavity.
  - Spontaneous pneumothorax may occur secondary to the rupture of air-filled cysts.
- Immune-mediated, eosinophilic, and lymphomatoid pulmonary granulomatosis are typically associated with hilar lymphadenopathy.

Neoplasia

- Primary lung tumors are relatively uncommon and are usually carcinomas.
  - Bronchogenic carcinoma is usually hilar in location and occurs most commonly as a large, irregularly marginated soft tissue mass in the caudal lung lobes, most commonly on the right side.
  - Cavitation is uncommon but may develop in large necrotic tumors.
  - Primary lung tumors may metastasize to other regions of lung.
  - Although pulmonary carcinomas commonly metastasize to hilar lymph nodes, these metastases generally are not large enough to be evident radiographically.
- Metastatic neoplasia generally appears as multiple, variably sized nodules randomly distributed throughout the lung. When small, it may be difficult to distinguish pulmonary nodules from end-on pulmonary blood vessels.

Unstructured Interstitial Pattern

This pattern is one of the most difficult to diagnose because it is commonly mimicked by poor radiographic technique secondary to respiratory motion, pulmonary underinflation, and radiographic underexposure. The lung generally appears more radiopaque than normal (Fig. 159-5). Diseases causing diffuse, unstructured interstitial infiltration have a widespread or caudodorsal distribution.

▼ ***Key Point*** A key radiographic feature of an unstructured interstitial pattern is a blurring of the vascular markings.

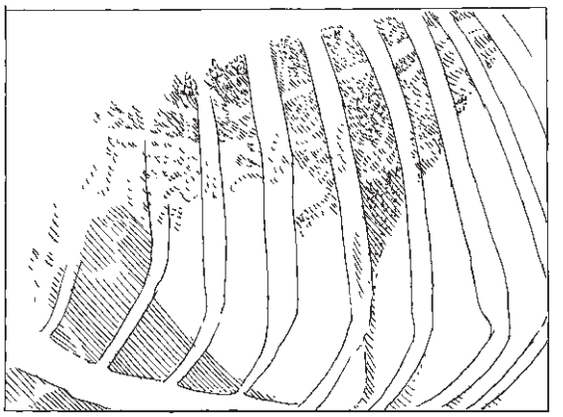

Figure 159-5. Diffuse dorsal caudal interstitial pattern.

Pulmonary Edema

Initially, pulmonary edema, both cardiogenic and noncardiogenic, usually appears as an interstitial pattern. As the disease progresses, fluid extends farther into the alveoli, resulting in an alveolar pattern.

▼ ***Key Point*** Lymphosarcoma may cause a diffuse interstitial pattern secondary to thoracic lymphatic occlusion by tumor emboli that results in fluid build up in the pulmonary interstitium.

Pneumonitis

- Interstitial pneumonia of fungal, parasitic, and especially viral etiology typically causes a diffuse increase in interstitial opacity of the dorsal and hilar lung regions. Hematogenous pneumonia, unlike bronchopneumonia, also tends to have a more caudodorsal-to-diffuse pulmonary distribution.
- Interstitial pulmonary disease secondary to metabolic or toxic disturbances, such as uremia, pancreatitis, smoke inhalation, or paraquat poisoning, are often diffuse.
- Interstitial pulmonary disease secondary to allergies often has a peribronchial distribution *(peribronchial cuffing).*

Pulmonary Fibrosis

- Lung fibrosis is a very common cause of diffuse interstitial opacity, especially in older dogs. It has been recognized as a congenital disorder in certain dog breeds (West Highland White Terriers) and may cause decreased lung compliance in severe cases.

Neoplasia

- Most neoplastic processes of the lung tend to be nodular; however, in some neoplasms there is a less

structured and more diffuse increase in interstitial pulmonary opacity. These neoplastic cells may reach the lung via the lymphatics (e.g., pulmonary lymphoma) or hematogenously (e.g., scirrhous mammary adenocarcinoma, scirrhous bronchogenic adenocarcinoma). Differentiation of this type of neoplastic infiltration from other causes of diffuse interstitial opacity is difficult.

- Clinically affected animals may present with a degree of respiratory distress disproportionate to the degree of pulmonary infiltration.
- Fine-needle aspiration of the lung, bronchoalveolar lavage, and/or lung biopsy may be needed for diagnosis.

Vascular Pattern

The vascular pattern of pulmonary disease is primarily determined by the size of the pulmonary arteries and veins.

Hypovascularity

Pulmonary underperfusion results in a decreased size to both the arteries and veins. Potential causes of pulmonary hypovascularity include:

- Congenital shunting of blood in a right-to-left direction, thus bypassing the lungs (e.g., tetralogy of Fallot, reverse patent ductus arteriosus).
- Acquired circulatory problems such as acute blood loss, shock, and cardiac tamponade.
- Decreased vascular diameter may be seen secondary to pulmonary thromboembolism. Affected portions of lung may appear hyperlucent.

Hypervascularity

- Hypervascularity can refer to the enlargement of both the arteries and veins, the arteries alone (pulmonary arterial hypertension), or the veins alone (venous congestion).
- Enlargement of both the pulmonary arteries and veins usually is associated with overhydration, secondary to over-zealous intravenous fluid administration, or with some type of congenital cardiac left-to-right shunt, resulting in pulmonary overcirculation (e.g., patent ductus arteriosus, ventricular septal defects).
- High-output states such as hyperthyroidism also may produce prominent pulmonary vascularity.
- Severe left-sided heart failure due to cardiomyopathy or chronic mitral valve insufficiency with long-standing venous congestion and secondary pulmonary hypertension also may lead to enlarged arteries and veins.

Acquired Pulmonary Arterial Hypertension

- In the dog, this condition most commonly is the result of heartworm disease.

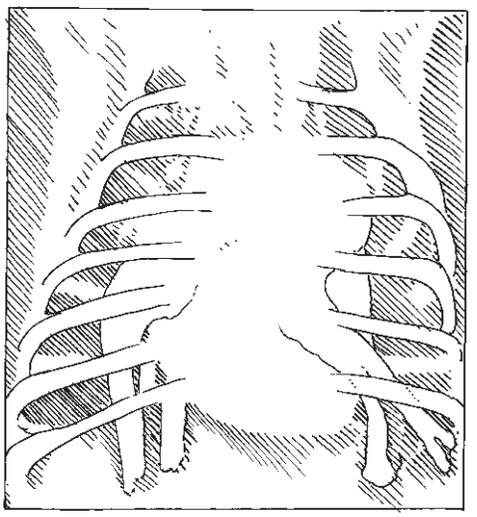

Figure 159-6. Radiographic appearance of heartworm disease. Note large, truncated lobar arteries.

- In early heartworm disease, there is right heart enlargement and a mild to moderate increase in interstitial opacity in the dorsal lung lobes.
- As the condition progresses, the right ventricle becomes more rounded, giving a "reversed D" shape to the cardiac silhouette on the radiographic view, and the main pulmonary artery segment and peripheral pulmonary arteries become enlarged and tortuous (Fig. 159-6).

▼ ***Key Point*** In advanced cases of heartworm disease, truncation or abrupt termination of the peripheral vessels, also called the *pruned tree* effect, is commonly seen in the caudal lobar vessels.

- Focal areas of pulmonary infarction appear as patchy alveolar opacities, primarily around the caudal lobar vessels.
- Pulmonary arterial hypertension also occurs in the cat and may be due to heartworm disease or aelurostrongylosis.

Venous Congestion

- Venous congestion, characterized by enlarged pulmonary veins, usually is associated with left heart failure from congenital or acquired cardiac disease.
- Early interstitial edema, which in the dog is usually restricted to the hilar area, causes a symmetric increase in interstitial opacity of the hilar area of the lung, with blurring of the veins on radiographs.
- As the pulmonary edema progresses, alveolar infiltrates become evident in the caudal lobes.
- In the cat, pulmonary edema is somewhat less predictable in its distribution and may appear more focal and asymmetric than that in the dog.

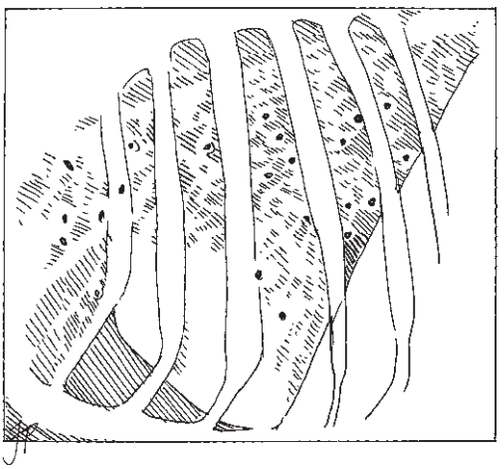

Figure 159-7. Bronchial pattern.

Bronchial Pattern

- Increased bronchial prominence in the dog may occur as a normal aging change or may be secondary to chronic bronchial inflammation.

▼ ***Key Point*** Bronchial wall mineralization, *without airway wall thickening,* may be seen as a normal aging change in dogs.

- Radiographic changes in animals with acute bronchitis may be absent or restricted to pulmonary overinflation or air trapping (e.g., feline asthma)
- As the disease progresses, the bronchial walls tend to appear thickened. This often results in a relative decrease in luminal diameter and is best appreciated on cross-sectional views in which the bronchi appear as thick-walled doughnut-like structures (Fig. 159-7). Airway inflammation may extend into the peripheral bronchial interstitium (bronchointerstitial pattern).
- When viewed longitudinally, the bronchial walls appear as paired, nearly parallel linear opacities (like tram lines) extending into the lung periphery.
- Bronchial mineralization is a common sequela of chronic bronchitis, especially in cases with an allergic or immune-mediated etiology.

Bronchial Prominence in Cats

- This pattern in cats is most commonly associated with bronchitis or feline asthma, although infection with *Aelurostrongylus abstrusus* may occasionally cause this appearance.
- Cats presenting with acute respiratory distress generally show evidence of thoracic overexpansion with a flattened diaphragm and a barrel-shaped thorax in addition to bronchial prominence.
- Asymptomatic animals may appear radiographically normal unless the disease is chronic and the animal has had several acute episodes of dyspnea.
- Some cats with chronic bronchitis have chronic consolidation or atelectasis of the right middle lung lobe, the result of mucus plugs in the middle lobe bronchus, chronic fibrosis, and volume loss in this lobe.

▼ ***Key Point*** Fluid-filled or mucus-filled bronchi, imaged in cross-section, may be mistaken for a nodular interstitial pattern.

Bronchiectasis

- Bronchiectasis, or *irreversible* bronchial dilation, generally occurs secondary to chronic bronchial disease.
- The bronchial dilation may be varicose, cylindrical, or saccular in shape, and on cross-sectional views the affected bronchi have prominent walls that appear relatively thin compared with the enlarged bronchial lumen.
- Animals with bronchiectasis are prone to secondary bronchopneumonia because of poor mucociliary pulmonary clearance.

Mixed Patterns

Although the pattern approach to pulmonary evaluation is helpful in arriving at a differential diagnosis, many disease processes result in a mixture of the aforementioned patterns. These patterns often vary depending on the stage of the disease process during which the animal is evaluated. Diseases commonly causing a mixed pattern include heartworm disease (interstitial—vascular), left-sided heart failure and pneumonia (interstitial—alveolar), and chronic bronchitis and pneumonia (bronchointerstitial).

Pulmonary Hyperlucency

- Abnormal pulmonary radiolucency is probably easiest to recognize when it is focal.
- Thin-walled, air-filled bullae or blebs often occur secondary to pulmonary trauma. They are generally subpleural in location and usually resolve spontaneously.
- Congenital bullae, cysts, and pneumatoceles may be located anywhere in the pulmonary parenchyma.

▼ ***Key Point*** Spontaneous rupture of a bullae, bleb, cyst, or pneumatocele may lead to a pneumothorax.

- Thicker-walled cavitary lesions may be the result of parasitic cysts (e.g., *Paragonimus kellicotti*), congenital bronchial cysts, cavitated abscesses, neoplasms, and granulomas. These may be single or multiple, and their location within the lung is variable.
- Horizontal beam radiographs may be helpful in determining if fluid or cellular debris is present in the cystic areas.

Emphysema

- Emphysema may occur as a compensatory change following surgical removal of a lung lobe or volume loss in one of the lung lobes; it also can be the result of aging or of true histologic breakdown of the alveolar septa. True emphysema, as seen in humans, is relatively uncommon in dog and cats.
- True emphysema with rupture and confluence of alveoli must be differentiated from causes of reversible hyperinflation including asthma or tracheobronchial obstruction (e.g., foreign body).
- Radiographically, hyperinflation is recognized by:
  - Relative pulmonary hyperlucency.
  - Flattening or tenting of the diaphragm.
  - Increased separation of the heart and diaphragm (widened cardiophrenic angle).
  - Apparent decreased size of the pulmonary vessels.
  - A barrel-shaped chest.
  - Decreased differences in diaphragmatic excursion between inspiratory and expiratory films.
- Radiographic overexposure and severe hypovascularity are other causes of apparent pulmonary hyperlucency but usually are not accompanied by the other radiographic signs seen in generalized emphysema.

ALTERNATE IMAGING MODALITIES

Ultrasound

It is not possible to image structures located beneath air-filled regions because of the large acoustic mismatch between the air and soft tissue. Air produces a reverberation artifact whereby spurious echoes are reflected back and forth between gas and the ultrasound transducer.

- Abnormal accumulations of fluid (e.g., pleural effusion), superficial soft tissue masses (e.g., laryngeal, tracheal), or peripheral pulmonary masses may be imaged sonographically.
- In animals with pleural effusion, the lung is displaced away from the body wall, allowing assessment of the character of the pleural fluid to determine if it is cellular or noncellular. Pleural fluid can serve as a window to imaging regions of atelectatic or diseased, non-aerated lung.
- Focal areas of pulmonary infiltration may be evaluated as long as they extend to the pulmonary periphery.
- Mediastinal masses may be imaged if they abut the thoracic wall or are surrounded by fluid rather than aerated lung.
- Mediastinal masses may be solitary or multiple; solid, vascular, or cystic; mineralized or non-mineralized. They may or may not invade regional vasculature. These masses are typically imaged via an intercostal or thoracic inlet approach.
- Ultrasonography has been used to evaluate for diaphragmatic hernia but a negative ultrasound exam does not rule out a rent in the diaphragm. Radiography +/− positive contrast peritoneography are still considered more sensitive than ultrasound in diagnosing diaphragmatic tears, particularly when organ displacement is not present.

▼ ***Key Point*** Ultrasound is quite useful for guiding aspirate and biopsy sampling.

Nuclear Medicine

- Nuclear medicine is rarely used in animals and is mostly limited to referral centers.
- Perfusion-ventilation studies are commonly done in humans and were first used in dogs to evaluate the effects of heartworm disease.
- Special aerosol masks and trapping mechanisms are used to deliver the radioactivity for the ventilation portion of the study.
- The perfusion part of the study involves IV administration of technetium 99m macroaggregated albumin (MAA). Because this agent is trapped in the capillary network of the lung on the first pass following an IV injection, it can be used to detect areas of decreased pulmonary perfusion, as with pulmonary thromboembolism.
- Distal intratracheal instillation of technetium 99m sulfur colloid has been used to evaluate for ciliary dyskinesis in the dog. In normal animals, the radiopharmaceutical will be swept proximally up the trachea by the functional cilia. In dogs with amotile cilia, the radiopharmaceutical will stay at the point of instillation. Affected dogs typically present with a history of chronic, recurrent bronchitis from birth.

Computed Tomography

Whereas conventional radiography produces summed images of an object, tomographic scanners rotate to divide the object and to organize it into spatially consecutive, parallel image sections. In computed tomography (CT), a computer stores x-ray attenuation data and generates a matrix of values, depicted in various shades of gray. Images can be reconstructed into multiple planes. Compared to radiographs, CT produces images with superior spatial and contrast resolution that are free from superimposition by overlapping structures.

Nasal Cavity

- General anesthesia is a requirement for CT scanning.
- Where available, CT has all but replaced radiography of the nasal cavity.
- CT is superior to radiography in defining the extent of disease processes and in differentiating infectious rhinitis from neoplasia.

- Features commonly recognized with nasal neoplasia include a soft-tissue dense-mass effect and bony lysis.
- Features commonly seen with rhinitis include turbinate thickening early on and then turbinate atrophy and lysis later in the disease process.
- Features particular to fungal (aspergillosis) rhinitis include severe turbinate loss, soft tissue dense plaque formation along the walls of the nasal passage, and productive bone formation secondary to fungal osteomyelitis when the frontal sinuses are involved.
- Radiodense, foreign bodies may be identified and are most typically found in the caudoventral nasal passages.
- Erosion of the cribriform plate with extension into the calvarial vault may occur with neoplasia or fungal (aspergillosis) rhinitis but is seldom seen in other cases of rhinitis.
- CT is useful in identifying nasopharyngeal polyps as soft-tissue–dense, pedunculated, poorly contrast-enhancing structures.
- It is important to acquire pre- and post-IV contrast images to differentiate a fluid density from a vascular soft-tissue dense mass.

Pleural Space, Mediastinum, and Lung

- CT of the thoracic cavity is usually performed following radiography to better define an abnormality identified on survey radiographs (Fig. 159-8).
- CT is more sensitive than radiographs at detecting discrete pulmonary metastases and is often recommended prior to removal of the primary tumor (e.g., limb amputation for osteosarcoma).
- CT is more sensitive than radiographs at discriminating mediastinal masses from cranial pulmonary masses.

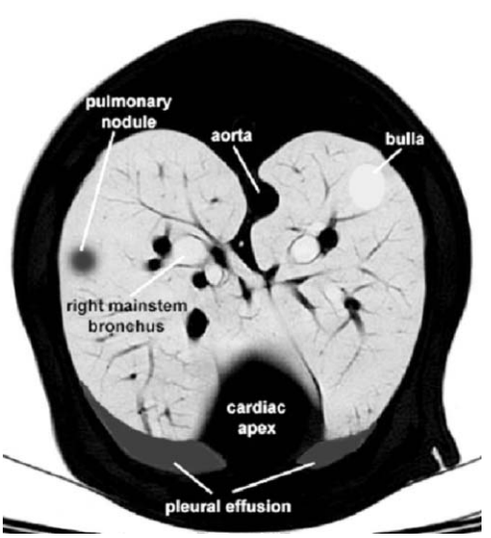

Figure 159-8. Transverse image of the thorax caudal to the bifurcation of the mainstem bronchi from the trachea.

- Pleural fluid will distribute to the dependent portion of thoracic cavity allowing better evaluation of aerated lung for pathology masked by effusion on survey radiographs.

▼ ***Key Point*** CT is quite useful for guiding aspirate and biopsy sampling.

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is a cross-sectional imaging modality that relies on computer generation of an image from returning signals. MRI signal intensity is a complex function of hydrogen concentration (proton density), the rates at which the nuclei realign along the magnetic field and lose synchronization with each other's spins, and blood movement. The relative weight of these components in the signal is dependent on the pulsing sequence used. Images may be acquired in multiple planes of a section.

- General anesthesia is a general requirement for MRI scanning.
- MRI has been used to evaluate nasal disease in small animal patients and is considered equally as sensitive as CT.
- Because MRI is extremely sensitive to motion, there are severe limitations to thoracic imaging due to cardiac and respiratory motion.

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Chapter

160 Surgery of the Nasal Cavity and Sinuses

Cheryl S. Hedlund

Signs in dogs and cats with chronic nasal and paranasal sinus disease may include nasal discharge, epistaxis, sneezing, gagging, stertorous breathing, nasal discomfort, and nasal deformity. Causes of nasal cavity and paranasal sinus diseases can be difficult to identify, but most cases are traumatic, infectious, inflammatory, mechanical, neoplastic, or parasitic in origin. Hemostatic abnormalities may lead to epistaxis. Most of these nasal diseases can be diagnosed and treated without surgery. However, rhinotomy may be necessary to arrive at a definitive diagnosis and may facilitate treatment of some diseases.

ANATOMY

Nasal Cavity

- The nasal cavity extends from the nostrils to the nasopharyngeal meatus and is divided into two chambers by the nasal septum. The rostral portion of the nasal septum is cartilaginous and difficult to evaluate radiographically.
- The rostral nasal chambers are occupied by the dorsal and ventral nasal conchae (turbinates) (Fig. 160-1).
- The caudal nasal chamber is filled with ethmoidal conchae (turbinates). The ethmoidal conchae extend into the frontal sinus, forming narrow communicating ostia between the frontal sinus and the nasal cavity (see Fig. 160-1).
- In the cat, the nasal cavity is shorter, the ethmoidal conchae are larger, and the nasal conchae are smaller than in the dog.
- The cribriform plate is a sievelike partition between the nasal and the cranial cavities (see Fig. 160-1). It articulates with the frontal bones dorsally and the presphenoid bones ventrally and laterally.
- The blood supply to the nasal cavity originates from the external carotid arteries via branches of the maxillary artery, including the sphenopalatine, ethmoid, greater palatine, dorsal nasal, lateral nasal, and maxillary labial arteries.

Paranasal Sinuses

- The paranasal sinuses enlarge with age and vary in size depending on the breed of the animal.
- The frontal sinus extends roughly from the medial canthus of the eyes to the temporal line. In dogs (but not in cats), it is divided into rostral, lateral, and medial compartments (see Fig. 160-1). The frontal sinus varies more in size than other cavities in the skull. The lateral compartment is particularly large in dolichocephalic breeds. Brachycephalic breeds have small lateral compartments, and the medial compartment may be absent.
- The maxillary sinus or recess is found dorsal to the roots of the third and fourth premolars and medial to the infraorbital canal. The maxillary recess in the cat is very narrow.
- Cats have a small sphenoid sinus. Dogs do not have a sphenoid sinus.

PREOPERATIVE CONSIDERATIONS

Disease Conditions

- Signs of chronic nasal disease can include unilateral or bilateral nasal discharge, epistaxis, sneezing, nasal discomfort, gagging, reverse sneezing, stertorous breathing, ocular discharge, and facial or nasopharyngeal distortion. Neurologic signs are seen if the disease extends into the cranium.
- The most frequent causes of chronic nasal and paranasal sinus disease are neoplasms, infections, and foreign bodies.
- Other causes include parasites *(Pneumonyssoides caninum, Capillaria aerophila, Linguatula serrata),* dental disease, trauma, lymphocytic-plasmacytic inflammation, and congenital anomalies. Nasal polyps, which are benign lesions, occur rarely.

Tumors

- Tumors of the nasal cavity and paranasal sinuses account for approximately 1% of all neoplasms in cats and dogs.

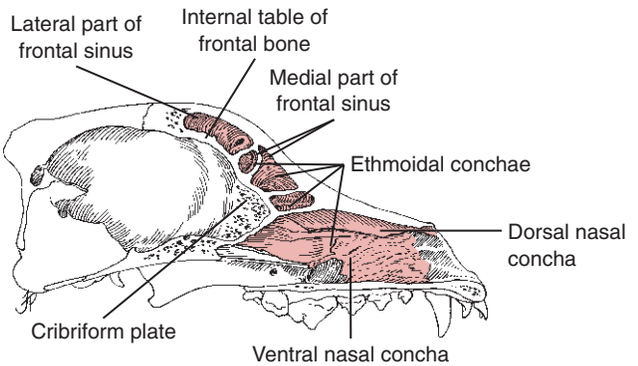

Figure 160-1. Sagittal section of the skull illustrating the anatomy of the nasal cavity and paranasal sinuses in relationship to the cranium. (Redrawn with permission from Evans HE [ed]: Miller's Anatomy of the Dog, 3rd ed. Philadelphia: WB Saunders, 1992.)

- Most intranasal tumors are diagnosed in older dogs and cats (>8–10 years) and in large-breed dogs.
- Tumors in the nasal cavity are usually found in the caudal third of the nasal passages.
- Most intranasal tumors are malignant (80%). Adenocarcinomas are most common, but squamous cell carcinoma, fibrosarcoma, chondrosarcoma, osteosarcoma, lymphosarcoma, hemangiosarcoma, undifferentiated sarcomas or carcinomas, and mast cell and transmissible venereal tumors also occur.
- The prognosis for malignant nasal neoplasms is guarded because of rapid local invasion and recurrence after therapy. Typically, these tumors do not metastasize until late in the course of the disease.
- Therapies that may help control some tumors include radiotherapy, immunotherapy, cryotherapy, and chemotherapy (see Chapter 26). These modalities are sometimes combined with surgical debulking of the lesion.

Infections

- Infections, especially those caused by fungal organisms, frequently cause nasal and paranasal cavity disease.
- Systemic diseases such as distemper, feline upper respiratory viral infections, and Rocky Mountain spotted fever can also cause acute or chronic rhinitis.
- Primary bacterial rhinitis is uncommon and usually is associated with foreign bodies, immunosuppression (feline leukemia virus [FeLV], feline immunodeficiency virus [FIV]), or dental disease.

Fungal Rhinitis

- The most commonly reported pathogenic fungi are *Aspergillus* and *Penicillium* species in dogs and *Cryptococcus neoformans* in cats. Other reported pathogens are *Rhinosporidium* and *Alternaria alternata.*
- Dogs with fungal rhinitis due to *Aspergillus* or *Penicillium* are usually young (1–7 years).
- Patients with fungal rhinitis generally do not have facial distortion but may exhibit ulceration of the nares and more nasal discomfort than dogs with nasal neoplasia.
- Treatment of fungal rhinitis is primarily medical, although surgery may be necessary for definitive diagnosis or creating ports for medical therapy.
- Medical therapy may be systemic (itraconazole, ketoconazole, or thiabendazole), topical (enilconazole or clotrimazole administered directly into the nasal cavity), or both (see Chapter 163 for details).
- If indicated, perform topical therapy by placing fenestrated balloon catheters via endoscopy or rhinoscopy, placing indwelling fenestrated tubes into the frontal sinuses and nasal cavity, or creating a nasal stoma for nasal irrigation or swabbing.
- Nasal rhinosporidiosis is treated by surgical excision of the lesion.

Diagnosis

Follow a standard protocol of evaluation, including a thorough history and physical examination, for all dogs and cats presenting with chronic nasal disease. Besides a complete blood count (CBC), serum chemistry profile, and urinalysis, consider a coagulation profile, radiography, enzyme-linked immunosorbent assay (ELISA) for FeLV and FIV in cats, computed tomography (CT) or magnetic resonance imaging (MRI), fungal serology, antegrade and retrograde rhinoscopy, and nasal biopsy.

History

The clinical history can provide important diagnostic clues.

- Suspect a destructive process if the discharge changes from unilateral to bilateral.
- Sneezing suggests involvement of the midnasal and rostral nasal chambers.
- Gagging or reverse sneezing suggests nasopharyngeal involvement or postnasal drainage.
- Reverse sneezing suggests nasal parasites *(Pneumonyssoides caninum)* in endemic areas.
- A history of trauma or dental disease suggests an oronasal fistula.

Physical Examination

- Facial or palatal deformity suggests neoplasia.
- Mouth breathing indicates nasopharyngeal obstruction.
- An ocular discharge may indicate nasolacrimal duct erosion.
- A small midline opening at the junction between the nasal planum and the skin suggests a nasal dermoid sinus cyst.
- Neurologic signs may indicate disease extension into the brain.

Laboratory Studies

- A CBC, serum chemistry profile, and urinalysis can assess the patient's overall status.
- A coagulation profile is indicated if exploratory rhinotomy is planned. If epistaxis is a major clinical sign, perform a cross-match for blood transfusion.

Diagnostic Imaging

Radiography

Obtain radiographs of the thorax in the conscious patient, and obtain radiographs of the nasal cavity and paranasal sinuses with the patient under general anesthesia.

- Include lateral, ventrodorsal, rostrocaudal, and rostroventral-caudodorsal open-mouth or occlusal radiographic views (see Chapter 4).
- The two most useful radiographic views are the ventrodorsal view of the maxilla using intraoral radiographic film and the rostrocaudal projection highlighting the frontal sinuses.

▼ ***Key Point*** To avoid iatrogenic fluid densities within the cavities, schedule radiography before performing any rhinoscopic, flush, or biopsy procedures.

Computed Tomography or Magnetic Resonance Imaging

Although costly, CT or MRI should be performed when possible to localize lesions more accurately than is possible with radiography. (See Chapter 4 for an overview of these imaging modalities.)

Rhinoscopy

Perform rhinoscopy in the anesthetized patient following skull imaging. The nasal mucosa is very sensitive to manipulation, and exposure can be obliterated by hemorrhage. Therefore, use gentle manipulation, lavage, and suction techniques.

- The rostral aspect of the nasal cavity may be seen with an otoscope, cystoscope, or small fiberoptic scope. A flexible pediatric bronchoscope or 2- to 3-mm diameter rigid telescope facilitates examination of the remainder of the cavity and allows retropharyngeal examination of the choanae for lodged foreign bodies, nasal mites, mucosal invasion (mycoses), or extruding nasal tumors.
- It may be impossible to perform a rhinoscopic examination on very small dogs and cats because of the size discrepancies between the scope and the nasal passages. However, examine the pharynx and choanae in these animals.
- Use rhinoscopy to obtain specimens for biopsy, cytology, and culture.

Biopsy

During the rhinoscopic procedure, lesions can be biopsied using endoscopic biopsy instruments. Biopsy the nasal mucosa even if no obvious lesions are found.

Other Diagnostic Procedures

- Perform *nasal flushing* or coring procedures with the patient still under anesthesia if endoscopic biopsy was not possible or successful.
  - In this procedure, slide a stiff plastic tube (e.g., the plastic cover of a Sovereign [Sherwood Medical, Ireland] indwelling catheter) vigorously in and out of the nasal passages (inserted through the nares and not extending beyond the medial canthus) while flushing and aspirating saline.
  - Premeasure the catheter to avoid trauma to or beyond the cribriform plate.
  - Pack gauze sponges in the nasopharynx and be sure the endotracheal tube cuff is adequately inflated prior to flushing.
  - Collect the lavage fluid and debris and examine for tissue fragments, foreign bodies, and parasites.
- *Nasal swabs* for culture or cytologic evaluation are of limited value. Positive fungal cultures can be obtained in about 40% of normal dogs, so diagnosis should also rely on identifying characteristic mucosal lesions grossly and on histopathology. Occasionally, cryptococcosis organisms are identified by examining a stained, direct smear.
- *Serologic evaluation* for *Aspergillus* and *Penicillium* species is useful, but false-positive results are possible. Latex agglutination test for *Cryptococcus neoformans* is useful in cats.
- Perform *rhinotomy* as a diagnostic procedure if a diagnosis is not achieved by other means.

Anesthesia

- Begin preemptive analgesia such as placing a fentanyl patch 8 to 12 hours prior to surgery to enhance postoperative analgesia. (*Note:* Prevent ingestion of the patch.) See "Appendix" for dosage recommendations for fentanyl patches.
- Induce and maintain routine general anesthesia for diagnostic and surgical procedures (see Chapter 2).
- Prior to extubation, examine and suction the nasopharyngeal area. Leave the endotracheal tube cuff partially inflated to prevent tracheal aspiration of blood clots, fluid, and debris.

SURGICAL PROCEDURES

Objectives

- Obtain sufficient tissue samples to achieve a definitive diagnosis for the patient's chronic rhinitis or sinusitis.

- Completely remove or debulk the lesion.
- Facilitate administration of adjuvant therapy.
- Minimize blood loss.
- Maintain a cosmetically acceptable appearance.

Equipment

- Standard general surgical pack and suture
- Umbilical tape, vascular tape (Vas-Tie, Sil-Med Corp., Taunton, MA), or bulldog vascular clamps for temporary carotid occlusion
- Periosteal elevator
- Oscillating saw, air drill, pins and pin chuck, and/or osteotome and mallet to create bone flap
- Gelpi retractor
- Bone curette, rasp, bur, rongeur, and trephine
- Fenestrated, indwelling tubes or balloon catheters to facilitate application of topical medications
- Synthetic mesh to span the bony defect (usually not needed)

Temporary Bilateral Carotid Artery Occlusion

This procedure is performed prior to entry into the nasal cavity or paranasal sinuses if major surgery such as rhinotomy and turbinectomy is to be performed. Carotid artery occlusion decreases blood loss and improves exposure during rhinotomy. *Not all surgeons choose to use this technique.*

Technique

1. Place the dog in dorsal recumbency with the front legs secured caudally and a rolled towel placed under the neck.
2. Clip and aseptically prepare the ventral neck from the caudal aspect of the mandibles to the manubrium.
3. Incise the skin and subcutis on the ventral cervical midline from the larynx to the midtrachea.
4. Separate the paired sternohyoideus muscles to expose the ventral trachea.
5. Bluntly dissect lateral to the trachea and palpate the carotid pulse.
6. Exteriorize the carotid sheath and separate the external carotid artery from the vagosympathetic trunk and internal jugular vein (Fig. 160-2).
7. Occlude the carotid artery with a vascular tie, umbilical tape, or vascular clamp (see Fig. 160-2).
8. Repeat the procedure on the opposite carotid.
9. Appose the separated sternohyoid muscles and skin in two layers with simple continuous suture patterns.
10. Cover the surgical site with sterile draping material and, if necessary, reposition the patient for rhinotomy.
11. Following rhinotomy, reexpose the carotids and release occlusion. Lavage the area and routinely close in three layers (muscle, subcutis, and skin).

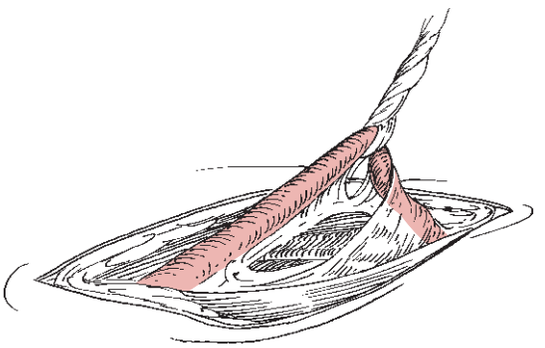

Figure 160-2. Exteriorize and incise the carotid sheath located lateral to the trachea, separate the common carotid artery *(top)* from the vagosympathetic trunk and internal jugular vein *(bottom)* and occlude.

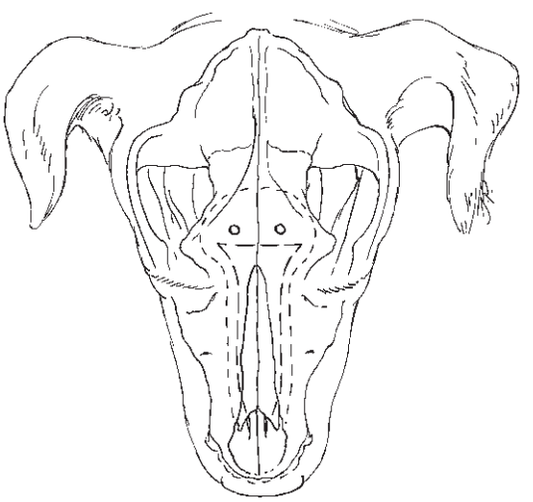

Figure 160-3. Dorsal rhinotomy. The outer dotted line delineates the approximate extent of the nasal cavity and frontal sinuses. The inner dashed lines delineate the bone flap for a unilateral or bilateral approach. The holes over the frontal sinuses indicate the site for insertion of drains. (Redrawn with permission from Bojrab MJ [ed]: Current Techniques in Small Animal Surgery, 3rd ed. Philadelphia: Lea & Febiger, 1990.)

Dorsal Rhinotomy

Following carotid occlusion, expose the nasal cavity and frontal sinuses for exploration and biopsy.

Technique

1. Position the patient in ventral recumbency insuring that the head is straight and not twisted to one side.
2. Prepare the nasal and frontal sinus areas for aseptic surgery.
3. Incise the skin and subcutis along the dorsal midline (Fig. 160-3).
4. Elevate the dense fascia and periosteum with a periosteal elevator and retract these tissues laterally with Gelpi retractors.

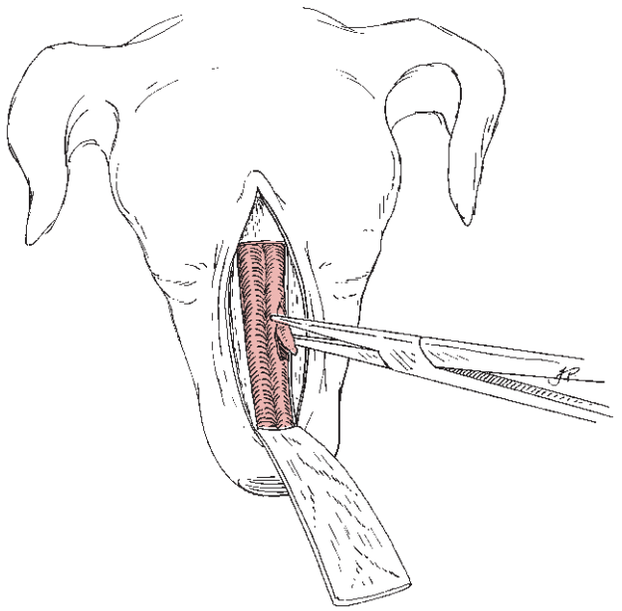

Figure 160-4. Reflect the bone flap rostrally or remove it. Perform turbinectomy using forceps, scissors, and curettes. (Redrawn with permission from Bojrab MJ [ed]: Current Techniques in Small Animal Surgery, 3rd ed. Philadelphia: Lea & Febiger, 1990.)

5. Create a unilateral or bilateral bone flap with an oscillating saw or drill. Bevel the edges of the bone flap so that the dorsal surface is slightly wider than the ventral surface if the flap is to be replaced after rhinotomy.
   a. Alternatively, make holes (drill or pin chuck) at the edges of the proposed bone flap and connect them with an osteotome and mallet.
   b. Another method is to make a hole into the nasal cavity with a trephine or pin and chuck; rongeur adjacent bone and discard.
6. Elevate the flap to expose the nasal cavity and the rostral portion of the frontal sinus for complete exploration (see Fig. 160-4).
7. Remove or debulk the lesion and involved conchae (turbinates), using forceps, Metzenbaum scissors, and/or a bone curette (Fig. 160-4). Save all tissues for culture and histologic evaluation.
8. Remove exudate from the frontal sinus, curette the lining to remove all diseased tissue, and enlarge the ostia to facilitate drainage.
9. Lavage and suction the nasal cavity and sinuses thoroughly with copious amounts of saline to dislodge debris and blood clots.
10. If required for adjuvant therapy or to minimize subcutaneous emphysema, place a fenestrated, indwelling tube (e.g., Brunswick feeding tube) into the frontal sinus and extending into the nasal cavity. Create the opening in the frontal sinus with a trephine, drill, or intramedullary pin.
11. To replace the non-diseased bone flap, drill holes in the bone flap and rhinotomy margins and place non-metallic sutures through adjacent holes to secure the flap (Fig. 160-5). Alternatively, discard the bone flap and proceed with soft tissue closure.
12. Close using continuous suture patterns in the fascial and periosteal layer, subcutaneous tissues, and the skin. When the defect is large and cosmetic appearance is critical, implant a synthetic mesh (e.g., Marlex mesh) across the bony defect and secure with non-absorbable, monofilament sutures.
13. The skin edges may be secured directly to the margins of the bony defect, creating a stoma into the nasal cavity to facilitate topical therapy or to prevent subcutaneous emphysema (Fig. 160-6).

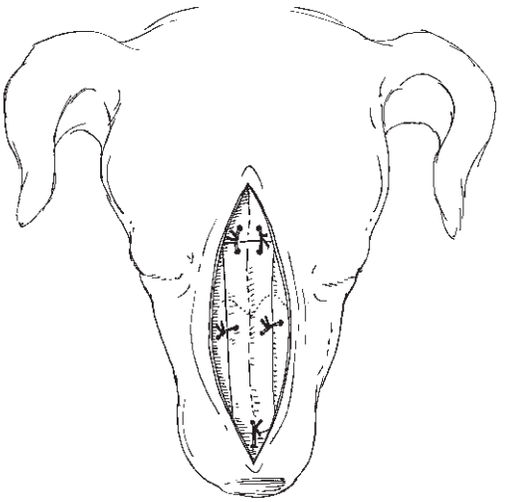

Figure 160-5. Replace the bone flap by placing sutures through holes drilled in the flap and margins of the defect. (Redrawn with permission from Bojrab MJ [ed]: Current Techniques in Small Animal Surgery, 3rd ed. Philadelphia: Lea & Febiger, 1990.)

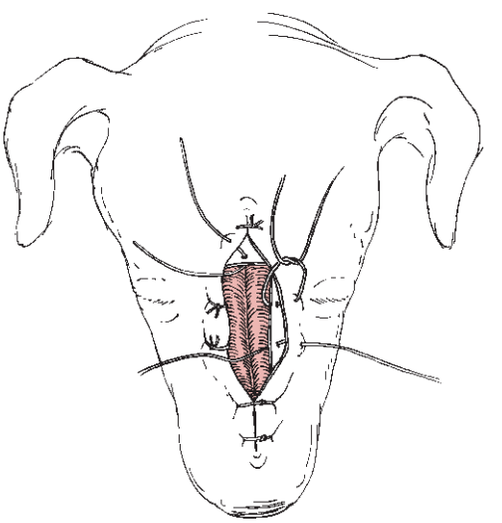

Figure 160-6. If a stoma following rhinotomy is desired, drill holes in the margins of the defect and pass sutures through these holes and the skin.

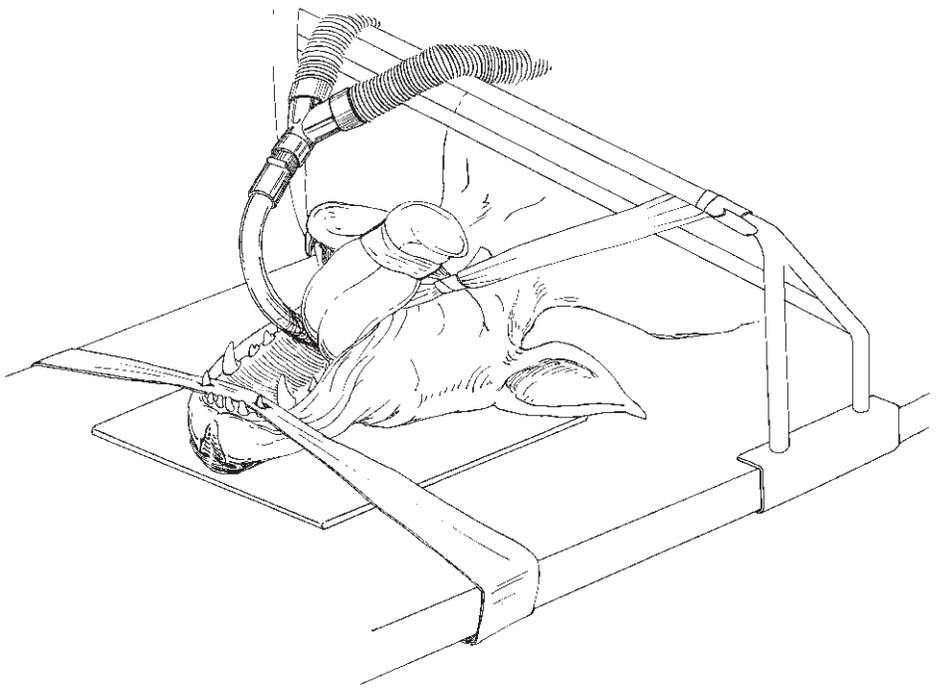

Figure 160-7. Positioning for ventral rhinotomy. (Redrawn with permission from Slatter DH [ed]: Textbook of Small Animal Surgery. Philadelphia: WB Saunders, 1985.)

14. If the stoma is small, it may heal by second intention; otherwise, following conclusion of medical therapy, debride, undermine, and appose the skin edges.
15. Dogs tolerate rhinotomy very well. Aggressive rhinotomy in cats can be associated with a higher rate of morbidity and mortality.

Ventral Rhinotomy

The nasal cavity and nasopharynx can be explored using a ventral approach. With this technique, evaluation of the frontal sinuses is limited to the rostral half.

Technique

1. Position the patient in dorsal recumbency with the oral cavity exposed by hanging and securing the mandible in a wide, open-mouth position (Fig. 160-7).
2. Cleanse the oral cavity, dental arcade, and nasopharyngeal area with a mild antiseptic solution (dilute chlorhexidine or povidone-iodine).
3. Incise the mucoperiosteum of the hard palate on the midline from the level of the canine teeth caudally to the fourth premolar or continue through the mucosa of the soft palate if the lesion extends into the nasopharyngeal area (Fig. 160-8).
   a. Alternatively, use a U-shaped mucoperiosteal incision parallel to the dental arcade (see Fig. 160-8).
4. Bilaterally reflect and retract the mucoperiosteum.
5. Identify and preserve the major palatine arteries. They penetrate the hard palate near the caudal aspect of the fourth premolar and run parallel to the course of the dental arcade about midway between it and the midline of the hard palate (see Fig. 160-8).
6. Create a window into the nasal cavity by removing a flap of hard palate with an oscillating saw, air drill, or osteotome and mallet (Fig. 160-9). Enlarge the window with a rongeur, if necessary.

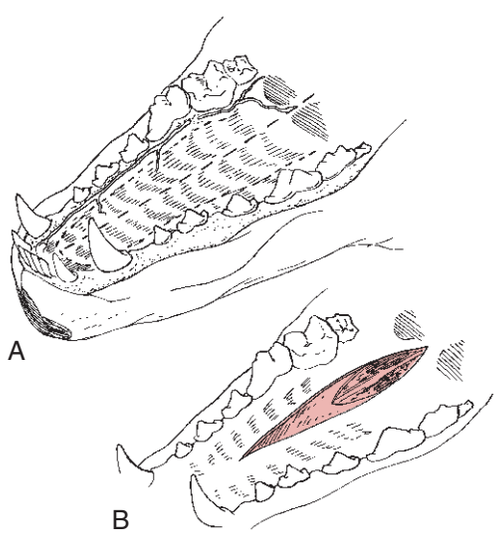

Figure 160-8. Ventral rhinotomy. Incise the mucoperiosteum on the midline or in the shape of a U, which parallels the dental arcade *(A)*. The incision may extend into the soft palate to expose lesions extending into the nasopharynx *(B)*.

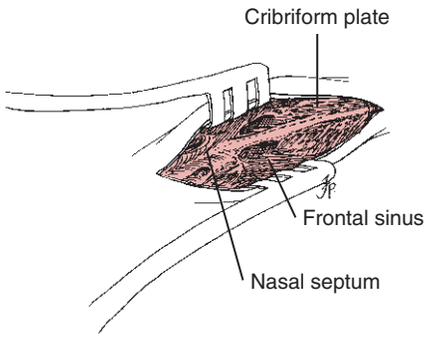

Figure 160-9. Exposure using ventral rhinotomy: cribriform plate, frontal sinus, remnant of nasal septum. (Rostral is to the left.)

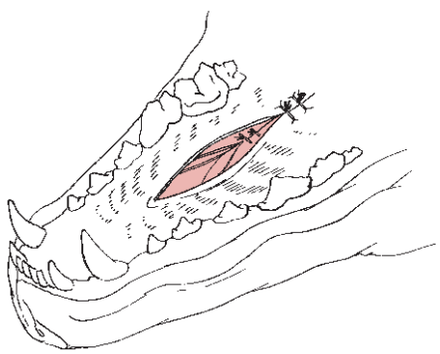

Figure 160-10. Following ventral rhinotomy, appose the mucoperiosteum with simple interrupted sutures. Appose the soft palate using two or three layers of simple interrupted or simple continuous sutures.

7. Remove the lesion and involved conchae (turbinates) with forceps and curettage.
8. Lavage and suction blood clots and debris from the area with copious amounts of saline.
9. Replace or discard the bone flap as for dorsal rhinotomy.
10. Close the mucoperiosteum with simple interrupted sutures. If possible, close the soft palate incision in two or three layers (nasal mucosa, muscle and connective tissue, pharyngeal mucosa) (Fig. 160-10).

Frontal Sinus Procedures

Chronic rhinitis or sinusitis (especially in cats) generally recurs in a variable period of time with either of the following procedures.

Technique for Sinus Flushing

1. Insert indwelling tubes for repeated frontal sinus flushing by first trephining a hole into the sinus.
2. Make an incision in the soft tissues and trephine a hole in the bone just lateral to the midline on a line connecting the rostral margins of the supraorbital processes.

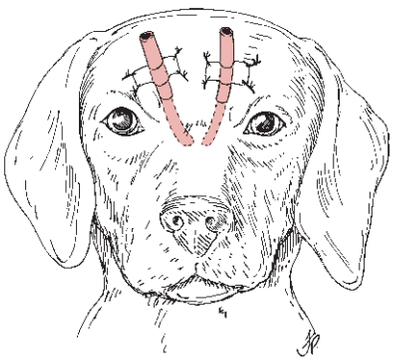

Figure 160-11. Position of tubes inserted into the frontal sinus and nasal cavity for topical treatment of chronic rhinitis and sinusitis. (Redrawn with permission from Slatter DH [ed]: Textbook of Small Animal Surgery. Philadelphia: WB Saunders, 1985.)

3. Collect biopsy and culture specimens.
4. Insert the fenestrated tube into the sinus and secure it to the skin (Fig. 160-11).
5. Following tube removal, allow the openings to heal by second intention.

Technique for Sinus Obliteration

1. Create a bone flap to expose the frontal sinuses and caudal nasal cavity.
2. Remove the compartment divisions and mucosal lining of the frontal sinus and aperture with a pneumatic bone bur. Complete removal of the lining is aided by the use of a dissecting or operating microscope.
3. Cover the aperture of the frontal sinus into the nasal cavity with a free fascial or muscle patch.
4. Lavage the area and fill the sinus with fat harvested from a secondary site (e.g., falciform ligament).
5. Close the periosteum, subcutaneous tissue, and skin.

POSTOPERATIVE CARE AND COMPLICATIONS

Patient Care

- Following rhinotomy, place the patient in a slightly head-down position and remove the endotracheal tube with the cuff slightly inflated to help remove fluid and debris.
- Give postoperative analgesics such as morphine (0.2–0.4 mg/kg IM or SC), fentanyl (1–5 µg/kg/hour continuous rate infusion), or buprenorphine (Buprenex, Norwich Eaton) (0.005 mg/kg IM or IV) for the first 24 hours and then as needed.
- Chewing on hard objects is forbidden if the bone flap from the hard palate is discarded.
- Prior to creating a nasal stoma, graphically describe to the client the postoperative appearance of the patient (optimally by viewing pictures of other

patients). Many clients are initially reluctant to accept their pets' appearance following rhinostomy.
- Following rhinotomy, discharge patients from the hospital within 2 to 3 days unless complications or adjuvant therapy dictates longer hospitalization.

Complications

- Expect sneezing and mild epistaxis for several days.
- Breathing sounds are harsh and resonant, often sounding "hollow."
- Appetite may be depressed for several days. Give cats diazepam or oxazepam to stimulate appetite if necessary.
- A serous to serosanguineous nasal discharge occurs for several days to weeks, depending on the primary disease condition and the effectiveness of adjuvant therapy. This discharge may continue indefinitely.
- Inward and outward movement of the skin flap may be observed with inspiration and expiration, respectively, if the bone flap is discarded, but this movement is usually temporary.
- Subcutaneous emphysema may occur. It is usually localized to the head and resorbs without treatment. If emphysema is excessive, place a tube in the frontal sinus to vent the air and aspirate the subcutaneous air.
- If carotid artery occlusion is not employed, blood loss during surgery may be excessive, requiring transfusions and vigorous fluid therapy.
- Airway obstruction is rare but may occur due to failure to mouth breath, mucosal edema, and anxiety. Sedate these animals and provide supplemental oxygen in a quiet, cool environment. Give corticosteroids to reduce mucosal edema.
- Disease erosion of the cribriform plate or curettage may result in exposure of the brain and cerebral edema. Treat brain edema with rapid-acting water-soluble IV corticosteroids, osmotic agents (mannitol), hyperventilation, hyperbaric oxygen, calcium channel blockers, and antioxidants.
- Indwelling catheters can be dislodged by the patient; therefore, some surgeons create temporary rhinostomies to facilitate topical therapy.
- Nasocutaneous or oronasal fistulas may form if healing is interrupted.
- Replaced bone flaps may sequestrate secondary to infection or radiation therapy.
- Chronic rhinitis or sinusitis and its causative agents will persist or recur if rhinotomy and turbinectomy (excision of nasal conchae) are performed without appropriate medical therapy (see Chapter 163). Exceptions may include nasal disease caused by foreign bodies or *Rhinosporidium* organisms.
- The chronic nasal discharge may persist because it is not possible to remove all diseased tissue during turbinectomy, and the epithelium may have undergone squamous metaplasia.

Prognosis

- Survival following various combinations of therapy for nasal neoplasms ranges from 4 to >24 months.
- Fungal rhinitis is refractory to antifungal agents currently available in about 50% of the cases. Antifungal agents are usually given for 6 to 8 weeks orally or repeated topically 1 to 3 times depending on the agent used. See Chapter 163 for medical treatment of infectious rhinitis and sinusitis.

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Chapter

161 Obstructive Upper Airway Disorders

Roger B. Fingland

Obstructive upper airway diseases typically are insidious in onset and result in progressively worsening respiratory stridor and dyspnea. The dimensions of the upper airway play a fundamental role in the efficiency of breathing and progression of disease. In narrowed regions of the upper airway, air velocity is higher and pressure is lower than elsewhere (Bernoulli effect), which tends to narrow susceptible regions of the upper airway still more.

ETIOLOGY

Congenital obstructive upper airway diseases are diagnosed so commonly in brachycephalic dogs that they are referred to collectively as the brachycephalic syndrome. Most other obstructive upper airway diseases are acquired and are diagnosed in middle-aged and older dogs. Obstructive upper airway diseases are diagnosed less frequently in cats.

Brachycephalic Syndrome

The brachycephalic syndrome consists of stenotic nares, elongated soft palate, and everted laryngeal saccules.

- Tracheal hypoplasia is a generalized narrowing of the tracheal lumen diameter diagnosed commonly in English bulldogs and, less commonly, in other brachycephalic breeds.
- Stenotic nares and elongated soft palate are congenital conditions diagnosed quite frequently in brachycephalic dogs.
- Laryngeal saccule eversion is a consequence of chronic upper airway obstruction.

Laryngeal Collapse

Laryngeal collapse is recognized most commonly in brachycephalic dogs with chronic obstructive upper respiratory disease (brachycephalic syndrome). Loss of the supporting function of the laryngeal cartilages results from pressure changes within the larynx induced by obstruction rostral to the rima glottidis. Laryngeal collapse is considered a progressive, end-stage disease. However, some dogs have a mild to moderate form of the condition and can do reasonably well with medical management.

Laryngeal Paralysis

This condition is seen primarily in old, large-breed, and giant-breed dogs. Interruption of the innervation to the intrinsic muscles of the larynx, particularly the cricoarytenoideus dorsalis muscle, results in failure of the arytenoid cartilages and vocal folds to abduct during inspiration. The condition is a congenital anomaly in some breeds, such as the Bouvier des Flandres, Siberian husky, and dalmatians. Laryngeal paralysis also has been associated with hypothyroidism (see Chapter 31) and diffuse polyneuropathies in dogs (see Chapter 129). In many cases laryngeal paralysis is idiopathic.

Nasopharyngeal Polyps

These inflammatory masses arise from the epithelium of the nasopharynx, auditory canal, or tympanic cavity (see Chapters 59 and 61).

- Polyps commonly occur in cats and may be congenital in young cats.
- Masses that arise from or involve the nasopharynx result in upper airway obstruction. Although nasopharyngeal polyps are rare in dogs, upper airway obstruction related to soft tissue proliferation can develop in dogs with hyperprogesteronism secondary to drug administration or excessive hormone production in the bitch.

Tracheal Collapse

This condition is seen primarily in old toy-breed dogs. Occasionally it is diagnosed in young dogs and may be congenital.

- The etiology of tracheal collapse is not known, but most likely it is multifactorial and related to changes in airflow dynamics due to primary small airway or upper airway disease. Potential etiologic factors include the following:
  - Predisposition in small-breed dogs
  - Obesity

- Degeneration of tracheal cartilages
- Chronic bronchitis

Tracheal Stenosis

Tracheal stenosis is usually a sequela of traumatic tracheal disruption. Animal bite wounds, traumatic intubation or extubation, and cervical gunshot wounds are common causes of tracheal injury.

Intraluminal Foreign Bodies

Tracheal foreign bodies rarely cause complete obstruction; large items usually are retained at the carina, whereas small ones often pass into the bronchi, leading to bronchial obstruction and pneumonia.

Primary Tracheal Neoplasia

These tumors are uncommon in dogs and rare in cats.

- Primary tracheal tumors reported in dogs include osteosarcoma, osteochondroma, chondrosarcoma, leiomyoma, mast cell tumor, adenocarcinoma, and squamous cell carcinoma.
- Primary tracheal lymphoma and adenocarcinoma have been reported in cats.

Extraluminal Compression of the Trachea

Segmental tracheal stenosis can be caused by compression from extraluminal masses such as parasitic granulomas *(Oslerus [Filaroides] osleri),* thyroid carcinoma (see Chapter 31), hilar lymphadenopathy (see Chapter 165), left atrial enlargement (see Chapter 149), mediastinal lymphoma (see Chapter 27), and mediastinal lipoma.

CLINICAL SIGNS

Stertor and Stridor

These signs of obstructive upper respiratory disease are so common in brachycephalic dogs that owners frequently do not recognize noisy breathing as abnormal.

- Stridor is a high-pitched inspiratory sound generated from obstruction of laryngeal airflow.
- Dogs with an elongated soft palate often have characteristic stertorous, or snoring, respiratory sounds that result from occlusion of the rima glottidis by the excessively long soft palate.
- Stridor and voice change are common in cats with nasopharyngeal polyps and in dogs with laryngeal paralysis. Dogs with laryngeal collapse can exhibit either stertor or stridor.

Dyspnea

Dyspnea is observed in most animals with obstructive upper respiratory disease.

- Inspiratory dyspnea, expiratory dyspnea, or a combination may be present, depending on the location and severity of obstruction.
- Collapse of the cervical segment of the trachea results in primarily inspiratory dyspnea, whereas collapse of the thoracic segment of the trachea often is associated with expiratory dyspnea.
- Animals with fixed upper respiratory obstruction such as tracheal stenosis and laryngeal collapse usually are continually dyspneic. Dyspnea may be intermittent and exacerbated by exercise, stress, or high ambient temperature in dogs with tracheal collapse or laryngeal paralysis.

Cough

Coughing is common in dogs with tracheal collapse and, less frequently, in dogs with tracheal stenosis or laryngeal paralysis.

- Approximately 50% of dogs with tracheal collapse have a characteristic "goose honk" cough associated with vibration in the collapsing segment. Other dogs with tracheal collapse do not have a characteristic cough, and some do not cough.
- Dogs with tracheal collapse rarely cough continuously. The cough may be intermittent, and paroxysms usually are exacerbated by stress, excitement, and mechanical stimulation of the trachea.

Decreased Exercise Tolerance

Occasionally, decreased exercise tolerance is observed in dogs with laryngeal paralysis, laryngeal collapse, tracheal stenosis, or brachycephalic syndrome.

Voice Change

This may be an early clinical sign in dogs with laryngeal paralysis. It is also common in cats with nasopharyngeal polyps.

Hyperthermia

Symptoms of laryngeal paralysis frequently are not apparent until the animal is exposed to high ambient temperature; some dogs with laryngeal paralysis are presented with profound hyperthermia.

▼ ***Key Point*** Evaluate laryngeal function in large-breed dogs requiring treatment for hyperthermia.

Gagging

Occasionally, gagging is observed early in the course of obstructive upper airway diseases such as laryngeal paralysis and elongated soft palate.

Dysphagia

Dysphagia may occur in cats with nasopharyngeal polyps and, rarely, in dogs with laryngeal paralysis.

Syncope

Fainting associated with exercise (overexertion), excitement, or coughing spells occurs in some dogs with tracheal collapse.

DIAGNOSIS

History

- Animals in the early stages of obstructive upper airway disease typically are asymptomatic at rest.
- Excitement, exercise, or stress leads to varying degrees of coughing, dyspnea, and stridor.
- Clinical signs may progress to constant, severe coughing and dyspnea.
- Some animals with severe obstructive upper respiratory disease are presented with a history of cyanosis or syncope.

Physical Examination

The physical examination often is unremarkable in dogs with obstructive upper respiratory diseases.

- Distinct lateral tracheal borders may be identified on cervical palpation in dogs with tracheal collapse. Gentle tracheal palpation may cause paroxysms of coughing.
- An ear discharge occasionally is identified in cats with nasopharyngeal polyps. Otoscopic examination may reveal polypoid masses within the external ear canal.
- Stenosis of the external nares may be evident in brachycephalic dogs.

Oropharyngeal Examination

A thorough oropharyngeal examination under light general anesthesia is diagnostic for most obstructive upper airway diseases.

Brachycephalic Syndrome

- The soft palate overlaps the tip of the epiglottis.
- Everted laryngeal saccules are identified as oval mucosal masses projecting into the ventral rima glottidis, lateral to the vocal folds.
- Enlarged tonsils and edematous pharyngeal mucosa are common.

Laryngeal Paralysis

- Animals with laryngeal paralysis are unable to abduct the arytenoid cartilages and vocal folds during inspiration.

▼ ***Key Point*** Use *light* anesthesia for evaluation of laryngeal function. A surgical plane of anesthesia will obliterate normal laryngeal reflexes and possibly result in a false-positive diagnosis.

- Slight, asynchronous abduction of the arytenoids may be observed in some cases.
- The majority of dogs with laryngeal paralysis have bilateral dysfunction of the cricoarytenoideus dorsalis muscle. Unilateral laryngeal paralysis (hemiplegia) is identified infrequently, perhaps because animals with unilateral involvement remain asymptomatic.
- Laryngeal edema and inflammation also may be seen.
- Evaluate arytenoid abduction during inspiration. Do not consider passive *expiratory* opening of the glottis and arytenoids as evidence of normal function.

Laryngeal Collapse

- The corniculate and cuneiform processes of the arytenoid cartilages are apposed or overlap, causing collapse of the airway.
- Abduction of the arytenoids is not observed.

Nasopharyngeal Polyp

- With the animal in dorsal recumbency, expose the polyp by gently retracting the soft palate ventrally and rostrally.

Radiography

Obtain radiographs of the pharyngeal, cervical, and thoracic regions.

- A soft tissue density cranial to the pharynx or an increased radiodensity of one of the osseous bullae may be identified on skull radiographs of cats with nasopharyngeal polyps. Computed tomography (CT) scan is also useful in identifying tympanic bulla changes in cats with polyps.
- The soft palate may appear thickened and lengthened in dogs with an elongated soft palate. Normally, the soft palate does not extend beyond the tip of the epiglottis.
- Narrowing of the tracheal diameter may be evident on lateral cervical and thoracic radiographs in dogs with tracheal collapse. Collapse occurs most commonly at the thoracic inlet. Tracheal collapse is a dynamic disease, especially in the early stages. Obtain full inspiratory and expiratory views because the trachea may not be collapsed during all phases of respiration. A normal or near-normal tracheal diameter on plain film radiographs does not rule out tracheal collapse.
- Tracheal stenosis is identified on a lateral cervical or thoracic radiograph as a focal reduction of the tracheal lumen diameter. Radiographs usually are adequate to establish a diagnosis of tracheal stenosis because of the static nature of the condition.
- Aspiration pneumonia is an infrequent sequela of obstructive upper respiratory disease. Aspiration pneumonia typically is characterized by a mixed alveolar-interstitial density in the dependent portions of the cranial and middle lung lobes (see Chapter 163).

Fluoroscopy

Fluoroscopy allows continual assessment of the tracheal lumen diameter during all phases of the respiratory cycle. In dogs suspected of having tracheal collapse, evaluate the entire trachea and both main stem bronchi during quiet respiration and induced coughing.

Tracheoscopy

Tracheoscopy is beneficial in assessing the location and severity of stenotic tracheal lesions. Perform tracheoscopy under general anesthesia and pay close attention to patient oxygenation.

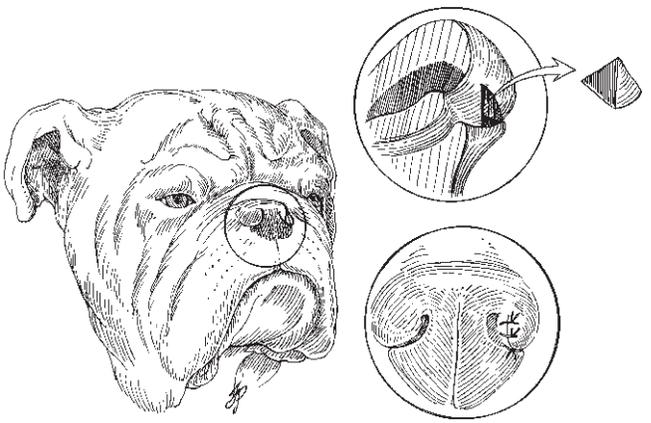

Figure 161-1. Wedge resection of the alar fold for stenotic nares.

TREATMENT

Brachycephalic Syndrome

Nasal Wedge Resection

Surgical Anatomy

In the dog, the nasal vestibule is occupied by the end of the ventral nasal concha, called the alar fold.

Preoperative Considerations

- Administer oxygen through a face mask for 3 to 5 minutes prior to induction (preoxygenation). Minimize stress to the patient.
- Consider temporary tracheostomy in brachycephalic dogs undergoing upper respiratory tract surgery.
- Rapid induction of anesthesia and control of the airway is essential. Mask induction is discouraged.
- Thoroughly evaluate the upper airway in animals with stenotic nares. Staphylectomy (soft palate excision) and laryngeal sacculectomy probably will be necessary.

Surgical Procedure

Objective

To increase the cross-sectional area of the nasal vestibule

Equipment

- #15 or #11 blade
- 4-0 or 5-0 monofilament nylon or polypropylene suture material
- Standard minor surgery pack

Technique

1. Excise a vertical triangular or elliptical wedge of tissue extending from the wing of the nostril caudally to include part of the alar cartilage. The base of the wedge should include one-third to one-half of the free edge of the nostril (Fig. 161-1).
2. Close the incision with 4-0 or 5-0 nylon or polypropylene suture material in a simple interrupted pattern.
3. If the cross-sectional area of the nasal vestibule has not been increased adequately, remove the sutures and excise more tissue. Remove the same amount of tissue on each side to ensure symmetrical nostrils.

Postoperative Care and Complications

- Carefully monitor the dog during recovery and for several hours after surgery.
- Incisional hemorrhage may occur but resolves with direct pressure.
- Signs of respiratory obstruction persist following nasal wedge resection if concurrent obstructive upper respiratory diseases have not been managed properly.

Staphylectomy (Correction of Elongated Soft Palate)

Surgical Anatomy

- The soft palate is a valve-like partition composed of mucosal and muscular layers.
- The free edge of the soft palate should appose or slightly overlap the epiglottis.

Preoperative Considerations

- See preceding discussion under "Nasal Wedge Resection."
- Just prior to beginning the procedure, administer dexamethasone sodium phosphate (0.2 mg/kg IV) to reduce tissue edema and inflammation associated with the surgery.

Surgical Procedure

Objectives

- To shorten the soft palate so that the free edge apposes or barely overlaps the epiglottis

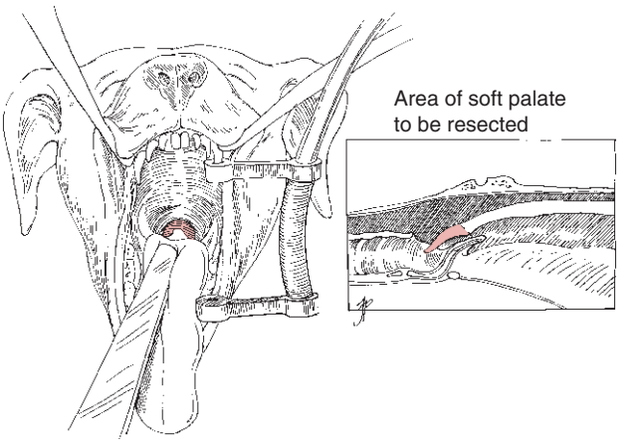

Figure 161-2. Staphylectomy for elongated soft palate. The area of soft palate to be resected is in red.

- To minimize pharyngeal and laryngeal edema by using an atraumatic technique

Equipment

- Standard instrument pack and suture
- Babcock forceps

Technique

1. Position the dog in ventral recumbency with the mouth held open with an oral speculum or adhesive tape sling.
2. Determine the portion of the soft palate that is excessive (Fig. 161-2) by placing it adjacent to the epiglottis. Alternatively, excise that portion of the soft palate that extends beyond an imaginary line across the *caudal* pole of the tonsils.
3. Place traction sutures of 4-0 absorbable suture material in the lateral aspect of the soft palate adjacent to the point at which the epiglottis touches the soft palate.
4. Grasp the center of the free border of the soft palate with Babcock forceps and retract it rostrally.
5. Incise approximately one-half the width of the soft palate with curved Metzenbaum scissors. Suture the incised mucosal edges with 4-0 absorbable suture material in a simple continuous pattern. The nasal mucosa tends to retract caudally.
6. Continue the "cut-and-sew" technique (Fig. 161-3) until the palate is resected and closure is complete.
7. Avoid using crushing clamps and electrocautery.

Postoperative Care and Complications

- Laryngeal edema is a common postoperative complication in brachycephalic dogs that have had surgery on the upper respiratory tract.

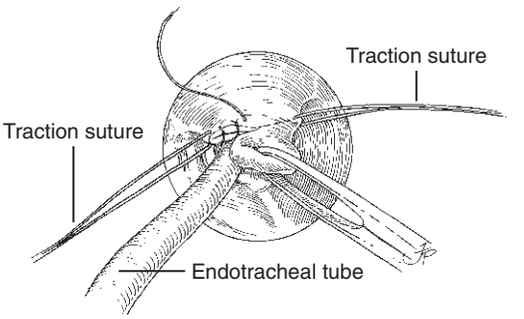

Figure 161-3. "Cut-and-sew" procedure for soft palate resection.

▼ ***Key Point*** Excessive resection of the soft palate may allow aspiration of food postoperatively because the shortened palate is unable to close the nasopharynx during swallowing.

- Clinical signs may persist if resection of the palate was inadequate.

Laryngeal Sacculectomy

Surgical Anatomy

Laryngeal saccules are small, mucosa-lined outpouchings that lie lateral to the vestibular folds.

Preoperative Considerations

See discussion under "Nasal Wedge Resection" and "Staphylectomy (Correction of Elongated Soft Palate)."

Surgical Procedure

Objective

To remove the everted laryngeal saccules and thereby relieve the obstruction

Equipment

- Metzenbaum scissors
- Babcock or Allis tissue forceps

Technique

1. Position the dog in ventral recumbency with the mouth held open with an oral speculum or adhesive tape sling.
2. Grasp the saccule with Babcock or Allis tissue forceps and retract it rostrally.
3. Amputate the saccule at its base with Metzenbaum scissors.
4. Use direct pressure to control hemorrhage. The cuff of the endotracheal tube can be used to apply pressure.

Postoperative Care and Complications

See discussion under "Staphylectomy (Correction of Elongated Soft Palate)."

Laryngeal Paralysis

Surgical Anatomy

- The larynx is supported by the cricoid and thyroid cartilages.
- Left and right arytenoid cartilages covered with mucous membrane are located at the rostral end of the larynx and form the dorsal part of the glottal cleft. The corniculate and cuneiform processes of the arytenoid cartilages project into the glottal cleft.
- The vocal folds form the ventral part of the glottal cleft.
- The cricoarytenoideus dorsalis muscles are innervated by the recurrent laryngeal nerves and are the only abductors of the arytenoid cartilages and vocal folds.

Preoperative Considerations

- Medical therapy for hyperthermic dogs in acute cyanotic crisis includes oxygen administration, alcohol or ice water baths, IV fluid therapy, and corticosteroids (prednisolone sodium succinate, 2.5 to 5.0 mg/kg IV, and dexamethasone, 0.5 mg/kg IV).
- Sedation may be necessary (e.g., acepromazine) to calm hyperthermic animals.
- Temporary tracheostomy (see Chapter 3) may be necessary for animals that do not respond to initial conservative treatment.
- Evaluate thyroid function (see Chapter 31). Also, perform a neurologic examination to evaluate the animal for polyneuropathy.
- Preoxygenate the dog and gain control of the airway rapidly during induction of anesthesia (i.e., via tracheal intubation).
- Prepare for tracheostomy tube insertion.

Surgical Procedure: Arytenoid Lateralization

Objective

To increase the diameter of the rima glottidis by lateralizing the arytenoid cartilages, which is also known as a tie-back procedure.

Avoid excessively lateralizing the arytenoid, which could predispose to aspiration pneumonia.

Equipment

- Standard surgical pack and suture
- Narrow malleable retractors
- Gelpi or Weitlaner retractors

Arytenoid lateralization involves freeing the arytenoid cartilage from its cartilaginous attachments and placing a non-absorbable suture to permanently abduct the cartilage, thus increasing the diameter of the rima glottidis. The procedure should be performed unilaterally, since that is usually successful in alleviating clinical signs.

Advantages

Advantages of arytenoid lateralization over other techniques, such as arytenoidectomy, are as follows:

- Intraoperative hemorrhage and postoperative edema are less compared with intraoral procedures.
- Postoperative laryngeal scar formation is uncommon.
- Voice change is minimal because a ventriculocordectomy is not performed.
- Temporary tracheostomy is seldom needed.

Technique

1. Prepare the ventral and lateral cervical region for aseptic surgery.
2. Place the dog in dorsolateral recumbency with the neck extended over a small, rolled towel. Approach either the right or the left side of the larynx, depending on the preference of the surgeon.
3. Make a paramedian incision adjacent to the larynx, approximately in the jugular furrow.
4. Continue the incision through the superficial muscle and subcutaneous fat, and identify the thyropharyngeus muscle.
5. Grasp the dorsal edge of the thyroid cartilage through the thyropharyngeus muscle. Rotate the thyroid cartilage ventrally.
6. Transect the thyropharyngeus muscle along the dorsal edge of the thyroid cartilage (Fig. 161-4).
7. Elevate the exposed dorsal edge of the thyroid cartilage and incise the articulation of the thyroid and cricoid cartilages. The intrinsic muscles of the larynx are exposed. Identify the cricoarytenoideus dorsalis muscle.
8. Transect the cricoarytenoideus dorsalis muscle near its insertion on the muscular process of the arytenoid cartilage (Fig. 161-5). Preserve a section of the muscle for histologic analysis.
9. Retract the remainder of the cricoarytenoideus dorsalis muscle rostrally and identify the cricoarytenoid articulation.
10. Separate the cricoarytenoid articulation with Mayo scissors.
11. Retract the arytenoid cartilage laterally.
12. Pass Mayo scissors between the arytenoid and the cricoid cartilages and transect the arytenoid-arytenoid articulation on the dorsal midline of the larynx. Some surgeons chose not to transect this articulation, and adequate arytenoid lateralization still results.

▼ ***Key Point*** Wound infection and postoperative stricture formation are more likely if the laryngeal mucosa is incised during this procedure.

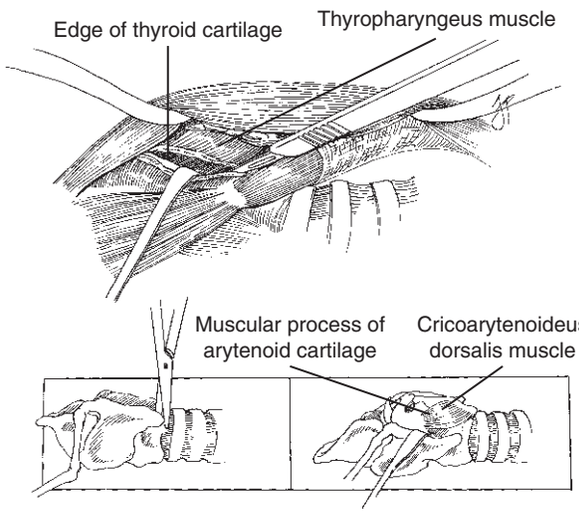

Figure 161-4. Arytenoid lateralization. Transect the thyropharyngeus muscle and expose the arytenoid cartilage. *Below left,* Transect the cricothyroid articulation. *Below right,* expose the arytenoid cartilage by retracting the thyroid cartilage.

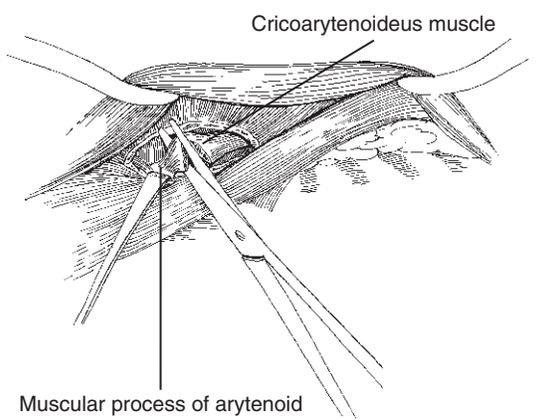

Figure 161-5. Arytenoid lateralization. Transect the cricoarytenoideus dorsalis muscle.

13. Pass a monofilament non-absorbable suture (0 nylon or polypropylene) from the muscular process of the arytenoid cartilage to the caudodorsal portion of the thyroid cartilage (Fig. 161-6). Alternatively, pass the suture from the muscular process of the arytenoid cartilage to the caudodorsal aspect of the cricoid cartilage (see inset in Fig. 161-6).
14. Temporarily extubate the patient and have an assistant perform an oral examination to evaluate the degree of arytenoid lateralization. Temporary extubation is not necessary if anesthetic gases are being delivered through an endotracheal tube passed through a temporary tracheostomy.
15. Tighten the suture as an assistant evaluates the position of the arytenoid cartilage. Knot the suture at the point of maximal abduction.

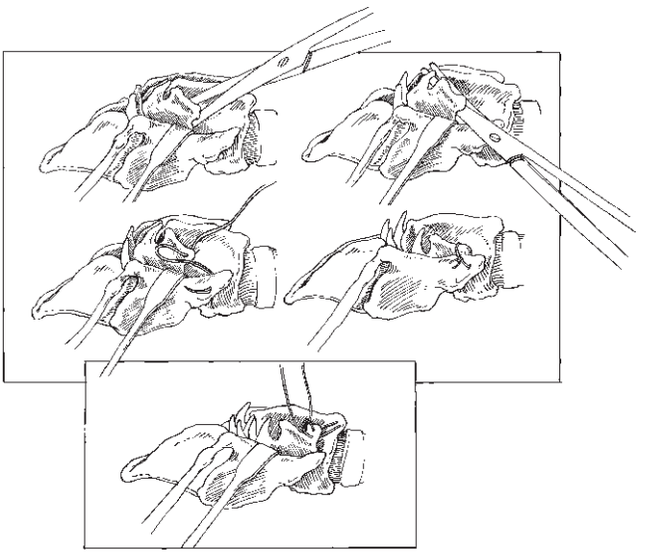

Figure 161-6. Arytenoid lateralization-suture adduction. *Top,* Transect the arytenoid-cricoid articulation *(left),* then the arytenoid-arytenoid articulation carefully *(right),* avoiding incising the laryngeal mucosa. Suture the muscular process of the arytenoid cartilage to the caudodorsal portion of the thyroid cartilage. *Inset,* In the alternative LaHue approach, suture from the muscular process of the arytenoid to the dorsocaudal aspect of the cricoid.

16. Replace the endotracheal tube if it was removed.
17. Close the thyropharyngeus muscle with 3-0 absorbable suture in a simple continuous pattern.
18. Close the subcutaneous and skin layers routinely.

Postoperative Care and Complications

- Laryngeal edema is a common sequela of laryngoplasty. Carefully monitor postoperative laryngoplasty patients that do not have a tracheostomy tube for signs of upper respiratory obstruction. Administer corticosteroids and supplemental oxygen if laryngeal edema develops. Be prepared for emergency tracheostomy.
- Manage tracheostomy tubes meticulously. Clean the tube as needed (at least every 2 hours). Double-cannula tracheostomy tubes are ideal (see Chapter 3).
- Laryngeal scar formation resulting in cranial glottic stenosis is a potential complication of arytenoidectomy, especially when excision of the vocal folds or arytenoid cartilages extends into the dorsal or ventral commissures; however, the lateralization procedure avoids this complication.
- Failure to open the rima glottidis adequately may result in recurrence or persistence of clinical signs after surgery.
- Consider lateralization of the contralateral arytenoid cartilage if signs recur or persist after unilateral arytenoid lateralization.
- Consider arytenoidectomy (Fig. 161-7) only as a last resort when bilateral lateralization fails.

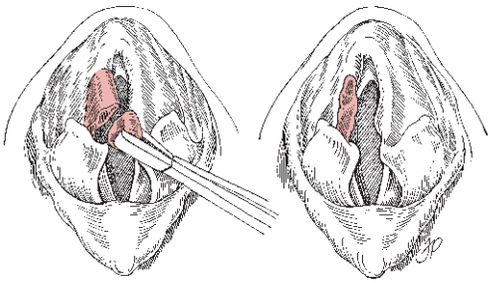

Figure 161-7. Partial arytenoidectomy for laryngeal paralysis.

- Bilateral arytenoidectomy or excision of excessive arytenoid tissue during partial arytenoidectomy may result in laryngeal dysfunction or excessive enlargement of the lumen characterized by episodes of aspiration pneumonia and gagging. Surgical amelioration of this condition is unlikely. Permanent tracheostomy can be performed as a salvage procedure.

Laryngeal Collapse

Treat the predisposing factors, such as stenotic nares, everted laryngeal saccules, and elongated soft palate. Also, recommend an integrated program of medical therapy consisting of weight control, prevention of hyperthermia, and intermittent use of sedatives (e.g., acepromazine) and corticosteroids as needed. If clinical signs persist, reevaluate the respiratory tract. Persistence of clinical signs after appropriate medical and surgical management of predisposing factors may necessitate a permanent tracheostomy.

Permanent Tracheostomy

Preoperative Considerations

- Permanent tracheostomy is a salvage procedure that usually is indicated for treatment of end-stage laryngeal disease. Permanent tracheostomy can be performed following laryngectomy for laryngeal neoplasia.
- Detailed client communication is vital prior to performing permanent tracheostomy. Explain the procedure, potential postoperative complications, and activity restrictions (see below).
- Make certain the segment of the trachea distal to the proposed tracheostomy site is normal. Tracheoscopy or fluoroscopy is preferable; however, inspiratory and expiratory cervical and thoracic radiographs may be adequate to evaluate the integrity of the distal trachea.
- Use an endotracheal tube with a high-volume, low-pressure cuff that has been checked for leaks. Place the cuff distal to the proposed tracheostomy site.

Surgical Procedure

Objective

To create a permanent stoma in the cervical segment of the trachea

Equipment

- Standard surgical pack and suture
- Tracheostomy tube with a high-volume, low-pressure cuff (tube must be long enough to allow positioning of the cuff in the caudal cervical trachea)

Technique

1. Place the dog in dorsal recumbency with the neck extended over a rolled towel. Prepare the ventral cervical region for aseptic surgery.
2. Make a ventral cervical midline incision through the skin and subcutaneous tissues, beginning at the larynx and extending caudally approximately 10 cm. Center the incision over the proposed tracheostomy site.
3. Separate the paired sternohyoideus muscles, exposing the trachea.
4. Bluntly dissect the cervical fascia from the entire circumference of the trachea between the second and the sixth tracheal cartilages.

▼ ***Key Point*** Identify and avoid the recurrent laryngeal nerves when dissecting the cervical fascia from the trachea.

5. Preplace two horizontal mattress sutures (2-0 polydioxanone) between the sternohyoideus muscles, passing *dorsal* to the trachea where the cervical fascia was dissected.
6. Tie the horizontal mattress sutures. This apposes the sternohyoideus muscles dorsal to the trachea, decreasing tension on the mucocutaneous anastomosis by deviating the trachea ventrally to the level of the skin.
7. Make a partial-thickness rectangular incision in the tracheal wall. Make the segment to be excised three tracheal cartilages long (include the third, fourth, and fifth cartilages) and approximately one-third the width of the tracheal circumference (Fig. 161-8).

▼ ***Key Point*** Do not make a full-thickness incision in the tracheal wall. Incise the tracheal wall to the level of the mucosa.

8. Bluntly elevate the tracheal cartilages and annular ligaments from the tracheal mucosa inside the boundaries of the rectangular incision. Remove the cartilages and annular ligaments, leaving the mucosa intact.
9. Excise a rectangular section of skin adjacent to the stoma bilaterally. Make each section equal to the

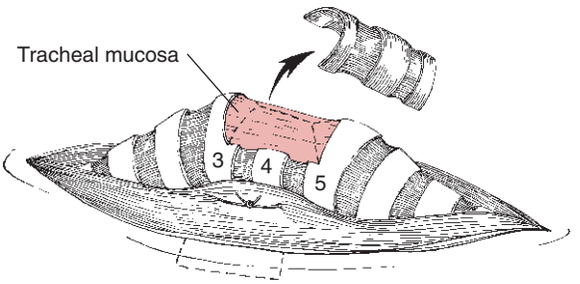

Figure 161-8. Permanent tracheostomy. Remove the segment of ventral trachea with remaining mucosa intact *(red)*. The dotted line indicates the area of mucosa and skin to be incised to complete the stoma.

length and approximately one-half the width of the tracheal stoma (see Fig. 161-8).

10. Secure the skin to the trachea by placing simple interrupted sutures (2-0 polyglycolic) between the dermis (not the skin edge) and the fascia on the lateral aspect of the trachea.
11. Check the endotracheal tube position and make certain that the cuff is inflated. The cuff should be positioned approximately 2 cm distal to the stoma.
12. Incise the tracheal mucosa, as shown in Figure 161-9.
13. Place simple interrupted sutures (4-0 monofilament nylon) 2 mm apart between the skin and the tracheal mucosa. Precise apposition is important.

▼ ***Key Point*** Make certain that there is no tension on the mucocutaneous sutures. Tension predisposes to dehiscence and stenosis.

14. Close the skin incision cranial and caudal to the stoma.
15. Gently suction the tracheal lumen proximal to the cuff to remove clotted blood.

Postoperative Care and Complications

- Clean the stoma every 4 to 6 hours for 48 hours after surgery. Cleaning is needed less frequently after 48 hours. Instruct the owner to clean the stoma once a day.
- Protect the stoma from self-trauma. Elizabethan collars are not recommended. Rarely, rear-limb hobbles are necessary to keep the animal from scratching the surgery site.
- Apply petroleum jelly to the skin around the stoma once a day for approximately 2 weeks to prevent irritation from dried secretions. This usually is not necessary after hair regrows. Avoid putting petroleum jelly in the stoma.
- Trim the hair around the stoma frequently.
- Dirty, dusty environments and swimming must be avoided.
- Skin fold occlusion of the stoma resulting in episodes of respiratory distress is the most common postoperative complication. Excision of redundant skin may be necessary, especially in brachycephalic breeds.
- Approximately 60% of dogs and cats are unable to bark or purr after permanent tracheostomy.
- All tracheostomies stenose approximately 20% to 40%. The degree of stenosis is variable and can be minimized by meticulous surgical technique.
- Closure of the stoma rarely is indicated. Closure is accomplished by resection of the stomal segment and primary anastomosis (see discussion under "Tracheal Resection and Anastomosis").

Nasopharyngeal Polyp

Surgical Anatomy

- The auditory (eustachian) tube extends from the nasal pharynx to the rostral portion of the tympanic cavity. The pharyngeal opening of the auditory tube is an oblique, slit-like opening that lies on the lateral

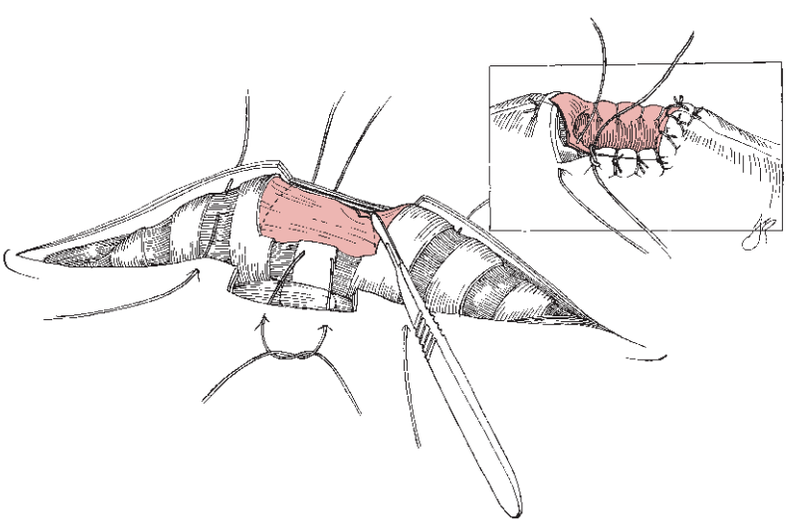

Figure 161-9. Permanent tracheostomy. After the mucosa is incised and reflected laterally, suture the skin directly to the peritracheal fascia and the annular ligament. Complete the stoma by closing the mucosa and skin with simple interrupted sutures *(inset)*.

wall of the nasal pharynx above the middle of the soft palate.
- The tympanic bulla is a smooth bulbous enlargement of the temporal bone, located between the retroarticular and the jugular processes.

Preoperative Considerations

- Obtain skull radiographs or a CT scan preoperatively. Evaluate the tympanic bulla and petrous-temporal bone for evidence of middle ear infection, including osseous bulla thickening, increased density within the tympanic cavity, and sclerosis of the petrous-temporal bone.
- Be prepared to perform a ventral bulla osteotomy in cats with radiographic signs or clinical signs of otitis media.

Surgical Procedure

Objective

To remove the polyp from the pharynx and bulla

Equipment

- Standard surgical pack and suture
- Atraumatic spay hook
- Allis tissue forceps
- Steinmann pin
- Rongeur
- Curette

Technique

1. If a ventral bulla osteotomy is indicated, position the cat in dorsal recumbency and prepare the ventral cervical region for aseptic surgery.
2. Perform a ventral bulla osteotomy (see Chapter 62) on the side with radiographic evidence of otitis media. If the cat is affected bilaterally, perform the osteotomy on the side of origin of the polyp. If the side of origin cannot be determined, perform the osteotomy on the side with the most pronounced radiographic changes.
3. Expose both the dorsomedial and the ventrolateral compartments of the tympanic cavity and carefully remove all inflammatory tissue. Submit tissues for histologic analysis. Avoid curettage of the dorsomedial aspect of the tympanic cavity.
4. Submit material from the bulla for bacterial culture and sensitivity testing.
5. Place a small rubber drain in the bulla that exits from an opening in the skin adjacent to the primary incision.
6. Place the cat in sternal recumbency with the mouth held open by a mouth speculum or adhesive tape sling.
7. Retract the soft palate cranially and ventrally with an atraumatic spay hook.
8. Grasp the nasopharyngeal polyp with an Allis tissue forceps and apply slow, steady traction until the mass is removed. A long stalk should be attached at the base.
9. Submit the excised tissue for histologic evaluation.

Postoperative Care and Complications

- Observe for laryngeal edema.
- Horner syndrome is a common complication of bulla osteotomy in cats. Clinical signs typically resolve within 4 weeks.
- Leave the drain in the bulla osteotomy site for 3 to 5 days.
- Administer antibiotics based on results of culture and sensitivity testing.

▼ ***Key Point*** Nasopharyngeal polyps may recur as a result of incomplete excision of inflammatory tissue. Failure to perform a bulla osteotomy in cats with middle ear involvement is a common cause of recurrence.

Tracheal Collapse

Application of Extraluminal Prostheses

Surgical Anatomy

- Individual C-shaped cartilage rings provide structural rigidity for the trachea.
- The space left by failure of the cartilage rings to meet dorsally is spanned by the transversely oriented trachealis muscle and connective tissue, collectively referred to as the dorsal tracheal membrane.
- The left recurrent laryngeal nerve lies on the left lateral or dorsolateral aspect of the trachea.
- The trachea is supplied by the cranial thyroid, caudal thyroid, and bronchoesophageal arteries. These arteries are enmeshed in delicate sheets of connective tissue on the lateral aspects of the trachea called lateral pedicles. Small, transversely oriented branches penetrate between tracheal rings and arborize in the tracheal submucosa.

Preoperative Considerations

- Consider surgical management on initial presentation only in dogs that are experiencing life-threatening dyspnea or syncope. Treat other dogs medically (Table 161-1) for approximately 4 weeks before considering surgical management. Dogs with mild to moderate tracheal collapse that respond well to medical management may not require surgery.
- Perform a tracheal wash, preferably bronchoscopically, and submit samples for routine cytology and bacterial culture and sensitivity testing.

- Identify the location of collapse using radiography or bronchoscopy.
- Anesthesia (see Chapter 2 for details on drug dosages):
  - Choose an endotracheal tube that is long enough to reach the thoracic inlet. Test the cuff.
  - Premedicate with diazepam.
  - Administer a *light* dose of thiobarbiturate.

▼ ***Key Point*** Always evaluate laryngeal function in dogs with tracheal collapse.

  - Induce anesthesia and rapidly gain control of the airway by passing an endotracheal tube.
  - Prepare for mechanical ventilation.
  - Administer cefazolin (25 mg/kg IV) at induction of anesthesia and 2 hours after the first dose.

Table 161-1. MEDICAL TREATMENT OF TRACHEAL COLLAPSE

Patient Management

Avoid airborne irritants or allergens.
Identify and then minimize exacerbating factors. Excitement, stress, extremes of air temperature, and humidity should be avoided.
Control daily activity. Minimize fatigue, episodes of exercise-induced cough, or dyspnea.
Provide nutritional counseling. Correct overweight body condition.
Schedule routine preventive dental care. Dental prophylaxis reduces bacterial contamination of the pharynx and upper airway.
Prevent dehydration. Adequate hydration maintains low viscosity of airway secretions and thereby promotes clearance.
Promote clearance of airway secretions. Liquefy secretions using humidifier or vaporizer treatments (probably more effective than expectorant drugs), and then facilitate their removal using physiotherapy (light exercise, coupage, or percussion).
Prevent infectious tracheobronchitis (kennel cough complex). Vaccination for parainfluenza, adenovirus, and *Bordetella* is preventive.

Drug Therapy

Antibiotics. If complicating bacterial airway infections are suspected, use amoxicillin-clavulanate cephalosporins, trimethoprim-sulfa, quinolones, or others as guided by tracheobronchial cultures; aerosol administration (gentamicin, 50 mg q12h for 5–7 days) may be more effective for eliminating *Bordetella* from the airways.
Reduce airway inflammation. Use an oral corticosteroid (prednisone, 1–2 mg/kg/day for 1–2 weeks; if improvement is noted, then continue with alternate-day maintenance.
Bronchodilator therapy. See Chapter 162 for a table of drug dosages. Administer drugs such as aminophylline, theophylline, oxtriphylline, or terbutaline, although the reversibility of lower airway obstruction in canine bronchitis and tracheobronchitis may be limited.
Antitussive therapy. See Chapter 162 for a table of drug dosages. Administer drugs such as hydrocodone to control a cough that is distressful to the owner or that causes exhaustion or episodic collapse in the animal; use cautiously and only intermittently if possible, because suppression of the cough reflex may be detrimental to clearance of airway secretions in chronic bronchitis.

Surgical Procedure

Objective

To provide rigid support for the collapsed tracheal segment and maintain function of the mucociliary system

Equipment

- Spiral- or ring-shaped prostheses made from the case and barrel of a 3-ml polypropylene syringe case (Fig. 161-10)
- 4-0 polypropylene suture material with a tapercut needle
- Standard instrument pack and suture
- Small Gelpi retractors

Technique

1. Place the dog in dorsal recumbency with the neck extended over a small, rolled towel.
2. Prepare the ventral cervical region for aseptic surgery.
3. Incise the skin on the ventral cervical midline from the larynx to the manubrium.
4. Separate the paired sternohyoideus and sternothyroideus muscles on the midline and retract the muscles laterally with Gelpi retractors. Partially myotomize the sternocephalicus muscles at the manubrial attachment.
5. Identify the left recurrent laryngeal nerve.
6. Beginning approximately 2 cm caudal to the larynx and preserving the caudal thyroid artery, dissect the lateral pedicle from the left side of the trachea to the level of the thoracic inlet.
7. Make a 5-mm window in the right lateral pedicle 2 cm caudal to the larynx, preserving the caudal thyroid artery.
8. Place a right-angle forceps dorsal to the trachea through the window in the right lateral pedicle; grasp the spiral prosthesis and direct the prosthesis around the trachea.
9. Rotate the prosthesis onto the trachea, making a small window in the right lateral pedicle where the

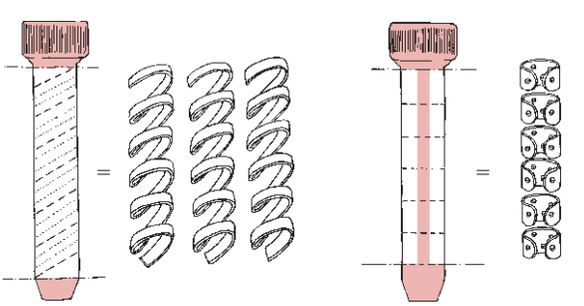

Figure 161-10. Extraluminal prosthesis. The barrel of a 3-cc polypropylene syringe case can be used to make spiral or ring-shaped tracheal prostheses.

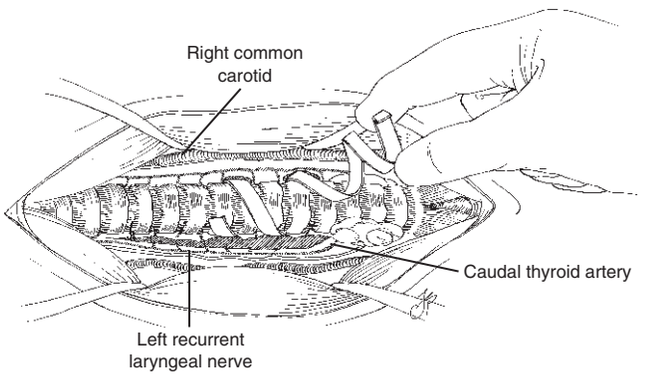

Figure 161-11. Extraluminal prosthesis. Rotate the prosthesis onto the trachea.

prosthesis passes around the right lateral aspect of the trachea. Place the prosthesis over the collapsed segment of the trachea (Fig. 161-11).

10. When applying total-ring prostheses (C-shaped rings), simply make small windows through the right and left lateral pedicles to allow placement of the rings.
11. Deflate the endotracheal tube cuff and reposition the tube either cranial or caudal to the prosthesis. Reinflate the endotracheal tube cuff.
12. Suture the prosthesis to the trachea with 4-0 polypropylene suture material placed in simple interrupted fashion. Place a row of sutures laterally, ventrally, and dorsally, including the dorsal tracheal membrane. All sutures enter the tracheal lumen (Fig. 161-12).
13. Apply additional prostheses caudally as needed. Gentle cranial traction on the cervical trachea affords limited exposure to the segment of the trachea in the thoracic inlet.
14. Deflate the endotracheal tube cuff and gently move the tube in the trachea to ensure that sutures have not been placed through the endotracheal tube cuff. Reinflate the cuff.
15. Appose the sternocephalicus, sternohyoideus, and sternothyroideus muscles. Close the subcutaneous tissue and skin in a routine manner.
16. The intrathoracic segment of the trachea can be supported by performing a right third intercostal thoracotomy (see Chapter 167) and applying prostheses, as described above.

Postoperative Care and Complications

- Leave the endotracheal tube in place with the cuff inflated until the dog has a strong swallowing reflex. Deflate the cuff prior to removing the tube.
- Administer supplemental oxygen postoperatively as needed.
- Administer corticosteroids immediately postoperatively and at 6 hours postoperatively to minimize tracheal mucosal swelling. See discussion under "Staphylectomy (Correction of Elongated Soft Palate)" for drugs and dosages.
- Continue antibiotic therapy for 14 days after surgery.
- Continue antitussive and bronchodilator therapy as needed to control coughing (see Table 161-1).
- Observe the dog for subcutaneous emphysema and signs of tracheal obstruction for 5 days after surgery.
- Ischemic necrosis of the trachea resulting from dissection of the lateral pedicles occurs in a limited number of cases. Gentle tissue handling and minimizing dissection of the lateral pedicles reduces the incidence of this complication.

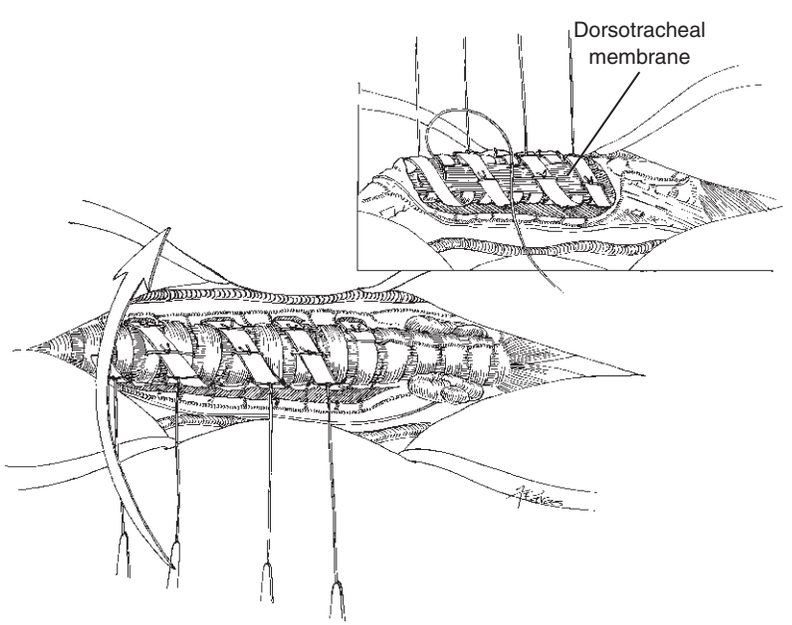

Figure 161-12. Extraluminal prosthesis. Suture the prosthesis to the trachea laterally, ventrally, and dorsally. All sutures enter the tracheal lumen.

Placement of an Intraluminal Prosthesis

Recent reports have indicated successful placement of intraluminal tracheal prostheses, or stents, in some dogs with tracheal collapse. Stent placement requires specific materials, endoscopic equipment, and an experienced clinician. Complications, such as stent migration and infection, have been reported. Refer the patient to a specialist for this procedure.

Tracheal Foreign Body Retrieval

Tracheal foreign bodies often can be removed with a fiberoptic endoscope. Various transendoscopic retrieval devices are available for flexible and rigid endoscopes.

Technique

1. General anesthesia is required for this procedure. Attach a Y-shaped swivel adapter that has a self-sealing port for passage of the endoscope (Fiberoptic Scope/Suction Catheter Adapter with Swivel, Portex; Wilmington, DE) to the endotracheal tube. This allows simultaneous tracheoscopy and inhalation anesthesia in dogs intubated with a tube with an inner diameter of >7.5 mm.
2. Anesthetize small dogs and cats with an intravenous anesthetic and pass the endoscope directly into the trachea.
3. Place the animal in sternal recumbency with the head elevated.
4. Insert an oral speculum to prevent the animal from biting and damaging the endoscope.
5. Carefully insert the endoscope into the trachea. Examine the larynx, trachea, and bronchi and locate the foreign body.
6. Critically evaluate the type and position of the foreign body before attempting to remove it. Foreign bodies that are embedded in the tracheal mucosa or that have sharp edges may not be amenable to transendoscopic removal.
7. Pass the retrieval instrument through the operative port of the endoscope. Position the retrieval instrument either cranial (forceps) or caudal (basket device) to the foreign body.
8. Grasp the foreign body and *gently* retract the endoscope and foreign body together. Tracheotomy or tracheal resection and anastomosis may be necessary if the foreign body is firmly lodged in the trachea.

▼ ***Key Point*** Excessive traction on a foreign body firmly lodged in the trachea may cause severe tracheal trauma.

9. After the foreign body has been removed, replace the endoscope and perform a thorough, systematic inspection of all accessible parts of the trachea and bronchial tree.

Postoperative Care and Complications

- Complications are rare after transendoscopic removal of a tracheal foreign body.
- Moderate coughing from tracheal irritation is common but transient.
- If the foreign body was firmly lodged in the trachea and removal was difficult, closely monitor the animal for signs of tracheal trauma (e.g., subcutaneous emphysema) for 48 to 72 hours.

Segmental Stenosis

Tracheal Resection and Anastomosis

Tracheal resection and anastomosis is indicated for treatment of tracheal stricture and tracheal neoplasia and, rarely, for removal of a tracheal foreign body. Meticulous surgical technique is imperative to minimize postanastomotic stenosis.

Surgical Anatomy

- Review surgical anatomy in the tracheal collapse section.
- The tracheal cartilages are joined ventrally and laterally by 1-mm-wide fibroelastic bands called annular ligaments.

Preoperative Considerations

- Identify the extent of the stenotic lesion radiographically and/or endoscopically.
- Anesthesia:
  - Gain control of the airway by rapidly passing an endotracheal tube. Mask induction is not advisable.
  - Endotracheal intubation may be difficult or impossible when the cranial cervical segment of the trachea is stenotic. Be prepared to perform a tracheostomy for delivery of anesthetic gases.
  - Administer cefazolin (25 mg/kg IV) at induction of anesthesia and 2 hours after the first dose.

Surgical Procedure

Objective

To remove the stenotic segment of the trachea and create an airtight anastomosis under minimal tension.

Equipment

- Standard surgical pack and suture
- Gelpi retractors
- 2-0 and 3-0 polypropylene suture material with a tapercut needle

Technique

Many techniques for tracheal resection and anastomosis have been described. The split-cartilage technique is

ideal because the technique is easy to perform and results in more precise anatomic alignment with less luminal stenosis compared with other anastomotic techniques.

1. Patient positioning and surgical approach are the same as for application of tracheal prostheses.
2. Dissect the right and left lateral pedicles from the stenotic segment of the trachea.
3. Place stay sutures one cartilage cranial and one cartilage caudal to the stenotic segment to prevent retraction and facilitate manipulation of the incised ends.
4. Reposition the endotracheal tube so that the cuff is distal to the stenotic segment. Perform the resection and anastomosis over the endotracheal tube if possible. Do not manipulate the distal segment with the endotracheal tube cuff inflated.
5. Using a #10 blade, circumferentially split in half one tracheal cartilage at each end of the stenotic segment. Incise the stenotic segment longitudinally and remove it. Submit the diseased segment for histologic evaluation.
6. Preplace four to six simple interrupted, tension-relieving sutures with 2-0 polypropylene suture material between the cranial and the caudal tracheal segments. Pass each suture around the second or third tracheal cartilage cranial and caudal to the anastomotic site.
7. Bring the cranial and caudal segments into apposition by tying the tension sutures.
8. Place 8 to 12 simple interrupted sutures, encompassing the split tracheal cartilage at the end of the cranial and caudal segments. Penetrate the tracheal lumen and tie knots on the outside of the trachea. Make certain that the edges of the dorsal tracheal membrane are apposed.

Postoperative Care and Complications

- Leave the endotracheal tube in place with the cuff inflated until the dog has a strong swallowing reflex. Deflate the cuff and then carefully remove the tube.
- Observe for signs of tracheal obstruction. Mucosal swelling rarely is a problem after resection and anastomosis.
- Discourage extension of the neck if the resected segment was large (i.e., more than five tracheal cartilages).
- Obtain cervical radiographs 1, 2, and 3 months after surgery. Follow-up tracheoscopy to assess healing is ideal.
- Postanastomotic stenosis is the most common complication. Excessive anastomotic tension usually is the cause. Complications such as air leakage, infection, mucostasis, and dehiscence occur rarely.

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Chapter

162 Bronchopulmonary Disease

Lynelle R. Johnson

Diseases of the tracheobronchial tree and pulmonary parenchyma are very common in canine and feline patients and are responsible for substantial morbidity in the pet animal population. Determining the underlying disease responsible requires an understanding of clinical signs, interpretation of laboratory and radiographic findings, and collection and analysis of airway samples. Individualized therapy will be most likely to lead to amelioration of signs. Many respiratory tract diseases are chronic in nature, and the goals of therapy become controlling clinical signs and avoiding progression of disease.

CLINICAL SIGNS

Coughing, respiratory distress, abnormal breathing, and exercise intolerance are the presenting complaints most commonly observed in cats and dogs with diseases involving the respiratory tract.

- Early in the course of disease, disorders of the conducting airways primarily cause cough.
- As disease progresses, shortness of breath and decreased ability to exercise may become more evident. Parenchymal disorders usually are associated with abnormal respiratory rate and effort as well as exercise intolerance and signs of systemic illness.
- In chronic airway disease or parenchymal lung disorders, complications such as syncope and cyanosis may arise from progressive respiratory disease.

Overview in Dogs

A wide variety of infectious, inflammatory, degenerative, and neoplastic diseases cause clinical signs referable to the respiratory tract in dogs.

- Common causes of respiratory disease in dogs include tracheal or bronchial collapse, chronic bronchitis, and infectious or inflammatory lung disease. Clinical signs of cough and exercise intolerance are common to all three conditions, and further diagnostic testing is needed to further define the underlying disorder. Isolated cervical tracheal collapse may be suspected by the observation of a high-pitched, honking cough in a small breed dog in combination with inspiratory difficulty; however, lower-airway inflammatory disease may complicate the clinical picture and will be easily missed unless a full evaluation is completed. Additionally, some dogs with tracheal collapse have concurrent laryngeal paralysis, detected by the presence of dramatic stridor over the larynx along with voice change. Chronic bronchitis is a very common disease of small-breed dogs; however, large breed dogs are equally affected.
- Acute respiratory distress, characterized by extreme tachypnea, cyanosis, or collapse, may be observed in animals with decompensated chronic tracheobronchial or interstitial disease. This should be distinguished from other causes of acute respiratory signs such as pulmonary edema (cardiogenic and noncardiogenic), pulmonary thromboembolism, and disease of the pleural space (pneumothorax or pleural effusion).
- Hemoptysis is relatively uncommon in dogs and cats, but this finding may be observed with pulmonary infiltrates with eosinophils, *Paragonimus* infection, heartworm disease, pulmonary hypertension, pulmonary neoplasia, anticoagulant rodenticide toxicity, and pulmonary foreign body.

Overview in Cats

Cats may present with a history of acute or chronic respiratory disease. Cats with chronic respiratory disease may present emergently with acute signs of respiratory discomfort because stress can lead to rapid physical decompensation.

- The most common cause of respiratory signs in cats is lower-airway inflammatory disease (chronic bronchitis and asthma). These airway diseases have many features that parallel the same disorders in people, including spontaneous airflow limitation, airway inflammation, and bronchial hyper-responsiveness.
- Cats are susceptible to pulmonary infection with bacteria, although bacterial infection of feline airways is a relatively uncommon phenomenon. Similarly, aspiration pneumonia, which is common in the dog, occurs relatively uncommonly in the cat. Isolation of *Mycoplasma* spp. from the lower airways of a cat

should be considered indicative of infection since this organism is not found in the lower airways of healthy cats. This is important to recognize because isolation requires special culture techniques, and, in some studies, this organism is the most common cause of primary lung infection in the cat. *Yersinia pestis,* the cause of bubonic and pneumonic plague, is an additional primary pathogen to consider in cats from New Mexico (see Chapter 19).

- Other infectious agents to consider as causes of respiratory signs in cats include systemic mycoses (particularly cryptococcosis, blastomycosis, and histoplasmosis), parasites (lungworms and heartworm), viruses (calicivirus, herpesvirus, feline infectious peritonitis), and protozoa (toxoplasmosis).
- Additional causes of cough that should be considered are tracheobronchial foreign body, tracheal neoplasm, and chylothorax. Other differential diagnoses for cats with primarily shortness of breath include pleural effusion (chylothorax, pyothorax, hydrothorax, hemothorax), pneumothorax, pulmonary thromboembolism, neoplasia, and cardiac failure.

TRACHEAL COLLAPSE

Etiology

- Hypocellular tracheal cartilage with deficient production of glycosaminoglycans and chondroitin sulfate has been found in some dogs with tracheal collapse. These metabolic deficiencies cause a reduction of bound water within tracheal cartilage and result in decreased turgidity of the ring structure. The abnormalities in chondrogenesis that result in tracheal collapse may be congenital or inherited, or may be related to dietary deficiencies.
- Collapse may be present in the cervical region, intrathoracic region, or both. In some dogs, collapse of smaller airways supported by cartilage can be seen. Collapse may be found solely at rest, or it may be dynamic, varying with the phases of respiration. In these situations, cervical collapse is found on inspiration, while intrathoracic collapse occurs on expiration. Inflammation within the airways may exacerbate airway collapse.
- In cats, tracheal collapse has been associated with masses that obstruct the upper airway.

Pathophysiology

- Loss of structural support in the cartilage of the tracheal ring allows fluctuations in airway diameter in association with changes in airway pressure that occur during respiration or cough.
- The trachea generally collapses in a dorsoventral orientation. Tracheal rings become flattened, leading to narrowing of airway diameter, elongation of the dorsal tracheal membrane, and prolapse into the airway. Concussive trauma between the dorsal tracheal membrane and the ventral epithelial surface of the trachea results in airway injury, mucus production, and perpetuation of cough. Reduction in the radius of the airway increases the resistance to airflow, which necessitates an increase in driving pressure to maintain normal air movement into and out of the lungs. Increased airflow can perpetuate airway inflammation and injury.
- Collapse is isolated to the cervical trachea in some dogs, but many dogs also have disease in the intrathoracic region.

Cervical Tracheal Collapse

Cervical tracheal collapse occurs on inspiration. During inspiration, intrapleural pressure drops, leading to a decrease in intrathoracic airway pressure and airflow from the glottis into the region of gas exchange in the lung. The cervical trachea is exposed to atmospheric pressure, and a pressure drop also occurs from the glottis down the airway. Dogs that lack rigidity in the cervical trachea will experience collapse on inspiration and will exhibit clinical signs of inspiratory distress. Inspiratory wheezing may also be evident. In dogs with concurrent upper-airway obstruction (everted laryngeal saccules, elongated soft palate, laryngeal paralysis), a larger pressure gradient develops in the cervical trachea and this increases the tendency of the airway to collapse and perpetuates upper-airway inflammation. Prolapse of the dorsal tracheal membrane into the airway lumen accentuates mechanical trauma to the wall of the trachea, leading to further mucosal irritation, inflammation, and cough.

Intrathoracic Tracheobronchial Collapse

Intrathoracic tracheal collapse or collapse of the mainstem bronchi is encountered on expiration when intrapleural pressure exceeds intra-airway pressures, and poorly supported airways tend to close. In some dogs, generalized airway collapse is encountered. It is unclear whether cartilaginous deficiency underlies this disease as it does with tracheal collapse. Airway collapse can be seen in conjunction with chronic bronchitis or airway inflammatory disease, perhaps because of irritation caused by cough or because of changes in the pressure gradients within the lung associated with obstruction of smaller airways. In addition, airway inflammation stimulates a cough, which can exacerbate signs related to airway collapse.

Clinical Signs

Signalment

Small-breed dogs are typically affected with tracheal collapse, and an increased prevalence is generally seen in the Yorkshire terrier, poodle, Pomeranian, and chihuahua. Any breed of dog can be affected by lower-

airway collapse, although typically smaller breed dogs are affected. Animals of any age may present with signs related to tracheal and/or lower-airway collapse.

History

A long-term history of chronic, intermittent cough is typically reported with or without episodes of respiratory distress. These signs have often been present since the patient was young. Stress, heat, humidity, eating, drinking, or external pressure on the trachea can all trigger clinical signs of disease.

- Coughing, gagging, and retching can be reported with tracheal collapse and may be mistaken for vomiting. Owners might also suspect a tracheal foreign body or "kennel cough" as a cause for signs.
- Paroxysms of coughing often occur and may lead to cough syncope. In general, cough and respiratory distress progress over time until the animal becomes debilitated or unable to function.
- Animals with tracheal collapse can have long periods of normalcy between episodes of apparent acute disease. Exacerbations of clinical signs may be associated with any additional respiratory-related complication including inflammation or infection (bronchitis or pneumonia), upper-airway obstruction (laryngeal paralysis or everted saccules), or congestive heart failure (CHF). A common cause for exacerbation of disease is intubation for a procedure under anesthesia. Finally, weight gain appears to worsen clinical signs of disease in affected animals.

Physical Examination

- Obesity is very common in dogs with tracheal and airway collapse. Hepatomegaly has also been reported, which may be a result of fat deposition in the liver.
- Dogs with tracheal collapse can appear normal at rest. Excitement induces a honking cough, and in more severe cases can result in airway obstruction and respiratory distress. Animals typically have marked tracheal sensitivity, and even gentle palpation can precipitate a crisis.
- High-pitched inspiratory noises are sometimes heard over the narrowed trachea in animals with cervical collapse. The presence of stridor indicates that concurrent laryngeal paralysis should be considered.
- An end-expiratory snap may be heard over the thorax with collapse of the intrathoracic trachea or mainstem bronchi.
- Auscultation of wheezes or crackles suggests the presence of concurrent bronchitis or interstitial lung disease.

Diagnosis

The presence of a honking cough in a small-breed dog is often considered diagnostic of tracheal collapse. Consider a full diagnostic workup in order to identify and treat all coincident disorders that complicate the clinical presentation.

Radiography

- Inspiratory and expiratory lateral views and a ventrodorsal view are recommended to evaluate tracheal luminal diameter, pulmonary infiltrates, and cardiac size.
  - The cervical trachea may be collapsed on inspiration.
  - It may be possible to confirm collapse of the intrathoracic trachea or mainstem bronchi on expiration.
- The trachea can appear radiographically normal in more than 50% of cases, and false-positive results are also common. Performing fluoroscopy during the induction of a cough can be used to aid in the diagnosis, although even this technique cannot identify all cases of collapsed trachea.
- Ultrasound of the cervical trachea has been reported as a modality for confirming trachea collapse by identifying the abnormal shape of the tracheal lumen.

Airway Sampling

Obtain respiratory samples for cytology and culture to rule out infectious or inflammatory conditions (pneumonia, bronchitis, or fibrosis) that can accentuate clinical signs. Endoscopy (bronchoscopy) offers the most complete evaluation of the respiratory tract and has the benefit of confirming the presence or absence of tracheal and airway collapse. Evaluate upper airway structure and function in all animals sedated for tracheal wash or bronchoscopy.

- Evaluate samples for cytologic abnormalities that might suggest inflammation or infection. Bacterial culture and special culture for *Mycoplasma* spp. are recommended (see discussion under "Chronic Bronchitis").

Transtracheal Wash

- Use sedation and oral intubation when performing a tracheal wash on a patient with tracheal collapse. To avoid tracheal irritation, use a sterile endotracheal tube of small diameter. Lidocaine gel applied lightly to the tube can lessen induction of cough. It is not necessary to expand the inflatable cuff during the short procedure, and this can also lessen the tendency for worsening of cough after the procedure.
- After intubation, pass a sterile polypropylene urinary catheter or feeding tube to the level of the carina (the fourth intercostal space), and inject sterile nonbacteriostatic saline (4–5 ml), and then aspirate back into the syringe. Stimulating a cough and performing coupage during aspiration will increase the return of fluid as will a sterile mucus trap system attached to a controlled suction device. Only 1 to 2 ml

of fluid are required for sample processing (cultures and cytology), and a second and third aliquot can be instilled if the sample recovered is inadequate. Alternatively, culture can be performed using a guarded swab passed through the endotracheal tube. This system will not be contaminated by the tip of the endotracheal tube.

Bronchoscopy

- When available, bronchoscopy is useful both for collection of airway samples and for grading the extent and severity of tracheal collapse. In small dogs, a bronchoscope with a diameter smaller than 5 mm diameter is most useful for assessing the airways. Flexible bronchoscopy has an advantage over rigid bronchoscopy because of the ability to assess lower airways as well. Bronchoscopy can confirm the presence of isolated cervical tracheal collapse and can identify passive or dynamic collapse of lower airways. Determining the extent of disease is important when deciding whether surgical correction or placement of an intraluminal stent is feasible.
- Bronchoalveolar lavage can be used to collect lower-airway samples. Culture can be obtained from the lavage fluid or from a guarded endoscopic microbiology brush. Veterinarians performing respiratory endoscopy and bronchoscopic-guided airway lavage should be intimately familiar with respiratory tract anatomy and trained in the procedures of bronchoscopy. Particular attention must be paid to coordinating the airway examination with anesthesia methods, and assuring sufficient ventilation and delivery of oxygen during the procedure.

Treatment

General

- Weight loss is beneficial for most patients. Reducing the amount of fat on the thoracic cage improves chest wall compliance and decreases the work of breathing. Many dogs will experience substantial reduction in cough and improvement in respiratory health with weight loss alone.
- Efforts should be made to limit exposure to environmental stressors such as high humidity and heat during exercise. A harness should be used in place of a collar.
- Sedatives may be required during periods of high stress. Acepromazine (0.05–0.25 mg/kg SC or IM) or butorphanol (0.05–0.2 mg/kg SC or IM) may be used alone or in combination. Use reduced dosages when the two drugs are used in combination.

Antitussives

Cough suppressants are needed at some stage in most cases of tracheal collapse to break the cycle of cough-induced airway injury.

- Opiates such as hydrocodone (0.2 mg/kg PO q6–12h) or butorphanol (0.5–11 mg/kg PO q6–12h) are most effective. The dosing regimen must be sufficiently flexible to control cough without inducing nausea or excessive sedation.
- Over-the-counter dextromethorphan-containing compounds are occasionally effective.

Bronchodilators

Dogs that have intrathoracic airway collapse and evidence of small airway disease may benefit from the use of bronchodilators (Table 162-1). Bronchodilators have no clinically significant effect on the large airways and do not result in an increased diameter in the tracheal lumen. Instead, these drugs act primarily on small airways, making it easier for air to flow out of the lungs and lessening the tendency for dynamic collapse of large airways.

Anti-Inflammatory Drugs

Treat concurrent chronic bronchitis as described in the next section. Occasionally, tracheal inflammation may require a short course of therapy with glucocorticoids for resolution of airway injury; 5 to 7 days of prednisone, 0.25 to 0.5 mg/kg PO q12–24h followed by rapid tapering of the dose is usually sufficient to treat inflammation.

Antibiotics

It is uncommon for clinically significant bacterial infection to complicate the course of tracheal collapse. When a bacterial infection is documented, the choice of antibiotics should be based on culture and sensitivity results.

- Before cultures become available, antibiotics with efficacy against oral bacteria, including *Mycoplasma* are recommended. Doxycycline and enrofloxacin both provide a good spectrum of activity and are efficacious against most of the bacteria typically encountered.

Surgical Stabilization

- Surgical placement of tracheal ring prostheses has been successful in reducing clinical signs in dogs with focal cervical tracheal collapse. The surgery is technically demanding and is associated with occasionally serious complications. However, most owners report that the surgery is beneficial in improving the quality of life for their pet (see Chapter 161).
- Placement of intraluminal stents has resulted in alleviation of clinical signs in dogs with severe tracheal collapse that failed to respond to medical management. Stents made from a nitinol metal alloy are placed fluoroscopically. Once placed, stents are generally not removable. Complications associated with obstruction of a principal bronchus, device fracture, and granuloma formation have been reported.

Table 162-1. BRONCHODILATORS COMMONLY USED IN CANINE AND FELINE BRONCHOPULMONARY DISEASE.

Drug	Dosage	Side effects
Methylxanthines		
Sustained-release theophylline	Dog: 10 mg/kg PO q12 h Cat: 10 mg/kg PO q24 h (PM)	Multiple drug interactions, gastrointestinal upset, tachycardia
Beta agonists		
Terbutaline	Dog and cat: 0.01 mg/kg SC, IV Dog: 1.25–5.0 mg/dog PO q12 h Cat: 0.625 mg PO q12 h	Tachycardia, hypotension
Terbutaline MDI	200 μg/puff q12 h by aerosol	
Albuterol	Dog: 50 μg/kg PO q12 h	
Albuterol MDI	90 μg/puff q12 h by aerosol	
Epinephrine	20 μg/kg IV, IM, SC, IT	Cardiac arrhythmias, hypertension, vasoconstriction

MDI, metered dose inhaler

Prognosis

Dogs with tracheal collapse generally have irreversible disease. The goals of preventive and acute therapy are to minimize clinical signs, prevent worsening of bronchopulmonary disease, and improve the overall quality of life.

CHRONIC BRONCHITIS

Etiology

The etiology of chronic bronchitis in the dog is unknown; however, it is likely that chronic mucosal irritation or immunologic stimulation is responsible for airway inflammation and clinical signs of disease.

- Smoking remains the major cause of chronic bronchitis in people, and exposure to air pollution or particulate matter may play a role in the canine disease.
- In addition, some dogs may suffer from chronic aspiration of small-volumes of gastrointestinal content sufficient to trigger airway inflammation.

Pathophysiology

- Chronic airway inflammation results in characteristic changes in lower-airway structure and function. Neutrophilic infiltration of the airway results in release of proteases and oxidant species that damage the mucosa, stimulating a chronic cycle of injury and repair of the epithelium.
- Chronic bronchitis is characterized by hypertrophy and hyperplasia of mucous glands and goblet cells. These changes result in accumulation of mucus within the airway with obstruction of airflow, leading to clinical signs of cough and exercise intolerance.
- Histopathologic changes reported in dogs with chronic bronchitis include inflammatory cells in the lamina propria, goblet cell proliferation, enlargement of mucous glands, epithelial erosion with healing by basal cell proliferation, and squamous metaplasia. Mild emphysema, characterized by increased alveolar air space and loss of interalveolar septae is occasionally seen, although dogs do not display clinical manifestations of emphysema.

Clinical Signs

Signalment

Most dogs with chronic bronchitis are middle aged to older. Both large and small breed dogs are affected, and often the animal is overweight or obese.

History

- The characteristic historical finding in chronic bronchitis is the presence of a chronic cough for at least 2 months' duration, in the absence of other disorders that can cause cough. An acute exacerbation of disease may cause the owner to seek veterinary attention, but often it is discovered that the dog has coughed for years when a careful history is obtained.
- The cough associated with chronic bronchitis can be a dry hacking cough or may be reported as moist or harsh. Swallowing or licking the lips after a cough suggests that the cough is productive, which is probably due to excessive mucus production.
- Exercise intolerance, fatigue, or increased panting may be reported in addition to cough, however, the typical dog with bronchitis is not systemically ill. This characteristic helps distinguish chronic bronchitis from other causes of cough including infective pneumonia, CHF, and thoracic neoplasia.

Physical Examination

- Animals with chronic bronchitis are often overweight.

- Chronic bronchitis is classified as an obstructive airway disease that classically results in a slow, deep respiratory pattern in order to decrease the work of breathing. When observed carefully, animals severely affected by chronic bronchitis may show prolonged expiration and an expiratory push. These animals may also be intermittently cyanotic or syncopal. Dogs with chronic bronchitis may also pant or appear short of breath when excited or agitated during an examination.
- Tracheal sensitivity is usually present but this is a nonspecific finding associated with airway inflammation. Concurrent tracheal or airway collapse is commonly present and may be detected by the characteristic goose-honk cough or as a snapping sound over the thoracic cage when intrathoracic airways collapse on expiration.
- The presence of normal lung sounds does not rule out the diagnosis of chronic bronchitis. Stimulating a large inspiration by causing breath holding or inducing a cough will increase the detection of abnormal lung sounds in many cases.
- Adventitious lung sounds are often found in dogs with chronic bronchitis. Coarse or harsh, diffuse crackles are reported along with expiratory wheezes.
- Cardiac auscultation may reveal concurrent mitral-valve insufficiency in older, small-breed dogs. Heart rate and rhythm may be helpful in ruling out CHF as a cause of cough, because these dogs typically exhibit a regular sinus rhythm or sinus tachycardia, whereas dogs with respiratory disease usually have a normal to slow heart rate, often with sinus arrhythmia due to increased vagal input from pulmonary disease.
- Determining the etiologic cause of cough in a dog with cardiomegaly, left atrial dilation, and collapse or compression of the mainstem bronchus can be challenging. In some dogs, increased left-atrial volume, causing compression of the bronchus is the primary problem, whereas in others, primary loss of cartilaginous support of the airway is the principal pathology resulting in cough. Some dogs might also suffer from airway inflammation that induces cough in conjunction with cardiac or airway structural abnormalities.

Diagnosis

The history of a long-term cough in an otherwise bright and healthy dog is suggestive of chronic bronchitis, which is largely a diagnosis of exclusion. Pneumonia and pulmonary neoplasia can cause similar signs. Also, dogs often have separate or concurrent cardiopulmonary conditions such as tracheal collapse, bronchial collapse, bronchial compression, or heart failure. A complete diagnostic workup assesses the role each condition might play in the generation of clinical signs and aids in developing a therapeutic plan. Laboratory evaluation (complete blood count [CBC], chemistry panel, urinalysis) should be done to evaluate systemic health, although there are no typical abnormalities for chronic bronchitis. The diagnosis is based on the history, clinical findings, chest radiographs, and airway sampling to rule out other pulmonary causes of cough.

Radiography

▼ ***Key Point*** Normal-appearing thoracic radiographs are common with chronic bronchitis. This does not rule out bronchitis as a diagnosis.

- Generalized peribronchial infiltrates are considered typical of chronic bronchitis. This pattern is usually characterized by "doughnuts" (end-on bronchi) or "tram lines" (airways seen in longitudinal section), which represent airway walls thickened by inflammation. In comparison to age-matched control dogs, dogs with bronchitis have thickening of bronchial walls and increased numbers of airway walls visible on chest radiographs. However, some older dogs demonstrate radiographic features of bronchial thickening without evident clinical signs of chronic bronchitis.
- Alveolar infiltrates are not typically found in chronic bronchitis and would suggest a diagnosis of pneumonia or pulmonary edema.
- Pulmonary infiltrates may be obscured by fat overlying the thoracic cage in obese animals. Obesity also leads to decreased thoracic compliance, which restricts expansion of the thorax and can lead to an apparent reduction in lung volume.
- Heart size can be difficult to interpret in patients with chronic bronchitis. True right-sided cardiomegaly may be seen in severely affected patients that develop pulmonary hypertension or cor pulmonale. However, many chondrodysplastic breeds will appear to have cardiomegaly due to breed conformation. Also, obesity can cause an enlarged cardiac silhouette as a result of intrapericardial deposition of fat. A vertebral heart score is a good method for objectively estimating heart size in many dogs (see Chapter 143).

Airway Sampling

Cytologic characterization and culture of the cellular infiltrate within the airways can identify or exclude infectious causes of cough and allows development of a rational therapeutic plan. Samples may be obtained through endotracheal or transtracheal wash or with bronchoscopy.

Transtracheal Wash

- An endotracheal wash through a sterile endotracheal tube can be performed as described under "Tracheal Collapse."

- A transtracheal wash can be performed by passing the needle of a jugular catheter between the tracheal rings (I prefer a puncture as low on the trachea as possible), and then threading a sterile catheter down the airway. Alternately, a through-the-needle catheter can be used to access the lower airways. After placement of the catheter and withdrawal of the needle, sterile tubing is passed through the catheter in order to collect the wash sample.
- A sterile preparation is performed in the site desired. Local anesthetic block can be achieved with SC infiltration with 2% lidocaine at the site of entry in the skin and in the trachea.
- The needle is placed into the skin several rings below the site where the trachea will be entered. By drawing the skin upward before penetrating the trachea, a SC tunnel will be created that lessens accumulation of air after the procedure. When the trachea has been entered, a slight "pop" is felt and the animal will usually cough. The catheter is threaded through the needle to the level of the carina (the fourth intercostal space).
- If a jugular catheter is used, the needle is withdrawn from the neck at this time, and the guard secured over the needle-catheter junction.
- When performing a transtracheal wash, the catheter should never be withdrawn back into the needle after the trachea has been entered, as this increases risk of shearing the catheter off into the airway.
- Tracheal washing is performed with one to three aliquots of 4 to 6 ml of sterile, non-bacteriostatic saline. Stimulation of a cough or coupage of the chest during aspiration can enhance recovery of fluid. Only 1 to 2 ml is necessary for sample processing.

Bronchoscopy

- Bronchoscopy is extremely useful in the diagnosis of chronic bronchitis, particularly in cases that lack typical radiographic findings. The procedure allows visualization of airway changes, localization of disease, collection of more specific airway samples, characterization of dynamic changes in airway caliber, and the opportunity to identify and biopsy lesions.
- Dogs with chronic bronchitis have variable degrees of airway hyperemia and a roughened appearance to the mucosa. The majority of dogs have increased mucus in the airways. Animals with long-standing bronchitis can have nodular proliferations of fibrous tissue protruding into the airway. These nodules are usually of varying size and are found throughout the airway. In some cases these must be differentiated from the nodules produced by the parasite *Oslerus osleri,* which are typically found on the floor of the airway just cranial to the carina.
- Bronchoalveolar lavage is performed as described under "Tracheal Collapse."

Tracheobronchial Cytology

- Healthy dogs have primarily ciliated, columnar epithelial cells in tracheal wash fluid. Rare inflammatory cells or macrophages from the lower airway are seen.
- Dog with bronchitis typically have elevated numbers of non-degenerate neutrophils in airway cytologic preparations. Increased mucus may be seen in airway fluid and occasionally Curschmann's spirals are seen, which represent bronchial casts of airway mucus.
- A large number of epithelial cells on cytology suggests sloughing of the airway mucosa. Squamous metaplasia also may be noted.
- Healthy dogs have 5% to 6% neutrophils, 5% to 6% eosinophils, 5% to 6% lymphocytes, and 75% to 95% macrophages in bronchoalveolar lavage fluid. An increased number or percentage of neutrophils is seen in most dogs with chronic bronchitis. This is usually a reflection of inflammation within the airway and does not indicate a septic process. However, the presence of toxic neutrophils or intracellular bacteria indicates that infection is likely.
- A smaller percentage of patients will have a predominance of eosinophils in airway washings, which may be a reflection of the generalized immune response, or in some cases may suggest a hypersensitivity response or parasitic infection. Further workup should be considered in these patients (see "Other Laboratory Tests").

Tracheobronchial Culture

- Airway samples should be submitted for aerobic culture and susceptibility testing and for Mycoplasma culture. Specialized transport media may be required to isolate Mycoplasma, and individual laboratories should be consulted.
- The lumina of the trachea and large airways are not sterile environments, and a variety of oral contaminants or commensal bacteria may be found in tracheal wash or bronchoalveolar lavage samples, despite careful attention to technique. Interpretation of positive culture results must take into account cytologic abnormalities.
- The presence of oral contaminants on cytology, such as squamous cells or *Simonsiella* bacteria, makes a positive culture result of questionable importance (Table 162-2).
- Quantitative aerobic culture of bronchoalveolar lavage fluid yielding large numbers of bacteria and detection of intracellular bacteria on cytology are most helpful in determining that true bacterial infection is present. Most animals with bronchitis have very small numbers of bacteria on culture and lack intracellular bacteria.
- In rare animals with chronic bronchitis, aspiration of oral bacteria may occur during episodes of coughing or panting, and these bacteria may overwhelm host

Table 162-2. BACTERIA RETRIEVED FROM THE AIRWAYS OF HEALTHY DOGS AND CATS

Dogs	Cats
Bordetella bronchiseptica	*Acinetobacter*
Corynebacterium spp.	*Bordetella bronchiseptica*
Escherichia coli	*Corynebacterium*
Enterobacter	*Enterobacter*
Klebsiella	*Flavobacterium*
Pasteurella	*Klebsiella*
Pseudomonas	*Pasteurella*
Staphylococcus	*Staphylococcus*
Streptococcus	*alpha-Streptococcus*

defenses. Previously stable bronchitic patients that develop an exacerbation of disease may be experiencing true bacterial infection or secondary bronchopneumonia.

Other Laboratory Tests

- Nonspecific abnormalities on the minimum database, such as a stress neutrophilia or eosinophilia, may be seen in animals with chronic bronchitis. The presence of neutrophilia with a left shift, neutropenia, or monocytosis indicates that other conditions such as pneumonia or bronchiectasis should be considered.
- Animals with eosinophilic airway washes should be screened for airway parasites and larval migration through appropriate fecal exams (see Chapter 158). Heartworm disease must be ruled out.
- An electrocardiogram often shows an exaggerated sinus arrhythmia and may give an indication of right atrial enlargement ($P > 0.4$ mV) or infrequently of right-sided cardiomegaly (S-waves in leads I, II, III, aVF).
- Pulse oximetry is useful as a screening test for detection of hypoxemia. If the S_pO_2 is less than 95%, an arterial blood gas should be performed.
- Arterial blood gas analysis may exhibit mild to moderate hypoxemia. Hypercarbia is not detected unless respiratory failure ensues or the dog is sedated and hypoventilating. In one study, nuclear ventilation scans confirmed the existence of patchy areas of deficient ventilation in dogs with chronic bronchitis.
- Tidal breathing flow volume loops in dogs with chronic bronchitis have shown reductions in expiratory flow and loop shapes similar to those seen in humans with chronic bronchitis.

Treatment

General

- Obesity worsens clinical signs in dogs with chronic bronchitis by decreasing thoracic wall compliance, increasing the work of breathing, and increasing abdominal pressure on the diaphragm. Gradual weight loss should be stressed for all overweight animals. Increasing amounts of exercise also can be useful in encouraging weight loss.
- Animals with concurrent tracheal collapse or marked tracheal sensitivity may benefit from using a harness instead of a collar.
- Environmental stressors, such as cigarette smoke, dust, pollutants, heat, and low humidity should be avoided whenever possible.
- Some patients may benefit from intermittent airway humidification via steam inhalation or nebulization. Owners should be instructed to coupage the chest after nebulization or encourage gentle exercise to facilitate clearance of secretions.
- Rarely, dogs with chronic bronchitis are also affected with chronic atopic-type skin allergies. The value of desensitization on bronchitis signs has not been evaluated clinically in dogs. Other aspects of treatment, such as introduction of a novel-protein diet can be considered as part of the overall treatment plan. Attention to diet may also benefit weight control, which is often a problem in dogs with chronic airway diseases.
- When airway cytology reveals a preponderance of eosinophils, consideration should be given to empiric deworming with a broad-spectrum drug such as fenbendazole.

Anti-Inflammatory Drugs

Airway inflammation is the cause of clinical signs of chronic bronchitis. This can be ameliorated by treatment with glucocorticoids. It is essential that infectious diseases have been ruled out and that concurrent abnormalities, such as severe dental disease or CHF, have been successfully treated prior to initiation of anti-inflammatory treatment.

- Prednisone or prednisolone is generally safe and effective in dogs with uncomplicated bronchitis. The dosage regimen should be tailored to the individual, with the severity of signs, chronicity of infection, and systemic health playing a role in decisions regarding treatment.
  - Dogs often require initial dosages of prednisolone of 0.5 to 1.0 mg/kg q12h for 5 to 7 days to induce remission of clinical signs. When the cough has reduced to a satisfactory level, the dosage should be decreased by half every 5 to 7 days until the lowest possible dose is achieved. Long-term therapy (2–3 months) should be expected in most cases.
  - Alternate-day use of steroids or possible discontinuation of medication should be the goal of therapy. Some clinicians attempt to reduce dependence on systemic corticosteroids by initiating treatment with inhaled fluticasone during the period of dose tapering (see "Feline Asthma"). The efficacy and

adverse effects of such treatment in dogs has not been studied critically, and such therapy is relatively expensive, but the approach merits consideration in dogs that experience substantial side effects but still require chronic therapy for control.
  - Animals that do not respond to steroids alone may benefit from addition of a bronchodilator (see "Bronchodilators").
  - Exacerbation of disease in the early stages of treatment requires returning to the higher dose of glucocorticoid that controlled clinical signs. It is very common for dogs to suffer recurrence of clinical signs throughout life. Repeated episodes require additional workup when complicating infections or other cardiopulmonary diseases contribute to illness.
- Owners should be instructed to monitor response to therapy closely and should understand that the goal of therapy is to control cough, not eliminate cough, since most dogs remain variably symptomatic. Failure to respond to glucocorticoids indicates that the diagnosis of non-infective, chronic bronchitis should be reconsidered.

Bronchodilators

Bronchodilators may be helpful in reducing clinical signs in dogs with bronchitis that do not show complete response to glucocorticoids. Bronchoconstriction is likely not a component of chronic bronchitis in the dog; however, bronchodilator therapy may provide a multitude of beneficial effects such as reducing airway inflammation, reducing work of breathing, and stimulating mucociliary clearance.

- The clinical effects of methylxanthine derivatives probably result from adenosine inhibition. Extended-release theophylline dosed at 10 mg/kg PO q12h has been shown to achieve predictable plasma levels in dogs that approximate the human therapeutic range (see Table 162-1).
  - Adverse effects reported with use of methylxanthines include gastrointestinal signs, nervousness, and hyperexcitability.
  - Theophylline metabolism is affected by a multitude of factors, including fiber in the diet, smoke in the environment, CHF, and other factors. Drug therapy must be tailored to the individual because there is a wide variation in the dose that causes side effects. In overweight dogs, it is prudent to begin at half the recommended dosage, then increase the dose if needed and if the dog tolerates the drug.
  - Enrofloxacin inhibits metabolism of theophylline. Use of the two drugs concurrently could result in toxic plasma levels of theophylline. At least a 30% reduction in theophylline dose is recommended when enrofloxacin is required to treat coincident infection.
- Beta-2 agonists are likely to provide more profound bronchodilation than methylxanthine derivatives due to direct relaxant effects on airway smooth muscle. Terbutaline and albuterol have been used successfully in cases of chronic bronchitis. Adverse effects include hyperexcitability, tremors, nervousness, and gastrointestinal signs.

Antitussives

Coughing serves an essential function in clearance of the viscid secretions associated with chronic bronchitis. However, chronic coughing can lead to repeated airway injury and may be responsible for syncopal events. Cough suppressants (e.g., hydrocodone or butorphanol) have an important role in management of chronic bronchitis after infection has been ruled out and after the majority of inflammation has resolved (see "Tracheal Collapse" for dosage).

Antibiotics

Antibiotic treatment is warranted when infection has been documented through appropriate culturing technique and cytologic findings. In general, infection is not a major component of the syndrome of canine chronic bronchitis; however, bronchitis can result in an abnormal environment in the airways and disrupt normal host defenses by altering mucociliary clearance and disrupting the mucosal barrier. Therefore, every animal should be screened for concurrent infection and treated if needed. In particular, *Mycoplasma* and *Bordetella bronchiseptica* should be excluded.

- Antibiotics should be based on culture and sensitivity results when possible. Chosen drugs should have a broad spectrum of activity against bacteria commonly found in the conducting airways, should be lipophilic in order to facilitate penetration of the airway, and should be relatively free of side effects. When possible, I prefer use of doxycycline or possibly chloramphenicol. Potentiated sulfa drugs can also be efficacious. Potentiated penicillin drugs can be used, but have no efficacy against *Mycoplasma*. Enrofloxacin should not be used in uncomplicated bronchitis; it should be reserved for cases with pneumonia.
- Infection plays a predominant role in cases that have concurrent bronchiectasis (see next section). In these patients, long-term antibiotic therapy is indicated.

Prognosis

Owners should be informed that bronchitis is a chronic disease. The goals of therapy should be to (1) control the degree of inflammation present, (2) diagnose and treat infection when it occurs, (3) limit clinical signs, and (4) prevent worsening airway disease that might lead to debilitating sequellae such as bronchiectasis and cor pulmonale.

BRONCHIECTASIS

Etiology

- Bronchiectasis is characterized by irreversible dilation of the airways and is typically accompanied by concurrent suppuration.
- Possible etiologies include chronic inflammation due to uncontrolled bronchitis, chronic infection due to unresolved pneumonia or a bronchial foreign body, or as a sequela to an airway insult such as smoke inhalation. Bronchiectasis can also be encountered in association with primary ciliary dyskinesia or with eosinophilic lung disease.
- Bronchiectasis occurs more commonly in dogs than in cats and is associated with more dramatic clinical manifestations of disease.

Pathophysiology

- Proteases and elastases released from neutrophils during a chronic inflammatory or infectious process destroy the support structure of the bronchial walls. The negative pressure in the surrounding pulmonary tissue pulls the airways open, resulting in dilation.
- Dilated airways lack normal mucociliary clearance and trap secretions distally. Airflow is obstructed by airway secretions, and mucus-laden airways stimulate a productive cough. Chronic recurrent pneumonia can develop because the bronchial environment is primed for continual bacterial growth.
- Because bronchiectasis is difficult to recognize clinically, proper therapy is often delayed. As a result, it is common for airway changes to have progressed beyond the reversible stage by the time of diagnosis.

Clinical Signs

Signalment

- Bronchiectasis is a disease primarily affecting dogs; it is rarely documented pre- or postmortem in cats. Cocker spaniels have an increased reported prevalence of bronchiectasis.
- Animals with primary ciliary dyskinesia are typically young when the condition is diagnosed and have a history of chronic nasal discharge or airway infection. Other animals are generally older on presentation, with a history of pulmonary disease, typically chronic bronchitis.

History

- A chronic, productive cough and recurrent pneumonia are the primary historical complaints. Failure to respond to standard therapy for chronic pulmonary disease, along with frequent and serious exacerbations of disease, seem to be characteristic of patients with bronchiectasis.
- In some dogs, hemoptysis may be reported.

Physical Examination

- Animals often display systemic signs resembling pneumonia, such as fever, cachexia, and tachypnea. A noxious oral odor may be noted.
- Tracheal sensitivity is usually marked, and animals often expectorate and swallow mucus. Lung sounds are generally abnormal. Loud bronchial noises can sometimes be heard over dilated airways. Loud crackles may be ausculted in mucus-filled air spaces. Lobar consolidation may result in a region of absent lung sounds.

Diagnosis

Laboratory Evaluation

The CBC may show signs that reflect the chronic nature of the inflammatory process. Neutrophilia, monocytosis, anemia, and hyperglobinemia may be present.

Radiography

- Radiography may be confirmatory, but it is generally insensitive for detecting dilation of the airways. Bronchography was previously used in human medicine but has been replaced by thin-section computed tomography (CT).
- Ventral consolidation of the lung is seen when airways are obstructed with mucus or purulent secretions. Dilated airways are more visible when a pneumonic infiltrate is present.
- CT reveals focal or diffuse regions of increased airway space in conjunction with thickened airway walls. Pneumonic processes are generally more visible on CT.

Bronchoscopy

Bronchoscopy can be very useful in documenting dilation of the airways in dogs. In addition, foreign bodies can be identified and removed, bacterial cultures can be obtained, and the extent of disease can be assessed.

- Bronchiectasis often results in reddening of the mucosa and accumulation of a large amount of yellow to green viscid mucus. Airways lose the normal elliptical shape when bronchiectasis develops, airway bifurcations become very thinned, airways are dilated, and some airways can be obstructed with mucus.
- Bronchoalveolar lavage fluid is characterized by a preponderance of neutrophils. Cells should be assessed for the presence of intracellular bacteria. Blood-tinged fluid may be recovered or macrophages may contain hemosiderin as an indicator of previous alveolar hemorrhage.
- Both aerobic and anaerobic cultures should be obtained because suppuration can support growth of bacteria in an anaerobic environment. In veterinary patients, occult (culture negative) infections may also

occur, a finding that can complicate decisions regarding therapy.

Other Laboratory Tests

Electron microscopy on biopsies of ciliated airway epithelium (nasal or tracheal samples) can be used to document primary ciliary dyskinesia.

Treatment

General

- When present, foreign body removal greatly assists in resolution of clinical signs of disease. However, focal bronchiectasis can result, which then serves as a source of chronic reinfection or recurrent signs. In these patients, lobectomy should be considered as part of treatment.
- Nebulization, chest coupage and postural drainage assist in the removal of secretions from the airway. Maintenance of systemic and airway hydration through oral intake, intravenous fluids, or nebulization should be used when necessary.
- Cough suppressants should be avoided in virtually every instance because failure to remove infectious and inflammatory secretions will perpetuate disease.

▼ ***Key Point*** Antibiotics are the mainstay of therapy, and long-term or lifelong therapy may be required.

Antibiotics

Choose antibiotics based on culture and sensitivity results. The occurrence of occult infection makes it difficult to choose specific therapy in some cases. Use broad-spectrum antibiotics that penetrate the pulmonary tissue.

- Fluoroquinolones are useful agents; however, resistance by streptococcal species poses a serious concern and these drugs have no efficacy against anaerobes. Therefore a second drug must be used in conjunction.
- Chloramphenicol, doxycycline, and clindamycin have been used with success.
- Trimethoprim-sulfa would most likely be useful, although side effects preclude long-term use of this drug.
- Azithromycin is a useful drug when susceptibility has been proved and this drug is well tolerated long term.
- When long-term (6 months to lifelong) antibiotics are required, a monthly rotation of several drugs should be considered to avoid development of resistant species.

Prognosis

Bronchiectasis associated with a foreign body may be partially resolved by retrieval of the material and with aggressive antibiotic treatment, but most cases of bronchiectasis are at continued risk for infection and worsening lung disease.

FELINE BRONCHIAL DISEASE

Etiology

- Feline bronchial disease appears to result from the initiation of an inflammatory process within the airways that results in mucosal edema, smooth muscle hypertrophy, hypertrophy of mucous glands with increased bronchial mucus, and reversible bronchoconstriction.
- Triggers of the inflammatory condition in spontaneously diseased cats have not been identified and it is likely that individual susceptibility to the induction of airway inflammation and hyper-responsiveness is quite variable.
- Environmental conditions or infectious agents have not been proven to cause bronchial disease; however, they may be responsible for exacerbation of preexisting disease. Some studies have found an association with *Mycoplasma* airway infection in asthmatic cats.
- The lungworm *Aelurostrongylus abstrusus* and the heartworm *Dirofilaria immitis* have been proposed as causes of hypersensitivity lung disease, but are present in just a fraction of affected cats.

Pathophysiology

- Current research suggests that cats with bronchial disease have hyper-responsive airways, analogous to asthma in humans. Human asthma is associated with an accumulation of inflammatory cells and mediators within the airway.
- Degranulation of mast cells with release of histamine and serotonin is associated with an acute inflammatory response within the airways. Release of inflammatory mediators aids in recruitment and activation of T lymphocytes and eosinophils.
- T lymphocytes contribute to airway inflammation through production of cytokines including interleukin-5, which enhances expression of leukocyte adhesion molecules and facilitates the ingress of eosinophils.
- The products of eosinophils are likely contributors to the pathology seen in feline bronchial disease. Major basic protein, eosinophil-derived cationic protein, eosinophil peroxidase, and eosinophil-derived neurotoxin are released from eosinophil granules. Major basic protein is particularly damaging to the airway, causing ciliostasis, epithelial cell death, and bronchoconstriction.
- Inflammatory injury to the mucosal lining exposes sensory endings in the lung, resulting in enhanced neural responsiveness to noxious stimuli. Thus, inflammation leads to a perpetual state of airway hyperexcitability and potential hyper-responsiveness.

Clinical Signs

Cats of all ages and of either sex are affected. There is a suggestion of an increased incidence and severity of disease in the Siamese cat.

History

- Cats with bronchial disease may have a long-term history of coughing, gagging, and decreased activity levels, suggesting chronic disease. Occasionally owners will report noisy breathing or wheezing. Another subset of cats will develop respiratory distress and cyanosis acutely and require emergency care, typical of an acute asthmatic attack.
- Feline bronchial disease can be misdiagnosed as a vomiting disorder because cats tend to retch and bring up bronchial secretions during a cough.
- Signs of upper respiratory tract infection can precede the onset of bronchial signs. This may be similar to viral-induced asthmatic symptoms in susceptible human patients.

Physical Examination

- Physical examination and thoracic auscultation are normal in some cats, whereas others exhibit adventitious lung sounds ranging from subtle wheezes to harsh crackles. Expiratory sounds are expected since asthma is classified as an obstructive airway disease of small airways. Pulmonary function testing has shown prolonged expiratory times in most cats examined. This can be observed in some cats at rest; however, excitement induced in the exam room often leads to tachypnea or panting.
- Cats with bronchial disease usually have increased tracheal sensitivity, and post-tussive crackles can be ausculted.
- Decreased thoracic compliance may be detected due to hyperinflation of the lungs.
- Open-mouthed breathing with or without cyanosis occurs in some cats and represents a medical emergency.

Diagnosis

The history and physical examination are helpful in establishing a presumptive diagnosis of bronchial disease. The remainder of the diagnostic workup may elucidate a primary cause of underlying airway hyperreactivity, such as lungworm, heartworm, or *Mycoplasma* infection, and it can rule out complicating conditions.

Laboratory Evaluation

- Peripheral eosinophilia is present in some cats with bronchial disease. Neutrophilia and monocytosis may reflect the chronicity of disease.
- Fecal examination, by zinc sulfate centrifugation-flotation and Baermann procedure, are useful in detecting parasitic infection. Heartworm testing (antibody, antigen, and echocardiography of the pulmonary arteries) should be considered in endemic areas when radiographs suggest pulmonary vascular disease and should also be considered in the cat that presents with both coughing and vomiting as clinical signs.
- Hyperglobulinemia may be present but is a nonspecific finding.

Radiography

- Normal chest radiographs do *not* rule out the diagnosis of bronchial disease.
- An interstitial peribronchial pattern with "doughnuts" and increased linear markings is considered classic for feline bronchial disease. Animals presenting in respiratory distress may show hyperinflation of the lungs with caudal displacement of the diaphragm and evidence of aerophagia.
- Occasionally a larger airway retains a mucus plug, resulting in atelectasis of the lobe supplied by that bronchus. This most commonly occurs in the right-middle lung lobe due to its dependent position; however, this is found in a minority (10%) of cats. Excessive mucus accumulation and plugging of more peripheral airways can result in a patchy alveolar pattern that must be distinguished from pneumonia, pulmonary edema, or neoplasia.
- CT can reveal thickened airway walls, mucus plugging, and emphysematous change with asthma or bronchitis.

Airway Sampling

Evaluation of airway washings through transoral (endotracheal) wash or bronchoscopy is recommended for patients that are stable enough to undergo the procedure. Anesthetic protocols that include ketamine are generally safe and effective for the procedure. Pretreatment with terbutaline prior to the anesthetic procedure can reduce the likelihood of bronchoconstriction. The drug can be given orally (0.625 mg PO q12h) or by injection (0.01 mg/kg sSC).

Airway Evaluation

- Bronchoscopy can reveal viscid mucus accumulation, mucus plugging, and nodular irregularities of the airways. Hyperemia is not a prominent finding.
- Cytologic findings in feline bronchial disease can include eosinophilic, neutrophilic, or mixed inflammatory responses. Normal feline airways are rich in eosinophils, and it is not uncommon for healthy cats to have greater than 25% eosinophils in an airway wash. Increased numbers or percentages of eosinophils or neutrophils are consistent with the diagnosis of feline bronchial disease and the level of inflammation correlates with the severity of disease. This can be helpful in determining therapy.

Table 162-3. ANTI-INFLAMMATORY AGENTS USED IN THE TREATMENT OF FELINE ASTHMA

Drug	Dosage	Mechanism of Action
Glucocorticoids:		Decrease influx of inflammatory cells, stabilize lysosomal membranes, decrease capillary permeability.
Prednisolone	1–2 mg/kg PO, IM q12–48 h	
Methylprednisolone acetate	10–20 mg/cat IM every 2–8 weeks	
Prednisolone sodium succinate	50–100 mg/cat IV	
Fluticasone proprionate (MDI)	110 µg/puff by aerosol q12–6 h	
Cyproheptadine	1–2 mg/cat PO q12 h	Blockade of serotonin receptor
Cyclosporine	10 mg/kg PO q12 h (adjust dosage to produce trough levels in the blood >500 ng/ml)	T-cell inhibition

MDI, metered dose inhaler.

- Studies have reported that 25–42% of airway cultures are positive for bacteria or *Mycoplasma*. When cytologic findings suggest airway infection, these positive cultures likely represent true infection, but a large percentage of healthy cats have positive airway cultures. Also, bacteria may establish temporary residence in the respiratory tract of cats with bronchial disease during episodes of respiratory distress without causing true infection.

Other Laboratory Tests

Pulmonary function tests can be performed in certain referral institutions. Anesthesia is required for measurement of airway resistance and lung compliance. Cats with bronchial disease exhibit higher airway resistance due to bronchoconstriction. Administration of terbutaline decreases resistance in some cats indicating partial reversibility of smooth muscle contraction.

Treatment

Emergency Therapy

▼ ***Key Point*** Minimization of stress is one of the most important aspects in management of the cat in acute respiratory distress. Provide a quiet, cool environment with supplemental oxygen.

Cats often benefit from concurrent administration of a bronchodilator such as terbutaline or albuterol, which are smooth muscle relaxants and generally provide rapid bronchodilation. A near immediate response to bronchodilator therapy is supportive of a clinical diagnosis of bronchial asthma.

- The suggested dose of terbutaline is 0.01 mg/kg SC. Monitor the cat for improvement in respiratory rate and effort for 15 minutes after administration. If no alterations are seen, give a second dose.
- Though often available, parenteral aminophylline is a poor substitute for terbutaline, as bronchodilatory effects are relatively minimal. Aminophylline is painful when administered by SC or IM injection, and agitation may occur following IV injection.
- An alternative approach used in many emergency practices involves administration of one or two puffs of albuterol from a metered dose inhaler delivered into a pediatric or feline spacer. The face mask attached to the spacer should be appropriate for a feline face and create a good seal; the mask should be maintained in place for 6 to 10 breaths.
- In cases of life-threatening bronchoconstriction, epinephrine can be administered cautiously if terbutaline is not available. Beta-2 agonist effects will produce reliable bronchodilation; however, cardiovascular stimulatory actions can cause side effects.
- If treatment with terbutaline, albuterol, or epinephrine fails to improve effort of breathing, the diagnosis of reactive bronchial disease is less likely. However, many cats with chronic bronchial disease show signs mainly as a consequence of inflammation so that the use of short-acting parenteral corticosteroids will often result in a relatively rapid improvement in clinical signs (Table 162-3).
- Signs of successful therapy result in reductions of respiratory rate, expiratory effort, and cyanosis.

Chronic Management

- Anti-inflammatory agents are the mainstay of therapy. Oral or inhaled steroids are the most commonly used agents and are generally successful in alleviating clinical signs (see Table 162-3). Prednisolone is the preferred anti-inflammatory agent, using a high dose initially (1–2 mg/kg PO q12h) for 3 to 10 days, and then tapered according to clinical response. Approximately 50% of cats can be stabilized and medication can be discontinued.
- Cats that cannot be medicated orally can be treated with long-acting steroid injections; however, this is a

less desirable method of treatment and leads to a number of systemic side effects. In these patients, the use of inhaled medications is preferred, either alone or preferably after stabilization and during the tapering of oral medication. Administer Flovent (fluticasone proprionate) 110 µg/puff q12h using an aerosol chamber or spacer device (AeroKat or Optichamber) and mask. Following one actuation of the metered dose inhaler into the chamber, cats should inhale 6 to 8 breaths to receive an adequate amount of drug.

- Alternate anti-inflammatory agents occasionally used in animals that cannot tolerate corticosteroids include cyproheptadine, a serotonin blocker, which is effective in vitro, and cyclosporine, an inhibitor of T cells (see Table 162-3). Side effects associated with cyclosporine limit its use to severe and refractory cases.
- Bronchodilators may help control clinical signs and decrease the dosage of corticosteroids required. Terbutaline, a beta-agonist, and extended release theophylline, a methylxanthine derivative, can be used. Individual cats will react differently to the drugs available. If the initial response to terbutaline is not adequate or if pills can be given only once daily, substitute a theophylline derivative. Consider prescribing inhaled albuterol by metered dose (see "Emergency Therapy") for use in the home setting for emergency management of asthmatic attacks.
- Some cats suffer exacerbation of disease in dusty or polluted environments, in response to cigarette smoke, or when they encounter specific noxious elements or stressful situations. Recognition and elimination of these triggers can reduce the frequency of attacks of respiratory distress or coughing episodes. Use of HEPA filters in the home may benefit indoor cats.

Contraindications

- Cats have significant sympathetic innervation to the airway. Blockade of beta receptors with propranolol (a nonselective beta blocker) or atenolol (a selective beta-1 blocker) can result in bronchoconstriction and respiratory distress in cats with bronchial disease. These drugs should be avoided.
- Diuretics and anticholinergic agents should not be used. There are no primary indications for these classes of drugs, and they have the negative effects of dehydrating the mucus layer and increasing mucus trapping.

Prognosis

Feline bronchial disease can be a chronic disorder and cats often exhibit either chronic persistent signs or recurrent episodes of clinical disease. Owners should be informed of this probability, encouraged to follow anti-inflammatory therapy closely, and to pursue regular communication with their veterinarian for follow-up care.

INTERSTITIAL LUNG DISEASE

Etiology

The etiopathogenesis of interstitial lung diseases is unknown, and the origin of disease is most likely multifactorial.

- Hundreds of inhaled agents, drugs, chemicals, and chronic infection or inflammation have been shown to lead to interstitial pneumonias or pulmonary fibrosis in humans. It is likely that chronic exposure to any of these substances could lead to similar conditions in dogs and cats.
- Genetic factors may play a role in the development of interstitial lung disease since West Highland white terriers and other terrier breeds seem more likely to develop this condition.

Pathophysiology

- Exposure to a variety of insults can lead to the release of inflammatory mediators in the lung, which initiate a chronic progressive inflammatory disease in the interstitium. Accumulation of the inflammatory products and cellular components of neutrophils and macrophages causes thickening of the alveolar wall and destruction of alveolar architecture.
- The presence of cellular debris within the alveoli and the formation of enlarged, dysfunctional alveolar units result in mismatching of ventilation and perfusion with subsequent hypoxemia.
- Interstitial lung disease results in a thickened barrier to diffusion for gas exchange. Diffusion impairment leads to hypoxemia during exercise and in severe cases can cause clinical signs at rest.
- Lung compliance is decreased by fibrosis causing increased work of breathing and tachypnea. End-stage restrictive lung disease develops.

Clinical Signs

Signalment

Terrier-type dogs, particularly the West Highland white terrier, and perhaps other small-breed dogs seem to be at increased risk for development of interstitial lung disease. Males and females are equally affected. Any age is susceptible; however, animals are usually older on presentation, perhaps because of prolonged exposure to inciting agents or due to compensatory mechanisms that preserve pulmonary function. A similar disease resulting in pulmonary dysfunction has been reported in cats.

History

- The classic history in an animal with interstitial lung disease is shortness of breath and exercise intolerance. Owners may attribute easy fatigability to advanc-

ing age and fail to recognize the presence of respiratory disease.
- Syncope can result from hypoxemia, pulmonary hypertension, or inappropriate baroreceptor responses following coughing or excitement.
- In cats, findings of respiratory distress and cough mimic those seen in feline bronchial disease.

Physical Examination

- Patients may appear relatively normal at rest, but develop shortness of breath and possibly cyanosis on exertion. Most animals are tachypneic and may exhibit respiratory distress.
- Pulmonary auscultation may be relatively unremarkable; however, the hallmark of pulmonary fibrosis is the presence of diffuse inspiratory crackles across the thorax. Crackles may be fine and localized or may be diffusely present and audible without a stethoscope.
- In patients that have developed pulmonary hypertension, cardiac auscultation may reveal a prominent pulmonic component to the second heart sound, a split S_2, or a murmur of tricuspid regurgitation.

Diagnosis

Definitive diagnosis of interstitial lung disease requires an open-lung biopsy. However, exclusion of other diseases that result in shortness of breath and crackles (e.g., pneumonia, bronchitis, CHF), along with failure to respond to standard treatment for bronchitis, is suggestive of the diagnosis.

Radiography

- Radiographs may be relatively normal, particularly in view of the degree of respiratory distress present in the patient. Classically, a generalized, diffuse interstitial pattern is detected.
- True cardiomegaly in these patients is characterized by right-sided cardiomegaly, and this may be an indicator of pulmonary hypertension. Artifactual cardiomegaly can be present due to breed conformation, decreased inspiratory volume, or reduced lung expansion.
- CT is valuable in documenting and characterizing the interstitial lung diseases in humans and further use of this modality may improve diagnostic capabilities in affected animals.

Airway Sampling

- Bronchoalveolar lavage will show an increase in the percentage of neutrophils, usually to greater than 25% (normal 5–6%). It is not possible to differentiate interstitial lung disease from chronic bronchitis based on cytologic findings alone; however, absence of increased bronchial mucus or anatomic changes at bronchoscopy argues against a diagnosis of chronic bronchitis.
- Cultures are usually negative unless infection complicates the disease.
- Pathologic assessment of affected lungs in cats reveals interstitial fibrosis, alveolar epithelial metaplasia and alveolar interstitial smooth-muscle metaplasia. In affected West Highland white terriers, expansion of the extracellular matrix with collagen rather than fibroplasia leads to thickening of the alveolocapillary barrier. Inflammation does not appear to be a substantial component of this disease.

Other Laboratory Tests

- Arterial blood gas analysis can show extreme hypoxemia at rest, while other animals may be normoxemic at rest.
- Doppler echocardiography may be used to document pulmonary hypertension when either tricuspid regurgitation or pulmonic insufficiency is present.

Treatment

General

- Exposure to identifiable inhaled or ingested risk factors should be minimized.
- Weight control is desirable to improve thoracic compliance.
- In general, animals diagnosed with interstitial lung disease respond poorly to treatment and have a poor prognosis. Underlying neoplasia may be present in some animals.

Anti-inflammatory Drugs

- Animals that will benefit from steroid therapy should show a response after 2 to 3 weeks of treatment with prednisone or prednisolone at 1 to 2 mg/kg PO q12h. High-dose therapy may result in continued improvement over 1 to 2 months, but the risk of severe immunosuppression and other complications must be considered.
- Variable success has been found in human patients when cytotoxic agents are used alone or in combination with glucocorticoids. The risk of systemic side effects related to immunosuppression or myelosuppression increases dramatically when cyclophosphamide is used. Anti-fibrotic drugs have not proved successful in human medicine and have unacceptable side effects in dogs. While interferon-gamma had initial success in treatment of humans, further studies have not supported its use.

Bronchodilators

- It is reasonable to consider a trial on bronchodilators in animals suspected of having an interstitial lung disease. Theophylline or beta-2 agonists may reduce respiratory distress and improve cardiac and respiratory muscle function in some patients (see Table 162-1).

Prognosis

- The prognosis for control of disease is guarded. Some animals can be made relatively comfortable for variable amounts of time, but respiratory distress typically worsens.
- Patients with pulmonary fibrosis are at risk for pulmonary hypertension and cor pulmonale.

PULMONARY INFILTRATES WITH EOSINOPHILS

Etiology

- Eosinophils accumulate in the canine airway in response to infection with heartworm, lungworms *(Filaroides hirthi, Capillaria aerophila),* or with parasitic bronchitis *(Oslerus osleri, Paragonimus kellicotti)*. Larval migration can also result in an eosinophilic pulmonary infiltrate.
- Hypersensitivity or an immune directed reaction can trigger eosinophil deposition in the airway and idiopathic eosinophilic lung disease. This condition is called eosinophilic bronchopneumopathy by some authors.
- Pulmonary eosinophilia has also been observed in cases of neoplastic-associated hypereosinophilic syndrome (see Chapter 22), in pulmonary fungal infections (see Chapter 20), and in dogs with pulmonary granulomatosis.

Pathophysiology

- Eosinophils in the airway release effector molecules such as major basic protein and eosinophil-derived cationic protein, which normally act to kill parasites or to combat an immunologic insult. The products of eosinophils damage cells of the respiratory system, resulting in ciliary paralysis and erosion and sloughing of the mucosa.
- Eosinophils stimulate release of preformed mediators from mast cells such as histamine and serotonin, and increase circulating levels of leukotrienes and platelet activating factor. These substances increase the permeability of the epithelium, increase secretion of mucus, and may also mediate smooth muscle contraction, causing bronchoconstriction.
- Eosinophil activation causes an increase in airway mucus, leading to increased resistance to air flow and subsequent hypoxemia.

Clinical Signs

History

The most common clinical complaint is a cough that is unresponsive to antibiotic treatment. Hemoptysis may be present in dogs with pulmonary infiltrates with eosinophils. Dogs are often short of breath, anorexic, and exhibit exercise intolerance.

Physical Examination

- The animal may be bright and alert or show variable degrees of depression and weight loss. Occasionally, severe systemic signs are present.
- Loud bronchial noises can be heard along with diffuse coarse crackles. Marked tracheal sensitivity is often present.

Diagnosis

Laboratory Evaluation

- The CBC often shows leukocytosis with eosinophilia and basophilia; however, peripheral eosinophil numbers may be normal despite significant pulmonary involvement.
- Heartworm disease must be ruled out with an occult heartworm test, and animals should have multiple fecal examinations (zinc sulfate centrifugation-flotation or Baermann procedure) performed to detect possible lungworm infection.

Radiography

- Thoracic radiographs typically show a mixed infiltrative pattern with bronchial, interstitial, and alveolar densities. Young animals with larval migration have a primarily caudodorsal distribution of infiltrates.
- *Paragonimus* infection may show the characteristic thick-walled cystic structures on radiographs. Occasionally, rupture of a cyst can lead to pneumothorax.
- Heartworm infection is characterized by a prominent right ventricle and enlarged pulmonary arteries.

Airway Sampling

- High numbers of eosinophils are seen on cytology from tracheal wash fluid or on bronchoalveolar lavage. Cytology preparations should be carefully searched for parasite eggs and larvae.
- Bronchoscopy generally reveals markedly hyperemic airways. Yellow-green mucus, polypoid proliferations on the epithelium, bronchiectasis, and airway collapse are variably seen.

Other Laboratory Tests

- Intradermal skin testing might be considered in an attempt to identify an offending allergen, but has never been well correlated to spontaneous canine lung diseases.

Treatment

- Removal of an offending allergen can result in resolution of clinical signs, but most animals also require glucocorticoid therapy.
- In dogs with suspected eosinophilic lung disease, empiric therapy for lungworm infection or larval migration could be considered in animals that are

stable. In that case, Fenbendazole is recommended at 50 mg/kg PO q24h for 10 days. Specifically identified parasitic infections and larval migration should be treated with appropriate anthelminics.

- The primary treatment for eosinophilic infiltration of the airways or pulmonary parenchyma is based on immunosuppression with glucocorticoids. Prednisone is used initially at 1 mg/kg PO q12h for 5 to 10 days. The dose is slowly tapered as signs resolve and the drug can often be discontinued in 4 to 6 months. Too rapid tapering of drug can result in failure to eliminate signs or early recurrence, and recurrence of clinical signs requires a return to the higher dose of steroid. Some dogs require sustained treatment.

GRANULOMATOUS PULMONARY DISEASES

Etiology

- In endemic regions, granulomatous pulmonary disease is commonly seen with systemic fungal infections (histoplasmosis, blastomycosis, and coccidioidomycosis; see Chapter 20).
- Noninfectious granulomatous lung diseases are uncommonly encountered in the dog and cat.
  - Eosinophilic pulmonary granulomatosis is a nodular lung disease that has been linked to occult heartworm infection in the majority of cases.
  - Pulmonary lymphomatoid granulomatosis has been described in dogs and is similar to a neoplastic condition in humans characterized by proliferation of T lymphocytes. Some animals with lymphomatoid granulomatosis have had a history of heartworm disease.

Pathophysiology

- Fungal elements typically incite a type IV hypersensitivity immune response with infiltration of macrophages and lymphocytes.
- Eosinophilic granulomatosis may be induced by an immune reaction to heartworm antigens, dirofilarial immune complexes, or other unidentified stimuli. Characteristics of type III and type IV hypersensitivity reactions are present, with proliferation of epithelioid cells, macrophages, and eosinophils within the parenchyma.
- Histopathologic lesions are typically described as an angiocentric infiltrate of mononuclear cells, lymphocytes, plasma cells, mast cells, and occasionally eosinophils.

Clinical Signs

Signalment

Any age or breed of animal may develop granulomatous pulmonary disease, although young to middle-aged, large-breed dogs and young cats are more commonly affected.

History

These diseases often result in a chronic course of disease with signs present from 1 to 12 months prior to diagnosis.

- Respiratory signs include a nonproductive cough, abnormal breathing, respiratory distress, and exercise intolerance.
- Systemic signs such as fever, anorexia, and weight loss are often present.
- A relentless course of disease is typical, and treatment with glucocorticoids results in worsening disease in the case of fungal disease or minimal improvement with granulomatous disease. These disorders are also unresponsive to antibiotic treatment.

Physical Examination

- Systemic involvement is indicated by the generally debilitated state of the patient. Additional organs are often affected in cases with systemic mycoses (see Chapter 20) but not in primary granulomatous pulmonary diseases.
- Respiratory abnormalities include an elevated respiratory rate, increased tracheal sensitivity, harsh coarse crackles, and loud bronchial wheezing noises.

Diagnosis

Laboratory Evaluation

- The CBC typically shows a leukocytosis with variable degrees of neutrophilia, monocytosis, eosinophilia, or basophilia. Hyperglobulinemia may be present in association with chronic antigenic stimulation.
- Occult heartworm testing and fungal titers are recommended in suspected cases. Positive titers for histoplasmosis and blastomycosis may reflect only exposure to disease.

Radiography

- Fungal disease typically results in a nodular pattern on chest radiographs, with a homogeneous population of small or large nodules, depending on the type and duration of fungal infection.
- The presence of multiple pulmonary masses varying in size is suspicious for a granulomatous disease, metastatic neoplasia, or malignant histiocytosis. Pulmonary masses ranging from 1 to 7 cm and lobar consolidation have been reported in eosinophilic and lymphomatoid granulomatosis.
- Hilar lymphadenopathy is present in virtually all granulomatous lung diseases and can be severe. Partial obstruction of a main stem bronchus often occurs due to enlargement of hilar nodes.

Airway Sampling

- In myocotic infections, fungal elements may be seen on transtracheal wash, bronchoalveolar lavage, or on fine-needle aspiration of the lung.
- Definitive diagnosis of nonfungal granulomatous disease is based on characteristic histopathologic findings from biopsy of a lung mass. Eosinophils are commonly encountered on cytology of eosinophilic granulomatosis and may also be seen in lymphomatoid granulomatosis.

Treatment

- Treat pulmonary mycosis as described in Chapter 20.
- Therapy for eosinophilic or lymphomatoid granulomatosis should begin with treatment of heartworm disease, when present. Treatment for the granulomatous component of disease requires the use of immunosuppressive and cytotoxic drugs. Prednisone along with cyclophosphamide or cyclophosphamide/vincristine has been used with some success; however, prognosis is guarded for these conditions. A remission rate of less than 25% has been reported in one series of advanced canine patients.

NON-CARDIOGENIC PULMONARY EDEMA

Etiology

Non-cardiogenic pulmonary edema can be categorized as high-pressure edema or permeability edema. High-pressure edema may be more amenable to therapeutic intervention.

- **High-pressure edema** results from overexpansion of the extracellular fluid volume by overzealous administration of fluids, from decreased oncotic pressure, or in association with pulmonary overcirculation, which may occur with pulmonary thromboembolism.
- **Permeability edema** can result from pulmonary insults such as aspiration of acidic gastrointestinal contents, near drowning, and smoke inhalation, or from extrapulmonary insults such as pancreatitis, disseminated intravascular coagulation, sepsis, and anaphylaxis. A number of these conditions activate the systemic inflammatory response syndrome (SIRS), a disorder known to predispose to noncardiogenic pulmonary edema,
- Combination of these two types of noncardiogenic pulmonary edema may result from electric cord shock, upper airway obstruction, or in re-expansion pulmonary edema (i.e., after alleviation of chronic atelectasis due to long-standing pleural effusion or chronic diaphragmatic hernia).

Pathophysiology

- Noncardiogenic pulmonary edema is not associated with primary cardiac insufficiency. In high-pressure edema, overexpansion of plasma volume or decreased oncotic pressure leads to fluid accumulation in the lung due to a disruption of Starling forces.
- Damage to the alveolocapillary membrane results in permeability edema and allows protein-rich fluid to flood the alveoli. This results in refractory hypoxemia, decreased pulmonary compliance, and eventual hyaline membrane formation. In humans, the severest form of this condition is known as acute (or adult) respiratory distress syndrome (ARDS).

Clinical Signs

Dogs or cats with serious systemic illness that develop signs of refractory respiratory distress or tachypnea should be suspected of having non-cardiogenic pulmonary edema and/or pulmonary thromboembolism. Typically, animals with non-cardiogenic pulmonary edema are poorly responsive to conventional therapy.

History

The history usually reveals an acute or chronic pulmonary or multisystemic illness requiring significant supportive care. Non-cardiogenic edema may be associated with chronic vomiting syndromes. Respiratory abnormalities noted include tachypnea, respiratory distress, and cyanosis.

Physical Examination

- Thoracic auscultation reveals tachypnea and often the fine crackles of pulmonary edema. Underlying lung disease may result in coarse crackles or absence of lung sounds due to lobar consolidation.
- The remainder of the physical examination may provide clues to the inciting event, such as electric cord burns, peripheral edema, neurologic abnormalities, stridor, abnormal abdominal palpation, or other physical exam abnormalities.

Diagnosis

The history of a precipitating catastrophic event or trigger for systemic inflammation along with acute onset of respiratory distress is highly suggestive of the diagnosis. Alternative considerations should include pneumonia, pleural effusion, and pulmonary thromboembolism. Refractory hypoxemia despite aggressive supportive care increases the index of suspicion for non-cardiogenic pulmonary edema.

Radiography

- Patchy interstitial and alveolar densities are found, particularly in the periphery or caudodorsal lung lobes. The pattern of distribution helps distinguish this type of pulmonary edema from cardiogenic edema in the dog. Typically, with non-cardiogenic pulmonary edema, the infiltrate is severe and bilat-

eral rather than perihilar in distribution, and it fails to clear with diuretic therapy.
- Radiographic signs of aspiration pneumonia such as cranioventral alveolar infiltrates or consolidation of middle lung lobes may be present in some cases.

Arterial Blood Gas

Arterial blood gas analysis is helpful in following the course of disease and in determining prognosis. Animals are hypoxemic, there is an increased alveolar to arterial gradient, and oxygen responsiveness is minimal.

Treatment

Use aggressive therapy to correct the primary disease. Acid-base imbalances and electrolyte abnormalities are identified and normalized early in the course of disease. Prognosis is guarded in most cases.

High Pressure Edema

In cases with high-pressure edema, *discontinue* intravenous fluid support as soon as the problem is identified. Overhydration can usually be resolved with diuretic therapy. Oncotic pressure may be elevated transiently through infusion of plasma or dextrans, and this may clear the pulmonary infiltrate.

Permeability Edema

Animals that develop non-cardiogenic pulmonary edema due to increased permeability in the alveolocapillary membrane often have more severe derangements in gas exchange and are more difficult to stabilize.

- Unfortunately there is no specific therapy for non-cardiogenic pulmonary edema and many cases require short-term ventilation support to survive.
- Use oxygen therapy to increase the pO_2.
- Use sedation (butorphanol, 0.1–0.2 mg/kg IM) to reduce anxiety.
- Administer IV fluids *very* cautiously to avoid alveolar flooding; generally fluid therapy will exacerbate the edema. This relationship can create real problems when there is a need for fluid resuscitation, but the clinician should understand that large volume infusions will likely precipitate a need for ventilator therapy.
- Use diuretic therapy cautiously because it can deplete intravascular fluid volume and lead to hypotensive shock while failing to clear pulmonary congestion. Reducing capillary hydrostatic does lower the tendency towards edema formation, but this point must be weighed against the loss of cardiac filling and tissue perfusion.
- Plasma infusion can be helpful by replacing proteins lost through the alveolocapillary membrane and maintaining oncotic pressure; however, colloid not maintained within the vascular space may worsen the edema.
- There is no clear evidence that corticosteroids are efficacious in patients with non-cardiogenic pulmonary edema. Steroids may be useful in rare cases of non-cardiogenic pulmonary edema associated with shock or anaphylaxis.
- Bronchodilators are of uncertain value. Long-acting theophylline might increase the strength of respiratory muscles but at the risk of anxiety and gastrointestinal disturbances. Terbutaline in dogs has been shown to reduce lung water in experimentally induced permeability edema.
- Positive inotropic support may be helpful in certain cases to maintain blood pressure, especially when fluid intake is restricted.
- Progressive respiratory distress, desaturation despite oxygen therapy, hypercarbia and other signs of respiratory failure, or obvious respiratory fatigue require tracheal intubation and mechanical ventilation.

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Chapter

163 Respiratory Infections

John D. Bonagura

The respiratory system is a common portal of entry for infectious agents of all varieties, with many of these infectious agents have been identified as respiratory pathogens (Table 163-1). The purpose of this chapter is to emphasize clinical aspects of common respiratory infections in dogs and cats. For details concerning specific infectious diseases, the reader is referred to Chapter 11 for respiratory virus and chlamydia infections of the cat, Chapter 12 for bordetellosis and viral tracheobronchitis of the dog, Chapter 13 for canine distemper, Chapter 20 for the systemic mycoses, and Chapter 21 for toxoplasmosis. Diagnostic procedures relevant for respiratory infections are summarized in Table 163-2 and are discussed in Chapters 158 and 159. Management of noninfective bronchopulmonary diseases and of chronic bronchitis in the dog and cat are described in Chapter 162. Management of pleural infections is described in Chapter 164.

- The nasal cavity, nasopharynx, larynx, and the trachea are normally inhabited by a variety of microorganisms. Aspirated bacteria from the upper respiratory tract intermittently populate the tracheal-bronchial tree. Thus the potential for *secondary* opportunistic infection is high when underlying pulmonary injury is present or when the host is immunologically compromised. In addition, the clinician can expect to culture microorganisms such as *Pasteurella* spp. from the upper airways when performing diagnostic studies. These results must be interpreted with care.
- Many infectious agents are *primary* pathogens of the respiratory epithelium, pulmonary interstitium, or pleural space. This is particularly true of upper respiratory infections caused by viral agents or bacteria like *Bordetella bronchiseptica.*
- The respiratory system also may be involved in *multisystemic* infections. This is common with the systemic mycoses, *Blastomyces dermatitidis* and *Histoplasma capsulatum.*
- Certain infectious agents, such as *Bartonella* spp., are emerging as potential causes of respiratory infection at multiple levels. Some of these agents are intracellular, others very difficult to culture. Diagnosis of these infections relies increasingly on molecular laboratory methods.
- It is helpful to identify the principal *anatomical site(s)* of infection, as many infectious agents produce a characteristic pattern of respiratory disease. This approach may help the clinician in the differential diagnosis and in directing appropriate laboratory studies. Good examples of localized respiratory disease are the viral upper respiratory infections of cats and canine infectious tracheobronchitis. Because clinicians generally speak in terms of the anatomic diagnosis—rhinitis, sinusitis, laryngitis, tracheitis, bronchitis, pneumonia, pleuritis, or mediastinitis—respiratory infections will be discussed using this classification (see Tables 163-1 and 163-2).

▼ ***Key Point*** Because many respiratory infections are secondary to another condition, consider the possibility of *underlying* respiratory disease or the possibility of host immunosuppression.

- The subject of infectious disease is extensive. For more detailed information on specific infections, the reader is directed to other sources such as *Greene's Infectious Diseases of the Dog and Cat.*

RHINITIS AND SINUSITIS OF INFECTIOUS ETIOLOGY

Infections of the nasal cavity and paranasal sinuses are common, and clinical signs may also involve the nasopharynx. Acute rhinitis is frequently caused by viral and bacterial pathogens that directly invade the nasal mucosa. Chronic rhinitis often can be traced to another predisposing problem such as immunosuppression, foreign body, or tumor. Because the nasal cavity is not sterile, standard culture and sensitivity tests are of little value in diagnosis and management of these diseases.

Etiology

- Infections of the nasal cavity and nasal sinuses are not uncommon, especially those associated with acute, contagious viral infections in dogs and cats. Etiologic agents are summarized in Table 163-1.

History

- Cardinal signs of upper airway infection are sneezing, nasal discharge, and often a dry cough. Involvement

Table 163-1. CLASSIFICATION OF COMMON RESPIRATORY INFECTIONS BY ANATOMIC LOCATION

Rhinitis and Sinusitis

Herpesvirus (rhinotracheitis) [F][†]
Calicivirus [F][†‡]
Chlamydia psittaci
Parainfluenza virus [C][†]
Canine distemper virus [C][†‡]
Adenovirus-2 [C][†‡]
Salmon poisoning rickettsial agent [C]
Bordetella bronchiseptica [C,F][†‡]
Secondary bacterial infection (find predisposing cause)
Aspergillus flavum [C]
Penicillium spp. [C]
Rhinosporidium seeberi [C]
Cryptococcus neoformans [F]
Cuterebra and other grubs
Pneumonyssus (Pneumonyssoides) caninum [C]
Eucoleus boehmi [C]

Tracheitis

Upper respiratory virus (see above)
Bordetella bronchiseptica [C][‡]
Osleri (Filaroides) osleri [C]

Bronchopulmonary Infections[§]

Some upper respiratory viruses (see above)
Canine influenza virus
FIV infection—can cause alveolitis in cats
Bacteria bronchopneumonia—both gram-positive and gram-negative infections
Bordetella bronchiseptica [C, F]
Gram-negative bacteria: *Escherichia coli, Klebsiella* spp., *Pseudomonas* spp., *Pasteurella* spp.
Gram-positive bacteria: *Streptococcus* spp., *Staphylococcus* spp.
Mycoplasma spp. [F > C]
Parasitic infections [F, C]
Aelurostrongylus abstrusus [F]
Paragonimus kellicotti [C, F]
Capillaria aerophilia [C, F]
Osleri (Filaroides) infection *(F. milksi, F. hirthi)* [C]
Aspergillosis (endobronchial infection)
Viral infections: feline calicivirus; canine distemper virus
Chlamydia psittaci [F]
Rickettsial infections (*Ehrlichia canis;* Rocky Mountain spotted fever) [C >> F]
Toxoplasma gondii [F > C]
Hematogenous bacterial infection
Nocardia spp., *Actinomyces,* anaerobes[¶]
Leishmania donovani [C]
Systemic mycoses: *Histoplasma encapsulatum, Blastomyces dermatitidis, Coccidioides immitis, Cryptococcus neoformans* [C > F]
Response to parasitic infection: migrating nematodes [C]
Dirofilaria immitis [C > F]
Lungworms and flukes [F, C]

Pleuritis and Pleuropneumonia

Feline infectious peritonitis
Anaerobic bacteria
Aerobic bacteria (*Pasteurella* spp., *E. coli,* etc.)
Nocardia asteroids
Actinomyces spp.
Blastomyces dermatitidis [C >> F]
Toxoplasma gondii [F >> C]

*This list is not comprehensive; important clinical conditions are indicated with the most commonly affected species designated as [C] = canine; [F] = feline.
[†]Infection commonly extends to the larynx and trachea.
[‡]Infection commonly extends to the bronchi and may cause pneumonia.
[§]Alveolar involvement may develop in some cases of interstitial pneumonia.
[¶]Pulmonary abscess, pleuropneumonia, and pyothorax may develop with these agents.

of or discharge into the nasopharynx may cause reversed sneezing or gagging.

- Contagion is an issue with some causes of upper respiratory infections, especially with agents associated with the feline upper respiratory infections (see Chapter 11).
- Acute viral rhinitis is usually self-limiting within 1 to 2 weeks.
  - Persistence of viral or bacterial rhinitis or sinusitis can occur in immunocompromised cats infected with feline leukemia virus (FeLV) or feline immunodeficiency virus (FIV).
  - In addition, feline herpesvirus persists in a latent subclinical carrier form in recovered cats, and this occasionally recrudesces to result in episodic or persistent rhinitis (or conjunctivitis).
- Primary bacterial rhinitis and sinusitis are uncommon (except with *Bordetella bronchiseptica*); however, secondary bacterial infection can develop as a sequel to mucosal injury or obstructed nasal passages caused by upper respiratory viral infection, foreign body, periodontal disease and root abscesses, oral-nasal fistula or cleft palate, trauma (sequestrum), allergic rhinitis, lymphocytic-plasmacytic rhinitis, congenital ciliary dyskinesia (including the Kartagener syndrome), polyps, neoplasia, and fungal infection.
- *B. bronchiseptica* infection can lead to significant rhinitis as well as tracheobronchitis.
- Chronic bronchitis or lobar pneumonia can predispose to sinusitis, and vice versa. It is likely that a sinubronchial route of migration reinforces each infection.
- Bacterial isolates in rhinitis/sinusitis are variable and typify bacteria normally encountered in the nasopharynx, including gram-positive, gram-negative, and anaerobic organisms. Recently *Bartonella* spp. has been incriminated as a possible cause of nasal cavity discharge, including epistaxis, in dogs.
- Fungal infection of the nasal cavity or sinuses (see Table 163-1) can also be associated with immunosuppression; however, this immunodeficiency may be difficult to demonstrate in dogs. *Aspergillus flavus,* for example, is a normal inhabitant of the nasal cavity, but may invade respiratory epithelium in dogs with altered immunity or preexistent inflammation (e.g., lymphocytic-plasmacytic rhinitis, foreign body, or trauma).
- Nasal parasites, such as the nasal mite, *Pneumonyssus (Pneumonyssoides) caninum,* and the nasal nematode, Eucoleous, are uncommon in most localities, but are a potentially treatable cause of upper nasal/nasopharyngeal signs; this should be considered, especially in young dog with rhinitis and reversed sneezing.

Clinical Signs

- Sneezing, nasal discharge, and gagging or retching from postnasal drip are the typical signs of infectious rhinitis and sinusitis.

Table 163-2. DIAGNOSIS OF RESPIRATORY INFECTIONS

Nasal Cavity and Paranasal Sinuses

Signalment (age, breed, sex), vaccination status, history
Physical examination (emphasis: head, eyes, nose, oral cavity, regional lymph nodes, skin)
Auscultation
Serologic tests (aspergillosis, FeLV, FIV, and cryptococcus)
Skull, dental, and nasal radiographs
CT or MRI of the nasal cavity and paranasal sinuses
Examination of the teeth, oral cavity, oropharynx, and tonsils under anesthesia (inspection, palpation, examination with dental probes and mirrors)
Rhinoscopy (nasal cavity and retroflex rhinoscopy of the nasopharynx and posterior choanae)
Nasal culture (bacterial, fungal)
Aspiration biopsy/cytology (swab or nasal flush) of nasal exudate
Mucosal biopsy of the nasal cavity
Fine-needle aspiration biopsy/cytology of enlarged regional lymph nodes or mass lesions
Surgical exploration of the nasal cavity and paranasal sinuses for culture, biopsy, and debridement
Virology: Immunocytologic identification of viruses (e.g., immunofluorescence for canine distemper, feline herpes) and virus isolation (e.g., feline calicivirus)

Larynx

Ultrasonography of larynx
Visual examination of the larynx during light anesthesia
Radiography

Trachea

Radiography (cervical and thoracic)
Fluoroscopy
Tracheoscopy (endoscopy)
Cytologic examination of tracheal lesions (brush cytology of the tracheal mucosa)

Bronchopulmonary Diseases

History and physical examination (observation, auscultation, percussion of the thorax)
Thoracic radiography
Complete blood count
Heartworm (HW) tests (enzyme-linked immunosorbent assay [ELISA] antigen tests for dogs and cats, microfilaria tests for dogs, HW antibody test for cats)
Fecal examinations (flotation and Baermann sedimentation to detect lung parasites)
Serologic testing
(e.g., immunodiffusion or other tests for systemic mycoses, IgM ELISA for toxoplasmosis)
Arterial blood gas
Pulse oximetry
Bronchoscopy
Culture of tracheobronchial secretions
(transtracheal wash, endotracheal approach using a guarded culture swab, or aspiration through sterile tubing advanced through a sterilized endoscopic port)
Cytologic examination of the bronchi or lower airways
- Transtracheal wash of tracheobronchial secretions
- Endotracheal aspiration cytology
  - Via a catheter placed in the trachea or bronchial tree
  - Via an endotracheal tube (method sometimes used in cats and very small dogs)
- Brush cytology of the bronchial mucosa
- Bronchial aspiration cytology (selective, via a bronchoscope catheter)
- Bronchoalveolar lavage with a wedged bronchoscope

Fine-needle aspiration (FNA) of the lung or a mass lesion
Lung biopsy
Pulmonary function testing

Diseases of the Pleural Space

History and physical examination (observation, auscultation, percussion of the thorax)
Thoracic radiography (pre- and post-thoracentesis)
Thoracentesis
Cytology of pleural effusate
Culture and sensitivity of pleural effusate
Serological testing when appropriate (FIV, FIP)
Biochemical tests (e.g., serum/pleural effusion triglyceride concentration)
Ultrasound examination
Computed tomography (CT) or magnetic resonance imaging (MRI) of thorax
Lymphangiography

Diseases of the Mediastinum

History and physical examination (observation, auscultation, percussion of the thorax)
Thoracic radiography
Ultrasound examination
CT or MRI of mediastinum
FNA of mediastinal masses
Barium swallow and esophagram
Tracheoscopy/bronchoscopy

- Reversed sneezing (violent, inspiratory movements against a closed glottis) may occur with nasopharyngeal irritation from any source.
- Involvement of the ocular conjunctiva is not uncommon with contagious causes of rhinitis. Corneal involvement may suggest herpesvirus infection. Chorioretinitis may develop consequently to infectious canine distemper virus or cryptococcosis.
- Cough may indicate postnasal drip with pharyngeal irritation or concurrent involvement of the larynx, trachea, or bronchial tree.
- Some dogs retch and expectorate secretions that have accumulated in the pharynx.
- A serous discharge is typical of acute viral disease, whereas mucopurulent nasal exudate suggests a bacterial or fungal component.
- Other clinical findings such as fever, enlargement of the tonsils, bony swelling, regional lymphadenopathy, oral ulceration, and ocular or neurological involvement may be evident depending on the underlying causes of disease.

Diagnosis

- The differential diagnosis of upper respiratory infections is extensive (Table 163-3), including primary infectious diseases, secondary infections, and a large number of non-infective disorders. The age, vaccination status, history, and physical examination tend to focus the diagnostic considerations in most cases. The diagnostic studies chosen depend on the presumptive diagnosis and response to initial therapy (see Table 163-2).
- Primary infectious diseases, nasal mites, and foreign bodies with secondary infection are the important cause of rhinitis and sinusitis in younger dogs and cats. Older pets (older than 8 years of age) tend to be afflicted with nasal tumors complicated by secondary nasal infection.
- The poorly understood, idiopathic, lymphocytic-plasmacytic rhinitis of dogs and cats is a very common biopsy diagnosis that may be associated with allergy or infection. This disorder may allow for opportunistic secondary mucosal invasion by bacteria or fungi.
- Suppurative rhinitis is a less common biopsy diagnosis of the nasal mucosa. Primary and secondary bacterial infection may be involved; infection by *Bartonella* spp. should be considered.
- Infections caused by *Aspergillus* spp. and *Penicillium* spp. require histologic examination of nasal tissue, sometimes with special staining (e.g., silver stains) to detect hyphae. A positive agar gel immunodiffusion (AGID) test may also be supportive of the diagnosis. Routine culture is nonspecific because these fungi can be normal inhabitants of the nasal cavity.

▼ ***Key Point*** Because bacteria and fungi can be cultured normally from the nasal cavities, a careful exclusion of an underlying condition is essential and over-interpretations of positive cultures must be avoided.

- The typical *canine work-up* for signs of nasal disease requires general anesthesia. Routine laboratory tests can be obtained including a complete blood count (CBC) and serologic tests for aspergillosis and polymerase chain reaction (PCR) for *Bartonella*. Regional lymph nodes can be aspirated if enlarged, and routine thoracic films exposed to exclude concurrent bronchopulmonary infection. However, most diagnoses are made under general anesthesia.
  - At a minimum, diagnostic imaging should include an open mouth radiograph of the nasal cavity. Abnormal findings include focal or multifocal lesions, increased soft tissue or fluid density, loss of turbinate detail, nasal septal deviation, and boney destruction. These findings are not diagnostic of any specific condition, and each is compatible with some form of chronic infection.
  - Optimally computed tomography (CT) of the nasal cavity, paranasal sinuses, and nasopharynx should be done and interpreted by an expert in this form of imaging.
  - After radiological procedures, initiate anesthetic examination with careful inspection of the oral cavity, oropharynx, tonsils, and larynx. Follow this with antegrade rhinoscopy via the nostrils and retrograde rhinoscopy across the nasopharynx using a retroflexed endoscope.
    Unfortunately, rhinoscopy is limited in small dogs (and cats) related to availability of appropriate sized endoscopes.
    Visual findings of disease may include abnormal mucosal color (hyperemic, white); plaque formation (fungus or lymphocytic-plasmacytic rhinitis); puff ball (rhinosporidiosis) or nasal mites; and destruction of turbinate structure or friable mucosa. An obvious foreign body or mass lesions may be observed in some cases. Hemorrhage may obscure the examination field.
  - Then undertake mucosal biopsy of the nasal cavity, preferably guided by findings at endoscopy or radiography/CT.
    Blind biopsy based on location of clinical signs is also appropriate.
    In some cases of chronic rhinitis, large chunks of nasal turbinate bone may be obtained during this procedure. Request special stains (e.g., silver stains) for suspected cases of fungal rhinitis.
- At the end of the procedure the nasal cavity is flushed bilaterally with cooled saline (ensure that the endotracheal tube is inflated and the caudal airways packed with sponges; put the nose "down" to prevent aspiration and swallowing of fluid). Inspect the collection sponges at the conclusion of the procedure for any foreign material or tissue that may be appropriate for cytologic or histopathologic examination.

Table 163-3. DIFFERENTIAL DIAGNOSIS OF UPPER AIRWAY INFECTIONS

Causes of Nasal Discharge

Infectious causes of nasal discharge in dogs and cats (see Table 163–1)
Inflammatory causes of nasal discharge
  Lymphocytic plasmacytic rhinitis
  Idiopathic, including "allergic" rhinitis
  Postinflammatory scars at posterior choanae
Congenital diseases predisposing to nasal discharge
  Ciliary dyskinesis
  Congenital—cleft palate
  Imperforate posterior choanae openings
  Immunodeficiency disease (IgA)
Physical disorders leading to nasal discharge
  Foreign body
  Acquired—oro-nasal defect
  Trauma leading to nasal bleeding or fracture/sequestrum
  Abnormal drainage from the nasal cavity due to inflammatory or congenital webs, tumors, or polyps
Neoplastic causes of nasal discharge

Dogs—Malignant Tumors

Adenocarcinoma (most common)
Chondrosarcoma
Fibrosarcoma
Mast cell tumor
Osteosarcoma
Squamous cell carcinoma
Transmissible venereal tumor

Cats—Malignant Tumors

Squamous cell carcinoma
Adenocarcinoma
Lymphoma

Benign Tumors (Dogs and Cats)

Polyps (more common in cats)
Adenoma
Fibroma

Causes of Epistaxis

Thrombocytopenia from any cause
Thrombocytopathia
Ehrlichiosis
Hyperglobulinemia or other hyperviscosity syndromes
Polycythemia (serous discharge or epistaxis)
Hypertension (including pheochromocytoma)
Coagulopathy with normal platelets (not typical; usually due to platelet problems)
Neoplasms
Foreign bodies
Violent sneezing from any cause
Some chronic infections

Other Upper Airway Disorders

Inflammatory polyps
Disease of the tonsils
Laryngeal edema consequent to inflammation, trauma, or increased work of breathing
Unilateral or bilateral laryngeal paresis
Inflammatory nodules on the vocal folds
Eversion of the laryngeal saccules
Airway obstruction
Collapse of the glottic opening
Congenital tracheal lesions (segmental lesions)
Tracheal collapse
Relentless barking
Foreign body or foreign material
Swallowing disorders, esophageal masses, or megaesophagus
Trauma leading to hematoma, edema, fracture, perforation, laceration, or disruption
Iatrogenic injury (traumatic intubation, excessive cuff inflation)
Mass lesions: granulomas, tumors, and neoplastic conditions

Other Respiratory Disorders

Mediastinal lymphadenopathy or heart base tumors causing airway compression
Primary bronchial collapse
Left main bronchus compression by an enlarged left atrium
Primary chronic bronchitis (noninfectious)
Heartworm disease
Lungworms
Pulmonary neoplasm
Granulomatous disease

- Positive fungal cultures for aspergillosis are not necessarily diagnostic for the disease, but invasion of nasal mucosa with hyphae or a positive immunodiffusion or enzyme linked immunosorbent assay (ELISA) test are supportive of the diagnosis.
- Mucosal biopsies can be cultured for bacteria. A positive culture is more likely to be significant when compared to a flush or swab (superficial) culture, but results must be interpreted carefully.
  - Rarely, surgical exploration of the nasal cavity and paranasal sinuses is needed for definitive diagnosis.
- The typical *feline work-up* for signs of nasal disease is often completed in two stages:
  - Initially, submit a CBC and feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), and Cryptococcus ELISA tests to the laboratory.
  - Obtain a chest radiograph if the condition is chronic or there are lower airway signs.
  - Send a swab of nasal discharge to the lab with specific instructions to stain the smear for Cryptococcus neoformans.
  - Submit advanced virus diagnosis tests (immunofluorescence; PCR) for herpesvirus infection.
  - Following this first set of treatments, treat the cat empirically with a single course of antibiotics (amoxicillin, clavulanate, or doxycycline with food) and lysine (for possible herpesvirus infection) while awaiting the test results. Clients are instructed to provide good home nursing care and a stress-free environment for the cat.
  - If these studies fail to yield a diagnosis and empiric therapy is not curative, then anesthetic procedures

including nasal cavity imaging, rhinoscopy, and biopsy are needed, as described above for the dog.

- When clients cannot pursue advanced imaging and rhinoscopy, an "intermediate" and less costly (but more superficial) approach can be taken using a very short period of general anesthesia.
  - Premedicated the cat with butorphanol (0.25 mg/kg, IM) with acepromazine (0.1 mg/kg, unless contraindicated), accomplish IV anesthetic induction, and intubate the cat with a cuffed endotracheal tube.
  - If permitted, obtain one open-mouth radiograph of the nasal cavity.
  - Use a warmed dental mirror and a strong focal light source to evaluate the retropharyngeal space to rule out a polyp or obvious foreign body. Pull the soft palate in a rostral and ventral direction using a spay hook, and place the mirror in the caudal oropharynx to direct reflected light into the nasopharynx.
  - Then obtain two or three empiric nasal mucosal biopsies from the affected side(s) using 2- to 3-mm biopsy forceps.
  - At the conclusion of the procedure, flush the nasal cavity gently with sterile saline using a soft red-rubber tube to dislodge accumulated secretions or foreign material. The glottis should be protected by inflation of the cuff, packing with clean sponges (inspect at end of procedure), and by keeping the cat in a nose-down position so that most fluid exits the pharynx via the mouth.

Treatment of Viral and Bacterial Rhinitis

- Treatment of *acute upper respiratory infection* depends on the underlying condition. In cases of viral rhinitis, supportive nursing care, maintenance of hydration, and prevention of secondary bacterial infections by administration of a broad-spectrum antibiotic represent a typical therapy (avoid tetracyclines in puppies, enrofloxacin in growing animals, and chloramphenicol in cats). Ophthalmic medications may be useful for conjunctivitis or in cases of herpesvirus associated corneal ulcers (avoid corticosteroids).
- Dogs or cats with respiratory infection caused by bacterial infection may respond to doxycycline. This is especially true for *B. bronchiseptica* or *Bartonella* infections, which may be primary. Tetracyclines should not be used in pregnant bitches or in young dogs or cats if permanent teeth have not yet erupted (as staining will occur). Because *B. bronchiseptica* is an inhabitant of the mucosal brush-border, it can be difficult to eradicate infection with systemic antibiotics. In well-defined cases, empiric therapy with nebulized gentamicin can be considered (for details, see "Infectious Tracheobronchitis").
- For cats with chronic bacterial rhinitis of uncertain cause, a recurring cycle of intermittent antibiotics may be needed. Amoxicillin-clavanalate, doxycycline (5–10 mg/kg PO daily, always followed by food), and a 5-day course of azithromycin (5–10 mg/kg daily for 5 days; thereafter 10 mg/kg q72h) may provide symptomatic relief. A course of clindamycin also may be considered as it has some efficacy against *Mycoplasma* spp. Lysine (250 mg/day once or twice daily, crushed in food) can be tried if herpesvirus is thought to be a predisposing cause.
- Treat immunosuppressed cats with secondary bacterial rhinitis with broad-spectrum antibiotics if clinical signs worsen or if lower respiratory infection develops. For cats with FIV or FeLV viral-related immunosuppression, the empiric use of diluted human interferon alpha 2a (30 units, PO for 7 days, every other week) or of recombinant feline alpha interferon has been advocated, but more studies are needed. Cats do form antibodies against human interferon, which may limit effectiveness long term.
- In bacterial rhinitis associated with tooth root abscesses, management of the dental disease, along with a long-term course of antibiotics, may be curative. Any oronasal fistula should be closed.

Treatment of Fungal Rhinitis

A variety of treatments have been suggested for well-defined *fungal rhinitis/sinusitis*. Treatment recommendations depend on the specific agent, and protocols can be complicated and, in many cases, unsuccessful.

- General principles of therapy
  - Patients with fungal rhinitis represent complicated cases, and the clinician should consult detailed textbooks or current literature before embarking on any course of therapy for these serious conditions. It may be helpful to discuss options with an internist or a surgical specialist.
  - Oral medical therapy with an azole antimicrobial represents the least complicated approach to treatment. However, the drugs are expensive and many patients will not respond. Furthermore, these drugs may have significant adverse effects, such as hepatotoxicity, that must be discussed with the client.
  - The use Foley-type balloon catheters or red-rubber tubes, placed by endoscopy or by surgery, allows for instillation of antifungal medication. Some imidizoles are available in liquid form and can be infused directly into the nasal cavity and frontal sinus.
  - Surgical debridement may be considered a possible adjunct to therapy. Non-surgical debridement can be done via an endoscope or with devices used for dental cleaning (Water-pik) dislodge infected material.

- *Rhinosporidiosis* is associated with "puff-ball granulomas" in the nose. These can be treated by surgical extraction.
- *Aspergillus flavus* and *Penicillium* spp. are most commonly treated with nasal tubes placed by endoscopy or surgery.
  - The endoscopic method involves general anesthesia; placement of two infusion catheters in the nasal cavity (or frontal sinus if visible); multiple Foley or balloon catheters within the nostrils rostrally and in the cranial soft palate (via the nasopharynx); and infusion of antifungal medication with the dog placed in varying recumbent positions during the procedure. Before treatment, the balloons are inflated to create a nearly sealed nasal cavity. A one-time treatment of liquid enilconazole is administered (1% or 10 mg/ml, enilconazole) or clotrimazole (approximately 120 ml of a 1% solution) for 1 hour. A slow, constant infusion process maintains continual filling of the space and contact with the mucosa. This may be preceded by debridement of affected tissues (controversial). Enilconazole is also effective as a vapor, which may enhance its local effect.
  - One-treatment cures with enilconazole and clotrimazole have been reported. In one study of 24 dogs an 80% response rate was observed. In another study of 36 dogs, almost 95% responded to local treatment of enilconazole (about 55% responded to a single treatment). A second treatment 3 to 4 weeks later provided a positive outcome for most dogs that did not respond to a single infusion. One study of 60 dogs treated with clotrimazole reported about a 90% response rate.
  - An alternative method is placement of nasal tubes in the frontal sinus either surgically or by use of an endoscope to instill enilconazole (10 mg/kg, in 10 ml of solution divided between each nasal cavity) for 10 to 14 days. This approach is more labor intensive and may have a higher success rate, but has largely been supplanted by the endoscopic method.
  - Oral therapy of nasal aspergillosis may be attempted as a primary treatment or as a supplement to local therapy. A number of drugs have been used with varying success.
    Itraconazole at 5 mg/kg PO q12h for 2 to 3 months.
    Thiabendazole, which is less effective (40–50% positive response) and is more hepatotoxic, but can be administered at a dose of 10 to 20 mg/kg PO q12h with food (start at lower dose) for 6 to 8 weeks. The main advantage is a lower drug cost.
    Ketoconazole (Nizoral 5–10 mg/kg PO q12h for 6–8 weeks) is about as effective as thiabendazole.
- *Cryptococcus neoformans* infection of the upper airways is treated with fluconazole, itraconazole, ketoconazole, or amphotericin B (alone or in combination with flucytosine). Fluconazole seems to be useful at 50 mg total dose per cat q24h for 2 to 4 months. Itraconazole at 5 mg/kg q12h may be an alternative and needs to be continued even after the control of nasal discharge. Occasionally, higher doses are needed.

INFECTIOUS TRACHEOBRONCHITIS

General Points

- Acute tracheobronchitis refers to an inflammation of the trachea and bronchial tree of recent onset and short duration.
- Canine infectious tracheobronchitis (ITB), also known as the kennel cough complex, refers to a group of acute contagious infections in dogs that cause inflammation of the larynx, trachea, and bronchi. ITB is discussed in Chapter 12.
- Feline upper respiratory infection (URI) complex refers to a group of acute contagious upper respiratory diseases in the cat that may also involve the trachea or bronchial tree (see Chapter 11). In some cases the lung is involved as well.
- The clinical signs of tracheobronchitis typically include a paroxysmal, harsh, dry cough that can last for days to weeks.
- The condition may be accompanied by other signs of upper respiratory infection such as nasal discharge and sneezing (which are typical in cats and may be noted in dogs with *Bordetella* infection). In many cases, signs are isolated to the tracheobronchial tree.
- Common canine infectious agents include *B. bronchiseptica,* canine parainfluenza virus, canine adenoviruses (types 1 and 2), canine distemper virus, canine reoviruses (types 1 and 2), and canine herpesvirus. *B. bronchiseptica* is the most common bacterial infection, and canine parainfluenza virus is the most common viral isolate noted in the dog with canine infectious tracheobronchitis (ITB).
- Recently a new canine influenza virus, mutated from an equine strain, has been identified in dogs. This virus can cause signs identical to those of other "kennel cough" agents.
- In cats, feline herpesvirus and calicivirus are considered the most common causes of contagious upper respiratory disease. Calicivirus is more likely to involve the lower airways. Mycoplasma infection and bordetellosis should also be in the differential diagnosis for lower airway disease in cats.
- Many of these infectious diseases are very contagious and associated with high-density populations. The infectious agents can be transmitted by aerosol or fomite. Incubation periods are typically between 3 and 10 days. Vaccinations confer partial to complete protection against many of the ITB agents in most cats and dogs.
- In addition to infectious (contagious) causes, other conditions may *predispose* to tracheobronchial infection or inflammation. Some of these include:

- Abnormal local immunity
- Boarding kennels/catteries
- Racetracks
- Ciliary dyskinesis (rare)
- Contagious diseases
- Debilitation/poor nutrition
- Drying of the mucous membranes
- General anesthesia (intubation; aspiration)
- Poor vaccination history
- Recurrent or chronic bronchial disease

- Acute tracheobronchitis indicates an inflammatory reaction. The usual consequences of this inflammation are variable increases in tracheobronchial secretions and cough. If respiratory clearance mechanisms or immunity is insufficient, pneumonia may develop from the primary agent (e.g., bordetellosis) or from secondary bacterial invaders.

Diagnosis of Tracheobronchitis

- In general, one diagnoses feline upper respiratory infections and canine infectious tracheobronchitis from the history and physical examination. The long list of potential causes of signs of acute tracheobronchitis includes the conditions listed in the lower portion of Table 163-3.
- Some conditions (e.g., noninfective bronchitis, neoplasia) are more likely in mature animals and should be excluded initially by examination and thoracic radiography.
- The duration of signs and the response to supportive treatment will largely determine which diagnostic considerations are pursued. In classic kennel cough with no constitutional signs, diagnostic studies are generally negative and are not indicated. Poor responders should be worked up.

Diagnostic Tests

- Routine hematologic tests and radiographs are usually unremarkable; however, the client must understand that a number of other conditions can lead to similar clinical signs and should be prepared to support further examinations if indicated. If the patient is very ill, or if the clinical course of expected improvement is not met, additional tests are indicated.
- A CBC and serum chemistry panel (especially renal function, glucose) is appropriate for sick animals.
- Fecal flotation and empiric deworming with pyrantel is recommended for puppies and kittens.
- If significant ocular signs such as photophobia or anisocoria are noted, stain the cornea for ulcers; if results are positive, give antibiotics (without steroids).
- In previously untested cats, perform FeLV and FIV tests to screen for immunosuppressive diseases.
- Radiography of the thorax is probably the most indicated of studies and can be justified to rule out bronchiopneumonia and other causes of acute cough. The right middle lung lobe is predisposed to secondary infection in upper respiratory diseases, and pulmonary involvement is best seen on a VD or DV projection.
- Culture and cytology of the tracheobronchial airway secretions are indicated in unresponsive cases or those with confounding bacterial pneumonia. A transtracheal wash in cooperative dogs or an endotracheal wash in puppies or cats can be used to obtain a diagnostic sample.
- Other diagnostic tests may be considered in ruling out the differential diagnosis. These are indicated in Table 163-3.

Therapy of Infectious Tracheobronchitis

- The viral causes of these diseases are usually self-limiting, and often no treatment is necessary. This is especially true in mild, uncomplicated cases with minimal constitutional signs (i.e., animals that are without fever, still eating, and not acting sick).
- Specific supportive, symptomatic, and antimicrobial therapy for infectious tracheobronchitis is described in Chapters 11 (cats) and 12 (dogs).

Prevention of ITB

- Vaccination in dogs can be performed routinely with the following antigens: *B. bronchiseptica*, canine parainfluenza virus, canine adenovirus type 2, and canine distemper virus (see Chapter 7). Cats can be vaccinated against herpes-, calici-, and panleukopenia (parvo) viruses and bordetellosis (see Chapter 7).

BRONCHOPNEUMONIA

Etiology

- Pulmonary infections are common in dogs and in cats. Bacterial pneumonia is an important cause of morbidity and mortality in dogs and cats.
- Though numerous infectious agents (viruses, rickettsia, and systemic mycoses) can cause interstitial pneumonia, most cases of bronchopneumonia are bacterial in origin. Common microorganisms responsible for pneumonia are indicated in Table 163-1.
- The route of infection is typically inhalation.
- Hematogenous spread of bacterial pneumonia to the lungs is less common and can be very difficult to treat.
- The clinician should appreciate possible risk factors and predisposition for pneumonia, including:
  - Contagious upper respiratory infection (e.g., infective tracheobronchitis after boarding)
  - Preexistent bronchopulmonary disease (including noninfectious bronchitis, lung contusion, heartworm disease, smoke inhalation, pulmonary atelectasis, thromboembolic disease)

- Inhalation or aspiration of pharyngeal or gastric fluid or contents (due to anesthesia, swallowing disorders, megaesophagus, neuromuscular disease, laryngeal paralysis, posterior fossa lesion, stupor, vomiting, prolonged recumbency), or opiates and postoperative sedatives
- Oro-nasal sources of infection (sinusitis, dental disease)
- Immunosuppression caused by another virus (FeLV, FIV, canine distemper, parvovirus) or disease (e.g., hyperadrenocorticism, diabetes mellitus, generalized demodecosis)
- Immunosuppressive drug therapy (glucocorticoids, anticancer chemotherapy)
- Abnormal respiratory defense mechanisms (Cushing's disease, chronic bronchitis, ciliary dyskinesia, neutrophil dysfunction syndromes)
- Bronchial foreign body
- Foreign body aspiration pneumonia (e.g., food, mineral oil in cats)
- Debilitation, hospitalization, nosocomial infection

- Sedation with opiates.
  - Indwelling intravenous catheter sepsis (hematogenous spread)
  - Contaminated endotracheal tube, tracheostomy tube, or bronchoscope
  - Aspiration or inhalation of liquid foreign material during diagnostic or therapeutic procedures (barium sulfate, medications, mineral oil, nutritional supplements)
  - Following thoracic surgery
- Prompt recognition and treatment of bronchopneumonia is important. It is equally important to identify the predisposing cause so that further episodes can be prevented or anticipated.

Clinical Signs

- The history often indicates a predisposing factor for bronchopneumonia.
- Tachypnea, respiratory distress, productive cough, and fever are typical findings.
- Constitutional signs—depression, anorexia, and listlessness—may be observed as the only features of disease.
- Mucopurulent nasal exudate may be present.
- Pulmonary adventitious sounds—especially rhonchi and crackles—may be ausculted; however, loud or asymmetric bronchial sounds can be the only auscultatory finding.

Diagnosis of Bacterial Bronchopneumonia

▼ ***Key Point*** Point Clinical signs, radiography, and the CBC are usually sufficient to make a presumptive diagnosis of bacterial pneumonia.

- Thoracic radiographs are key to the diagnosis of bronchopneumonia.
  - The typical findings are increased lung density that is most commonly alveolar in nature leading to border effacement (silhouetting) of the heart. The lobe may become consolidated, producing a fluid density lobar sign.
  - The right middle lung lobe is most prone to bacterial infection; the cranial lobes also are frequently involved. In contrast, dorso-caudal pulmonary infiltrates are very unlikely to be associated with bacterial infection of the lung with the exception of atypical microorganisms (mycoplasmas, fungal infections, mycobacteria), or hematogenous pneumonia (from sepsis), which is diffuse, beginning as an interstitial pattern and progressing to alveolar.
  - A cranioventral distribution of bacterial bronchopneumonia is typical.
  - With some foreign bodies, the intermediate lobe may be involved.
  - Lung consolidation may occur, leading to an eventual loss of air bronchograms except in the most proximal portion of the lobe.
- *Radiographic differential diagnosis* is important.
  - Hilar or sternal lymphadenopathy is uncommon with bacterial infection.
  - Nodular densities are more typical of fungal disease, granulomatosis, or pulmonary neoplasia.
  - The combination of bronchopneumonia with concurrent septic pleural effusion (pyothorax) is very uncommon in dogs and cats. These findings are suggestive of an atypical infectious agent such as *Nocardia asteroides* or actinomycosis, presence of a foreign body, concurrent malignancy, or pulmonary embolus.
  - Pneumonia caused by viral, protozoal (e.g., toxoplasmosis), rickettsial, or fungal infection is typically interstitial in distribution. Fungal and *Toxoplasma* infections produce granulomatous lesions in the lung, and with systemic mycoses, hilar lymphadenopathy can be pronounced.
  - Esophageal air or dilatation may indicate simple air swallowing or a more serious condition such as megaesophagus or myasthenia gravis.
- *CBC*—Leukocytosis, left shift, and monocytosis are typical abnormalities on the CBC; however, the magnitude of change is not consistently related to the extent of infection. Overwhelming fulminant bacterial pneumonia may cause a neutropenia with degenerative left shift.
- *Serology*—Infected cats also may be FIV or FeLV positive. FIV infection has also been associated with nonbacterial alveolitis and interstitial pneumonia.
- *Airway cytology and culture* can confirm the diagnosis.
  - Transtracheal or endotracheal aspiration cytology demonstrates neutrophilic inflammation, often with degenerative PMNs and intracellular bacteria.

- Cocci are usually streptococcus, and rods are usually gram-negative bacteria.
- The culture is typically positive for bacterial growth (see Table163-1).
- Special media are needed for effective culturing of Myocoplasma spp.; mycoplasma culture should be requested in most cases, and especially in cats.
- While a fine-needle aspiration of a collapsed lung can provide diagnostic tissue, in general, one should avoid percutaneous needle aspiration of a consolidated lung in order to prevent inoculation of the pleural space.

▼ ***Key Point*** Bronchopneumonia is typically a complication related to another disorder, general anesthesia, or medical or surgical treatments. The precipitating cause should be identified.

Treatment of Bacterial Bronchopneumonia

- Keep the patient well hydrated and warm. Fluid therapy is often required to prevent dehydration and inspissated respiratory secretions.
- Perform thoracic coupage 4 to 6 times daily. Once the patient feels better, brief walks, followed by coupage, help to mobilize tracheobronchial secretions.
- Airway humidification may assist in expectoration of secretions. Expectorants like guaifenesin are of uncertain merit and are not usually prescribed.
- Bronchodilator therapy (sustained release theophylline at 10–20 mg/kg PO q12h for dogs) is of unproven efficacy but may reverse irritative bronchoconstriction and strengthen respiratory muscle effort in dyspneic animals.

▼ ***Key Point*** Cough suppressants are *contraindicated* in bronchopneumonia.

- Humidified oxygen should be administered to dyspneic, cyanotic, or hypoxemic animals.
- Antibiotics should be prescribed *for at least 3 weeks.* The duration of therapy may be longer pending clinical results and radiographs.
- Antibiotic choice should be based on culture and sensitivity (obtained by transtracheal or endotracheal washing) and with consideration of current or prior antibiotic therapy. Request a Gram stain on expectorated material or a cytoprep from an airway washing.
- *Initial/Empiric antibiotic therapy* is initiated when culture results are pending, when cultures are reported as "no growth," or when airway culture is simply unavailable. An extended or broad-spectrum antibiotic is generally indicated in dogs and in cats. The choice depends on a number of factors including the species, age of the patient, severity of pneumonia radiographically, respiratory status (oxygen saturation, respiratory rate and depth), previous antibiotic therapy, and suspected source and type of microorganism. In cases of nosocomial (hospital-acquired) infection, a more aggressive antibiotic protocol may be indicated. There is no one best choice for antibiotic therapy in pneumonia, and the best approach is to culture fluid from the lung and target a specific microorganism based on sensitivity testing.
  - Cephalosporins and amoxicillin-clavulanic acid are generally effective with activity against gram-positive and gram-negative bacteria, as well as against anaerobes. They are generally well tolerated by dogs and cats, including most young animals. Rapid IV administration of cefazolin can cause vomiting. These drugs do not demonstrate significant activity against *mycoplasma* spp.
  - Sulfadiazine-trimethoprim is a reasonable drug for first-line therapy of bronchopneumonia in dogs.
  - Azithromycin is increasingly used for treatment of infections in dogs and cats, and is proabably a good drug for empiric therapy of pneumonia. There is demonstrated activity against *mycoplasma* spp.
  - Fluoroquinolones (enrofloxacin or orbifloxacin) are broad-spectrum drugs available for both parenteral and oral use. These antibiotics should not be used for trivial infections. There is some activity against *mycoplasma* spp.
- Resistant or complicated bronchopneumonia
  - Doxycycline is an excellent choice for unresponsive pneumonia, in part related to strong activity against bordetellosis and myoplasma infection. However, the overall spectrum is limited and it is not generally chosen as a single drug for empirical therapy. In resistant pneumonia in cats, doxycycline is a good choice because of the high probability of *mycoplasma* infection.
  - In cases of life-threatening or poorly responsive pneumonia, the spectrum of a cephalosporin or amoxicillin-calvulanic acid can be extended with parenteral amikacin, once daily (provided hydration and renal function are satisfactory). This combination does not affect *mycoplasma* spp.
  - In cases of pulmonary consolidation, a combination of a fluoroquinolone combined with clindamycin, metronidazole, or amoxicillin is a reasonable choice.
  - In life-threatening bronchopneumonia, consider a combination of IV enrofloxacin plus IV amoxicillin or a third generation cephalosporin.
- Management of bacterial pyothorax requires thoracostomy tube drainage and antibiotics. Because anaerobic organisms are commonly involved in pyothorax, treatment with penicillin (20,000–40,000 units/kg PO or IV q6–8h), alone or in combination with sulfadiazine-trimethoprim, or clindamycin is recommended.

Follow-Up

- Obtain thoracic radiographs to ensure resolution of infection. Areas of lobar consolidation may take 2 to 6 weeks to become totally clear. Failure of steady clinical and radiographic improvement indicates a need to reevaluate the patient and to consider a tracheal wash or bronchoscopy with bronchial fluid aspiration.
- Recurrent pneumonia also is common, particularly in those animals with persistence of predisposing factors, including swallowing disorders, chemotherapy, ciliary dyskinesis, and acquired or congenital immune deficiencies. Infrequently, an unresponsive or refractory single lobe infection requires surgical lobectomy for resolution of the problem. Surgery is also indicated in cases of lung abscess or pneumonia due to a foreign body that cannot otherwise be retrieved. Surgical results are generally rewarding in this clinical situation.

RESPIRATORY PARASITES

Etiology

- A number of respiratory parasites have been identified in dogs and cats. The life cycle of some respiratory parasites is complex and involves intermediate and transport hosts. Some of the more important infections include:
  - *Aelurostrongylus abstrusus* is a parasite of cats. This nematode requires a snail or slug as an intermediate host. Cats are often infected by eating transport hosts including birds, small mammals, and reptiles.
  - *Paragonimus kellicotti* is a fluke parasitic to dogs and cats. Infection follows ingestion of an intermediate host (crayfish, aquatic snail) or a transport host (e.g., raccoon).
  - *Capillaria aerophilia* is a nematode parasite of the dog and cat that has a direct life cycle. Pathogenic potential appears very low.
  - *Crenosoma vulpis,* the fox lungworm, infrequently infects dogs.
  - *Osleri/Filaroides* spp. are nematodes that invade the respiratory tract of the dog. Transmission is direct, often from bitch to pups. Three related species have been associated with respiratory disease, *O. osleri* (found in granulomas near the tracheal bifurcation), *F. milksi* (a bronchopulmonary parasite), and *F. hirthi* (a lung parasite of importance to research colonies).
  - *Dirofilaria immitis* infects the pulmonary arteries, causing secondary pulmonary injury (see Chapter 152).
  - *Toxoplasma gondii* is a protozoan capable of multisystemic infection that is usually subclinical, but occasionally can cause pneumonia (see Chapter 21). Immunosuppression predisposes to toxoplasmosis.
- Parasites of the nasal cavity include cuterebra and other grubs, the microscopic nematode *Eucoleus boehmi,* nasal mite *Pneumonyssus (Pneumonyssoides) caninum,* and the gapeworm *(S. ierei).*

Clinical Signs

- Signs depend on the specific parasite, site and severity of infection, and the magnitude of the host reaction.
- Mild cases are asymptomatic and only detected if ova are identified during routine fecal examination.
- Clinically apparent infections occur most often in younger animals (<2 years) that are heavily infested.
- Sneezing, nasal discharge, and reversed sneezing are signs of nasal mite infestation.
- A chronic cough is typical of *O. osleri* infection; some dogs develop marked reactions to the parasites, leading to productive coughing of white foam and even airway obstruction from tracheal granulomas.
- Coughing is the most common sign of lower respiratory parasitic infections. Exercise intolerance and weight loss also may occur.
- Fever and tachypnea are typical of toxoplasmosis but not of other respiratory parasites. Multisystemic disease may be present in toxoplasma infection including neurological signs, anterior uveitis, chorioretinitis, and hepatitis.

Diagnosis

- Diagnosis of respiratory parasites is made following clinical examination, endoscopy, radiography, or identification of either ova or larvae in fecal samples or respiratory secretions.
- Eosinophilia is not uncommon in lungworm or fluke infections.
- Diagnosis of nasal mites or other nasal parasites is by direct visualization, often using a retroflexed bronchoscope. Diagnosis of *E. boehmi* requires mucosal biopsy or identification of the ova on a fecal examination.
- Diagnosis of *O. osleri* usually requires tracheoscopy, identification of nodules (which contain small, filamentous worms), or biopsy of a granuloma. There are no obvious radiographic changes unless soft tissue granulomas proximal to the carina are observed within the air-filled trachea. Occasionally, larvae may be obtained via tracheal washings.
- Radiographs are helpful in the recognition of advanced lungworm infections.
  - *Aerulostrongylus* causes an indistinct interstitial-nodular pattern in the lung. Distribution of infiltrates varies but caudal lung lobes are typically involved.
  - *Paragonimus* generally causes a granulomatous interstitial reaction with appearance of air-filled cystic structures (especially in the dog).

  - *Filaroides* infections can cause a diffuse interstitial infiltrate ranging from severe *(F. milksi)* to mild. *F. hirthi* seldom leads to clinical disease.
  - *Toxoplasma* when manifested in the lung leads to a mixed interstitial-alveolar infiltrate.
- Fecal flotation can identify ova from some parasites (double-operculated *Capillaria* ova, single-operculated *Paragonimus* ova) or larvae of *Aelurostrongylus* or *Osleri/Filaroides* spp. Baermann fecal sedimentation techniques may be required to identify larvae.
- Transtracheal washing or aspirations of tracheobronchial secretions may demonstrate parasitic ova or larvae. In some cases, ova are scarce. An eosinophilic pulmonary infiltrate with accompanying neutrophilia is typical.
- Diagnosis of pulmonary toxoplasmosis depends on clinical signs and serological evaluation.

Treatment

- Treatment of respiratory parasites involves destroying the infective organism, reducing parenchymal reaction, and instructing the owner about the prevention of further infection. A number of drugs (at varying dosages) have demonstrated efficacy against respiratory parasites, though treatments for some parasites are difficult.
- Fenbendazole (Panacur) is generally the safest antiparasitic drug. In cases of severe eosinophilic pulmonary reaction, adjunctive therapy with prednisolone (0.5 mg/kg, orally, once or twice daily for 7–14 days) may be quite helpful.
- Nasal parasites are treated by manual removal of large parasites or by treatment with oral injectable ivermectin (consult a parasitologist or specialist). Nasal mites may require high-dose ivermectin for control (800 mcg/kg SC single dose) or topical selemactin (6–24 mg/kg topically every 2 weeks for 3 total doses), or extra-label use of milbemycin (1 mg/kg PO every 10 days for 3 total doses). Dogs treated in these ways must be heartworm and microfilaria negative; do not use in collies.
- Aelurostrongylosis is treated with fenbendazole (Panacur, 50 mg/kg, orally, once daily for 10 days).
- Paragonimiasis is treated with either fenbendazole (as above), praziquantel (Droncit, 25 mg/kg, orally, q8h for 2 days), or albendazole (25–50 mg/kg orally q12h for 10–20 days).
- *Filaroides* spp. are treated with fenbendazole, albendazole, or oral ivermectin (200 µg/kg/wk for 3 doses or 400 µg/kg once; do not administer to collies).
- Capillaria infection is often asymptomatic but can be treated as per *Filaroides* infection.
- The prognosis for recovery and elimination of signs is generally good unless severe granulomatous disease has developed, in which case, residual cough may occur.

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Chapter

164 Pleural Effusion

Robert G. Sherding / Stephen J. Birchard

Pleural effusion is an abnormal accumulation of fluid within the pleural space and is a clinical manifestation of conditions such as pyothorax, feline infectious peritonitis, congestive heart failure, intrathoracic neoplasia (e.g., lymphoma, thymoma, pulmonary neoplasia, mesothelioma), chylothorax, heartworm disease, hemothorax, hypoalbuminemia, lung lobe torsion, and diaphragmatic hernia. Pleural effusion is usually suspected from clinical signs and physical findings and is confirmed by thoracentesis or thoracic radiography.

ETIOLOGY

Pleural effusion occurs when one or, more often, a combination of the factors that determine pleural fluid dynamics are altered so as to increase fluid formation, decrease fluid absorption, or both. For example, pleural effusion is often associated with congestive heart failure (CHF) because increased capillary hydrostatic pressure results in increased pleural fluid formation. Extreme hypoalbuminemia may lower systemic colloidal osmotic pressure sufficiently to cause increased formation and decreased absorption of pleural fluid. Inflammation of the pleura may increase the formation of pleural fluid because of increased blood flow (hydrostatic pressure) and permeability of the pleural capillaries along with increased intrapleural colloidal osmotic pressure due to a higher concentration of protein in the fluid. Pleural effusion may also result from lymphatic insufficiency caused by thoracic duct obstruction, intrathoracic neoplasia, pleural thickening, or lymphatic hypertension secondary to CHF. The major causes of pleural effusion in dogs and cats are listed in Table 164-1.

CLINICAL SIGNS

- Dyspnea and exercise intolerance (inactivity) are the most consistent presenting signs of pleural effusion. Dogs and cats generally accommodate to small to moderate increases in the volume of intrapleural fluid by gradually decreasing their level of activity. Thus the signs of early pleural effusion are subtle and often imperceptible to the owner. As the accumulation of intrapleural fluid becomes substantial, however, tachypnea and respiratory distress become apparent during mild exertion and eventually even at rest.
- To facilitate breathing, the animal may prefer a sitting or crouched sternal posture, with the head and neck extended and the elbows abducted away from the thorax. An anxious facial expression and open-mouth breathing with forceful abdominal efforts during inspiration may be observed. Cyanosis may be seen in severe cases.

▼ ***Key Point*** Any struggling or increased distress during examination procedures may worsen dyspnea and induce respiratory arrest because of limited respiratory reserve.

- Other clinical signs associated with pleural effusion depend on the underlying cause but may include anorexia, depression, weight loss, dehydration, pallor, fever, hypothermia, or cough. Cough in animals with pleural effusion may indicate tracheal compression by a mediastinal mass (lymphoma, thymoma), intrapulmonary involvement (e.g., lung tumor, pulmonary edema, heartworm disease, pneumonia), or the presence of pleuritis.

DIAGNOSIS

Suspect pleural effusion on the basis of clinical signs and physical findings. Confirm pleural effusion by thoracentesis (see Chapter 3) or thoracic radiography (see Chapter 159). The cause is often determined through analysis of pleural fluid obtained by thoracentesis, in conjunction with post-thoracentesis radiographs. Depending on the suspected etiology, consider other diagnostic procedures such as laboratory evaluations, cardiac evaluations, ultrasonography, and specialized imaging procedures (contrast radiography, scintigraphy, computed tomography [CT]). Rarely, exploratory thoracotomy is required for definitive diagnosis.

Table 164-1. CAUSES OF PLEURAL EFFUSION AND CRITERIA FOR DIAGNOSIS

Causes of Pleural Effusion	Distinguishing Radiographic Findings	Fluid Patterns	Other Diagnostics
Common Diseases			
Pyothorax	Effusion may be unilateral or encapsulated; rounded or collapsed lung lobes (constrictive pleuritis)	Septic exudate	CBC; fluid culture
Feline infectious peritonitis	Concurrent abdominal effusion in some cases; rounded or collapsed lung lobes (constrictive pleuritis)	Nonseptic exudate (pyogranulomatous)	Fluid protein electrophoresis; Serology; PCR, immunostain
Congestive heart failure	Cardiomegaly; pulmonary edema and venous congestion; dilated caudal vena cava; abdominal effusion (rare)	Pure transudate; modified transudate; chylous effusion	Echocardiography; electrocardiography; angiocardiography
Heartworms (dirofilariasis)	Prominent pulmonary arteries; right-sided heart enlargement	Modified transudate; chylous effusion	Heartworm tests; echocardiography
Mediastinal neoplasia (lymphoma, thymoma)	Mediastinal mass (widened mediastinum; dorsally displaced trachea; caudally displaced heart and carina; esophageal compression)	Neoplastic: modified transudate; nonseptic exudate; chylous effusion	Ultrasound; fine-needle aspiration cytology
Bronchopulmonary neoplasia (carcinoma)	Pulmonary mass or infiltration	Neoplastic (variable): modified transudate; nonseptic exudate; chylous effusion; hemorrhage	Ultrasound; fine-needle aspiration cytology; thoracotomy
Chylothorax	Rounded or collapsed lung lobes (constrictive pleuritis); effusion may be unilateral	Chylous effusion	Fluid triglyceride; lymphangiogram; evaluate for underlying causes
Uncommon Diseases			
Diaphragmatic hernia	Other signs of thoracic trauma; loss of diaphragm shadow; displaced abdominal organs; concurrent abdominal effusion	Modified transudate; nonseptic exudate	Ultrasound; contrast peritoneography
Hemothorax	Other signs of thoracic trauma	Hemorrhage	If nontraumatic: coagulation tests; evaluate for underlying causes
Lung lobe torsion	Opaque lung lobe (right middle or either cranial lobe)	Nonseptic exudate; hemorrhage	Ultrasound, bronchoscopy; thoracotomy
Hypoalbuminemia	Concurrent abdominal effusion	Pure transudate	Evaluate kidneys, liver, and GI tract
Mesothelioma	No distinguishing characteristics	Neoplastic (variable): modified transudate; nonseptic exudate	Ultrasound; fine-needle aspiration cytology; thoracotomy
Thymic branchial cyst	Mediastinal mass (similar appearance to mediastinal neoplasia)	Modified transudate; nonseptic exudate	Ultrasound; thoracotomy
Pancreatitis	Concurrent abdominal effusion	Nonseptic exudate	Abdominal ultrasound; serum pancreatic lipase immunoassay
Pulmonary thromboembolism	Hypovascularity of lung; blunted pulmonary arteries; right-sided heart enlargement	Modified transudate; nonseptic exudate	Angiography; pulmonary perfusion scan

Physical Examination

Thoracic Auscultation and Percussion

- Auscultation generally reveals muffled or inaudible heart and lung sounds ventrally, while breath sounds are preserved dorsally.
- On percussion, pleural effusion causes the thorax to sound dull and hyporesonant, and a horizontal fluid line may be demonstrable.

Other Physical Findings

- Fever suggests an inflammatory, infectious, or neoplastic process.
- Jugular venous distention or pulsations and auscultation of murmurs, gallops, and arrhythmias are signs suggestive of cardiogenic pleural effusion. Pleural effusion can be associated with congestive heart failure in cats with hyperthyroidism; thus, palpate the thyroid region for the presence of thyroid gland nodules or enlargement.
- Decreased compressibility of the cranial thorax is suggestive of a mediastinal mass, usually lymphoma or thymoma. Mediastinal lymphoma can also compress the esophagus, causing signs of dysphagia and regurgitation; it also can impinge on the sympathetic innervation of the eye, causing Horner syndrome.
- Animals with pleural effusion should also be thoroughly examined for evidence of a tumor in any location, since extrathoracic neoplasms may metastasize to the lungs or pleural cavity and cause pleural effusion (e.g., mammary adenocarcinoma).
- Ophthalmoscopy may reveal lesions of chorioretinitis in cats with feline infectious peritonitis (FIP).
- External signs of trauma may indicate hemothorax or diaphragmatic hernia.

Thoracic Radiography

Routine thoracic radiography is generally effective for confirming pleural effusion.

▼ ***Key Point*** If the animal is in extreme respiratory distress, perform pleural drainage to stabilize the patient before radiography. Otherwise, the stress of restraint and manipulation during radiography could prove fatal.

The radiographic signs of pleural effusion include separation of the lung lobes from the parietal pleura and sternum by extrapulmonary fluid density (i.e., compression of lung lobes by a pleural fluid density), fluid-filled interlobar fissures producing a scalloped appearance to the edges of the lungs, and obscuring of the cardiac and diaphragmatic shadows, which is referred to as the silhouette sign (see Chapter 159). There is also widening of the mediastinum and blunting or filling of the costophrenic angles by intrapleural fluid density on a ventrodorsal view. In addition, the various causes of pleural effusion may be associated with other radiographic findings of diagnostic significance (see Table 164-1).

- A rounded contour to the caudal lobar borders, often accompanied by atelectasis of the cranial and middle lobes, is suggestive of a chronic fibrosing reaction of the visceral pleura that is exerting a constrictive and restrictive effect on the lung lobes (especially in cats with chronic chylothorax). Atelectatic lobes may be mistaken for pulmonary masses, hilar masses, or lung lobe torsion.
- Although most pleural effusions are bilateral, unilateral effusion is seen occasionally. This is most suggestive of pyothorax because the natural walling-off response to septic suppuration can cause extensive pleural thickening, which may seal off the mediastinum and limit the effusion to one side. Pleural thickening associated with chylothorax can also result in unilateral effusion. In addition to pyothorax and chylothorax, unilateral effusion is occasionally observed in traumatic hemothorax, diaphragmatic hernia, pulmonary neoplasia, and lung lobe torsion.
- Pleural effusion is sometimes found in combination with ascites. Simultaneous pleural and peritoneal effusions (dual-cavity effusion) occur most often in cats with FIP but also in dogs or cats with severe hypoalbuminemia, diaphragmatic hernia, widely disseminated neoplasia, pancreatitis, and CHF.

▼ ***Key Point*** Because many intrathoracic structures are obscured by the presence of pleural effusion, obtain radiographs *after* the removal of pleural fluid to facilitate visualization of such abnormalities as mediastinal mass, cardiomegaly, intrapulmonary lesions (masses, infiltrates, vascular changes), lung lobe torsion, or diaphragmatic hernia (see Table 164-1).

- Both right and left lateral radiographic views of the thorax may be indicated when a unilateral lesion is suspected (e.g., focal fluid accumulation, pulmonary mass or focal density, lung lobe torsion). Horizontal beam radiography (e.g., standing lateral view) can be used to confirm small-volume effusions, to demonstrate fluid encapsulation, and to facilitate visualization of thoracic structures by shifting fluid away from the structures of interest.

Thoracentesis and Fluid Analysis

In most animals with pleural effusion, the combination of radiographic findings and fluid analysis establishes the diagnosis or determines the direction for additional diagnostic evaluations. Drainage of the pleural fluid also provides therapeutic benefit and may be lifesaving in patients with hypoxemia.

Thoracentesis

- Thoracentesis is a safe and generally effective method for removal of fluid from the pleural space.

See Chapter 3 for a description of thoracentesis techniques.

- Following the collection of diagnostic specimens, enough fluid should be aspirated to relieve respiratory distress. In some animals it may be difficult to obtain an adequate volume of fluid if the fluid is compartmentalized within the pleural space by adhesions or if it is viscid and full of fibrin or debris. In this case, or if repeated pleural drainage is anticipated, place a thoracostomy tube (see Chapter 3).

Pleural Fluid Analysis

Perform the following analyses on the pleural fluid.

- Perform cytologic examination of direct smears and centrifuged cell concentrate smears stained with routine hematologic stains. In scanty aspirates, smears for cytologic examination are the first priority.
- Measure total nucleated cell count (differentiates transudates from exudates).
- Determine physical and biochemical characteristics, such as color, turbidity (correlates with nucleated cell count in non-chylous fluids), odor (foul odor suggests pyothorax), specific gravity and total protein concentration (differentiates transudates from exudates), viscosity and clot formation (indicates fibrinous exudate as in feline infectious peritonitis [FIP]), and presence of chylomicrons (tests for triglyceride indicate chylous effusion).
- Consider non-routine chemical analyses; e.g., pH (<6.9 in pyothorax), glucose (<10 mg/dl in pyothorax), lactic dehydrogenase (>200 IU/L in exudates), adenosine deaminase (elevated in inflammatory exudates), and fibronectin (elevated in neoplastic effusion).
- If infection is suspected, consider Gram stain, acid-fast stain, culture and sensitivity testing for aerobic and anaerobic bacteria, and, in some cases, culture for fungi.
- If FIP is a possibility, set aside an aliquot of fluid in case protein electrophoresis and a polymerase chain reaction test are later warranted based on preliminary findings (see under Feline Infectious Peritonitis).

Classification of Pleural Fluid Patterns

On the basis of these analyses, pleural effusions are generally classified into one of several patterns: transudate, modified transudate, nonseptic exudate, septic exudate, chylous effusion, or hemorrhage (Table 164-2). In addition, any of these can be subcategorized as neoplastic versus non-neoplastic depending on whether or not neoplastic cells are present on cytologic evaluation. There can be considerable overlap between these various categories; nevertheless, they are helpful for understanding the pathogenesis and determining the cause of pleural effusions.

Transudate

Transudative effusions are generally associated with alteration of capillary hydrostatic pressure caused by CHF or decreased plasma colloidal osmotic pressure caused by hypoalbuminemia. The typical features of a pure transudate are low protein concentration and low cell count consisting predominantly of mesothelial cells; this is comparable to the characteristics of normal pleural fluid.

Modified Transudate

Long-standing transudative effusions often become modified transudates, as they acquire greater cellularity and protein content. Modified transudates and nonseptic exudates can be very similar.

Table 164-2. PLEURAL FLUID ANALYSIS PATTERNS*

Fluid Category	TP	WBC/μl	Disease Associations
Transudate	<1.5	<1,000	CHF (early); hypoproteinemia
Modified transudate	2.5–5	1,000–7,000	CHF; neoplasia (e.g., lymphoma); diaphragmatic hernia; pulmonary thromboembolism
Nonseptic exudate	3–6	5,000–20,000	FIP; neoplasia; diaphragmatic hernia; lung lobe torsion; pancreatitis; pulmonary thromboembolism
Septic exudate	3–7	5,000–300,000	Septic pleuritis (pyothorax)
Chylous effusion	2.5–6	1,000–20,000	CHF; lymphoma; thoracic lymphangiectasia; heartworms; jugular vein thrombosis (catheter-induced); diaphragmatic hernia; lung lobe torsion
Hemorrhage	>3.0	5,000–20,000	Trauma, coagulopathy, neoplasia, lung lobe torsion

TP, total protein (g/dl).
*The six basic fluid patterns and their most frequent clinical associations are indicated. Any of these can be subcategorized as neoplastic if neoplastic cells are present on cytologic evaluation.

Septic Exudate

Septic exudates are purulent effusions consisting of numerous degenerating neutrophils, usually in association with intra- and extracellular bacteria. The fluid usually has marked turbidity, high protein concentration, and a foul odor, whereas the color is variable. The presence of a septic exudate within the pleural space indicates septic pleuritis (pyothorax) and is an indication for culture and Gram stain of the effusion (see under Pyothorax).

Nonseptic Exudate

Nonseptic inflammation and disorders that cause lymphatic or venous obstruction, such as neoplasia, diaphragmatic hernia, lung lobe torsion, pulmonary infarction, and thymic branchial cysts may result in a nonseptic exudative effusion that is difficult to distinguish from a modified transudate. Some clinicians subclassify such effusions as neoplastic effusions if neoplastic cells are evident cytologically.

- *Feline infectious peritonitis* causes a nonseptic pyogranulomatous exudate that has fairly distinctive characteristics—yellow and translucent in appearance with a viscous consistency, high protein concentration (approximating serum levels), high fibrin content, and low-to-moderate cellularity consisting mostly of non-degenerate neutrophils and macrophages (see under Feline Infectious Peritonitis; see also Chapter 10). If FIP is suspected, consider performing protein electrophoresis of the fluid. If gamma globulin is greater than 32% of the protein in effusates, FIP is strongly considered; conversely, if more than 48% of protein is albumin or if the albumin-to-globulin ratio is greater than 0.81, FIP is unlikely.
- *Eosinophilic effusion* (>10% eosinophils) can be either an exudate or modified transudate. The most frequent cause has been intrathoracic neoplasia (e.g., systemic mastocytosis, lymphoma). Eosinophilic pleural effusion has also been associated with heartworm disease, allergy, bronchointerstitial lung disease, eosinophilic granulomatosis, and trauma.

Chylous Effusion

Chylous effusions are caused by extravasation or leakage of intestinal lymph (chyle) from an obstructed or ruptured thoracic duct. Chylothorax in dogs and cats may be idiopathic or associated with trauma, thoracic lymphangiectasia, intrathoracic neoplasia, heart disease, heartworms, venous thrombosis, diaphragmatic hernia, or lung lobe torsion (see under Chylothorax). The milky white opaque fluid contains mostly lymphocytes accompanied by variable numbers of neutrophils, depending on the duration of the effusion and the extent of the resulting pleuritis (see Table 164-2). Chylous effusions are confirmed by the presence of chylomicrons, which can be demonstrated by the ether clearance test, by the presence of a cream layer on refrigeration, and microscopically by the presence of Sudan-positive orange fat droplets, but these are relatively insensitive methods.

▼ ***Key Point*** The most reliable test for chylous effusion is the comparison of the triglyceride and cholesterol concentrations measured simultaneously in the fluid and serum. Chylous effusion is characterized by a high triglyceride concentration (usually >300 mg/dl) compared with that of serum and a pleural fluid cholesterol-to-triglyceride ratio of less than 1. The fluid cholesterol concentration is less than or equal to that of serum.

Hemorrhagic Effusion

Hemorrhage into the pleural space may be associated with trauma, hemostatic abnormalities, or neoplasia. The physicochemical and cytologic features of the effusion are similar to those of defibrinated peripheral blood. The presence of erythrophagocytosis by macrophages confirms that the hemorrhage is not merely the result of a traumatic collection.

Laboratory Evaluations

Various laboratory evaluations may provide useful diagnostic information depending on the suspected underlying cause of pleural effusion.

- The complete blood count may reveal a neutrophilia with a left shift in pyothorax, FIP, lung lobe torsion, and neoplasia. Lymphopenia is common in animals with chylothorax, but it can also be a nonspecific manifestation of stress. Anemia and various other hematologic abnormalities may be associated with lymphoma and feline leukemia virus (FeLV).
- Serum protein determinations may reveal hypoalbuminemia, a cause of transudation, or hyperglobulinemia, a common finding in FIP and other conditions of chronic immune stimulation. Severe proteinuria would be expected on the urinalysis of a dog or cat with hypoalbuminemia and transudation associated with nephrotic syndrome.
- Diagnostic testing may be indicated for infectious and parasitic diseases that have been associated with pleural effusion, such as FeLV, feline immunodeficiency virus (FIV), FIP, heartworm disease, and aelurostrongylosis. Specific aspects of these various diagnostic tests are described in the appropriate chapters elsewhere in this book.
- In cats with cardiogenic pleural effusion, the serum concentrations of thyroxine and taurine may be indicated for the diagnosis of hyperthyroid cardiomyopathy and taurine-deficient cardiomyopathy, respectively (see Chapter 150).

Cardiac Evaluations

- Echocardiography is the most useful procedure for diagnosis of cardiogenic causes of pleural effusion such as cardiomyopathy (idiopathic, taurine deficiency, hyperthyroidism), pericardial diseases (pericarditis, neoplasia), congenital heart defects, and heartworm disease.
- Angiocardiography is also helpful for determining the underlying cardiac abnormality in selected cases of cardiogenic pleural effusion. A detailed discussion of cardiac evaluation is found in Chapters 142 and 143.

Ultrasonography

The inability of ultrasound to penetrate air-filled structures limits the diagnostic usefulness of ultrasound examination of the lungs; however, in animals with pleural effusion, ultrasonography can provide meaningful information because the pleural fluid provides an "acoustic window" for transmission. Thoracic ultrasonography is possible when an air-filled lung is collapsed, displaced (by fluid, mass, or herniated abdominal viscera), replaced (by neoplastic tissue), or consolidated. Because the presence of pleural fluid actually enhances ultrasound transmission, it is preferable to perform the procedure prior to evacuation of the pleural fluid.

- Pleural fluid usually appears as an anechoic or hypoechoic space between the thoracic wall or diaphragm and lung. The fluid in pyothorax and hemothorax may contain internal echoes.
- In addition to confirming pleural effusion, ultrasonography is helpful for the diagnosis of pulmonary, mediastinal, and pleural neoplasms; pulmonary abscesses associated with pyothorax; lung lobe torsion; cardiac abnormalities; and diaphragmatic hernia.
- Ultrasonography can also be used to guide needle placement accurately for fine-needle aspiration or biopsy of pleural, mediastinal, and pulmonary masses.

Specialized Imaging Techniques

Depending on the suspected etiology of the pleural effusion and the results of other diagnostic evaluations, specialized imaging techniques may be indicated, such as contrast radiographic procedures (contrast peritoneography for the diagnosis of diaphragmatic hernia, contrast lymphangiography for the diagnosis of chylothorax, contrast pleurography), lymphoscintigraphy, and CT.

Positive Contrast Peritoneography

When diaphragmatic hernia is suspected but cannot be confirmed on routine thoracic and abdominal radiographs, ultrasonography should be the next approach; however, if ultrasound is unavailable, positive contrast peritoneography is an alternative method for diagnosis of diaphragmatic hernia. Inject an aqueous contrast iodide (Renovist; 1 ml/kg) into the peritoneal cavity, and roll the animal from side to side for several minutes to distribute the contrast agent. Obtain radiographs to determine whether the contrast agent has entered the pleural space through a defect in the diaphragm.

Lymphangiography

Positive-contrast lymphangiography is used to evaluate the thoracic duct lymphatic channel in dogs and cats with unexplained chylous effusion. This is usually done by catheterizing an intestinal lymphatic just prior to, and in preparation for, surgical ligation of the thoracic duct to treat chylothorax. The reader is directed to surgical clinical literature and texts for a technical description of this procedure.

SPECIFIC DISEASES

Pyothorax (Septic Pleuritis)

Pyothorax is the accumulation of purulent exudate (pus) within the pleural space as a result of intrapleural bacterial infection (septic pleuritis) or, rarely, mycotic infection.

Etiology

Microorganisms

A diversity of microorganisms has been isolated from the pleural fluid of dogs and cats with pyothorax; mixed bacterial infections composed mostly of obligate and facultative anaerobes are found most consistently.

- In many cases, the infection consists entirely of anaerobic bacteria. The most frequent isolates are *Bacteroides* spp., *Clostridium* spp., *Peptostreptococcus* spp., *Fusobacterium* spp., *Pasteurella multocida,* and *Actinomyces* spp. The isolates from cats with pyothorax and their relative frequency closely resemble those found in subcutaneous cat bite abscesses and mirror the normal oropharyngeal flora of the cat.
- Other bacteria found sporadically include *Pseudomonas* spp., *Escherichia coli, Klebsiella* spp., *Proteus* spp., *Streptococcus* spp., *Staphylococcus* spp., *Corynebacterium pyogenes, Nocardia* spp., *Borrelia* spp., *Eubacterium* spp., and mycoplasmas.
- Fungi, such as *Cryptococcus neoformans, Blastomyces dermatitidis,* and *Candida albicans,* are rare causes.
- In addition, pleuritis has been reported as a rare manifestation of infection with Aelurostrongylus abstrusus, the feline lungworm.

Source of Infection

The source of infection is not identified in most dogs and cats with pyothorax. Microorganisms may poten-

tially enter the pleural space through penetrating chest wounds (e.g., bite wounds), perforations of mediastinal structures (i.e., esophagus, trachea, bronchi), migrating pleural foreign bodies (e.g., grass awns), and direct extension from the lung in bacterial pneumonia (parapneumonic effusion). Mediastinitis, pleuritis, and pyothorax are frequent complications of esophageal perforation caused by esophageal foreign bodies, especially those with irregular sharp edges, such as plastic, glass, wood, and bone. Iatrogenic esophageal rupture can occur during endoscopic foreign body retrieval or during balloon dilation of esophageal strictures. Intrapleural infection can also result from hematogenous or lymphatic spread from distant infection sites.

Clinical Signs

Dyspnea is the most consistent sign of pyothorax. Cough is observed in some cases. In addition, nonspecific systemic signs are common, including inactivity, exercise intolerance, fever, depression, anorexia, dehydration, weight loss, and pallor. Advanced cases may present in a moribund state with endotoxic shock and hypothermia.

Diagnosis

- Physical findings (auscultation and percussion) and radiographic findings in pyothorax are typical of pleural effusion. In some animals with pyothorax, the pleural fluid may become encapsulated or compartmentalized by fibrinous adhesions and fibrosis (walling-off process), producing radiographic signs of unilateral or non-gravitating effusion and rounded lobar edges.
- The hematologic findings in pyothorax are typical of a serious septic inflammatory process and support the diagnosis. A neutrophilic leukocytosis with a left shift and with toxic-appearing neutrophils are found in most cases, while a neutropenia with a degenerative left shift may develop terminally. The hemogram also usually reveals a mild to moderate nonregenerative, normochromic, normocytic anemia of chronic infection.
- Confirm the diagnosis of pyothorax with pleural fluid analysis, which indicates septic inflammatory (purulent) exudate. The fluid is usually malodorous and cloudy or opaque, with color varying from red to brown to yellow. The fluid also may contain a flocculent sediment of fibrinous and cellular debris. The total protein concentration generally exceeds 4.5 g/dl and there are usually 50,000 to 100,000 or more nucleated cells/µl, consisting of mostly (greater than 85%) degenerating neutrophils. Cytologic examination usually reveals abundant intra- and extracellular bacteria.
- Culture the pleural fluid for confirmation of the diagnosis and for determination of optimal antibacterial therapy. In most cases, a mixed infection (see earlier, under Etiology) involving primarily anaerobic bacteria is found. If only routine aerobic culture techniques are used, only the aerobic component of the infection will be identified, and because some dogs and cats with pyothorax have an exclusively anaerobic infection, there may be no growth at all. Thus, perform both aerobic and anaerobic cultures.
- Because retroviral status may influence prognosis, test cats with pyothorax for FeLV (see Chapter 8) and FIV (see Chapter 9).

Treatment

Treat pyothorax with systemic antibiotics, closed-chest drainage, and lavage by means of an indwelling chest tube thoracostomy (see elsewhere for thoracic tube placement). The chest tube provides for repeated drainage and irrigation of the pleural space.

Antibiotics

Start antibiotic therapy intravenously and then continue orally at home for at least 4 to 6 weeks. Until the results of culture and sensitivity of the effusion are available, assume that a mixed anaerobic and aerobic infection is present (see earlier, under Etiology). Most isolates are susceptible to antibiotics of the penicillin family, such as penicillin G, ampicillin, amoxicillin, or amoxicillin with clavulanate; thus, standard dosages of any one of these are a good initial choice (see Table 164-3), although approximately 20% of anaerobes may be resistant to the penicillin-ampicillin group. Other effective antibiotics for anaerobic infections include clindamycin and metronidazole (see Table 164-3). For gram-negative infections, add an aminoglycoside (amikacin), enrofloxacin, or trimethoprim-sulfadiazine. Trimethoprim-sulfadiazine is indicated for *Nocardia* spp.

Pleural Drainage and Lavage

Place a thoracic drainage tube to drain purulent material from the pleural space and allow lavage of the pleural cavity. Although some animals with severe effusion may require continuous chest drainage, intermittent drainage is adequate for most patients.

- Perform thoracic drainage at least twice daily. For pleural lavage use sterile isotonic saline or lactated Ringer's solution warmed to body temperature. Prior to each irrigation procedure, evacuate any fluid that has accumulated since the previous lavage and record the quantity. Warm the irrigation solution to body temperature and infuse 10 to 20 ml/kg body weight slowly over about 5 minutes through the chest tube. If respiratory distress occurs, stop the infusion.
- Leave the solution in the thorax for 5 to 10 minutes while the animal is gently rolled to enhance distribution; then aspirate as much as possible. A return of 75% or more of the irrigation solution is expected, which can sometimes be facilitated by repositioning

Table 164-3. USEFUL ANTIBIOTICS FOR TREATMENT OF PYOTHORAX

Antibiotic	Trade Name	Dosage	Indications
Penicillin G	generic	20,000–40,000 U/kg q6–8h IV IM	anaerobes,* *Pasteurella, Actinomyces*
Ampicillin	Omnipen	20 mg/kg q6–8h IV IM SC	anaerobes,* *Pasteurella* and some other gram negatives
Amoxicillin	Amoxi-Tabs	20 mg/kg q8–12h PO	anaerobes,* *Pasteurella* and some other gram negatives
Amoxicillin/clavulanate	Clavamox	20 mg/kg q12h PO	anaerobes,† *Pasteurella* and many other gram negatives
Chloramphenicol	Chloromycetin	50 mg total/cat q12h IV SC PO	anaerobes,† gram-positive and gram-negative aerobes
Clindamycin	Antirobe	10 mg/kg q12h PO	anaerobes†
Metronidazole	Flagyl	10–15 mg/kg q8–12h PO IV	anaerobes†
Enrofloxacin§¶	Baytril	*Dogs:* 5 mg/kg q12h PO, IV, SC; *Cats:* 5 mg/kg q24h PO, IV, SC	most gram-negative and gram-positive aerobes
Trimethoprim-sulfadiazine	Tribrissen	15 mg/kg q12h PO	*Nocardia*
Amikacin‡	Amiglyde-V	10 mg/kg q8–12h IV IM SC	gram negatives§
Cefoxitin	Mefoxin	20–30 mg/kg q8h IV IM	anaerobes,† gram-negatives
Ticarcillin	Ticar	30–50 mg/kg q6h IV IM	anaerobes,† gram-negatives, *Pseudomonas*

*Excluding Bacteroides fragilis.
†Including most penicillin-resistant strains of Bacteroides fragilis.
‡Caution: uncorrected dehydration may potentiate aminoglycoside nephrotoxicity.
§Enrofloxacin and aminoglycosides are ineffective against anaerobes; thus, always use in combination with penicillin or other antibiotic with activity against anaerobes when treating pyothorax.
¶Doses exceeding 5 mg/kg daily are retinotoxic in cats and may cause blindness.

the animal or rolling it from side to side during aspiration.

- If the animal is initially dehydrated, rehydration should be accomplished before, or simultaneous to, the first lavage; otherwise, much of the instilled fluid will be absorbed from the pleural space with very little returned on aspiration.
- Obtain samples of interlavage fluid for cytologic examination on a daily basis and examine for disappearance of microorganisms and degenerative neutrophils. Remove the chest tube once the interlavage pleural fluid becomes characteristic of a modified transudate (clear in appearance and free of microorganisms and degenerative neutrophils) and the quantity that accumulates is small and can be accounted for merely by the presence of the drain itself (i.e., up to 2–3 ml/kg/day). There should also be radiographic resolution of pleural effusion.
- The duration of the pleural drainage phase of therapy in most cases is 4 to 7 days. Monitor serum proteins and electrolytes (especially potassium) because depletion can occur with prolonged lavage. Evaluate thoracic radiographs about 1 week following tube removal to ensure resolution, and continue systemic antibiotics for a minimum of 4 to 6 weeks.

Complications

Adverse sequelae to pyothorax may include restrictive pleuritis, pleural adhesion formation, and pulmonary abscessation. Occasionally, adhesions render closed-chest drainage and lavage ineffective. In such cases, perform a thoracotomy (see Chapter 167) to manually break down adhesions, drain pockets of exudate, remove debris, and place a drainage tube in the most favorable location for postoperative thoracic lavage. In addition, thoracotomy may be necessary if a migrating pleural foreign body is suspected.

Chylothorax

Etiology

Chylothorax results from the leakage or extravasation of chylomicron-laden intestinal lymph (chyle) into the pleural space from an obstructed, ruptured, or anomalous thoracic duct or its collateral branches. The cause of chylothorax is frequently not apparent; however, chylous pleural effusions in dogs and cats have been associated with lymphangiectasia of intrathoracic lymphatics (resulting from obstruction of thoracic duct inflow into the cranial vena cava), traumatic rupture of the thoracic duct, intrathoracic neoplasia (mediastinal lymphoma, thymoma), heart disease (cardiomyopathy, heartworms, hyperthyroidism, pericarditis), diaphragmatic hernia, peritoneopericardial diaphragmatic hernia, lung lobe torsion, and vena caval thromboembolism (iatrogenic from indwelling jugular venous catheterization). Idiopathic chylothorax has a predilection for Afghan hounds, Smiba Inus, and Oriental cat breeds (Siamese, Himalayan).

Clinical Signs

In addition to typical signs of pleural effusion, such as dyspnea and tachypnea, it is noteworthy that dogs and cats with chylothorax often present with coughing.

Diagnosis

- Confirmation that pleural fluid is chyle depends on demonstration of the presence of chylomicrons. The most reliable criteria for chyle are an increased concentration of triglycerides in the fluid compared with serum and a fluid cholesterol-to-triglyceride ratio of less than 1 (see under Classification of Pleural Fluid Patterns).
- In the veterinary literature, many milky effusions have been called pseudochylous (which implies lipid in the form of cholesterol and lecithin derived from degenerating cells) when, in fact, if triglyceride analysis had been performed, these effusions would probably have been true chyle.
- The predominant cell in chyle is usually the small lymphocyte. However, over time the irritant effect of chyle results in an influx of inflammatory cells, especially neutrophils.
- Once chylothorax is confirmed, use routine radiography and other clinical evaluations (e.g., ultrasonography, echocardiography, heartworm testing) to search for underlying causes, such as heart disease, heartworms, neoplasia, or diaphragmatic hernia.

Medical Treatment

- If an underlying cause is identified, treatment is directed toward the underlying primary disorder. In the rare case when there is a history of recent thoracic trauma, conservative medical management may be tried for a 2-week period in hopes of spontaneous healing of the injured lymphatic. This consists of (1) pleural drainage by either periodic thoracentesis or continuous chest tube drainage, and (2) decreasing thoracic duct flow by exercise restriction (cage rest).
- A fat-restricted diet supplemented with medium-chain triglycerides (MCTs) has been recommended in the past; however, this has not been effective clinically, and in normal dogs it has been shown experimentally that altering dietary fat content or using MCTs does not significantly affect thoracic duct lymph flow and that orally administered MCTs are carried in thoracic duct lymph.
- Anecdotal reports have indicated some success with the administration of a benzopyrone compound, Rutin (50mg/kg PO q8h). The proposed mechanisms of action of rutin include reducing leakage from blood vessels, increasing protein removal by lymphatic vessels, increasing the macrophage phagocytosis of chyle, increasing tissue macrophage numbers, and increasing proteolysis and removal of protein from tissues. However, clinical results from the use of this drug for dogs and cats with chylothorax have been inconsistent.

Surgical Treatment

- If no underlying medically treatable cause of chylothorax is found, surgical intervention is indicated. The surgical approach to treatment of chylothorax involves ligation of the thoracic duct at the level of the diaphragm in association with evaluation of the thoracic duct and intrathoracic lymphatics by pre- and immediate postoperative contrast lymphangiography. Lymphangiography is performed by cannulating a mesenteric lymphatic vessel via a flank abdominal approach. After delineating the thoracic duct and its branches with the dye study, the duct is ligated via a 10th intercostal space thoracotomy (right side in dogs, left side in cats). Ligate the duct as close to the diaphragm as possible, and be sure to occlude all branches. Postligation lymphangiography then confirms complete occlusion of the thoracic duct system. The details of these procedures are provided in Chapter 167.
- The reported success rate of this procedure varies from 20% to 60% in cats and 55–60% in dogs. Commercially available pump devices (e.g., Hakim-Cordis ventricular-peritoneal catheter, Cordis Corporation, Miami, FL; double-valve Denver peritoneal-venous catheter, Denver Biomaterials Inc., Evergreen, CO) are available for active pleuroperitoneal shunting of chylous effusion in refractory chylothorax. Disadvantages of shunt devices are that they are expensive, they are easily occluded, they require considerable owner compliance, and the complication rate is high.
- Recent clinical studies have shown improved results of surgical treatment when thoracic duct ligation is combined with partial pericardectomy. Although the reason for treatment successes with pericardectomy are unclear, subtle changes in thoracic venous and/or lymphatic pressures could account for the cessation of effusion due to improved flow through thoracic duct lymphatics. The authors currently create a pericardial window in conjunction with thoracic duct ligation for chylothorax in dogs and cats.
- When chylothorax is unresponsive to thoracic duct ligation or shunt procedures, pleurodesis using intrapleural instillation of a sclerosing agent such as tetracycline or sterile talc may be palliative. Pleurodesis is intended to reduce or stop pleural effusion by causing diffuse adhesions between the parietal and visceral pleura. It is an effective technique in humans but has not been efficacious in dogs, either with experimental or spontaneous effusion.

Complications

Chronic diffuse fibrosing pleuritis is a sequela of chylothorax that may cause constriction and collapse of lung lobes and restrict the expandability of the lungs. Radiographically, fibrosing pleuritis is indicated by rounded lung lobe borders and atelectasis of cranial or middle lobes. The atelectatic lobes may be mistaken for pulmonary masses, hilar masses, or lung lobe torsion. In order to avoid excessive pleural fibrosis, surgical

intervention in animals with chylothorax, especially cats, should not be delayed. Surgical removal of the layer of fibrin and fibrotic reaction covering the visceral pleura, a process called decortication, is difficult in cats and usually results in significant laceration of underlying lung tissue that requires continuous pleural drainage for postoperative pneumothorax and effusion.

Feline Infectious Peritonitis

Etiology

Feline infectious peritonitis is a highly fatal chronic progressive coronaviral infection of cats characterized by widespread immune complex-mediated vasculitis and pyogranulomatous inflammation (see Chapter 10 for a comprehensive description of the disease). In the effusive form of FIP, exudative peritonitis or pleuritis may occur.

Clinical Signs

Pleural involvement is manifested as dyspnea and by other signs of pleural effusion, often accompanied by nonspecific signs such as anorexia, depression, fever, and pallor. Pericardial effusion due to fibrinous pericarditis may accompany pleural FIP and is detectable by echocardiography, but only rarely is this extensive enough to cause cardiac tamponade.

Diagnosis

- The diagnosis can usually be established by analysis of a specimen of pleural fluid obtained by thoracentesis. The fluid of FIP is a nonseptic exudate, often described as pyogranulomatous or fibrinous. It is typically pale yellow to golden in color, is nearly translucent because of its relatively low cell count (usually 1,000–10,000 nucleated cells/μl), and is foamy because of its high protein content. The fluid of FIP may seem viscous, tenacious, and sticky, and it may contain flecks, strands, or clots of fibrin. The concentration of protein often approaches that of serum, ranging from 4 to 10 g/dl. Fluid protein electrophoresis is a reliable diagnostic indicator of FIP when gamma globulin composes more than 32% of the protein, albumin is less than 48% of the protein, and the albumin-to-globulin ratio is less than 0.81. A somewhat distinctive mixture of inflammatory cells characterizes the pyogranulomatous nature of FIP exudate, with non-degenerate neutrophils and macrophages predominating, but also including plasma cells and lymphocytes.
- Ancillary laboratory findings that may support the diagnosis of FIP include neutrophilic leukocytosis, neutropenia, lymphopenia, normocytic-normochromic nonregenerative anemia, and hyperglobulinemia.
- A high serum titer of anti-coronaviral antibody indicates the possibility of FIP but is not a confirmatory test. A polymerase chain reaction (PCR) test for coronavirus in pleural fluid is a useful diagnostic aid (low sensitivity but high specificity) providing that a validated assay is used. Also use fluid immunostaining.

Treatment

In general, the results of treatments for FIP have been disappointing, and the prognosis is considered poor. Nevertheless, occasional remissions have been obtained with immunosuppressive therapy and with drainage of the intrapleural exudate (see Chapter 10).

Congestive Heart Failure

Etiology

Pleural effusion can be a manifestation of CHF in dogs and cats (Chapter 147). It is most commonly associated with cardiomyopathy (see Chapter 150), but also occurs with cardiac arrhythmias, congenital cardiac defects, pericardial diseases, heartworm disease, and hyperthyroid cardiomyopathy. Although pleural effusion is considered primarily a sign of right-sided CHF, animals with severe or chronic left-sided failure also develop pleural effusion.

Clinical Signs

In animals with pleural effusion due to heart disease, presenting signs often include tachypnea, dyspnea, depression, inactivity, and weakness. Anorexia and vomiting may also be observed. Physical findings that may indicate a cardiogenic cause for pleural effusion include:

- Signs of low cardiac output, such as pallor, hypothermia, cold extremities and pinnae, and weak femoral pulses
- Jugular venous distention, jugular pulsation, or positive hepatojugular reflex
- Concurrent hepatomegaly (due to hepatic congestion) or ascites (although, unlike dogs, cats rarely develop significant ascites from CHF)
- Abnormalities of cardiac auscultation, such as murmurs, diastolic gallops, or arrhythmias
- Ophthalmoscopic lesions of taurine-deficient retinopathy in cats (see Chapter 138)
- A palpable thyroid nodule in hyperthyroid cats

Diagnosis

The diagnosis of cardiogenic pleural effusion can be difficult because the effusion may muffle the heart sounds on auscultation and obscure the cardiac silhouette on thoracic radiographs.

- Radiographic findings that suggest pleural effusion is associated with CHF include cardiomegaly, pulmonary infiltrates (edema), pulmonary venous distention, distended caudal vena cava, and hepato-

megaly. In many cases, these findings are more apparent on radiographs taken after fluid has been drained from the pleural space.
- Pleural fluid analysis may determine the effusate to be a transudate, modified transudate, or chylous effusion, the predominant cells being erythrocytes, mesothelial cells, and small lymphocytes.
- Echocardiography is often and sometimes angiocardiography, may be necessary to confirm and assess cardiac disease. Cardiac arrhythmias and conduction disturbances are evaluated electrocardiographically.

Treatment

The treatment options for CHF as described in Chapter 147 are used for control of cardiogenic pleural effusion.

Intrathoracic Neoplasia

Etiology

Intrathoracic neoplasia is one of the most common causes of pleural effusion in dogs and cats. Causes of neoplastic pleural effusion include mediastinal lymphoma and thymoma, primary and metastatic pulmonary neoplasia (see Chapter 165), and malignant pleural mesothelioma. The mechanism of pleural effusion in these conditions generally involves hemolymphatic obstruction.

Diagnosis

- Use radiography (both right and left lateral views) and ultrasonography to characterize or identify the location of an intrathoracic mass (see Chapter 159).
- The fluid can vary from modified transudate to nonseptic exudate to chylous effusion. Lymphoma is usually diagnosed cytologically. Confirmation of nonlymphomatous intrathoracic neoplasia can be a diagnostic challenge requiring biopsy by thoracoscopy or thoracotomy. Clumps of reactive mesothelial cells exfoliate into all pleural effusions and are easily mistaken for neoplastic cells, especially carcinoma cells. Ideally, similar-appearing cells should be aspirated from pulmonary or intrathoracic masses before a definitive diagnosis of neoplasia is made. Conversely, many primary and metastatic tumors do not exfoliate cells into pleural fluid; thus, an absence of neoplastic cells in pleural effusion does not necessarily exclude neoplasia as the cause.

Treatment

Chemotherapy for mediastinal lymphoma is discussed in Chapter 27. The surgical aspects of intrathoracic neoplasia (thoracotomy, lobectomy) are discussed in Chapter 167.

Hemothorax

Etiology

- Hemothorax, the accumulation of blood within the pleural space, may be associated with any form of thoracic trauma that lacerates the lung parenchyma or ruptures intrathoracic vessels (see Chapter 166). It can also be caused by disorders of hemostasis (see Chapter 23) or by intrathoracic neoplasms that rupture or erode into vessels. Lung lobe torsion and pulmonary infarction are rare causes.
- The seriousness of hemothorax depends on the rate and volume of blood loss. Bleeding from the venous circulation or the low-pressure pulmonary arterial circulation is usually self-limiting, whereas bleeding from high-pressure systemic arteries, such as the intercostal or bronchoesophageal arteries, may be more severe. Hemorrhage due to injury of the heart or great vessels results in massive hemothorax that is rapidly fatal.
- The two major consequences of hemothorax are shock due to loss of circulating blood volume into the pleural space and ventilatory impairment due to fluid compression of the lung. As a general rule, in rapidly developing hemothorax, fatal circulatory failure (exsanguination) occurs before the volume of pleural fluid that accumulates is sufficient to cause serious respiratory compromise. However, blood or fluid replacement therapy in the presence of continued bleeding may lead to greater accumulation of intrapleural fluid, resulting in severe lung compression and ventilatory failure.

Clinical Signs

Clinical signs of hemothorax are attributed to shock and pleural effusion—dyspnea, tachypnea, weakness, pallor, and weak femoral pulses.

Diagnosis

- The heart and lung sounds are usually muffled, and percussion of the ventral thorax may be hyporesonant. In the trauma victim, this is distinguished from the hyperresonance of pneumothorax.
- Confirm intrapleural fluid radiographically.
- Definitive diagnosis is made by aspiration of defibrinated (non-clotting) blood from the pleural space. Blood clots rapidly (within 45 minutes) in the pleural space; thus, unless there is ongoing or very recent bleeding, the aspirated hemorrhagic effusion will not clot or contain platelets.

Treatment

The treatment of hemothorax involves treatment of shock with intravenous fluids or blood, as well as relief of respiratory distress via thoracentesis if necessary. See

Chapter 166 for more details on treatment of hemothorax.

Lung Lobe Torsion

Etiology

Torsions of either the right middle lung lobe or the right or left cranial lung lobe have occasionally been found in dogs and cats with pleural effusions. The mechanism of lung lobe displacement that culminates in torsion is poorly understood. Lung lobe torsion can occur secondary to pleural effusion, or it can be the cause of a serosanguineous effusion.

Clinical Signs

The signs usually include dyspnea, tachypnea, depression, anorexia, and weight loss.

Diagnosis

- The diagnosis of lung lobe torsion is suggested by visualization of a consolidated cranial or middle lung lobe on post-thoracentesis radiographs. Radiographic differential diagnoses for lobar consolidation should include pneumonia, edema, hemorrhage, atelectasis, and neoplasia.
- The pleural fluid may be nonspecific (i.e., nonseptic exudate), or it may reflect the underlying disease state (i.e., chylous, septic, or neoplastic effusion).
- Ultrasonography is helpful for identifying lung lobe torsion in some animals with pleural effusion.
- Confirmation of lung lobe torsion can only be made by thoracotomy in many cases.

Treatment

The treatment is lung lobectomy of the affected lobe (see Chapter 167).

Thymic Branchial Cysts

Branchial cysts develop from vestiges of the fetal branchial arch system. These are rare, but when they develop in the thymus they produce an encapsulated, multilobulated, multicystic mass in the cranial mediastinum that compresses adjacent structures and usually cause pleural effusion. Pleural fluid is blood-tinged and characteristic of a modified transudate (obstructive pattern) or nonseptic exudate. On the basis of their radiographic appearance, thymic branchial cysts must be differentiated from other cranial mediastinal masses such as lymphoma and thymoma (see under Intrathoracic Neoplasia). Because of their cystic nature, branchial cysts should be distinguishable from solid mediastinal masses by ultrasonography. Treat branchial cysts by surgical resection.

Diaphragmatic Hernia

Pleural effusion can be a complication of diaphragmatic hernia, especially when the liver or omentum is incarcerated in the hernia. The effusion can complicate the radiographic diagnosis of diaphragmatic hernia. The pleural fluid is usually a modified transudate, but in some cases it may be blood or chyle. Diaphragmatic hernia is discussed further in Chapter 166.

Pancreatitis-Associated Effusion

Mild transient pleural effusion has occasionally been associated with acute pancreatitis. Accompanying peritoneal effusion may also be present. Pleural effusion is a well-known complication of pancreatitis in humans; the pathogenesis is not fully understood, but it has been attributed to chemical pleuritis associated with toxins and activated pancreatic enzymes such as lipase reaching the pleural cavity via intercommunicating lymphatics. Generalized vascular injury and increased vascular permeability associated with acute pancreatitis may also play a role. The pleural effusion is usually a small volume and self-limiting with resolution of the pancreatitis; thus, no specific treatment is necessary. See Chapter 73 for further discussion of pancreatitis.

Pulmonary Thromboembolism

Pleural effusion can occur in association with pulmonary thromboembolism whenever it is extensive enough to produce infarction and ischemic necrosis of the lung and inflammation of adjacent pleura.

- *Clinical signs* are unresponsive dyspnea and signs of right-sided heart failure.
- Underlying causes of pulmonary thromboembolism include heartworm disease, pulmonary neoplasia, and hypercoagulability caused by septicemia, amyloidosis, hyperadrenocorticism, and immune-mediated hemolysis.
- The effusion is usually a modified transudate or nonseptic exudate, but secondary infection of the infarcted lung can result in a septic effusion.
- Radiographically, blunted pulmonary arteries, hypovascularity of the affected lung, and evidence of right-sided heart enlargement or failure suggest pulmonary thromboembolism; however, the diagnosis can be difficult to document because radiographic abnormalities may be absent or very subtle.
- Specialized procedures such as right ventricular and pulmonary artery pressure measurements, angiography, and radionuclide lung perfusion scan may be required for definitive diagnosis.
- *Treatment* is based on resolving the underlying cause of the thromboembolism (see Chapter 153), providing pleural drainage as needed, supplemental oxygen therapy, and control of secondary bacterial infection.

Chapter

165 Respiratory Neoplasia

Marcia A. Carothers / Francisco J. Alvarez

Neoplasms of the respiratory tract are relatively uncommon in small animals representing 4% to 5% of all neoplasms in the dog and cat. More than 80% of respiratory tract tumors are malignant. In addition to primary tumors affecting the respiratory tract, the lungs are common sites of metastatic neoplasia.

NEOPLASMS OF THE NASAL PASSAGES AND PARANASAL SINUSES

- Neoplasms of the nasal cavity are more common in dogs than in cats and constitute approximately 75% of the respiratory tract tumors in dogs.
- The prevalence of nasal tumors has been reported to be 0.3% to 2.4% in dogs and 4.2% in cats. Approximately 80% of primary nasal tumors are malignant.
- Nasal tumors are likely to originate in the caudal two-thirds of the nasal passages and often invade the sinuses.
- Local invasion of the surrounding tissues is typical of these tumors. Paraneoplasic syndromes are rare and include hypercalcemia (associated with adenocarcinoma) and polycythemia (associated with fibrosarcoma).

Tumor Types

- Histologically, epithelial tumors are most common, representing 60%–75% of all nasal tumors in the dog.

▼ ***Key Point*** Of the tumors that occur most frequently in the dog, adenocarcinomas, squamous cell carcinomas, and undifferentiated carcinomas comprise approximately 66% of intranasal neoplasms. Chondrosarcomas, fibrosarcomas, and osteosarcomas comprise the remaining 33%.

- Nasal transmissible venereal tumors are uncommon, but the presence of such a tumor should always be considered in the differential diagnosis where the disease is endemic.
- Plasma cell tumors, mast cell tumors, and benign tumors are rarely seen in the dog.
- Although nasal tumors are locally invasive and the metastatic rate at the time of diagnosis is generally low, approximately 40% to 50% of patients have distant metastasis at the time of necropsy.
  - Mesenchymal tumors have the lowest rate of metastasis, whereas neuroendocrine tumors and neuroblastomas have the highest rate (80–100%).
  - Regional lymph nodes, brain, lung, and liver are the most common sites of metastasis.
- *In the cat* nasal and paranasal lymphoma are the most common types of malignancies, followed by adenocarcinoma and squamous cell carcinoma. Benign *nasopharyngeal inflammatory polyps* are more common in the cat than in the dog.

Table 165-1 lists tumors of the nasal passages and paranasal sinus occurring in dogs and cats.

▼ ***Key Point*** Malignant nasal tumors usually are locally invasive, with metastasis occurring late in the course of the disease.

Signalment

- Nasal tumors are more common in older animals. Mean ages range from 7 to 12 years in dogs, with chondrosarcomas having the lower mean (7 years) and neuroendocrine tumors having the higher mean (12 years). Cats have reported mean ages of 8 to 10 years.
- There is no sex predilection; however, in one study (Patniak, 1989), male canines had a slight higher predilection (1.8:1.0) than female canines.
- Dolichocephalic and medium- to large-breed dogs are predisposed to developing nasal neoplasms. Canine breeds reported to be at high risk for the development of nasal neoplasms include the Airedale Terrier, Bassett Hound, Old English Sheepdog, Scottish Terrier, Collie, German Shepherd, Keeshond, and German Short-haired Pointer.

History

- The average duration of clinical signs prior to diagnosis is approximately 3 months.

Table 165-1. NEOPLASMS OF THE NASAL PASSAGES AND PARANASAL SINUSES*

Malignant Tumors in Dogs	*Malignant Tumors in Cats*
Adenocarcinoma	Lymphoma
Squamous cell carcinoma	Squamous cell carcinoma
Chondrosarcoma	Adenocarcinoma
Osteosarcoma	Undifferentiated carcinoma
Fibrosarcoma	Neuroblastoma
Lymphoma	Fibrosarcoma
Histiocytic sarcoma or malignant histiocytosis	*Benign Tumors in Dogs and Cats*
Neuroendocrine tumors	Polyps (more common in cats)
Neuroblastoma	Adenoma
Transmissible venereal tumor	Fibroma
	Chondroma

*Listed in decreasing order of frequency.

- Sneezing, nasal discharge, epistaxis, and epiphora are the most common presenting signs.
- A partial response to antibiotic therapy can be observed initially; however, intermittent and progressive signs continue.

Clinical Signs

- Unilateral or bilateral nasal discharge (hemorrhagic, serohemorrhagic, or mucopurulent) and/or ocular discharge are the most common signs noted.
- Sneezing, snoring, or reverse sneezing may also been reported by the owner.
- Facial deformity (e.g., exophthalmos and nasal swelling) is common in dogs with skeletal neoplasms and may occur late in the curse of other types of nasal tumors.
- Seizures, blindness, and behavioral changes may result from invasion of the central nervous system (CNS) by direct extension. CNS involvement has been reported in 20% of the cases and is more common in neuroendocrine tumors and neuroblastomas than in other tumors.

▼ ***Key Point*** Chronic nasal discharge unresponsive to antibiotic therapy is likely to be caused by neoplasia.

Diagnosis

Diagnostic Imaging

- Plain radiographs (occlusal, dorsoventral, open mouth ventrodorsal, lateral, frontal sinuses, and ventrodorsal views) may demonstrate loss of trabecular pattern, increase in soft tissue density, septal destruction or deviation, facial bone destruction, frontal sinus opacification, and/or periosteal bone formation (see Chapters 4 and 159). The open-mouth view is the most useful for evaluating the nasal cavity.
- Computed tomography (CT) or magnetic resonance imaging (MRI) are useful for evaluating the extent of the tumor and for planning radiation therapy.
- Thoracic radiographs are necessary to determine the possibility of distant metastasis to the lungs.

Cytologic and Histopathologic Studies

- Cytologic and/or histopathologic confirmation is diagnostic. Procedures (and their specific uses) include:
  - Antegrade rhinoscopy, often performed with a cystoscope or an arthroscope, can be used for viewing the tumor and for acquiring tissue for cytology, histopathology, and culture.
  - Retrograde rhinoscopy, using a retroflexed endoscope or dental mirror, can demonstrate tumors extending caudal to the posterior choane.
  - Nasal flushes can be used for cytologic identification (see Chapter 160 for technique)
  - Blind biopsy procedures, using a biopsy needle, alligator biopsy forceps, catheter, or polypropylene tube, can be used to obtain diagnostic specimens for cytology-histopathology (see Chapter 160)

▼ ***Key Point*** Premeasure nasal biopsy devices to avoid penetration of the cribriform plate.

- Rhinotomy and nasal exploratory surgery can be used for direct exposure of the tumor and to obtain larger biopsy specimens.
- Transnasal curettage (through nostril) can be used to obtain tissue specimens for cytology and histopathology.
- Lymph node aspirates helps to determine the possibility of metastasis to regional lymph nodes.

Treatment

Radiation Therapy

With radiation therapy, the entire nasal cavity, including the bone, can be treated (cobalt, linear accelerator). The dose and fractionation often used is 40 to 54 Gray (Gy) delivered in 10 to 18 fractions over 2 to 4 weeks.

- Radiation has been shown to increase survival times in dogs and cats with nasal tumors. Orthovoltage (due to low tissue penetration) may be effective only when combined with surgical cytoreduction.
- Brachytherapy (intracavitary radiation), using iridium-192, has been reported to treat nasal tumors. Potential problems are associated with this type of treatment and lower survival times are achieved compared with other forms of radiation.

Complications

The following post-treatment complications have been reported:

- Rhinitis and mucositis may be severe but usually subside within 2 months.
- Nasal discharge and sneezing may persist.
- Ulcerative dermatitis may occur at the irradiated site but generally resolves with topical treatment.
- Ocular complications may include keratoconjunctivitis sicca, corneal ulcers, uveitis, retinal degeneration, and cataract formation.

▼ ***Key Point*** To maximize survival times and reduce complications of radiation therapy, include CT or MRI with radiation therapy to provide optimal treatment fields and minimize exposure to normal tissues (e.g., eyes and brain)

Surgical Cytoreduction

Surgical cytoreduction alone or followed by radiotherapy has been reported, but a high rate of acute and chronic morbidity is also associated. In addition, because survival times for animals treated with surgical cytoreduction alone are similar to that for untreated animals, surgical cytoreduction is rarely indicated.

- Rhinotomy (nasal flap) with curettage or turbinectomy is the most common procedure (see Chapter 160)
- Radiation therapy after surgery is recommended.
- Surgery is the treatment of choice for nasal polyps.

Chemotherapy

- Chemotherapy may be effective in certain tumor types (see Chapter 26 for discussion of chemotherapy).
- Platinum drugs (cisplatin, carboplatin) have been shown to benefit some dogs with nasal carcinoma (response rate <25%), but with short median survival times.
- Single-agent therapy with dactinomycin, doxorubicin, and mitoxantrone has had variable results, but in general are not effective for adenocarcinomas.
- A combination COP protocol (vincristine, cyclophosphamide, prednisone), followed by a maintenance protocol is recommended after radiation therapy for nasal lymphoma in cats and dogs.
- Vincristine, as a single agent, is the treatment of choice for transmissible venereal tumors.

Prognosis

Prognostic factors include histologic type and tumor size. Survival times of 3 to 5 months have been reported for animals with no treatment.

- Prognosis for nasal polyps is good, but recurrence is possible.
- Median survival time for nasal tumors treated with radiation ranges from 8 to 25 months, with 1-year survival from 20% to 80% of the cases and 2-year survival from 10% to 48% of the cases.
- Dogs with chondrosarcomas treated with radiation therapy have longer median survival times than dogs with adenocarcinomas.
- Shorter survival times are reported for squamous cell carcinomas and undifferentiated carcinomas.
- Larger and more extensive tumors have a poorer prognosis than smaller tumors.
- In cats with nasal lymphomas, it has been reported that more than 40% can achieve 1 year and approximately 15% can achieve 2 years of survival.

NEOPLASMS OF THE LARYNX

Table 165-2 lists the types of laryngeal neoplasms seen in dogs and cats. These tumors are uncommon and are usually locally invasive; however, distant metastasis has been reported.

- Malignant neoplasms are more common than benign tumors.
- Oncocytomas, which are usually benign tumors, are the second most common laryngeal neoplasm in dogs. There is speculation that oncocytomas may be a form of rhabdomyoma.
- Feline laryngeal tumors include lymphoma, squamous cell carcinoma, and adenocarcinoma.

Table 165-2. NEOPLASMS OF THE LARYNX

Primary Malignant Tumors in Dogs
Squamous cell carcinoma
Lymphoma
Osteosarcoma
Melanoma
Mast cell tumor
Adenocarcinoma
Chondrosarcoma
Metastatic Tumors in Dogs
Thyroid carcinoma
Lymphoma
Pharyngeal rhabdomyosarcoma
Primary Malignant Tumors in Cats
Lymphoma
Squamous cell carcinoma
Adenocarcinoma
Benign Tumors in Dogs and Cats (Uncommon)
Unilateral polyps, generally inflammatory in origin
Oncocytoma* and rhabdomyoma
Leiomyoma

*The second most common laryngeal tumor in dogs. See text for description.

Signalment

- Laryngeal tumors occur in middle-aged to older animals (5–15 years) with the exception of oncocytomas or rhabdomyomas, which occur in young to middle-aged dogs (2–8 years).
- Males appear to be at increased risk.

History

- Noisy breathing and respiratory distress are the most common complaints reported.
- Exercise intolerance, change in voice, and loss of bark or purr may be noted by the owner.

Clinical Signs

- Inspiratory dyspnea and cyanosis usually occur when the animal is stressed. Laryngeal stridor is common on inspiration.
- Coughing due to aspiration pneumonia may occur secondary to laryngeal dysfunction.
- Palpable laryngeal masses are uncommon except for those patients with rhabdomyomas.

▼ ***Key Point*** Inspiratory dyspnea is the most common sign of laryngeal obstructive disease. Neoplasia must be differentiated from laryngeal paralysis, foreign body, or other upper airway disorder via laryngoscopy.

Diagnosis

- The history and physical findings may suggest laryngeal disease.
- Radiography may demonstrate laryngeal distortion, increased soft tissue density of the larynx, and decreased laryngeal space. Ultrasonography may be useful for identifying mass lesions or secondary functional problems such as laryngeal paralysis.
- Laryngoscopic evaluation (using a laryngoscope or endoscope) may reveal a laryngeal swelling or mass. Differential diagnosis for a mass on the vocal fold includes an inflammatory polyp.
- Biopsy for histopathology provides a definitive diagnosis. Biopsy with alligator biopsy forceps, needle biopsy instruments, or bronchoscopic biopsy forceps is usually successful in obtaining a diagnosis.

Treatment

Surgery

- Surgical excision may be curative if the tumor is benign, but is only palliative for malignant disease.
- Complete laryngectomy with a permanent tracheostomy (see Chapter 161) has been done rarely in veterinary medicine because of associated complications.

Radiation Therapy

Radiation may be beneficial in the treatment of some laryngeal tumors (e.g., mast cell tumor and lymphoma).

Chemotherapy

- Lymphoma usually responds to combination therapy (see Chapter 27) but little information is available concerning laryngeal lymphoma.
- Other tumors may respond to chemotherapy (mast cell tumors, some carcinomas, and grade 2 and 3 sarcomas).

Prognosis

The prognosis for most laryngeal tumors is guarded because advanced disease usually is present at the time of diagnosis. However, if tumors are benign (e.g., polyps, oncocytomas, or rhabdomyomas) the prognosis is good with surgical excision.

NEOPLASMS OF THE TRACHEA

Tracheal tumors are rare in dogs and cats. See Table 165-3 for common types of tumors.

Signalment

- Young animals are at higher risk for osteochondromas; these usually are benign.

▼ ***Key Point*** Tracheal tumors are rare. Consider them malignant in older animals.

History

- Exercise intolerance, panting, and cough may be present for weeks before presentation.

Table 165-3. NEOPLASMS OF THE TRACHEA

Malignant Tumors in Dogs
Osteosarcoma
Chondrosarcoma
Lymphoma
Mast cell tumor
Adenocarcinoma
Malignant Tumors in Cats
Adenocarcinoma
Lymphoma
Squamous cell carcinoma
Benign Tumors in Dogs and Cats
Osteochondroma (dogs)
Leiomyoma
Polyps
Eosinophillic granuloma (cats)
Nodular amyloidosis (dogs)

Clinical Signs

- Cough, usually non-productive, is the most common sign.
- Stridor, usually inspiratory, may be noticed during exercise or panting.
- Tumors located at the carina cause both inspiratory and expiratory respiratory distress.
- Cyanosis, dyspnea, and collapse may occur with severe obstruction.

Diagnosis

- Radiography may demonstrate a soft tissue density within the tracheal lumen or decrease in lumen size.
- Tracheoscopy/bronchoscopy may be needed to reveal a tracheal mass.
- Biopsy and histopathology are diagnostic.
- In young dogs, consider Oslerus (Filaroides) osleri in the differential diagnosis.

Treatment

Surgical Excision

Surgery is the primary treatment for tracheal masses (see Chapter 161)

- Benign lesions may be cured with surgical resection.
- Tracheal resection and end-to-end anastomosis are usually the most appropriate surgical treatments (see Chapter 161).

Chemotherapy

- Local laryngeal lymphoma in dogs and cats can be treated with surgery or radiation therapy followed by a chemotherapy protocol.

Prognosis

- Benign tumors respond well to surgical excision.
- Complete remission can be achieved with tracheal lymphoma using chemotherapy with or without radiation or surgery.

NEOPLASMS OF THE LUNG

Primary pulmonary neoplasms represent approximately 1.2% and 0.5% of all tumors in the dog and cat, respectively. Primary lung tumors may metastasize to bronchial lymph nodes, lung, brain, bone, and pleura via lymphatics, airways, blood vessels, and transpleural space. Metastatic neoplasms to the lungs are more common than primary pulmonary tumors in the dog and cat.

Paraneoplastic syndromes are rarely recognized in dogs and cats.

- Hypertrophic osteopathy is the most common paraneoplastic syndrome associated with lung masses and has been reported in 3% to 15% of animals with pulmonary neoplasia.
- Leukocytosis (neutrophilia or eosinophilia) is a paraneoplastic syndrome that may be related to some types of pulmonary carcinoma.
- Other paraneoplastic syndromes include neuromyopathy, hypercalcemia, and secretion of adrenocorticotropic hormone resulting in clinical signs of hyperadrenocorticism.

Table 165-4. PULMONARY NEOPLASMS

Primary Tumors in Dogs
Carcinoma
Bronchoalveolar adenocarcinoma
Squamous cell carcinoma
Bronchogenic carcinoma
Anaplastic carcinoma
Sarcoma
Fibrosarcoma
Hemangiosarcoma
Osteosarcoma
Round cell tumors
Lymphoma
Malignant histiocytosis or histiocytic sarcoma
Benign
Lymphomatoid granulomatosis
Eosinophilic granuloma
Adenoma
Fibroma
Primary Tumors in Cats
Carcinoma
Adenocarcinoma
Squamous cell carcinoma
Bronchogenic carcinoma
Sarcoma
Hemangiosarcoma
Fibrosarcoma
Round cell tumors
Lymphoma
Malignant histiocytosis or histocytic sarcoma
Benign
Bronchial adenoma
Hemangioma
Metastatic Tumors in Dogs and Cats
Mammary carcinoma
Osteosarcoma
Thyroid carcinoma
Transitional cell carcinoma
Melanoma
Hemangiosarcoma
Squamous cell carcinoma

▼ ***Key Point*** Pulmonary neoplasia is the most likely diagnosis in dogs with hypertrophic osteopathy.

Tumor Types (see Table 165-4)

Primary Pulmonary Neoplasm

Carcinomas are the most common primary lung tumors in dogs, being bronchial, bronchoalveolar and alveolar, and they are graded as differentiated and undifferentiated.

- Differentiated carcinomas have a lower rate of metastasis than undifferentiated carcinomas and squamous cell carcinomas.
- The rate of metastasis at the time of diagnosis is approximately 50% for undifferentiated carcinomas and 80% for squamous cell carcinomas.
- In one report (Hahn, 1997), feline lung tumors had a metastatic rate of 75%.

Metastatic Pulmonary Neoplasms

These tumors are more common than primary pulmonary neoplasms. Metastasis occurs by the spread of tumor emboli via lymphatics or blood vessels.

- Because of the capillary network in the lungs, these tumor emboli are trapped and may proliferate and form nodules.
- See Table 165-4 for a list of common metastatic tumors.

Pulmonary Lymphomatoid Granulomatosis

- This is a condition that affects young to middle-age dogs. The etiology is unknown.
- The disease responds to immunosuppressive drugs and, in general, has a better prognosis than primary lung tumors.
- The most consistent laboratory finding is leukocytosis, eosinophilia, and/or basophilia.
- Eosinophilic granulomas have a good prognosis using immunosuppressive drugs.

Signalment

- Pulmonary neoplasms occur in older animals (>10 years), except lymphomatoid granulomatosis, which occurs in young dogs (1–6 years).
- Most studies do not recognize a breed or sex predilection.
- Larger dogs (>10kg) may be at increased risk.

History

History may vary depending on the tumor type, size, and doubling time. Many dogs are asymptomatic, and pulmonary nodules are discovered during a medical workup.

Clinical Signs

- Approximately 25% of dogs have no clinical abnormalities.
- Cough (harsh, nonproductive) is one of the most common presenting signs in symptomatic patients. The duration is usually chronic. Occasionally, hemoptysis is also present.
- Dyspnea, tachypnea, and cyanosis may be present and associated with pleural effusion and/or diffuse disease.
- Decreased exercise tolerance is usually related to respiratory compromise.
- Less common signs include anorexia, fever, weight loss, dysphagia, vomiting, regurgitation, and hemoptysis.
- Halitosis may be noted by the owner or during clinical examination.
- Lameness may be associated with hypertrophic osteopathy or with skeletal muscle and/or bone metastasis.
- Cats may present with multiple swollen digits and lameness associated with metastasis from primary pulmonary tumors (adenocarcinomas and squamous cell carcinoma).

Diagnosis

Diagnostic Imaging

Routine thoracic radiographs usually establish the diagnosis of a mass lesion(s). However, approximately 11% of pulmonary neoplasms are missed in survey radiographs because of:

- The small size of the lesions (<5–10mm).
- Lack of tumor contrast with pulmonary parenchyma or tumor site in a hidden location (e.g., the subpleural space or paraspinal recesses).
- The presence of pleural fluid.
- Atelectasis of one or more lung lobes.

▼ ***Key Point*** The evaluation of three radiographic views (ventrodorsal, right, and left lateral) of the thorax is recommended when primary or metastatic pulmonary neoplasia is suspected. MRI or CT scans may allow the detection of occult masses or lymph node enlargement.

Radiographic Pattern

- The most common radiographic pattern seen in dogs and cats with primary lung tumors is a well-demarcated spherical or smooth-edged mass that usually is solitary. However, metastatic lesions can be seen as a single nodule.
- Other, less common patterns that can be seen in primary lung masses, but are more common in metastatic disease, are multiple circumscribed nodules, interstitial disseminated reticulonodular pattern, mixed disseminated alveolar pattern, and homogeneous lobar consolidation.

Other Diagnostic Signs

- Radiographic changes associated with pulmonary tumors include: pleural effusion, pleural thickening, and thoracic lymphadenopathy.
- Calcification and cavitation of masses have been associated with adenocarcinomas.
- The caudal lung lobes are the most common locations of primary pulmonary neoplasms.

Other Diagnostic Evaluations

- Percutaneous transthoracic fine-needle aspiration for cytologic evaluation can be useful in peripheral masses, but it is common to have a nondiagnostic sample. Transthoracic needle aspiration biopsy for histopathologic evaluation may provide a diagnosis in more than 50% of the cases, but an approximate mortality rate of 10% was reported in one study.
- Cytologic evaluation of tracheal wash fluid, bronchoalveolar lavage fluid, and pleural fluid may detect neoplastic cells in some cases.
- Bronchoscopy may be valuable in perihiliar masses that extend into the bronchus, permitting tissue biopsy.
- Exploratory thoracotomy (see Chapter 167) and biopsy provide a definitive diagnosis and aid in staging the tumor. Lobectomy may be curative for an isolated mass lesion without lymphatic metastasis.
- Thoracoscopy may be used for obtaining a diagnosis in the case of multiple pulmonary lesions.

Treatment

Surgical Excision

- Surgical excision by lobectomy is the treatment of choice for solitary lung tumors (see Chapter 167).
- Biopsy samples from regional lymph nodes can be obtained when possible.
- Adjunctive chemotherapy may improve survival in some cases in which metastasis or local invasion is present or when complete clean margins have not been achieved.
- Metastectomy is recommended in some circumstances (e.g., complete control of the primary tumor for a long period of time [>300 days], no other metastatic sites, slow doubling time, and less than three metastatic lesions).

▼ ***Key Point*** Always submit lung tumors for histopathologic evaluation to establish diagnosis and prognosis.

Chemotherapy

- Chemotherapy may be beneficial in some tumors, mainly if used as an adjunctive therapy.
- Lymphomatoid granulomatosis may respond to combination chemotherapy with prednisone, vincristine, and cyclophosphamide. Eosinophilic granulomas may respond to immunosuppressive doses of prednisone alone.
- Carboplatin and gemcitabine are two drugs used for adjunctive therapy for excised primary pulmonary tumors.
- Malignant pleural effusion can be treated with intrapleural chemotherapy. 5-fluoruracil is an inexpensive drug that can be used safely in dogs. Cisplatin is other drug that can be used in dogs but is nephrotoxic. Cisplatin and 5-fluoruracil are fatal if used in cats.
- Some metastatic tumors that are responsive to chemotherapy include hemangiosarcoma (VAC protocol; vincristine, doxorubicin, and cyclophosphamide), lymphoma (COP with or without doxorubicin or L-asparaginase), and some malignant histiocytosis (lomustine with prednisone). Specific protocols for these types of tumors are described in the literature.

Prognosis

- Factors that decrease survival time include large tumor burden, thoracic lymph node involvement, and other metastases. Absence of lymphatic invasion by the lung tumor has been associated with increased survival times.
- Small (<5cm), solitary primary lung tumors without metastasis or malignant effusion are associated with prolonged survival (>1 year). Even large lobar masses can be removed successfully with a reasonable (>6 months) survival time.
- In cats, based in the histologic grade, poorly differentiated tumors have a median survival time of 2.5 months and those tumors that are moderately differentiated without evidence of metastasis have a median survival time of 23 months after surgery.
- Following treatment, monitor with routine thoracic radiographs every 1 to 3 months.

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Chapter

166 Thoracic Trauma

Dale E. Bjorling

Thoracic trauma in dogs and cats most often is the result of automobile accidents. The lack of apparent external injuries may be misleading; the diaphragm, thoracic wall, heart, or lungs may be severely damaged with little apparent damage to the overlying skin. Evaluate animals presented for treatment of thoracic trauma thoroughly but rapidly; if necessary, institute treatment prior to completing a full patient assessment. Animals with thoracic trauma may suffer concurrent abdominal or skeletal injuries.

Surgical correction of injuries associated with thoracic trauma may be required on an emergency basis; however, in general veterinary practice it is preferable to avoid emergency surgery of animals suffering thoracic trauma unless absolutely necessary.

This chapter discusses the major disorders caused by thoracic trauma: pulmonary and myocardial contusions, pneumothorax, rib fractures and flail chest, hemothorax, and diaphragmatic hernia; see Chapter 164 for discussion of chylothorax.

Injuries to abdominal viscera are discussed in respective organ-system chapters.

ETIOLOGY

Blunt Trauma

- Blunt trauma to the thoracic cavity usually is the result of automobile accidents. It may also be the result of being kicked by a human or farm animal (horse, cow), being struck by a heavy object, or falling from heights (e.g., falling from a window of a high-rise building).
- The severity of injury depends on the mass of the object delivering the blow, the velocity of the object, and the area to which the blow is delivered. It has been shown experimentally that when a blow equivalent to that delivered by a car is administered to the thorax of anesthetized dogs, the thoracic viscera may be compressed until the opposing parietal pleural surfaces underlying the ribs may almost be brought into contact. The ribs of young animals are pliable and tend to fracture less often than those of older animals.
- Blunt trauma can cause pneumothorax, hemothorax, pulmonary contusions, fractured ribs, or any combination of these.

Penetrating Trauma

- Penetrating trauma usually is the result of a gunshot. It may also result from a sharp instrument (e.g., a knife, screwdriver, stick, or arrow) or from deep bite wounds inflicted by a big dog on a smaller dog or cat.
- Consider the type of projectile, point of entry, and path of the penetrating object when attempting to diagnose thoracic trauma, even if wound entry is distant to the thoracic cavity. The path of a projectile may be altered if it strikes bony structures.
- It is often unclear whether thoracic injuries have resulted from penetrating wounds. Depending on the extent of injury, signs of cardiovascular collapse or respiratory distress may develop more slowly in patients suffering penetrating injuries of the thorax.
- In at least one study, mortality subsequent to bite wounds only occurred with thoracic or abdominal trauma, and exploratory thoracotomy failed to improve survival.

CLINICAL SIGNS

- *Tachypnea or dyspnea* (difficulty breathing) is a typical presenting sign in dogs and cats that suffer thoracic trauma. The animal may have an anxious or distressed appearance. The owner may or may not have observed the injury. Clinical signs of thoracic trauma may be delayed in onset, especially those associated with diaphragmatic hernia.
- *Hypovolemic shock* may result from internal or external hemorrhage or accumulation of fluid within tissue spaces. An animal suffering from hypovolemic shock has an increased heart rate, weak peripheral arterial pulses, cold extremities, and pale mucous membranes, and it often appears depressed or stuporous (see Chapter 156 for further discussion of shock).
- *Gastrointestinal signs* (diarrhea or vomiting due to obstruction) may be observed if a portion of the gastrointestinal tract has been displaced into the tho-

racic cavity through a diaphragmatic hernia. These signs are not commonly present immediately after the injury has occurred.

DIAGNOSIS

▼ ***Key Point*** Treatment of hypovolemic shock or other life-threatening disorders takes precedence over patient evaluation.

History

- Attempt to identify recent or past traumatic episodes.
- Question the owner regarding the onset and progression of the current clinical signs.
- Take the history while initial evaluation of vital signs is in progress so that life-threatening injuries (e.g., tension pneumothorax) can be detected and treated immediately.

Physical Examination

After initially determining the animal's vital signs (e.g., heart rate, respiratory rate, mucous membrane color and refill, temperature, and level of consciousness), examine the respiratory system using the following:

- Observation (of breathing)
- Palpation
- Auscultation
- Percussion
- Radiography

Observation

- Observe the rate, depth, and effort of respirations.
- Rapidly developing dyspnea usually is the result of pneumothorax, pulmonary contusion, or hypovolemia.
- Rapid, shallow, choppy breathing can result from restriction of the thoracic wall because of painful rib fracture.
- Paradoxical motion of the chest wall is caused by collapse of a portion of the rib cage on inspiration when multiple rib fractures create an unstable flail chest wall.
- Decreased hemithorax movement (fixation) can be seen on the side into which abdominal viscera have herniated through a ruptured diaphragm.
- Herniation of the lung into the intercostal space countercurrent with each respiration indicates torn intercostal muscles.

Palpation

- Palpate the thoracic wall for rib fractures, unstable (flail) segments, hematomas (usually adjacent to rib fractures), subcutaneous emphysema (crepitus), intercostal muscle tears (usually under intact skin), and abnormal location of the cardiac apex beat (displaced by herniation of abdominal viscera).
- Also palpate the abdominal cavity for concurrent intra-abdominal injuries. The absence of viscera suggests their displacement into the thoracic cavity.

Auscultation

- Carefully auscultate the entire thoracic cavity to determine whether breath sounds can be identified throughout the thoracic cavity. The absence of respiratory sounds strongly suggests displacement of the lungs by air, fluid (e.g., blood), or abdominal viscera. Crackles suggest intrapulmonary fluid accumulation.
- Auscultate the heart as well. A change in the location or pitch of heart sounds suggests displacement of the heart by air, fluid, or viscera. Ventricular arrhythmias may occur as the result of traumatic myocarditis or myocardial ischemia; however, their onset is more frequently observed 24 to 48 hours after the traumatic episode.
- See also Chapter 142.

Percussion

- Perform percussion of the thoracic wall to determine increased or decreased resonance. By placing one hand flat on the thoracic wall and tapping the knuckle of the middle finger with a percussion hammer or the tips of the fingers of the opposite hand, a sound of consistent frequency is produced in normal animals.
- In animals with air or air-filled viscera underlying the thoracic wall, the pitch is deeper and more resonant, whereas the sound produced in animals with fluid or solid viscera immediately under the thoracic wall is dull and less resonant.
- Percussion aids detection of pneumothorax, pleural effusion (e.g., hemothorax and chylothorax), diaphragmatic hernia, and consolidation of lung lobes.
- Skilled use of this technique requires frequent practice on normal animals to allow a distinction between normal and abnormal sounds.
- See also Chapter 142.

Fractures

- Thoracic injuries may occur in more than 30% of dogs and cats sustaining traumatic fractures.
- Examine the animal for the presence of fractures; do not be distracted by the obvious presence of broken bones but continue searching for evidence of more serious internal injuries.
- If spinal fractures are suspected, handle the animal with great care until these have been stabilized or it is determined radiographically that the spine is intact.
- The presence of fractures suggests that trauma of sufficient force to inflict injury to the thorax and its con-

tents has occurred. A survey of dogs injured in motor vehicle accidents found that more than 50% of animals with intrathoracic injuries also had fractured bones.

Surface Wounds and Abrasions

- Clip hair from the thoracic wall area as necessary to identify abrasions, bruises, or wounds that may point to likely sites of intrathoracic injury.
- Open wounds that freely communicate with the pleural space can cause progressive pneumothorax; unless the animal is stable, seal these immediately.

Thoracic Radiography

Take radiographs to evaluate the heart, lungs, pleural space, and thoracic wall (see Chapters 143 and 159 for a discussion of thoracic radiography).

- It is sometimes advisable to delay thoracic radiography of the injured animal until after higher priority conditions such as shock have been stabilized by emergency treatment. Pulmonary contusion, characterized by hemorrhage and fluid accumulation within the lungs, may not reach its greatest extent for 6 to 12 hours and then often may not appear radiographically to be improved for 7 to 10 days after injury.

▼ ***Key Point*** The full severity of pulmonary contusions may not be apparent on thoracic radiographs made within 1 to 2 hours of injury.

- A narrowed cardiac silhouette may suggest hypovolemia.
- Evaluate the pleural space carefully for fluid, air, or abdominal viscera, and evaluate the integrity of the diaphragmatic outline.
- Look for radiographic evidence of fracture or dislocation of skeletal structures and subcutaneous emphysema, which indicates leakage of air into the subcutaneous space from the environment, the thoracic cavity, or a major airway.
- Pneumomediastinum is seen as air outlining the mediastinal contents and is indicative of tracheobronchial rupture.
- If the animal's condition does not preclude this, obtain two radiographic projections.
- Often it is difficult to identify a diaphragmatic hernia on thoracic radiographs, particularly if obscured by accumulation of fluid within the pleural space. If a large quantity of pleural fluid is present, remove it and repeat the radiographs (see Chapter 159) or obtain an ultrasound examination, if readily available.
- Observations suggesting a diaphragmatic hernia include cranial displacement of the stomach, the loss of the caudal outline of the liver, and the presence of gas-filled viscous organs within the thoracic cavity.
- If a diaphragmatic hernia is suspected but unconfirmed by plain radiographs, consider positive-contrast celiography or abdominal ultrasonography (see Chapter 4).

Thoracocentesis

If indicated, perform thoracocentesis to obtain a sample of pleural fluid or to drain air from the pleural space (see Chapter 3 for technique).

- Analyze the fluid for the presence and concentration of red blood cells (RBCs) and plasma protein. The fluid may be whole blood, or it may be a combination of transudate, exudate, chyle, and blood, depending on the severity and duration of injury and the organs affected.
- Centrifuge an aliquot of the fluid and examine the cellular portion microscopically for degenerative neutrophils, bacteria, and organic matter (see Chapter 164). These findings may suggest a severe inflammatory process and possibly perforation of the esophagus or gastrointestinal tract.
- On rare occasions, the biliary tract may be ruptured in the presence of diaphragmatic hernia, and this can be identified by determining the concentration of bilirubin within pleural fluid. Biliary-pleural fistula has also been reported secondary to gunshot in a dog.

Blood Samples

- Draw blood and store the sample in anticoagulant and serum tubes (preferably before initiating treatment), unless analyzed immediately.
- Although these samples may not be needed, it is often helpful to determine the biochemical status of the animal at the time of hospital admission when attempting to distinguish between preexistent disease and that which has developed acutely after injury. These same considerations apply to the collection and storage of urine samples.

Packed Cell Volume and Plasma Protein Concentration

- Determine the packed cell volume (PCV) and plasma protein concentration (PPC) as soon as possible after the initial examination.
- It is critical to record these values because the diagnosis of continuing hemorrhage often relies on comparison of serial determinations of PCV and PPC.
- If hemorrhage is ongoing, these two values continue to decline at a similar rate. If, however, hemorrhage has ceased, it is not uncommon for the PPC to stabilize while the PCV continues to decline.
- The administration of IV fluids may further decrease these values; consider this when evaluating these parameters.

Arterial pH and Blood Gas Tensions

- These values give an indication of ventilatory function and gas exchange.
- Satisfactory oxygenation of the blood by the lungs requires adequate cardiac output, and decreased cardiac output caused by hypovolemic shock or depressed cardiac function may profoundly affect blood gas values.

Electrocardiography

- If available, obtain serial electrocardiograms to check for arrhythmias associated with myocardial injury.
- If electrocardiography is not available, closely monitor the animal's heart rate and rhythm and the occurrence of pulse deficits.

TREATMENT

Modify treatment to suit the individual needs of each trauma patient. Place and maintain at least one IV catheter for administration of fluids and drugs early in the course of treatment. In severely traumatized animals, place two IV catheters (one may be a central venous line) to allow more rapid infusion of IV fluids.

When confronted with a seriously injured animal, it is often difficult to develop a logical, disciplined treatment plan. The airway, breathing, and circulation (ABC) approach is a consistent, comprehensive plan for initial treatment of animals with thoracic trauma.

Airway, Breathing, and Circulation Approach

Airway

Be sure that the animal has a patent airway.

- Remove debris from the trachea and bronchi by forceps or suction or by passing an endotracheal tube.
- If the pharynx, larynx, or cranial portion of the trachea is severely damaged, consider performing a tracheostomy (see Chapter 3).

Breathing (Spontaneous or Assisted) and Oxygen Therapy

Restore thoracic wall integrity by sealing open ("sucking") chest wounds with an occlusive dressing and stabilizing flail segments so that the animal can ventilate effectively. Fluid and air should be removed from the pleural space. If the animal is not able to ventilate satisfactorily, institute assisted breathing.

- Assisted breathing requires an endotracheal or tracheostomy tube and may necessitate anesthetizing the animal or giving neuromuscular blocking drugs to paralyze the animal (see Chapter 2).
- Supplemental oxygen may be provided by an incubator or oxygen cage, face mask, nasal catheter (see Chapter 3), transtracheal cannula or catheter, or endotracheal or tracheostomy tube.
- When supplemental oxygen is administered to the animal in such a manner that it does not pass through the nasal passages, prewarm and humidify the air.
- A transtracheal catheter may be placed using a large-gauge (12–18) jugular catheter passed between the rings of the trachea.
- Secure the catheter to the skin and attach to the oxygen source. Deliver oxygen via the transtracheal catheter at an initial rate of 10 to 20 ml/kg/min.

Circulation

If myocardial function is satisfactory, administer IV fluids as needed to increase the circulating blood volume and cardiac output.

- In most cases of hypovolemic shock, administer a blood volume of IV fluids (90 ml/kg in dogs and 65 ml/kg in cats) as rapidly as gravity flow allows.
- In the presence of significant ongoing hemorrhage, fluid bags may be pressurized to increase the rate of administration.
- After the rapid infusion of a bolus of IV fluids equivalent to one blood volume, reassess the status of the patient and determine the need for ongoing fluid administration.
- If signs of hypovolemic shock have abated and hemorrhage has ceased, continue to administer fluids at a rate of 30 to 50 ml/kg q24h (see Chapter 156).
- If the animal's condition does not stabilize, continue rapid fluid administration.
- Auscultate the lungs for evidence of pulmonary edema and carefully monitor for other signs of edema (e.g., tachypnea, chemosis, tearing, tissue swelling, decreasing PCV and PPC).
- If necessary, monitor the central venous pressure (CVP) to determine the ability of the right side of the heart to eject the volume of blood presented to it (see Chapter 3 for CVP techniques). The relative change in CVP is more significant than the absolute value, and an increase of 7 to 10 cm of water indicates that the rate of fluid administration should be slowed.
- Because the low oncotic pressure of crystalloid fluids may contribute to fluid loss into the tissue space, a general rule for replacement of blood loss by crystalloid fluids is as follows:
  - For every 1 ml of blood lost, administer 3 ml of crystalloid fluid.

Pleural Space Drainage

- The pleural space may be drained intermittently by thoracocentesis using a hypodermic needle.
- If continuous or prolonged pleural drainage for removal of fluid or air is required, place a thora-

costomy tube (see Chapter 3 for thoracic drainage techniques).
- Attach thoracostomy tubes to a three-way stopcock to allow intermittent aspiration of the tube (e.g., q2–4h) or to a continuous suction device.
- If continuous suction is used, carefully control the negative pressure; it should not be less than −5 to −10 cm of water.
- Alternatively, attach the thoracostomy tube to a Heimlich one-way flutter valve.
  - If using this valve, carefully monitor the animal for complications.
  - Be aware that if the valve becomes cracked or the valve's diaphragm becomes wet, the one-way function of the valve may be lost and severe pneumothorax may develop.
  - This valve is available in two sizes, and animals weighing <10 kg frequently may be incapable of activating the larger valve, resulting in continued accumulation of air within the thoracic cavity.
- If fluid or air cannot be aspirated from the thoracostomy tube, the pleural space may be completely evacuated or the tube may be obstructed by a fibrin clot or by the tube bending on itself. Obtain thoracic radiographs and flush the tube with sterile saline to confirm patency.

Tube Removal

- Remove the tube when it is no longer needed.
- An indwelling thoracostomy tube results in continued production of a small volume of fluid (at least 3 ml q24h in a dog weighing 25 kg).
- It also is possible that a small volume of air may continue to accumulate within the pleural space due to air migration along the external surface of the chest tube or through leaks in the tubing.
- Therefore, it is often not possible to wait until there is no air or fluid accumulation within the thorax to remove the thoracostomy tube, and the tube usually is removed when the volume of air and fluid removed has reached insignificant amounts.

Treatment of Pneumothorax

Pneumothorax can be closed or open; in *closed* pneumothorax, the most common type, air escapes from the injured lung or airway into the pleural space; in *open* pneumothorax, air enters the pleural space through an open wound in the chest wall (e.g., bites, sharp objects, and projectiles).

Simple Pneumothorax

Accumulation of air in the pleural space that is not progressive is termed *simple pneumothorax* and is a common complication of thoracic trauma.

- Conservative treatment with thoracic drainage and cage rest usually is adequate. The air leak usually seals itself within hours, and residual intrapleural air is reabsorbed within a few days.
- Occasionally, oxygen therapy may be needed as initial treatment in animals that are severely dyspneic on presentation until the pleural space can be evacuated.
- Simple pneumothorax frequently is accompanied by other thoracic problems, such as pulmonary contusions and rib fractures, that can combine to cause serious problems with ventilation.

Tension Pneumothorax

Laceration of the lung, bronchus, or trachea may result in *tension pneumothorax,* the progressive accumulation of air in the pleural space that results in positive intrapleural pressure.

▼ ***Key Point*** Animals with tension pneumothorax need immediate life-saving thoracic drainage via a needle or thoracostomy tube to prevent lung collapse, decreased systemic venous return to the heart, and rapid death. This reestablishes negative intrapleural pressure and allows lung reexpansion.

- Intermittent thoracic drainage may not be adequate to allow proper ventilation, and continuous suction drainage frequently is necessary. In this case, connect the thoracic tube to a suction drainage unit such as Pleur-Evac (Deknatel, Fall River, MA).
- Consider exploratory thoracotomy (see later discussion in this chapter; also see Chapter 167) if the patient's condition fails to stabilize.

Treatment of Pulmonary Contusions

A pulmonary contusion is analogous to a bruise, with disruption of the tissues and capillaries resulting in extravasation of blood and accumulation of fluid within the pulmonary parenchyma. As mentioned previously in the discussion of IV fluid administration, aggressive fluid therapy may result in fluid accumulation within the lungs. This most likely is the result of decreased plasma oncotic pressure. IV infusion of the equivalent of one blood volume of crystalloid fluids over the course of 1 hour does not increase the extent of experimentally created pulmonary contusions in dogs. It is unlikely that IV fluid administration will increase fluid accumulation within pulmonary contusions unless the PPC is <3.0 g/dl or the plasma albumin concentration is <1.5 g/dl.

- Transfusions of plasma or whole blood or administration of colloid (hetastarch) helps maintain plasma oncotic pressure.
- Corticosteroids (2–4 mg/kg of dexamethasone phosphate or 30 mg/kg of methylprednisolone sodium succinate) may be useful in limiting the severity of pulmonary contusions if administered soon after injury.

- Diuretics have been recommended to remove excess water and limit the severity of contusions; however, diuretics may act to reduce total body fluid when volume expansion is critical to resuscitate the patient.
- Administer antibiotics to animals with pulmonary contusions to minimize the potential for development of bacterial pneumonia (antibiotic therapy for patients with thoracic trauma is discussed at the end of this chapter).
- In animals that are recumbent, frequent repositioning may help prevent hypostatic congestion, atelectasis, and pneumonia.
- Administer oxygen to treat or prevent hypoxemia.
- Bronchodilators (e.g., aminophylline at a dosage of 6–10 mg/kg q8h PO, IM, or IV in dogs and 6.6 mg/kg q12h PO in cats) may improve ventilation by keeping airways open.
- Closely monitor animals with moderate to severe contusions. If deterioration of respiratory function continues despite the above-mentioned measures, positive-pressure assisted ventilation may be necessary.

Treatment of Myocardial Contusions

Administration of corticosteroids as described for treatment of pulmonary contusions may be beneficial in the treatment of myocardial contusions, but the efficacy of any form of treatment is uncertain.

- Monitor ventricular arrhythmias (see Chapter 145) that develop as a result of traumatic myocarditis by continuous electrocardiography and treat initially with IV administration of lidocaine (2 mg/kg boluses to a maximum of 8 mg/kg/hour).
- If lidocaine therapy is effective but a constant infusion is required, administer lidocaine at a rate of 50 to 80 µg/kg/minute. Adjust the rate to achieve the desired effect.
- Procainamide may also be given (8–20 mg/kg q8h IM, 10–20 mg/kg q6h PO, or 20–50 mg/kg q8h extended release PO).
- See Chapter 145 for treatment of cardiac arrhythmias.

Treatment of Hemothorax

Hemothorax (blood accumulation in the pleural space) occurs secondary to any form of trauma that causes laceration of blood vessels, heart, lung, or thoracic wall (diseases other than trauma can cause hemothorax and are discussed in Chapter 164). Hemothorax causes two major problems: hypovolemic shock and impairment of ventilation. Massive hemorrhage from rupture of the heart or one of the great vessels usually causes rapid death.

- Treatment of traumatically induced hemothorax involves aggressive and rapid supportive care consisting of IV fluids and/or blood transfusions and pleural drainage (see Chapter 156 for details of treatment of hypovolemic shock).
- Consider autotransfusions for animals with significant hemothorax not complicated by an infectious or neoplastic process in the thorax.
- Aseptically collect the blood via a chest tube and return to the patient using a blood administration set.
- Closely monitor the patient's vital signs, PCV, and PPC.
- Consider exploratory thoracotomy for animals that fail to stabilize (see subsequent discussion in this chapter). However, surgical treatment of hemothorax may be unsuccessful because the source of hemorrhage is sometimes not identifiable.

Stabilization of Rib Fractures and Flail Chest

▼ ***Key Point*** Stabilization of rib fractures is required when a gross deformity has occurred, displacement of the fragments results in ongoing damage to the underlying viscera, or displacement or instability of the fragments interferes with ventilation (e.g., flail chest).

- Potential complications of rib fractures include the following:
  - Pneumothorax (from lung laceration by the sharp end of a fragment)
  - Pulmonary contusions
  - Hemothorax (bleeding from torn intercostal vessels, lacerated lung, or exposed rib marrow cavity)
  - Unstable chest wall (flail chest)
- *Flail chest* occurs when two or more adjacent ribs are fractured or dislocated both dorsally and ventrally, resulting in paradoxical movement of a segment of the thoracic wall during respiration. This may diminish lung volume and damage underlying viscera as the flail segment is displaced during respiration.
- Rib fractures may be stabilized by open fixation using pins and wires.
- Alternatively, secure the ribs to an external frame by percutaneous placement of sutures around the ribs (this procedure has been used successfully to stabilize flail chest).
- Place a frame made of malleable rodding used to construct splints and contour to the normal curvature of the thoracic wall. Bars pass over the dorsal and ventral aspects of the flail segment. Place at least two sutures around the ribs of the flail segment, dorsally and ventrally, and tie to the frame to displace the flail segment in a lateral, or outward, direction (Fig. 166-1). Alternatively, tongue depressors or other stiff materials of sufficient length to span the flail segment can be used to stabilize the damaged ribs.
- Damage to the underlying lung tissue usually does not occur during passage of the suture needle around the rib because of the presence of pneumothorax.

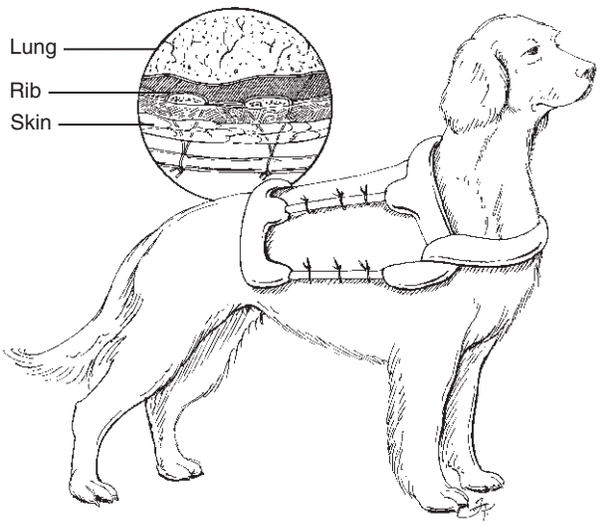

Figure 166-1. Fractured ribs can be secured to an external frame contoured to the body wall. Place sutures around the ribs dorsally and ventrally and tie them around the bars of the frame. (Redrawn from Bjorling DE, DeNovo RC, Kolata RJ: Flail chest: Review, clinical experience, and new method of stabilization. J Am Anim Hosp Assoc 18:269, 1982.)

Minimize the risk of potential damage to the underlying lungs by grasping a rib with a towel forceps and retracting the flail segment laterally.

- Keep the frame in place for at least 3 weeks.
- Do not apply tight bandages for stabilization of rib fractures because this displaces the ribs medially, resulting in continued damage to the underlying viscera and in healing of the ribs in such a position that lung volume is permanently decreased.
- Adjunctive therapy for rib fracture includes analgesia and intercostal nerve blocks to control pain (see Chapter 6), thereby promoting uninhibited cough and deeper, less restrictive breathing that helps prevent hypoventilation, atelectasis, retained secretions, and pneumonia.

Treatment of Open Chest Wounds

- Immediate treatment of open chest wounds consists of minor cleansing of the wound and application of a bandage to restore continuity of the chest wall.
- The defect in the chest wall should not be closed without treating associated pneumothorax with thoracocentesis or chest tube.
- Allow small penetrating wounds to heal as an open wound (if air is not leaking into the pleural space), or they may be explored, debrided, and sutured. Surgically explore, debride, and close large open wounds of the thoracic wall.
- It may be necessary to remove ribs that are devoid of musculature and vascular supply.
- Up to four adjacent ribs can be removed and the thoracic wall can be closed by apposing the remaining ribs.
- Larger defects require implantation of synthetic mesh (e.g., polypropylene) to compensate for the tissue lost.

Diaphragmatic Hernia Repair

Some hernias remain undetected for months or years before signs of pleural effusion, weight loss, gastrointestinal dysfunction, or jaundice occur (see Chapter 159 for radiographic diagnosis of diaphragmatic hernia).

- Minor perforations of the diaphragm usually seal without treatment.
- Surgically repair diaphragmatic defects (most can be closed by suture) that result in displacement of viscera into the thoracic cavity (see "Technique"). The liver, spleen, omentum, and gastrointestinal tract commonly are herniated.
- Timing of diaphragmatic hernia repair depends on the patient's condition.
- It is preferable to delay diaphragmatic hernia repair until the patient has stabilized; however, if respiratory function cannot be stabilized despite aggressive supportive care, it may be necessary to repair the diaphragmatic hernia on an emergency basis.

▼ ***Key Point*** Acute dilatation of herniated stomach or strangulation of herniated bowel requires emergency correction of a diaphragmatic hernia.

Surgical Procedure

Objectives

- Maintain pulmonary function by positive pressure ventilation during anesthesia and surgery.
- Replace viscera to the abdomen cavity.
- Inspect lungs, other thoracic viscera, and abdominal viscera for evidence of trauma.
- Repair the diaphragmatic defect with a monofilament absorbable suture.

Equipment

- Standard general surgical instrument pack and suture (plus various sizes of polydioxanone PDS)
- Long-handled instruments for deep-chested dogs
- Balfour and malleable retractors
- Thoracic drain tube and connectors

Technique

1. Keep the animal on mechanical ventilation throughout the repair.
2. Approach the diaphragm through a ventral midline abdominal incision.
3. Initially, it may be necessary to enlarge the diaphragmatic rent to reduce the herniated viscera. If so, make the incision ventrally to simplify repair.
4. Chronic diaphragmatic hernias are more commonly associated with formation of adhesions between

abdominal and thoracic viscera, and it has been observed that it may be necessary to perform a caudal median sternotomy to free abdominal viscera of adhesions from the lungs, mediastinum, and visceral pleura. If adhesions are extensive, a portion of the lungs or liver may have to be resected to allow repair of the hernia.

5. Following reduction of displaced organs and examination of the lungs and pleural space, close the rent with synthetic absorbable or monofilament nonabsorbable suture (simple continuous or horizontal mattress pattern).
6. Begin with the most dorsal aspect of the hernia and work ventrally to close the repair.
7. Grasp large "bites" of the abdominal wall musculature or ribs when suturing a diaphragm that has avulsed from the ventrolateral body wall. Identify and avoid the caudal vena cava.
8. If large portions of diaphragm have been destroyed, repair the defect with synthetic mesh or transposition of a transversus abdominis muscle flap, although this is rarely required.
9. Place a thoracostomy tube to remove air and fluid after surgery prior to closure of the diaphragmatic defect.

Postoperative Care and Complications

- Remove the thoracostomy tube when it is no longer needed.
- Advise the owner to limit the patient's activity for 2 to 4 weeks.
- Complications are rare and the prognosis usually is good.
- Reexpansion pulmonary edema rarely develops (more often in cats) and is characterized by fulminant pulmonary edema immediately after reexpansion of the lung lobes. Treat with diuretics and oxygen.

Exploratory Thoracotomy

Thoracotomy for treatment of ongoing hemorrhage or air leakage on an emergency basis is difficult and may be unrewarding. Exploratory thoracotomy failed to improve survival of dogs that sustained thoracic bite wounds. The animal is at significant risk due to the effects of anesthesia, and often it is difficult to identify and effectively treat the site of hemorrhage or air leakage.

- Before undertaking an exploratory thoracotomy, be sure that adequate equipment and personnel are available to successfully complete the procedure.
- Perform exploratory thoracotomy for treatment of traumatic injuries of the thoracic cavity only after aggressive medical therapy and thoracic drainage have failed to stabilize the animal's condition.
- If the site of injury can be identified, a lateral thoracotomy approach may be used (see Chapter 167). Unfortunately, this rarely is possible.
- A median sternotomy approach (splitting the sternum) allows exploration of both sides of the thorax (see Chapter 167).

Antibiotic Therapy

- Administer antibiotics to prevent the following:
  - Development of bacterial pneumonia resulting from traumatic injuries of the lungs
  - Wound infection as a result of disruption of the thoracic wall
- Initially give antibiotics intravenously to establish satisfactory tissue concentrations. This can be followed by oral administration of antibiotics.
- Prophylactic antibiotic treatment for pulmonary injuries should provide broad-spectrum antibacterial activity. A satisfactory combination is cefazolin (20 mg/kg q8h IM or IV) and gentamicin (2–4 mg/kg q12h or 4–8 mg/kg q24h SC, IM, or IV) or ampicillin (20 mg/kg q8h IM or IV) and enrofloxacin (5–10 mg/kg q12h PO or IM).
- Wound infections due to contamination of tissues with dirt most often are caused by gram-positive bacteria. Cephazolin or other cephalosporin antibiotics have good activity against the most common organisms involved.

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Chapter

167 Principles of Thoracic Surgery

Stephen J. Birchard / Eric R. Schertel

Thoracic surgery frequently is performed in small animals for a variety of disorders, especially in referral centers. Thoracotomy is commonly performed to correct routine cardiovascular defects such as patent ductus arteriosus and to evaluate and correct respiratory diseases such as pulmonary neoplasia. Exploratory thoracotomy may be indicated to determine the extent of diseases such as neoplasia and diffuse infection and to obtain biopsies to help establish a definitive diagnosis. It is important to be well versed in the anatomy and physiology of the thoracic cavity and its major structures and to be familiar with the principles of anesthetic management of the thoracic surgery patient.

Recently, minimally invasive thoracic exploratory (thoracoscopy) has become an alternative to traditional methods of thoracic surgery in veterinary medicine. Thoracoscopy requires specialized instrumentation and expertise, generally limiting its users to surgical specialists. Refer to the clinical literature and appropriate texts if more information on thoracoscopy is desired.

This chapter discusses surgical anatomy and physiology of the thorax, thoracic surgical technique, and patient care before, during, and after thoracic surgery.

SURGICAL ANATOMY

Bony Structures

- The bony structures of the thorax usually consist of 13 pairs of ribs and costal cartilages, 13 vertebrae, and 8 sternebrae.
- The first 9 ribs, called the sternal ribs, articulate with the sternum. The last 4 ribs are called the asternal ribs. The costal cartilages of ribs 10 to 12 make up the costal arch. The 13th pair of ribs is also called the floating ribs.
- The manubrium is the most cranial aspect of the sternum, and the xiphoid is located caudally. The xiphoid cartilage is the caudal extension of the xiphoid. Intersternebral cartilages are located between each sternebra. The sternebrae are very narrow structures, making midline division somewhat difficult. The sternebral midline is characterized by a slight bony ridge.

Soft Tissues

Muscles

- The external and internal intercostal muscles are located between each rib.
- Other surgically important muscles of the lateral thoracic wall are the serratus ventralis and serratus cranialis dorsalis, the scalenus, and the external abdominal oblique. The latissimus dorsi, a large, fan-shaped muscle extending from the ribs to the forelimb, is the first major muscle encountered during lateral thoracotomy.

Vessels and Nerves

- The intercostal arteries, veins, and nerves are located on the caudal aspect of each rib. The internal thoracic artery and veins run horizontally just lateral to the sternum, within the thorax.
- The cutaneous and muscular branches of the thoracodorsal artery are frequently encountered during lateral thoracotomy.

PREOPERATIVE CONSIDERATIONS

History, Physical Examination, and Diagnostic Tests

- Review the animal's history and perform a thorough physical examination.
- Give special consideration to the patient's cardiopulmonary status (mucous membrane color and refill time, heart rate and rhythm, pulse rate and character, heart and lung sounds, ventilation, thoracic palpation and percussion).
- Review diagnostic tests already performed and repeat if necessary.
- Evaluate thoracic radiographs and other diagnostic images to become familiar with the animal's disease and to plan the surgical approach. Thoracic ultrasound may assist in planning the surgical approach. Advanced imaging (computed tomography, magnetic resonance imaging) may be of benefit in selected cases.

- Evaluate blood tests, such as the complete blood count (CBC) and serum chemistry profile, to establish the patient's baseline before surgery. If the condition is severe, blood gas analysis may be helpful to further evaluate the patient's respiratory status.

Preoperative Treatment and Stabilization

General Supportive Care

- Closely observe the patient's condition. The clinical states of animals with thoracic disease may change rapidly.
- Administer appropriate medical therapy that will stabilize the animal and reduce the level of anesthetic and surgical risk.
  - For example, if a dog with patent ductus arteriosus is in congestive heart failure, treat with the appropriate drugs to improve cardiopulmonary function before anesthesia and surgery.
  - Correct fluid and electrolyte deficiencies.
- Maintain the animal's nutritional status. Consider placing a nasogastric, esophagostomy, or percutaneous endoscopic gastrostomy (PEG) tube if the animal will not eat and is becoming debilitated (see Chapter 3).

Thoracic Drainage

- If pleural fluid or air is present, perform thoracentesis before anesthesia to allow better ventilation (see Chapter 3).
- Place an indwelling thoracic drainage tube if fluid or air accumulation is recurrent (see Chapter 3).
- Use intermittent or continuous suction drainage.
- Quantify the amount of fluid or air recovered to establish a baseline before surgery.

Oxygen

- Administer oxygen to severely dyspneic or cyanotic animals.
- Place the animal in an oxygen cage with a 40% to 50% concentration or place a nasal oxygen tube to raise the concentration of inspired oxygen (see Chapter 3).
- If possible, analyze blood gases before and after oxygen administration to establish its effectiveness. Pulse oximetry may be useful as well.

Prophylactic Antibiotics

- Use prophylactic antibiotics if the planned operation will be a clean-contaminated, contaminated, or "dirty" procedure.
- Thoracotomy to open and/or resect a portion of the respiratory tract is considered a clean-contaminated procedure. However, we use prophylactic antibiotics only if there is a strong suspicion that contamination of the surgical field will occur (e.g., foreign bodies, abscess, necrotic tumor, or bacterial pneumonia). Thoracotomy for drainage and resection of the pericardium for pericarditis is an example of an indication for preoperative use of antibiotics.
- Administer the prophylactic antibiotic immediately before surgery to ensure sufficient blood concentrations of the drug at the time of surgery. Discontinue antibiotic administration 24 to 48 hours postoperatively unless evidence of infection is present.
- Choose an antibiotic that is effective against the suspected contaminant and that reaches therapeutic concentrations in the target tissues.

Blood

- Cardiac surgery or removal of large, vascular neoplasms may be associated with significant blood loss.
- Ensure that a blood donor or packed cells are available if significant blood loss is anticipated.
- Cross-match or type the donor's blood if multiple transfusions are anticipated.

Client Communication

Risks

- Major cardiac and respiratory surgery is associated with a high incidence of morbidity and mortality.
- Review the incidence of complications and death associated with the planned procedure and discuss this information with the client.

Cost

Thoracic surgery and patient care may be quite expensive. Discuss the cost of preoperative diagnosis and therapy, anesthesia and surgery, and postoperative intensive care with the client.

ANESTHETIC CONSIDERATIONS

The general principles of anesthesia described in Chapter 2 apply to thoracic surgery patients. Special considerations for thoracic surgery patients are outlined in this section.

Premedication

- Consider placing a transdermal fentanyl patch on the animal 12 hours prior to surgery for analgesia (see Chapter 6).
- Generally avoid phenothiazines such as acepromazine because of possible side effects of hypotension and myocardial depression. However, at low doses (up to 0.1 mg/kg SC or IM), they may be beneficial for calming animals with respiratory compromise but normal cardiac function. Acepromazine can be combined with one of the opiates (e.g., butorphanol) as an effective preanesthetic treatment (see Chapter 2).

- Diazepam (Valium) is a safe drug that can be used as a premedicant (0.2 mg/kg IV). It has minimal effects on the cardiovascular and respiratory systems.
- Xylazine (Rompun, Miles) causes undesirable cardiac and respiratory depression, making it a poor choice for thoracic surgery.
- Avoid using anticholinergics (e.g., atropine) because they increase viscosity of respiratory secretions, can increase anatomic dead space, and may induce cardiac arrhythmias.

Induction

- Diazepam, 0.2 mg/kg IV, followed by administration of a thiobarbiturate (e.g., thiopental), 6 to 10 mg/kg IV, provides relatively safe and rapid, smooth induction that allows immediate intubation and control of ventilation.
- The combination of ketamine and diazepam (1:1 mixture; 1 ml of mixture per 10 kg) also can be used for thoracic surgery patients. Hemodynamics is minimally compromised by this combination. However, ventilatory support may be necessary.
- Propofol is another choice for induction of anesthesia. See Chapter 2 for indications and dosage.

Maintenance

- Any of the commonly used inhalation anesthetics can be used successfully for thoracic procedures. Isoflurane is preferred because of less myocardial depression, although hypotension commonly occurs.
- Avoid nitrous oxide in patients with respiratory disease, pneumothorax, anemia, or hypoxia.
- Provide positive pressure ventilation by manual compression of the bag or with a mechanical ventilator (see Table 167-1 for ventilation guidelines).

▼ ***Key Point*** Adequate positive pressure ventilation in the thoracic surgery patient is essential for preventing hypoxia, respiratory acidosis, and atelectasis.

Table 167-1. GENERAL GUIDELINES FOR CONTROLLED VENTILATION

Physiologic Parameter	Value
Respiratory	8–12 breaths/min
Tidal volume	15–20 ml/kg of ideal body weight
Peak airway pressure	15–20 cm H_2O—closed 20–30 cm H_2O—open
Inspiratory time	1–1.5 sec
Expiratory time	2–3 sec
Inspiratory-to-expiratory ratio	1:2–1:4

Modified from Faggella AM, Raffe MR: Anesthetic management of thoracotomy. Vet Clin North Am 17:480, 1987.

Fluids

- Thoracotomy diminishes the functional reserve of the heart by decreasing effective filling pressures. This may be compensated for, in part, by fluid therapy.
- Place one or two intravenous catheters for fluid administration.
- Administer balanced electrolyte solutions at a surgical maintenance rate of 10 to 20 ml/kg/hour.

Monitoring

Cardiovascular

- The standard methods of cardiovascular monitoring (e.g., heart rate, color, pulse quality, and capillary refill) are very important, because alterations due to the disease or surgical manipulations are common.
- Electrocardiography (ECG) is helpful to monitor heart rate and detect arrhythmias.
- Blood pressure measurements obtained with an arterial catheter or a Doppler unit with a pneumatic cuff placed over an accessible artery (e.g., metatarsal artery) help monitor circulatory status during the anesthetic period.

Respiratory

- Carefully monitor the respiratory rate and depth. In the patient with respiratory compromise, be especially aware of spontaneous respirations before thoracotomy and immediately after closure of the thorax.
- Monitor blood gas analysis or pulse oximetry to determine respiratory status; make necessary adjustments.

Other

- Use standard techniques for monitoring depth of anesthesia (see Chapter 2).
- Ensure good communication between anesthetist and surgeon, which is essential for a smooth and successful procedure. Indicate to the anesthetist when major manipulations of the heart and lungs are imminent, and point out when problems arise such as atelectasis, due to inadequate ventilation, or acute blood loss. The anesthetist should keep the surgeon informed of the patient's overall status.

SURGICAL PROCEDURES

Instruments

A standard general pack is needed. See Table 167-2 for additional instruments that are particularly useful in thoracic surgery.

Table 167-2. SPECIAL INSTRUMENTS RECOMMENDED FOR THORACIC SURGERY

Scissors
Long-handled Metzenbaum
Potts

Needle Holders
Mayo-Hegar (long-handled)
DeBakey
French eye

Tissue Forceps
DeBakey general thoracic
DeBakey vascular

Other Forceps
Satinsky clamps
Angled or curved forceps
  Gallbladder
  Rumel thoracic and dissecting
  Mixter hemostatic and thoracic
  Lahey gall duct thoracic
Bronchus clamps
Vascular clamps

Retractors
Finochietto rib
Burford rib

Other
Rib approximator

Table 167-3. LOCATIONS OF THORACIC STRUCTURES VIA INTERCOSTAL THORACOTOMY

Thoracic Structure	Intercostal Space	
	Left	Right
Heart and pericardium	4, 5	4, 5
PDA, PRAA	4 (5)	
Pulmonic valve	4	
Trachea		3
Lungs	4–6	4–6
Cranial lobe	(4) 5	(4) 5
Intermediate lobe		5
Caudal lobe	5 (6)	5 (6)
Esophagus		
Cranial		3, 4
Caudal	7–10	7–10
Caudal vena cava	(6–7)	7–10
Diaphragm	7–10	7–10
Thoracic duct (caudal)		
Dog		8–10
Cat	8–10	

Modified from Orton C: Thoracic wall. In Slatter DH (ed): Textbook of Small Animal Surgery. Philadelphia: WB Saunders, 1985, p 539.
PDA, patent ductus arteriosus; PRAA, persistent right aortic arch.

Lateral Thoracotomy

Indications

This is the standard approach to most intrathoracic structures. See Table 167-3 for the locations of structures exposed through intercostal thoracotomy.

Objective

Gain access to the right or left hemithorax to expose the heart, lungs, or other structures.

Equipment

See Table 167-2 for specific instruments useful in thoracic surgery.

Technique

1. Place the animal in lateral recumbency. Place a towel or small pillow under the thorax to slightly arch the contralateral thoracic wall, making the surgical approach easier. Prepare the lateral thorax for aseptic surgery.
2. Count the intercostal spaces to approximate the location of the incision.
3. Incise the skin, subcutaneous tissues, and cutaneous trunci muscle, from dorsal to ventral, from the costovertebral junction to the sternum.
4. Incise the latissimus dorsi muscle from ventral to dorsal (Fig. 167-1).
5. Recount the intercostal spaces (by palpating underneath the latissimus dorsi muscle) from cranial to caudal unless the incision is located in the caudal thorax.
6. Incise through the remainder of muscles: serratus ventralis (can be bluntly separated rather than incised), scalenus, external abdominal oblique, and external and internal intercostals (Fig. 167-2). Penetrate the pleura (instruct the anesthetist to stop pos-

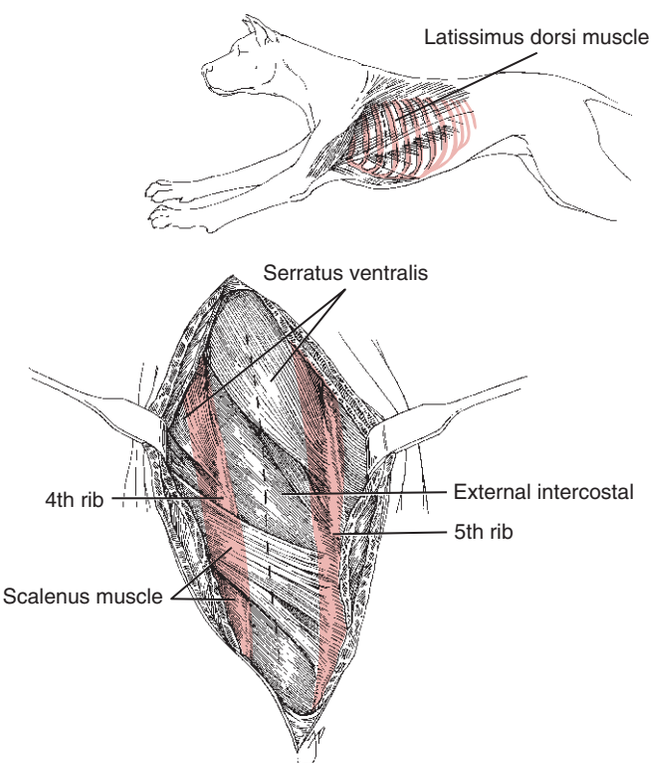

Figure 167-1. Thoracotomy technique. *Top,* Incise the skin at the intercostal space between rib 4 and rib 5 *(dotted line). Below,* Cut the latissimus dorsi muscle and retract to expose the serratus ventralis, dorsalis, scalenus, and external intercostal muscles.

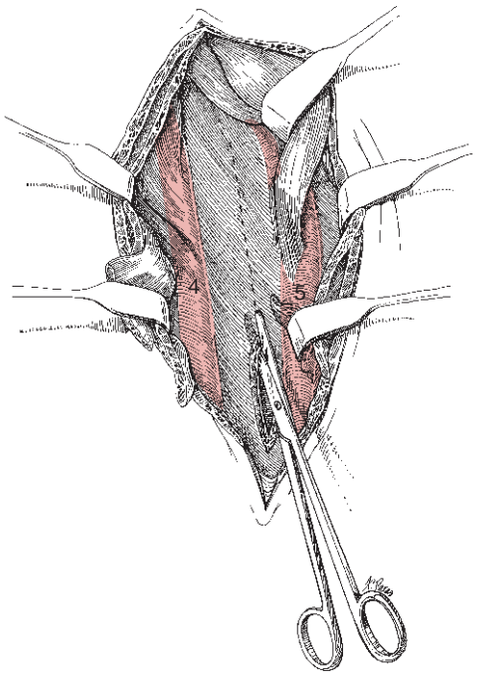

Figure 167-2. Cut or separate the serratus and scalenus muscles between rib 4 and rib 5 so that an incision can be made in the intercostal muscles and the pleura.

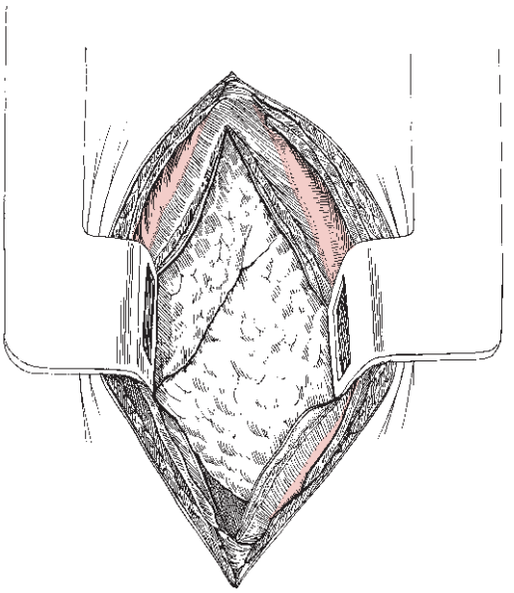

Figure 167-3. After the intercostal muscles and pleura are cut, retract the ribs to expose the lung.

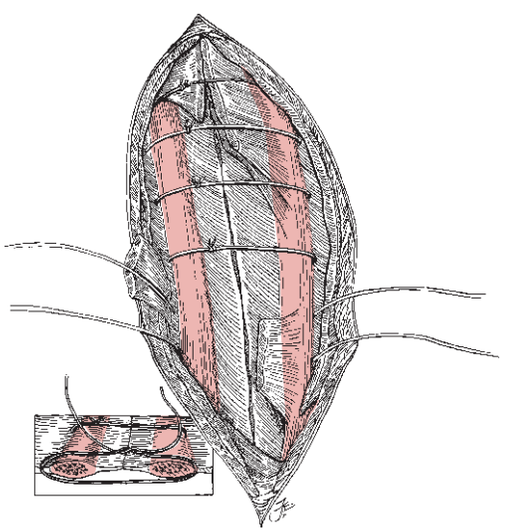

Figure 167-4. For lateral thoracotomy closure, place sutures around ribs 4 and 5 and secure each with a surgeon's knot.

itive pressure ventilation before introducing sharp instruments into the thorax), and incise the pleura dorsally and ventrally with Metzenbaum scissors. Avoid trauma to the internal thoracic artery when incising ventrally.

7. Protect the ribs and muscle tissue with moistened sponges and insert a self-retaining rib retractor (e.g., Finochietto) to expose the thoracic viscera (Fig. 167-3).
8. Closure
   a. Preplace a thoracic drain tube one to two intercostal spaces caudal to the thoracotomy.
   b. Perform an intercostal nerve block by injecting bupivacaine (Marcaine) adjacent to two rib heads on each side of the incision (administer a total dose of 1 mg/kg).
   c. Preplace several large (2-0, 0, or 1) absorbable sutures around the ribs. Hug the caudal rib during suture passage to avoid damage to the intercostal vessels and nerve. Avoid puncture of intrathoracic structures during needle passage around the ribs.
   d. While an assistant approximates the ribs by placing traction on the preplaced sutures, tie the rib sutures using a surgeon's knot (Fig. 167-4).
   e. Close the deep muscles in one layer (serratus, scalenus, external abdominal oblique, and intercostal muscles) in a simple continuous pattern (use absorbable suture for all layers except the skin).
   f. Close the latissimus dorsi muscle in a simple continuous pattern (Fig. 167-5).
   g. Close the cutaneous trunci muscle and subcutaneous tissues in the next layer in a simple continuous pattern; then close the skin routinely, using the pattern of your choice.
   h. Perform thoracocentesis using the thoracic tube to evacuate air or fluid.
   i. Place a light, loosely fitting bandage over the incision and thoracic tube.

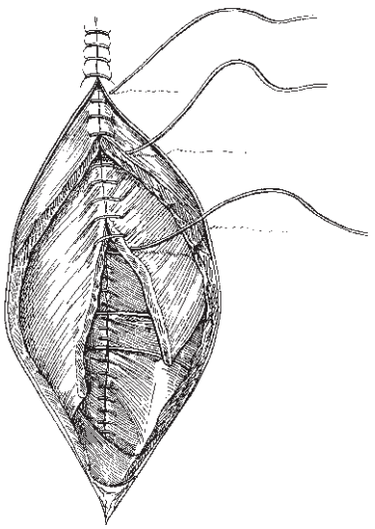

Figure 167-5. Close the latissimus dorsi muscle (simple continuous suture), the subcutaneous tissue (simple continuous suture), and the skin (simple continuous or interrupted suture).

Median Sternotomy

Indications

Median sternotomy is indicated when bilateral exposure of the thorax is necessary. Examples are as follows:

- Multiple lung lesions (e.g., multiple emphysematous bullae)
- Pericardiectomy
- Mediastinal tumors (e.g., thymoma)
- Alternate approach to the pulmonic valve or for other cardiac procedures
- Hepatic surgery
- Complicated diaphragmatic hernia or other diaphragmatic surgery

Objectives

- Obtain bilateral exposure of the thorax
- Achieve stable closure of the sternum to minimize postoperative complications

Equipment

See Table 167-2 for special equipment needed for thoracic surgery.

- Oscillating bone saw for medium to large dogs (an alternative is the Lebsche sternal knife; however, the saw is preferred)
- Osteotome and mallet
- Orthopedic wire (0.028–0.035 gauge) for medium to large dogs, wire cutters, and a wire-twisting instrument
- Electrocautery

Technique

1. Place the animal in dorsal recumbency.
2. Prepare the sternum and ventral half of the thorax for aseptic surgery.
3. Incise the skin and subcutaneous tissues from manubrium to xiphoid.
4. Divide the muscular attachments to the sternum along the thin, white fascial raphe to expose the sternum. This is best performed using electrocautery (Fig. 167-6).
5. Score the sternebrae precisely on the ventral midline with a scalpel or electrocautery (see Fig. 167-6).
6. Cut two-thirds of the thickness of the sternebrae with the bone saw. Finish the cut with an osteotome and mallet, being careful not to injure the heart or internal thoracic vessels.

▼ ***Key Point*** When performing sternotomy, make the sternal cut exactly on the midline to facilitate secure closure with full cerclage wire.

7. If possible, leave at least one sternebra uncut (e.g., cranial or caudal extent) to counteract sheer forces on the sternum after closure.
8. Protect the sternum with moistened sponges and retract with a rib retractor (e.g., Finochietto).
9. Closure
   a. Place a thoracic drain tube through an intercostal space lateral and dorsal to the sternotomy.
   b. Preplace cerclage wire or a heavy suture (e.g., 0 or 1 polypropylene in a cat or small dog) around each sternebra using hemostatic forceps (Fig. 167-7). Stay close to the bone to avoid the internal thoracic vessels. Tighten the wire using wire-holding forceps. If insufficient bone is present to wire the sternebrae directly, place the wires in a figure-eight pattern around the ribs where they attach to the sternum.
   c. Close the muscle tissue using an absorbable suture in a simple continuous pattern.
   d. Close the subcutaneous tissue and skin in a routine fashion.
   e. Perform thoracocentesis using the thoracic tube to evacuate air and fluid.
   f. Loosely place a lightly padded bandage over the incision and thoracic tube.

Lung Lobectomy

Indications

- Neoplasia
- Abscesses or granuloma of the lung
- Lung lobe torsion or severe trauma
- Irreversible atelectasis
- Bronchoesophageal fistula
- Emphysematous bulla
- Refractory lobar pneumonia

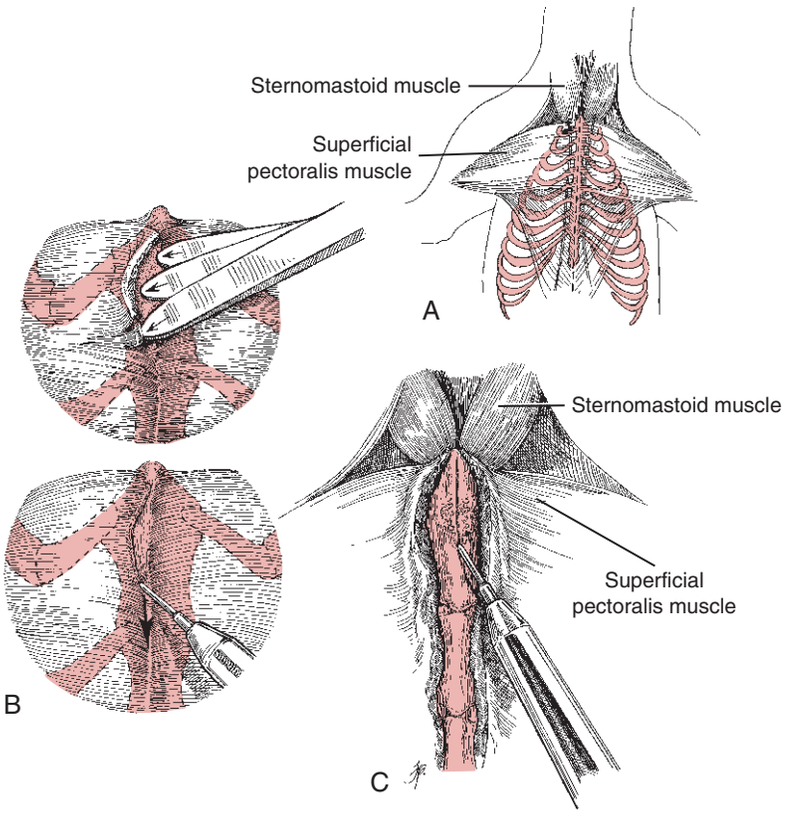

Figure 167-6. Technique for median sternotomy. *A,* Determine the middle of the sternum and associated muscle attachments. *B,* Bluntly dissect muscle off the sternum *(upper),* or incise muscle attachments with electrocautery *(lower). C,* Score the exposed periosteum on the midline.

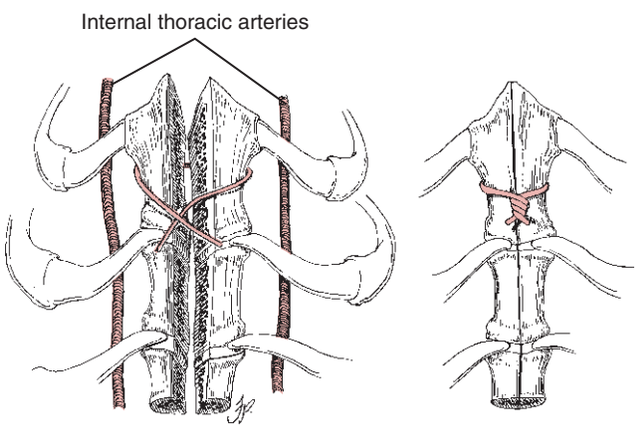

Figure 167-7. Close each sternebra with full cerclage wire twisted with a needle holder or wire twister.

Objectives

- Remove part or all of a lung lobe
- Maintain good hemostasis, especially of the major pulmonary blood vessels
- Establish an airtight seal of the bronchus and/or lung parenchyma
- Leave adequate pulmonary tissue to avoid compromise of the patient's cardiopulmonary status

Equipment

Use the same equipment as for lateral thoracotomy or median sternotomy, plus the following:

- Babcock tissue-holding forceps
- Small suture with swaged needle (e.g., 4-0 nylon or polypropylene)
- Tissue stapling device (30, 55, or 90 Thoracoabdominal Autosuture stapler; U.S. Surgical, Norwalk, CT) (optional)

Technique

1. See the preceding surgical techniques (lateral thoracotomy, median sternotomy) for descriptions of approaches to the lung lobes.
2. Explore the thorax and determine the extent of disease and which lobes are involved.
3. Determine which bronchus or bronchi supply the affected lobe(s).
4. Mobilize the lobe.
   a. For the caudal lung lobe, incise the pulmonary ligament that attaches the caudal aspect of the lobe to parietal pleura.
   b. Incise the pleural attachments between the affected lobe and the adjacent lobes.
   c. Gently incise or dissect adhesions between the lobe and the surrounding tissues (especially a problem in pulmonary neoplasia).

5. Partial lobectomy
   a. Place a non-crushing clamp (e.g., Satinsky) between the lesion and the hilus and incise distally to the clamp with scalpel or scissors.
   b. Close the remaining lung lobe parenchyma with 4-0 or 5-0 nylon or polypropylene in a continuous horizontal mattress pattern. Oversew the incised tissue with a simple continuous pattern to prevent air leakage.
   c. Alternatively, place the Thoracoabdominal Autosuture stapler between the lesion and the hilus. Staple the lung, incise distal to the stapler, and remove the diseased tissue.
   d. Check for hemostasis. Check for air leakage by flooding the lung incision with sterile saline, inflating the lung by positive pressure inspiration, and observing for bubbles. Place additional sutures if necessary to control leaks.
6. Complete lobectomy
   a. Dissect the pulmonary artery and vein free from the adjacent bronchus.
   b. Triple-ligate each vessel with silk or chromic catgut.
   c. Divide each vessel among the ligatures, leaving two ligatures with the animal.
   d. Place two clamps (e.g., Satinsky) across the bronchus and divide it between the clamps. Remove the lung lobe.
   e. Close the bronchus with monofilament nylon or polypropylene, using a horizontal mattress pattern followed by a simple continuous pattern.
   f. Alternatively, use the stapling device previously mentioned to close the hilar vessels and bronchus.

POSTOPERATIVE CARE AND COMPLICATIONS

Thoracic Drain Tubes

- If a thoracic tube has been placed, leave it in as long as necessary, depending on the animal's condition and production of air or fluid (see Chapter 3 for details on thoracic tube management).
- In routine procedures in patients without risk of recurrent pneumothorax or effusion, pull the tube as soon as negative pressure has been reestablished after completion of surgical closure.
- After pulmonary resection, consider leaving a thoracic tube in place for a minimum of 24 hours even if no air or fluid is recovered. Otherwise, leave the tube in until insignificant amounts of air or fluids are being recovered (<2 ml/kg/day).
- Obtain thoracic radiographs prior to removal of the thoracic tube to ensure that there is no significant pleural air or fluid.

Pain

- Thoracic surgery is associated with postoperative pain that causes discomfort and can inhibit ventilation by making the animal reluctant to expand the thorax.
- Be careful when handling the animal, especially around the thoracotomy site. Unilateral forelimb lameness is common after lateral thoracotomy but should resolve within several days.
- Local analgesia can be used as a method of decreasing postoperative discomfort. See lateral thoracotomy closure earlier in this chapter for intercostal nerve block technique.
- Systemic analgesia can also be used for those animals exhibiting significant pain. See Chapter 6 for discussion of postoperative analgesia.

Pneumothorax

- Small amounts of residual air in the pleural space are common after thoracic surgery and rarely cause a clinical problem.
- Persistent postoperative pneumothorax can be a serious problem after surgery of the lung or airways if continuing leakage occurs at the site of incision or excision.
- If pneumothorax causes respiratory compromise and a thoracic tube is not already present, tap the animal's chest with a butterfly needle, syringe, and stopcock (see Chapter 3). Place a thoracic tube and consider performing thoracic radiography if improvement in the animal's condition does not occur or if the pneumothorax is recurrent. Evaluate the heart, lungs, pleural space, and location of the thoracic tube.

Hemothorax

- Postoperative hemothorax can occur after any thoracic surgery but is more common after major cardiac or vascular surgery or after removal of large, highly vascular tumors. This can be a difficult complication to manage because reoperation does not usually reveal the source of bleeding.
- If large quantities of bloody fluid are aspirated from the thorax, obtain a packed cell volume (PCV) assay of the fluid. If the fluid is consistent with whole blood and the animal is losing considerable volume (i.e., clinical evidence of shock or PCV < 20), use supportive care to replace volume (isotonic or hypertonic fluids). A steadily declining PCV in evacuated pleural fluid is a good indicator of pending hemostasis.
- Perform autotransfusion if the blood is not contaminated with bacteria or neoplastic cells. Give whole blood from a donor dog if autotransfusion is not pos-

sible. (See Chapter 22 for more information on blood transfusions.)
- Monitor peripheral PCV and total protein until the animal's condition is stabilized.
- As a general rule, some surgeons recommend reexploration of the thorax if blood loss is >2 ml/kg/hour for 3 to 4 hours and unresponsive to conservative therapy.

Ventricular Arrhythmias

Cardiac arrhythmias are not uncommon and may develop 24 to 48 hours postoperatively (see Chapter 145).

Infection

- Postoperative infection after thoracotomy is uncommon but may occur if bacterial contamination occurs during the surgery or may be associated with the indwelling thoracic tube.
- Treat pleural infection with appropriate antibiotics (based on culture and sensitivity of the pleural fluid) and thoracic drainage (see Chapter 164). Rarely, thoracic lavage with fluids is necessary.

SUPPLEMENTAL READING

Evans HE, Christensen GC (eds): Miller's Anatomy of the Dog, 3rd ed. Philadelphia: WB Saunders, 1993, p 482.
Orton EC: Thoracic wall. In Slatter DH (ed): Textbook of Small Animal Surgery. Philadelphia: WB Saunders, 2003, p 373.

Section

12 Diseases of Avian and Exotic Pets

Barbara L. Oglesbee

Chapter

168 Avian Techniques

Barbara L. Oglesbee

RESTRAINT

For General Physical Examination (Fig. 168-1)

- Hold the bird's head firmly with one hand, placing the thumb and second finger under the mandibles and the first finger on the crown.
- With the other hand, grasp the bird with a towel wrapped securely around the body.

For Radiography

- Anesthesia with isoflurane may be necessary and reduces stress from the procedure.
- Use an acrylic positioning board (Silverdust, El Granada, CA).

Dorsoventral View (Fig. 168-2*A*)

- Lock the head in an acrylic shield.
- Extend the wings fully and place masking tape proximal to the carpus and on the primary feathers.
- Tape the legs in full extension.
- Align the keel bone over the spinal column.

Lateral View (Fig. 168-2*B*)

- Position the bird with the right side down.
- Lock the head in an acrylic shield.
- Pull the wings dorsally and tape with masking tape proximal to the carpi.
- Tape the legs caudally, with the right leg slightly anterior to the left leg.
- Restrain the tail with masking tape.

OPENING THE MOUTH

- A mouth speculum (Lafeber Co., Odell, IL) can be used to keep the mouth open (Fig. 168-3*A*).
- This procedure can cause cracking of the beak in some birds.
- Alternatively, loops of gauze can be used (Fig. 168-3*B*).
- Restrain the bird in a towel with one hand (see Fig. 168-1); with the other hand, pull down on a gauze loop placed over the upper beak.
- Instruct an assistant to pull a second gauze loop over the upper beak.

FORCED ALIMENTATION (GAVAGE FEEDING)

- Hold the bird in an upright position, using towel restraint if necessary (see Fig. 168-1).
- Hold the mouth open with a speculum or gauze loops (see Fig. 168-3).

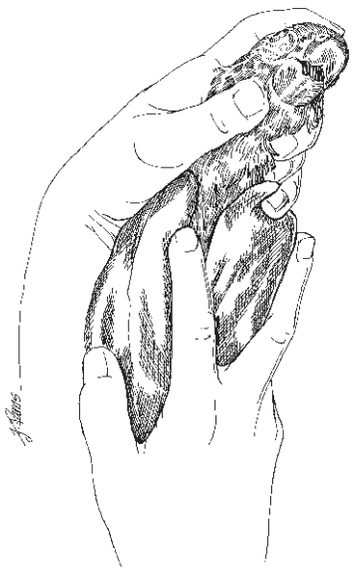

Figure 168-1. Restraint of parrot using a towel.

- Gently pass a rigid feeding tube (Lafeber Co., Odell, IL) or soft rubber catheter with an attached, gruel-filled syringe from the right side of the mouth into the crop (Fig. 168-4).
- Palpate the tube within the crop to check its position.
- Expel the contents of the syringe while monitoring the pharynx for reflux of food.
- Withdraw the tube and immediately release the bird.
- The volume of gruel to be administered varies with the size and age of the birds. Suggested volumes are budgerigar, 1 to 3 ml; cockatiel, 3 to 6 ml; Amazon parrot, 15 to 35 ml; and macaw 35 to 60 ml.
- The same procedure may be used to perform a *crop wash* for diagnostic sample collection. In place of gruel, instill 0.5 to 1 ml of sterile saline into the crop, then aspirate immediately.

SUBCUTANEOUS FLUID INJECTION

- Use a 25-gauge needle.
- Always use warmed fluids, 0.9% NaCl or lactated Ringer's solution (98°F).
- Divide volume of fluid into two equal injections in the groin area (Fig. 168-5).
- Approximately 1 to 2 ml of fluids per 100 g of body weight (BW) may be administered; the larger volume is given to smaller birds.

COLLECTION OF SAMPLES FOR CULTURE

Via the Choana (Fig. 168-6*A*)

- Hold the bird upright and open its mouth with a speculum or gauze loops (see Fig. 168-3).

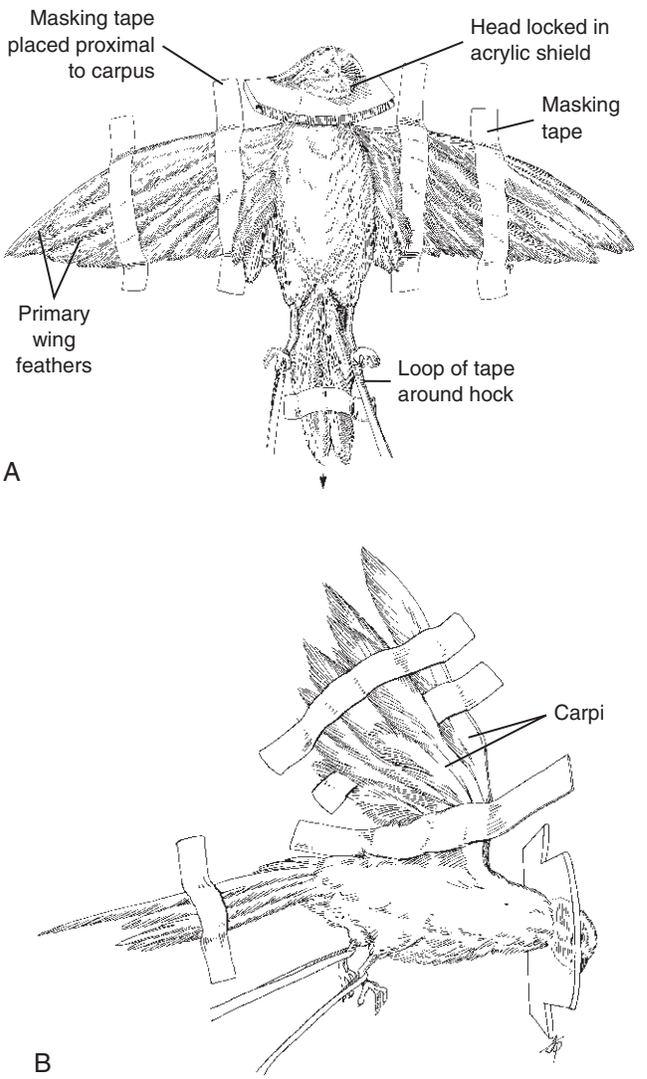

Figure 168-2. Restraint and positioning for radiography: *A,* dorsoventral view. *B,* lateral view.

- Insert a cotton-tipped swab into the most rostral portion of the choana.

Via the Cloaca (Fig. 168-6*B*)

- Restrain the bird in a towel.
- To avoid trauma to the mucosa, moisten the cotton-tipped swab with transport media or sterile saline solution before insertion into the cloaca.

VENIPUNCTURE SITES

▼ ***Key Point*** To prevent hematoma formation, always apply firm pressure after venipuncture.

The following sites are recommended for blood collection and infusion of bolus fluids.

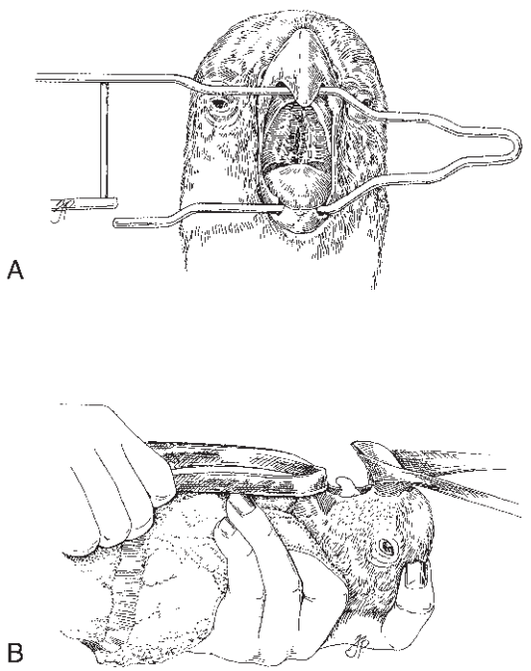

Figure 168-3. Opening the mouth using *(A)* a mouth speculum and *(B)* loops of gauze.

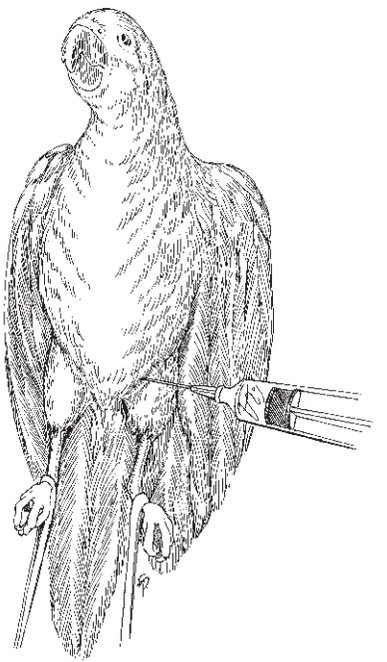

Figure 168-5. Subcutaneous fluid injection sites: interscapular region.

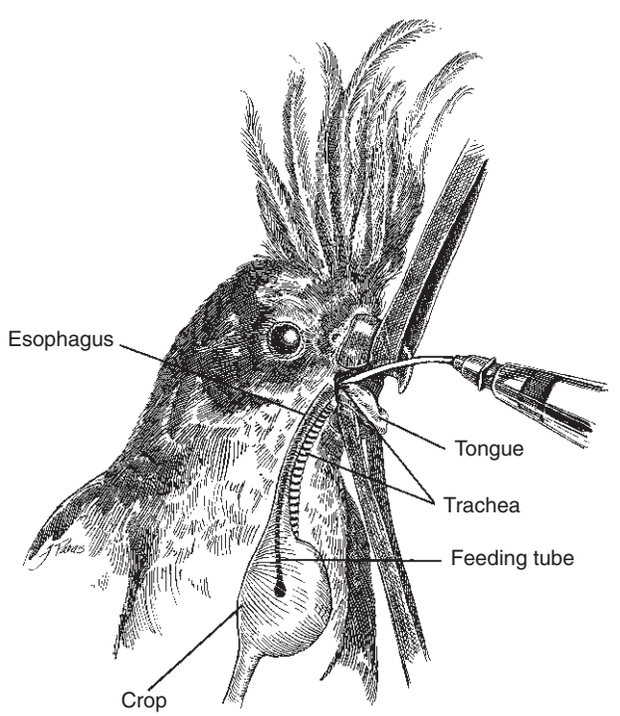

Figure 168-4. Forced alimentation.

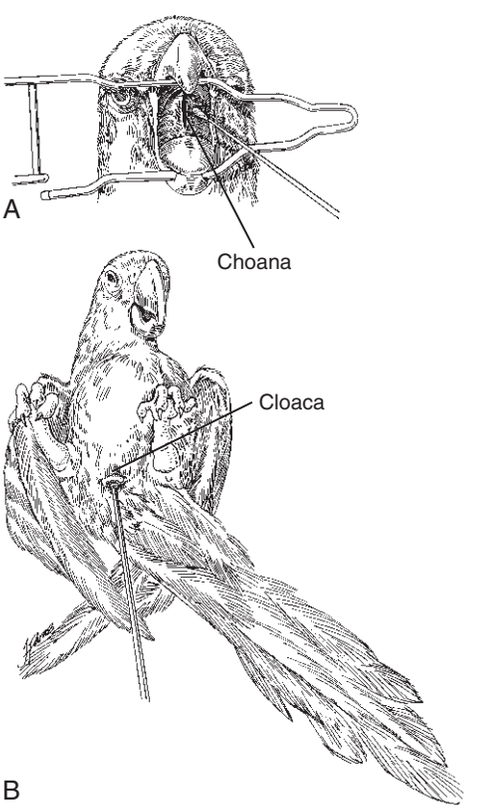

Figure 168-6. Collection of culture samples from *(A)* the choana and *(B)* the cloaca.

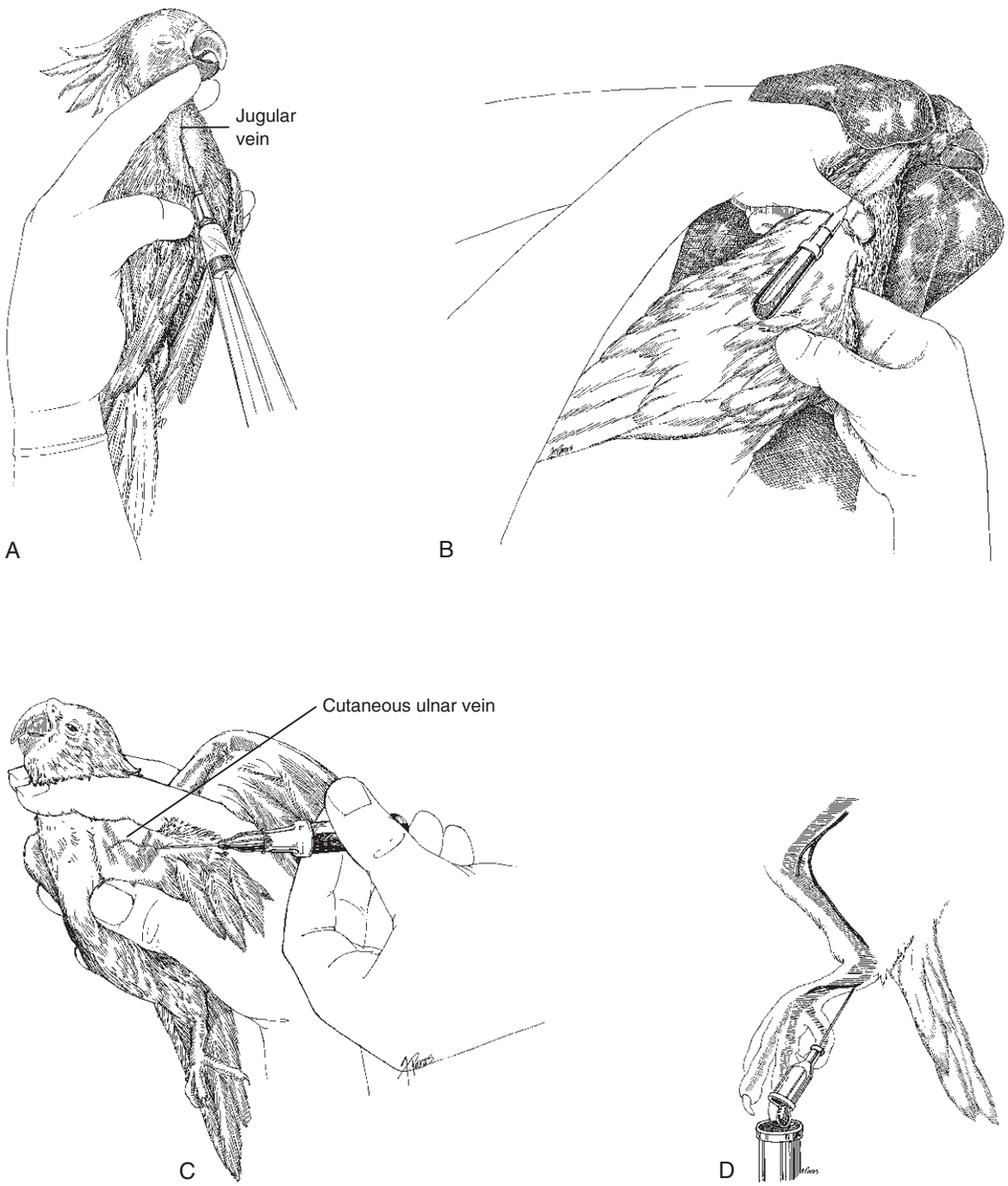

Figure 168-7. Venipuncture sites: *A,* jugular vein, birds weighing less than 200 g. *B,* jugular vein, larger birds. *C,* cutaneous ulnar vein. *D,* caudal tibial vein.

The volume of blood that may safely removed from a healthy bird for diagnostic sample collection is approximately 1% of BW (e.g., 1 ml of blood per 100 g of BW).

Jugular Vein

This venipuncture site is preferred for psittacine birds because of the relatively large size of the vessel and decreased tendency toward hematoma formation.

Birds Under 200 g (Fig. 168-7*A*)

- Use a hypodermic needle (25 or 27 gauge) and syringe (1 ml) for blood collection.
- The jugular vein is highly movable; make sure that the neck is in full extension.

Larger Birds (Fig. 168-7*B*)

- If an assistant is not available, larger birds (e.g., parrots) may require anesthetization with isoflurane.
- With the right hand, the assistant holds the feet and the right wing pulled caudally; with the left hand, he or she restrains the bird's head.
- Using a larger needle (22–27 gauge) and syringe (3 ml) for blood collection, apply firm pressure to the right jugular vein at the thoracic inlet.

Cutaneous Ulnar Vein (Fig. 168-7*C*)

- The cutaneous ulnar vein crosses the ventral surface of the humeroradioulnar joint.
- To collect blood, cannulate the vessel with a 25-gauge needle and aspirate with a 1-ml syringe.
- This vein is prone toward significant hematoma formation.

Caudal Tibial Vein (Fig. 168-7*D*)

- The caudal tibial vein passes on the medial side of the tibiotarsus just above the tarsal joint.
- To collect blood, cannulate vessel with a 25-gauge needle and allow blood to flow into a microcollection tube (Microtainer; Becton-Dickinson, Rutherford, NJ).
- Apply firm pressure for several minutes until bleeding stops.

INTRAMUSCULAR INJECTION (Fig. 168-8)

- If necessary, use towel restraint (see Fig. 168-1).
- Inject into the superficial pectoral muscles on either side of the keel bone. Alternate sides with subsequent injections.

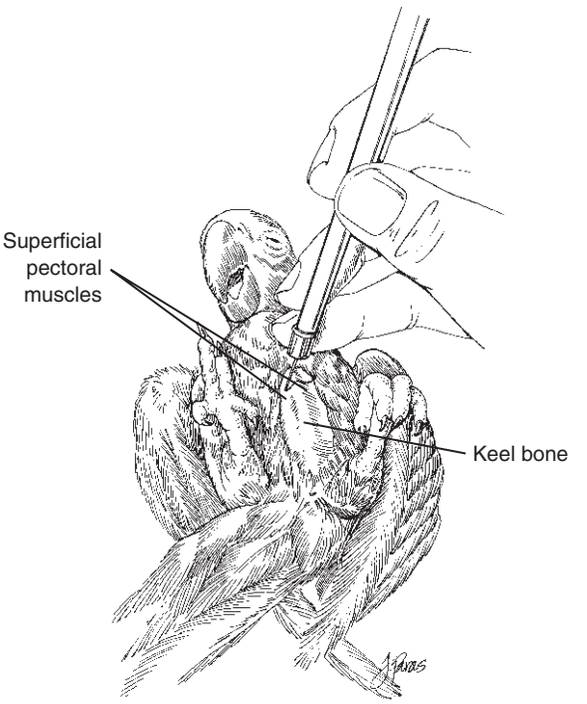

Figure 168-8. Intramuscular injection.

SINUS INJECTION OR FLUSH

Sinus Injection or Aspirate (Fig. 168-9*A*)

- Restrain the bird in a towel.
- Restrain the head firmly in a normal upright position.
- Insert the needle percutaneously into the sinus slightly above the commissure of the beak, midway between the upper beak and the medial canthus of the eye.

Sinus or Nasal Flush (Fig. 168-9*B*)

- Restrain the bird in a towel over a sink or collection bowl.
- Position the head so that it is slightly lower than the body, and restrain firmly.
- Press the syringe (without needle) against the naris opening.
- Inject 3 to 10 ml (depending on the size of the bird) of saline solution-antibiotic mixture into the nares with light pressure.
- If the flushing procedure is successful, the mixture will flow freely from the choana.
- Perform alternate flushes into each naris until all the mixture is used and/or no further exudate is produced.

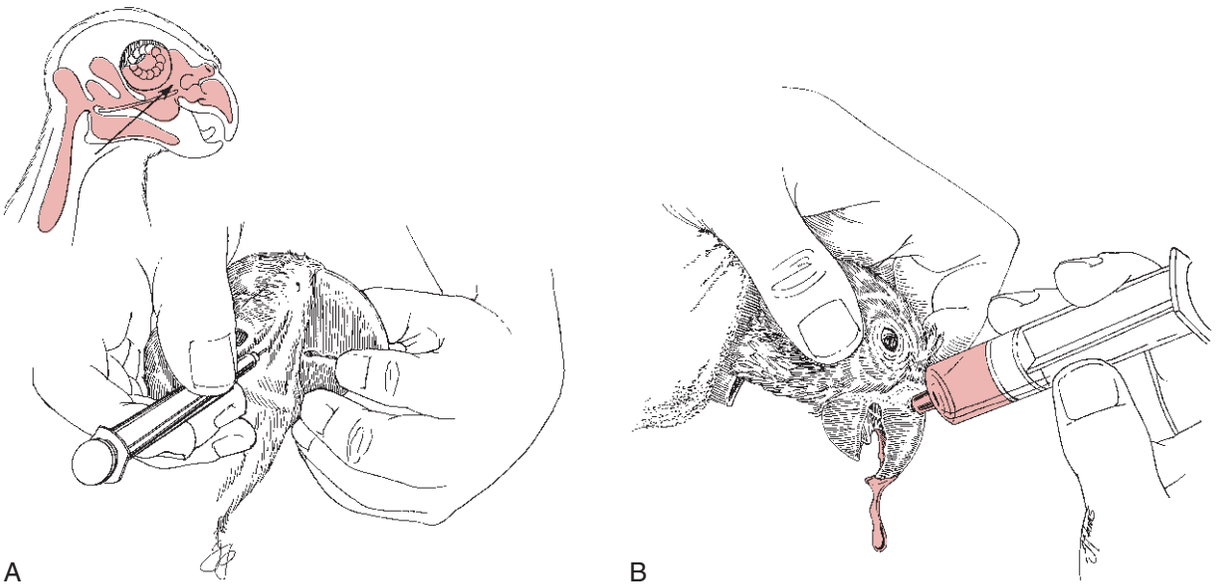

Figure 168-9. *A,* Sinus injection; *inset,* diagram of sinuses showing injection site *(arrow). B,* Sinus flush.

Figure 168-10. Tracheal injection or wash.

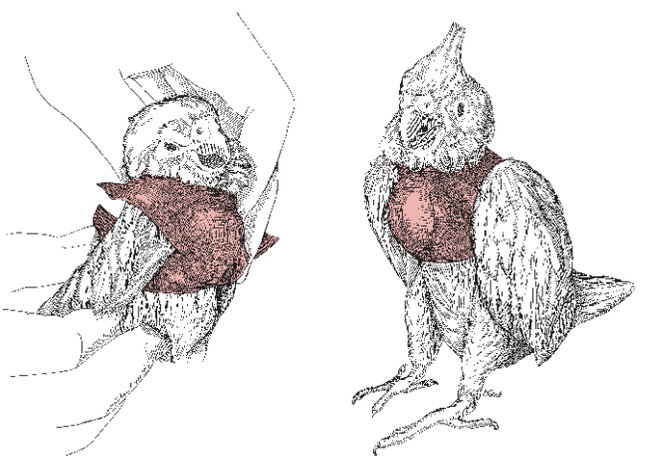

Figure 168-11. Crop supporter.

TRACHEAL INJECTION OR WASH (Fig. 168-10)

- Restrain the bird firmly.
- For tracheal injection, the bird may be held with the face upward, if desired.
- For tracheal wash, hold the bird in an upright position.
- Open the bird's mouth, using gauze loops or a speculum (see Fig. 168-1).
- Insert an open-ended tomcat catheter with attached syringe into the tracheal opening:
  - For tracheal injection—Inject medication.
  - For tracheal wash—Inject 1.0 to 2.0 ml of 0.9% NaCl/kg BW into the trachea, and then aspirate immediately.
- This method also may be used for tracheal endoscopy.

CROP SUPPORTER (Fig. 168-11)

- Cut the Vetrap longitudinally on each end.
- Position the longitudinal cuts above and below each wing.
- Secure in the back with tape.

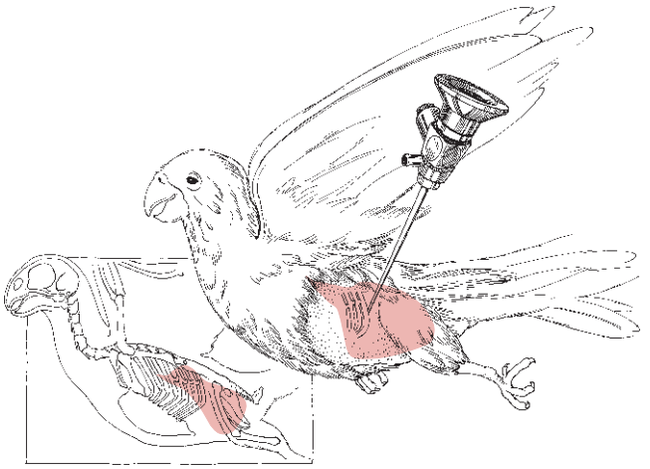

Figure 168-12. Preparation for endoscopy of the abdominal air sac; *inset,* trocar or cannula site.

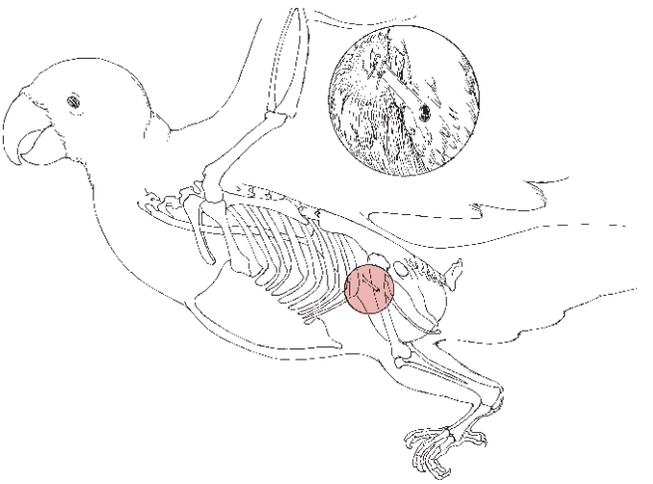

Figure 168-13. Abdominal breathing tube placement; *inset,* enlargement of placement site.

- When applying the Vetrap, maintain slight pressure inward to aid crop emptying.

PREPARATION FOR ENDOSCOPY OF THE ABDOMINAL AIR SAC (Fig. 168-12)

- Anesthetize the bird with isoflurane.
- Place the bird in lateral recumbency, right side down.
- Extend the wings out over the back; have an assistant hold them in this position.
- Pull the left leg as far caudally as possible.
- Push the right leg under the body to aid in maintaining true lateral recumbency.
- Pluck the area anterior to the proximal one-third of the femur free of feathers, and perform a sterile scrub.
- Apply clear drapes (3M, St. Paul, MN) over the area.
- Make a stab incision with a #15 scalpel blade through the skin anterior to the proximal one-third of the femur and caudal to the last rib.
- Bluntly separate the underlying musculature and peritoneum, using straight mosquito forceps.
- Introduce the trocar or cannula through the opened musculature to visualize the air sacs.

PLACEMENT OF ABDOMINAL BREATHING TUBE (Fig. 168-13)

- Enter the abdominal air sac using the technique described for endoscopy. Once the air sac is entered, the bird will begin breathing normally through the opening.
- Hold open the abdominal musculature or peritoneum with the inserted mosquito forceps.
- Place a 1- to 2-inch piece of a sterilized rubber catheter or shortened endotracheal tube in the opening and suture it in place with non-absorbable suture material.
- The catheter can be left in place for up to 2 weeks. If obstruction with mucus or exudate occurs, flush with a 0.9% saline solution.

Chapter

169 Avian Infectious Diseases

Don J. Harris / Barbara L. Oglesbee

ASPERGILLOSIS

Aspergillosis is an infectious but not contagious disease of pet and wild birds that is caused by the ubiquitous soil saprophyte *Aspergillus*. Infection generally occurs via inhalation of spores, resulting in primary lesions in the thoracic and abdominal air sacs and in the large airways (syrinx). Dissemination to other organ systems often occurs. Two forms of the disease, acute and chronic, commonly are seen.

- The acute form, which is seen most often in wild birds or psittacine birds under poor sanitary conditions, occurs after inhalation of an overwhelming number of spores. Severe dyspnea may result, with rapid progression to death.
- The chronic form, seen most often in psittacines, usually follows a stressful event or immunosuppressed state. Signs are often nonspecific and depend on the location of the infection and the immune status of the bird.
- The most common species isolated is *Aspergillus fumigatus*. *A. flavus, A. niger,* and other species play a lesser role.

▼ ***Key Point*** Aspergillosis is an opportunistic disease, requiring predisposing immunosuppressive factors such as stress, malnutrition, and environmental factors.

Etiology

Predisposing factors include the following:

- *Stress,* as may occur in shipping, quarantine, or movement to an unfamiliar environment. Stress also may result from a prolonged illness, such as chlamydiosis, or after a traumatic event, such as an injury or smoke inhalation.
- *Malnutrition* or vitamin deficiencies, especially hypovitaminosis A, often occur in birds on diets consisting of seed only.
- *Prolonged antibiotic or corticosteroid use* may cause underlying immunosuppression. For example, aspergillosis may occur after treatment for chlamydiosis owing to the immunosuppressive effects of tetracycline in conjunction with the debilitated state of a diseased bird.

▼ ***Key Point*** Suspect aspergillosis when clinical signs do not respond to or worsen with antibiotic treatment.

- Environmental factors:
  - Poor ventilation in conjunction with damp litter (especially corn-cob litter) soiled with feces promotes spore formation.
  - Poor sanitation, such as when nest boxes and incubators are cleaned inadequately, can predispose birds to aspergillosis.

Clinical Signs

Acute Form

- Signs include anorexia, dyspnea, and cyanosis.
- Sudden death may occur without signs.

Chronic Form

The onset is insidious, and signs vary depending on the location of the infection.

Respiratory System

Signs depend on the area affected. Respiratory signs will only occur if lesions impede airflow, for example, aspergillus granuloma formation in the syrinx, air sac thickening, and exudate accumulation in the air sacs.

Upper Respiratory Tract Signs

- Signs include a change in voice, reluctance to talk, and a respiratory click that can be heard when lesions involve the main airways, especially the syrinx.
- Severe, life-threatening dyspnea often occurs if the lesions are large enough to occlude the trachea or syrinx. In some cases, these may be the only lesions present.
- Mucoid to mucopurulent nasal discharge occurs in birds with *Aspergillus rhinitis* or *sinusitis*.
- Erosion of the nasal conchae and misshapened nares are seen in advanced cases of nasal aspergillosis.

▼ ***Key Point*** Suspect aspergillosis when the owner describes the bird as having "laryngitis."

Lower Respiratory Tract Signs

- With mild to moderate aspergillus airsacculitis, the air sacs are usually able to function normally (i.e., inflate and deflate to move air through the lungs). In these birds, respiratory signs are mild or absent, especially in birds that are sedentary.
- Dyspnea or exercise intolerance is seen in birds with extensive pneumonia or air sac involvement. Air sacs may become thickened or filled with caseous exudate, inhibiting their ability to move air.
- Respiratory signs are more likely to occur earlier in birds that are permitted to fly, as oxygen demand is greater in these birds.

▼ ***Key Point*** Birds with lower respiratory tract involvement often do not exhibit respiratory signs until disease is extensive. The most common clinical signs in birds with lower respiratory tract aspergillosis are nonspecific, such as weight loss, depression, and poor feathering.

Liver and Kidneys

Diarrhea, anorexia, and polyuria may be seen. Green discoloration of the urates (biliverdinuria) and hepatomegaly occasionally are seen.

Nervous System

Ataxia, torticollis, and paralysis may indicate central nervous system (CNS) involvement. Compression of the sciatic nerve by a granulomatous *Aspergillus* lesion has resulted in unilateral paralysis.

Nonspecific Signs

These are the most common signs. Weight loss, muscle wasting, depression, lethargy, and poor feathering often are the only clinical signs.

Diagnosis

History

- The history may identify an underlying environmental or immunosuppressive factor.

Physical Examination

- Examine the mouth and nares for mucus, exudates, or deformation of the nares. Take samples from the trachea or choana for fungal culture.
- Palpate the breast muscles and weigh the bird for evidence of weight loss and muscle wasting.
- Palpate the abdomen for evidence of organomegaly.
- Auscultate the trachea and chest for abnormal respiratory sounds and a respiratory click.

Laboratory Tests

- A severe leukocytosis often ranging from 25,000 to 100,000 white blood cells (WBCs) per microliter is often present.
- The differential count usually reveals heterophilia, monocytosis, lymphopenia, and anemia of chronic disease. Occasionally, the complete blood count (CBC) is normal.
- Increased serum total protein with an increased beta or gamma globulin portion is seen on plasma protein electrophoresis (EPH) in birds with chronic disease.
- Aspartate aminotransferase (AST), lactate dehydrogenase (LDH), and creatine phosphokinase (CPK) levels usually are increased, especially with hepatic involvement.

Endoscopy

▼ ***Key Point*** Endoscopy is invaluable for the diagnosis of aspergillosis.

- When there are episodes of severe dyspnea, tracheal endoscopy may reveal a single lesion occluding the syrinx.
- If a thick, white discharge or plaque is seen in the trachea, obtain a sample for cytologic examination and culture on Sabouraud's dextrose agar.
- Endoscopy of the abdominal air sacs may reveal diffuse cloudiness or white to yellow plaques. These plaques may become covered with a green-gray pigmented mold; obtain samples for culture and cytology.
- Samples for culture and cytology may sometimes be obtained by performing an air sac wash.

Radiography

- Radiographic changes may not be visible in early cases.
- Radiographs are generally not sensitive for defining tracheal granulomas, although if a soft tissue mass is seen within the trachea, aspergillosis should be suspected.
- In birds with nasal or sinus aspergillosis, perform cranial imaging such as skull radiographs, computed tomography (CT), or magnetic resonance imaging (MRI) to assess for the presence of granulomatous or caseated masses. Skull radiographs are less sensitive for picking up small lesions but are more readily available than CT or MRI.
- In advanced disease, radiographic abnormalities can include loss of definition of the air sacs, asymmetry of the air sacs due to air sac collapse or hyperinflation, and focal densities in the lungs or air sacs.
- Hepatomegaly or renomegaly may be visible radiographically when there is involvement of these organs.

Treatment

Treatment is most successful with early lesions confined to the nares or syrinx and when aggressive treatment is instituted early. A combination of topical treatment such as tracheal injection, sinus flush or nebulization (depending on the site of infection), systemic treatment, and debridement are usually necessary for successful outcome. Treatment is prolonged, requiring weeks to months of outpatient therapy. Continue treatment until clinicopathologic changes normalize and radiographic and endoscopic lesions resolve.

Antifungal Agents

- For birds with severe infections, administer amphotericin B (Fungizone, Squibb), 1.5 mg/kg q8h IV, for 3 to 7 days. Mask the bird with isoflurane anesthesia, and maintain an IV catheter for each injection.
- In birds with syringeal lesions, administer amphotericin B by intratracheal injection, using a tomcat urinary catheter (Sherwood Medical) at a dosage of 1 mg/kg q12h for up to 1 month.
- For nasal aspergillosis, a solution of 0.05 mg of amphotericin B per milliliter of sterile water may be used to flush the nares.
- For mycotic airsacculitis, make a solution of 1 mg of amphotericin B per milliliter of sterile water and nebulize q12h for 15 minutes. Alternatively, nebulize with clotrimazole (10 mg/ml in polyethylene glycol).
- Amphotericin B is potentially nephrotoxic and may cause bone marrow suppression. Monitor serum uric acid concentration to detect toxicity.
- Administer itraconazole (Sporanox, Janssen), 10 mg/kg q12h (with food) alone, in conjunction with, or following amphotericin B treatment. Usually at least 6 to 8 weeks of treatment are necessary; some birds may require treatment for months. Obtain a plasma biochemistry profile every 2 to 4 weeks to monitor for hepatotoxicity during treatment. African grey parrots appear to be more sensitive to the hepatotoxic effects of itraconazole. Use with caution, and discontinue use if anorexia occurs.
- Alternatively, administer fluconazole (Diflucan, Roerig), 15 mg/kg q24h PO, for up to 6 weeks with or after amphotericin B. Fluconazole is usually not as effective as itraconazole, but it may be better tolerated by some species, especially African grey parrots.
- Terbinafine (Lamisil, Novartis), 10 mg/kg q12h, PO has been anecdotally used to successfully treat aspergillosis in birds.
- 5-Fluorocytosine (Ancobon, Roche Labs), 50 to 150 mg/kg q12h PO, in conjunction with or after amphotericin B treatment has been used to treat aspergillosis in raptors. Give the higher dosage for active infections; use the lower dosage, often prophylactically, for 10 to 14 days in high-risk patients.

Antibiotic Therapy

- Antibiotic treatment based on culture and susceptibility testing may be necessary if a secondary bacterial infection is present.

Surgical Treatment

- Surgical removal of large accumulations of caseous material from air sacs in conjunction with systemic treatment and nebulization is often necessary for successful treatment.
- Surgical debridement of devitalized material from the upper airways and sinuses may facilitate topical therapy.

Supportive Care

- Fluid therapy, forced alimentation (see Chapter 168), and a warm environment are required for debilitated birds.

Prognosis

- The prognosis is poor to grave, depending on the severity of the disease.

Prevention

- Because *Aspergillus* is an opportunistic pathogen, attempt to reduce predisposing immunosuppressive factors such as stress and malnutrition.
- Treat birds with prolonged antibiotic therapy or other birds at risk with 5-fluorocytosine prophylactically (as previously described).

▼ ***Key Point*** To avoid inhalation of an overwhelming number of *Aspergillus* spores, house birds in a well-ventilated area. Do not use organic materials as bedding in nest boxes.

CHLAMYDIOSIS

Avian chlamydiosis is known as psittacosis when occurring in psittacine species and ornithosis when occurring in passerine species. The incidence in pet birds is high and is reportedly 15% to 30% of those tested.

Etiology

Avian chlamydiosis is caused by the obligate intracellular bacteria *Chlamydophila psittaci*. The organism infects many species of wild, domestic, and exotic birds, domestic mammals, and humans. Manifestation of this disease varies from subclinical to fatal, depending on the strain of *C. psittaci* involved and the species of bird affected.

▼ ***Key Point*** Chlamydiosis is potentially zoonotic and a reportable disease in many states. A valuable resource for practicing veterinarians, the compendium of psittacosis control is updated yearly by the Association of Public Health Veterinarians and is available at www.avma.org/.

Life Cycle and Transmission

Chlamydophila have a biphasic life cycle.

- Infectious, extracellular elementary bodies are shed in oral or nasal secretions and feces and may survive outside the host for a month or longer. Dissemination may occur via shared food dishes or aerosolized fecal dust.
- Elementary bodies are inhaled or ingested and enter host cells, where they undergo cellular rearrangement to form *reticulate bodies,* the replicating form of the organism.
- After replication, initial bodies reorganize to form *infectious* elementary bodies, which are released on rupture of the host cell. Elementary bodies then may be disseminated to cells of the liver, spleen, lungs, intestines, kidneys, gonads, and CNS.

Clinical Signs

▼ ***Key Point*** Clinical signs vary greatly, depending on the organ system affected, virulence of the organism, and immune status of the host.

- *Inapparent carriers* are common. These may be birds that have recovered from clinical illness or that may have never shown signs. High numbers of organisms may be shed intermittently from the feces or nasal or oral secretions, putting other pet birds and humans at risk.
- Clinical signs may develop in these carriers when they are stressed or otherwise immunocompromised.

Acute Form

- The acute form of the disease is seen more often in young or immunosuppressed birds. Signs may include the following:
  - Liver or gastrointestinal (GI) signs, such as inappetence, green-gray diarrhea, biliverdinuria (lime-green urates), and occasionally vomiting or regurgitation
  - Respiratory signs, including serous to purulent nasal or ocular discharge, labored breathing, blepharitis, and conjunctivitis
  - Nonspecific signs, including ruffled feathers, weight loss, and depression
- Without treatment, signs may progress over a few weeks, leading to prostration and death.

Chronic Form

- Nonspecific signs such as muscle wasting, poor feathering, lethargy, and inappetence may be the only signs. These signs are most often seen in birds with chronic hepatopathy.
- Recurrent conjunctivitis and mild respiratory signs are often seen.
- Occasionally, CNS signs (e.g., torticollis, seizures, and rear limb paresis or paralysis) may be seen alone.

Diagnosis

History

- Recently acquired birds may be at higher risk because of the increased exposure and stress associated with transport.

▼ ***Key Point*** Recently acquired birds are not the only ones at risk; birds may harbor the disease for months and even years before manifestation of clinical signs.

Physical Examination

- Findings may be normal in inapparent carriers.
- Suspect chlamydiosis in birds with poor feathering, weight loss, or signs of GI or respiratory disease.

▼ ***Key Point*** Lime-green urates are highly suggestive of chlamydiosis.

Laboratory Tests

- Leukocytosis, often >40,000 WBC per microliter demonstrating heterophilia with toxic heterophils, usually is seen in acute disease. Relative monocytosis and reactive lymphocytes and basophilia are often present.
- The WBC count may be normal in subclinical cases.
- A low packed cell volume is common in both acute and chronic disease.
- Serum protein usually is elevated as a result of chronic inflammatory stimulation. Plasma protein electrophoresis may demonstrate hypergammaglobulinemia and hypoalbuminemia.
- AST, LDH, bile acids, creatine kinase, and/or uric acid levels may be elevated, depending on the organ system affected.

Radiography

- Hepatosplenomegaly is the most common radiographic feature.
- Diffuse clouding of the air sacs may be present with airsacculitis.
- Often, no radiographic abnormalities are seen with chronic disease.

Antigen Capture

Immunoassay

- An immunoassay (IDEIA antigen system, California Avian Laboratories, Citrus Heights, CA) may be used to detect chlamydial antigen in naso-ocular discharges, pharyngeal swabs, and feces. The chlamydial organisms do not have to be viable for antigen to be detected.
- Shedding of organisms is often intermittent, producing false-negative results.
- Shedding is inhibited temporarily in birds tested within 1 to 2 weeks of treatment with erythromycin (e.g., Ornacyn, available in pet stores), doxycycline, tetracyclines, penicillins, chloramphenicol, tylosin, and quinolones.
- False-positive results also are common owing to cross-reactivity with some gram-negative bacteria. Confirm positive results using another method of testing.

Serology

Complement Fixation

- In the complement fixation (CF) test (Texas Veterinary Medical Diagnostic Laboratory, College Station, TX), single serum samples are of value if the titer is sufficiently high.
- Titers up to 1:8 are considered negative, 1:16 to 1:32 is suspicious, and >1:64 is positive. A fourfold rise in titer over a 4-week period is considered most significant. Titers may remain high following successful treatment.
- Young birds, budgerigars, cockatiels, canaries, and finches with chlamydiosis may not produce antibody titers high enough to be detectable by CF, making negative results unreliable in these birds.
- False negatives may occur when birds are tested early in the course of the disease, before sufficient antibody formation.

Latex Agglutination

- This test detects serum immunoglobulin M (IgM), which indicates a current infection.
- False-negative results are common in cockatiels, lovebirds, budgerigars, and some young birds, as well as in later stages of the disease.

Elementary Body Agglutination (Texas Veterinary Medical Diagnostic Laboratory)

- This test primarily detects IgM and is more sensitive than latex agglutination.
- IgM appears in the early phase of infection and wanes after approximately 3 weeks.
- False positives are rare, but false negatives are common.
- An elementary body agglutination titer of 80 suggests an active infection. Titers of 10 to 40 may be seen with low-grade infections, exposure, or recently treated infections.

Immunofluorescent Antibody

- This test primarily detects IgG, which appears in later stages of infection.
- False positives are more common than with other tests.

DNA Probe

- A highly sensitive and specific DNA probe for the detection of *Chlamydophila* infection is commercially available. Samples may be taken from blood, the oropharynx or cloaca.
- A positive result indicates an active infection, as false positives are unlikely.
- For *Chlamydophila* organisms to be detected in oropharyngeal secretions or cloacal swabs, the bird must be actively shedding organisms. Therefore, false-negative results are possible. However, a DNA probe is significantly more sensitive for detecting shedding than any other available method.
- For *Chlamydophila* organisms to be detected in blood samples, the bird must be bacteremic. Therefore, false-negative results are possible.
- To increase the likelihood of detecting infection, submit samples from the oropharynx, cloaca, and blood simultaneously.

Isolation on Culture

- Isolation requires live *Chlamydia* organisms.
- Success is highly dependent on proper transport medium, transport conditions, and previous antibiotic treatment.
- The chlamydial agent may be propagated in tissue culture, mice, or embryonated chicken eggs. Obtain postmortem samples from the spleen, liver, or air sacs.
- Isolation may be possible from antemortem exudate or fecal samples; however, shedding often is intermittent. This is the most reliable postmortem confirmation.

▼ ***Key Point*** False-negative results are common when testing for *Chlamydophila* organisms owing to intermittent shedding, administration of inhibitory antimicrobials, and production of low antibody titers in the face of active disease. Base the diagnosis of chlamydiosis on a combination of DNA probe and serologic testing, clinical signs, hematology, serum biochemical profile, plasma protein electrophoresis, and radiography.

Treatment

Tetracyclines are the most effective antibiotics against *Chlamydophila*.

▼ ***Key Point*** Tetracyclines must be administered for 45 days to be effective in eliminating infection. Client compliance is often a problem, especially when once- or twice-daily oral administration is prescribed. Treat clinically ill birds by a parenteral or direct oral route. Use food- and water-based dosage regimens in stable birds only. Monitor these birds to ensure that the treated food or water is being appropriately consumed.

- *Doxycycline* (Vibramycin, Pfizer) is the drug of choice for treatment of *Chlamydophila*. It is available in an oral (suspension, solution, or capsules) or IV form in the United States. The IV form should *not* be injected IM or SC.
  - The dosage of doxycycline varies, depending on the species. Administer 25 mg/kg q24h to macaws and cockatoos and 35 to 50 mg/kg q24h to African grey parrots, cockatiels, and Amazon parrots. Senegal parrots require 30 mg/kg q12h. Some birds will regurgitate on higher doses. Doxycycline may be mixed with a small amount of a favorite food, as long as that food is immediately and completely consumed.
  - For cockatiels and budgerigars, doxycycline may be added to a mixture of *hulled* millet seed and oats. Lightly coat the seed-oat mixture with sunflower oil, and add doxycycline at a rate of 300 mg/kg of seed mix. Feed birds this mix exclusively for 45 days. Use this route only in stable birds. Monitor birds to ensure that they are eating this diet.
  - Doxycycline for IM injection (Vibravenos, Pfizer) is available in countries outside of the United States and may be imported for use in birds. Administer 75 to 100 mg/kg IM every 7 days for 6 weeks.
  - Doxycycline may be effective for some birds when added to the drinking water. Use this route only in stable birds, and carefully monitor the birds to ensure that the water is palatable and that water consumption is normal. Birds may overconsume water during hot, dry periods or while on dry or pelleted diets, resulting in overdosage. Underdosage, resulting in treatment failures and possibly dehydration, may occur if birds refuse to drink treated water. Species that normally consume very little water, such as budgerigars *cannot* be effectively treated using water-based medication. Dosages are available for a limited number of species and include 300 to 400 mg/L water for cockatiels, 400 mg/L water for Goffin's cockatoos, and 600 to 800 mg/L water for African grey parrots.
- Secondary mycotic or bacterial infections owing to alterations of the normal enteric flora, stress, and immunosuppression are a common problem in birds treated with doxycycline.
- Thoroughly clean the environment following treatment to remove chlamydia organisms and prevent reinfection.
- Treat all birds sharing the same air space as birds diagnosed with *Chlamydophila* for 45 days.

Supportive Care

- Many birds with acute chlamydiosis are seriously ill and require supportive care such as fluid therapy, forced alimentation (see Chapter 168), and heat, as well as antibiotic therapy if secondary bacterial infection is present.

Prevention

- Because inapparent carriers are common and an accurate screening test is not available, it is difficult to prevent the introduction of *Chlamydia* organisms into a flock when purchasing new birds. A combination of serology and DNA probe to screen for chlamydiosis is recommended, with repeated yearly testing.

PSITTACINE VIRAL DISEASES

Psittacine Circovirus: Psittacine Beak and Feather Disease

Psittacine beak and feather disease (PBFD) is an infectious, sometimes fatal disease characterized by feather loss, feather dystrophy, occasional beak deformity, and destruction of the thymus and bursa. Originally believed to affect only white and pink cockatoos and a few other South Pacific psittacine birds, the disease has been reported in more than 30 species of Asian and South Pacific psittacine birds and is believed to be capable of causing disease in many others. Occurrence in Central and South American psittacine birds is rare. Death is attributed to secondary bacterial, viral, or mycotic infections or to general debilitation.

Etiology

- PBFD is caused by a non-enveloped, single-stranded DNA virus (PBFDV) that is structurally similar to the porcine circovirus and chicken anemia agent.

Transmission

- Virus may be recovered in the feces, crop secretions, and feather dust of infected birds. Being non-enveloped, PBFDV is thought to be extremely stable in the environment and may be resistant to many disinfectants.
- Infection may occur by inhalation or ingestion of the virus.
- PBFDV is believed to spread throughout the body of an infected bird via circulating WBCs. There is evidence that inapparent carriers may exist.

▼ ***Key Point*** Feather dust is a major method of transmission and environmental persistence of PBFDV. Feather dust may be dispersed through natural air flow and may contaminate food dishes, cages, bird carriers, insects, and human clothing.

Clinical Signs

PBFDV may cause peracute, acute hematologic, acute dermatologic, or chronic disease.

Peracute Form

This form is seen in neonates, most often cockatoos and African grey parrots, and may be associated with crop stasis, pneumonia, diarrhea, weight loss, and rapid death. There are few feather lesions.

Acute Hematologic Form

This form is seen almost exclusively in African grey parrots and on occasion in other African species.

- Patients usually present near or just after weaning age with severe weakness and depression.
- The primary hematologic feature is a marked pancytopenia, with WBCs sometimes absent and the hematocrit dropping to as low as 4%.
- Recovery is rare but has occurred with supportive care.

Acute Dermatologic Form

This form is seen in birds as young as 30 days of age, when feathers begin to replace neonatal down.

- Feather lesions include fractures, necrosis, hemorrhage, curvature, and premature shedding of affected feathers.
- GI signs include diarrhea, crop stasis, and anorexia. There may be few feather lesions, especially in young cockatoos, lovebirds, and African grey parrots.
- Death may follow the onset of clinical signs within days to several weeks.

Chronic Form

This form usually is recognized in psittacines younger than 3 years of age but has been reported in birds as old as 20 years of age. Birds may live for months to years before succumbing to secondary infections or chronic debilitation.

- Progressive feather abnormalities may be accompanied by beak lesions.
- Feather lesions include retained feather sheaths, bleeding within the pulp cavity, fractured feathers, clubbed feathers, circumferential constrictions within the feather shaft, curled or deformed feathers, and stress lines within feather vanes.
- Feather loss typically begins with powder down feathers. Contour, crest, wing, and tail feather loss is roughly symmetrical and progresses with each molt. Some birds become completely bald and remain so until death (months to years).
- Beak lesions often occur in galahs and Moluccan and sulfur-crested cockatoos but are not routinely seen in other species. Lesions may include oral ulceration and elongation and fractures of the beak, often accompanied by secondary mycotic or bacterial infections. Beak lesions usually occur after chronic feather loss but also can occur in birds with mild feather lesions. In cockatoos, the beak may appear shiny and black because of the absence of powder that settles on the beak during preening.

Diagnosis

Histopathology

- In affected feathers, typically there are ballooning degeneration and necrosis of epithelial cells in the epidermal collar and in the epidermal basal and intermediate zones of the developing rachis.
- Non-suppurative inflammation, characterized by perivascular accumulations of heterophils, plasma cells, lymphocytes, and macrophages, is the primary lesion seen in the feather pulp.
- Beak lesions histopathologically are similar to those seen in the feather shafts.
- The thymus and bursa typically are atrophied, with focal areas of necrosis and degeneration. These lesions are thought to cause immunosuppression.

Hematoxylin and Eosin Stain

- Basophilic intranuclear and intracytoplasmic inclusion bodies may be seen with hematoxylin and eosin (H&E) staining in the feathers, pulp, and follicular epithelium. These were once considered diagnostic for PBFDV; however, other viruses (e.g., avian polyomavirus) may induce similar intranuclear inclusion bodies.

DNA Probe

- A highly sensitive and specific viral DNA probe for the detection of PBFDV infection is commercially available (Infectious Diseases Laboratory, University of Georgia, Athens, GA). Birds latently infected can be detected by submitting 0.2 to 0.5 ml of whole unclotted blood. This test allows veterinarians to screen for birds subclinically infected with PBFDV.
- Birds testing positive on a blood DNA probe for PBFDV with *no* feather lesions should be retested in 90 days. If negative, the bird has cleared the virus and is likely immune. Birds continuing to test positive after 90 days are subclinically infected and may develop feather lesions at a later date.
- Birds testing positive on a blood DNA probe for PBFDV *with* feather lesions have an active infection. It is still possible that DNA-positive birds will mount

an immune response, clear the infection, and become blood DNA negative. However, keep birds with feather lesions strictly isolated until all feathers become normal. Abnormal-appearing feathers and their feather dust should be considered infectious. Monitor these birds for the development of normal feathers.
- Birds with feather lesions that continue to test positive and continue to grow abnormal feathers are unlikely to recover and will continue to be infectious to other birds as long as abnormal feathers are present.

▼ ***Key Point*** Keep all birds with abnormal feathers strictly isolated. Birds may become blood DNA negative before all affected feathers are molted. However, as long as abnormal feathers and their associated feather dust are present, the bird is continuing to shed virus and should be considered contagious.

Treatment

- There is currently no effective treatment for PBFDV.
- Provide supportive care (e.g., good nutrition, debridement of lesions, beak trimming, and heat) and antimicrobial therapy for secondary bacterial and fungal infections for chronically infected patients.

Prevention

▼ ***Key Point*** Using the DNA probe, test all birds for PBFDV prior to admission to the aviary.

- Isolate all birds testing positive for PBFDV to prevent contact with non-infected birds.
- Isolate all birds with feather lesions caused by PBFDV from direct or indirect contact with other birds until all abnormal feathers have been replaced with normal feathers.
- Exercise care to prevent feather or fecal dust from infected birds contaminating non-infected birds, particularly psittacine neonates.
- Viral particles, which are resistant to practically all disinfectants, may remain viable for more than 3 years in a contaminated environment.

Polyomavirus

Etiology

Polyomavirus is responsible for major economic losses in commercial budgerigar aviaries (budgerigar fledgling disease, BFD). Polyomavirus also has been reported to cause clinical disease in nearly all species of large psittacine birds and in passerine birds.

Budgerigars that survive BFD infection may develop feather abnormalities commonly referred to as "French molt." The lesions of French molt, however, also may be caused by psittacine circovirus.

Transmission

- Polyomavirus may be present in feces, feather dust, and oronasal and oral secretions. These contaminated materials may be inhaled or ingested by susceptible birds.
- Infected hens may pass the virus to offspring through the egg.
- Latent infections are common in budgerigars and are believed to be responsible for spread of this virus. Clinically normal parents may transmit polyomavirus to their offspring, some of which also become inapparent carriers.
- There is currently no evidence to support the existence of persistent infections in larger psittacine birds. However, some psittacine birds may become infected without demonstrating clinical signs and shed virus before eliminating the infection. Thus, birds with subclinical infections may be responsible for viral outbreaks, especially in pet stores and breeding facilities where susceptible neonates are exposed.

Clinical Signs

Hatchling Budgerigars <15 Days Old

- Signs include abdominal enlargement, delayed crop emptying, subcutaneous hemorrhage, retarded growth, and abnormal feathers.
- Sudden death is common. Reported mortality rates vary from 30% to 100% of affected hatchlings.

Budgerigars >15 Days Old

- Signs are similar to those described for hatchlings; however, the mortality rate is much lower.
- Fledglings may produce deformed primary flight feathers that break off at the base, leaving the birds unable to fly thus called "runners."

Neonatal Parrots

Non-budgerigar psittacine neonates are extremely susceptible to polyomavirus and are likely to develop clinical signs.

- Clinical signs usually develop at the time of weaning but may be seen anywhere from 14 to 150 days of age.
- Sudden death with and without clinical signs is common; birds that develop clinical signs usually die within 12 to 48 hours.
- Signs include diarrhea, delayed crop emptying, depression, anorexia, widespread hemorrhage, polyuria, and posterior paresis and paralysis.
- Unless immunosuppressed, adult non-budgerigar psittacine birds demonstrate mild or no clinical signs and eventually eliminate the virus. However,

these birds are likely to shed virus before recovery and thus serve as a source of environmental contamination.

Diagnosis

- Gross pathologic changes include hydropericardium, cardiomegaly, pale kidneys, ascites, hepatomegaly, splenomegaly, and diffuse petechial and ecchymotic hemorrhages in the subcutis, intestines, myocardium, epicardium, and serosal surfaces.
- Histopathologic demonstration of karyomegaly with basophilic intranuclear inclusion bodies in the kidneys, liver, spleen, heart, or feather follicles suggests polyomavirus.
- Confirmatory diagnosis requires the identification of viral antigen using virus-specific antibodies or the detection of viral nucleic acid using virus-specific DNA probes.
  - Highly specific and sensitive viral DNA probes (Infectious Diseases Laboratory, University of Georgia, Athens, GA or Avian Research Associates Laboratory, Milford, OH) can detect polyomavirus in infected tissue, cloacal swabs, and fresh feces of birds shedding virus. Identify birds that are shedding the polyomavirus by submitting a cloacal swab for testing. False-negative results may occur if the bird is not shedding virus at the time of testing.

Treatment

- Provide supportive care, as described for PBFD.

Prevention

▼ ***Key Point*** Quarantine all new birds for 30 days before entrance into an aviary. Perform DNA probe testing on all birds before entrance into an aviary. Isolate birds testing positive.

- Do not keep budgerigars in the vicinity of unvaccinated neonatal parrots.
- Do not mix neonates from different sources or return a neonate to the nursery after exposure to other birds.
- Disinfection with chlorine solution (50 ml/L of water) or prolonged contact with iodophors inactivates the virus.

Vaccination

A United States Department of Agriculture (USDA) approved inactivated avian polyomavirus is considered safe and effective (Biomune, Lenexa, KS). Administer the vaccine subcutaneously. Mild injection site reactions have been reported but should resolve within 3 to 6 weeks after injection. Follow vaccination guidelines provided by the manufacturer.

Pacheco's Disease

Also known as *herpes hepatosplenitis,* Pacheco's disease causes an acute, necrotizing hepatosplenitis that usually is rapidly fatal. The hallmark of Pacheco's disease is sudden death in birds that appear clinically normal until just before death. All species of psittacines of all ages, both imported and domestically raised, are susceptible.

Etiology

- Several strains of antigenically unrelated herpesvirus may cause Pacheco's disease; herpesvirus persists by inducing latent disease, with periodic reactivation and shedding. Clinical disease is dependent on the virus serotype, the species, and the immune status of the infected bird.

Transmission

- Although the exact route of Pacheco's disease virus transmission is unknown, this virus is present in high numbers in the feces and pharyngeal secretions of symptomatic and asymptomatic carrier birds. Thus, direct-contact contaminated aerosols and fecal-oral routes are the most likely routes of virus transmission.
- Herpesvirus is an enveloped virus and is relatively unstable in the environment. Anecdotal reports suggest that humans can serve as vectors, even with relatively long intervals between bird exposure. An incubation period of 3 to 7 days is common.

▼ ***Key Point*** Asymptomatic carriers of viruses that cause Pacheco's disease are common and often are incriminated in disease outbreaks. Any psittacine bird that has been exposed to or recovered from herpesvirus infection may potentially become a carrier.

Clinical Signs

- Sudden death without premonitory signs has been reported most frequently in Amazon parrots, cockatoos, lovebirds, Pionus parrots, and parakeets.
- Nonspecific signs include lethargy, anorexia, vomiting, diarrhea (sometimes hemorrhagic), biliverdinuria, naso-ocular discharge, and occasionally CNS signs.
- Signs often progress to death within several days; however, recovery has been reported in some birds with clinical signs consistent with Pacheco's disease virus.

Diagnosis

Antemortem Diagnosis

- Virus isolation from feces may reveal infection; however, viral shedding may be intermittent, making it ineffective for the detection of carrier birds.

- A reliable serologic test is not commercially available.
- A DNA probe is currently available that theoretically detects all known herpes serotypes affecting pet birds. Evidence suggests that the oral cavity or the cloaca is a highly reliable site for the collection of samples. To detect virus, birds must be shedding virus at the time the sample is taken, so false negatives are possible. The significance of a positive test is currently unclear at the time of this writing. A positive test result indicates that the bird is shedding a herpesvirus; however, what type of clinical disease, if any, that the detected herpesvirus may cause is unknown.

Postmortem Diagnosis

- Gross lesions may include hepatomegaly, splenomegaly, hemorrhagic enteritis, sinusitis, pneumonia, airsacculitis, and congestion and hemorrhage in the spleen, liver, and kidneys. Gross lesions may not be apparent in birds with peracute death.
- Histopathologic lesions often include hepatic and splenic necrosis.
- Virus may be isolated from liver, spleen, small intestine, and pancreas.

▼ ***Key Point*** Basophilic and eosinophilic Cowdry type A inclusion bodies, often present in the liver, spleen, kidneys, and pancreas, suggest herpesvirus infection.

Treatment

- Oral administration of acyclovir (Zovirax, Burroughs Wellcome) (80 mg/kg q8h × 7d) or the IV form given IM (40 mg/kg q8h) has been reported to decrease morbidity and mortality during Pacheco's disease outbreaks.
- Supportive care, including fluids, heat, assisted alimentation, and antibiotic therapy for secondary infections, may be of some benefit.

Prevention

- Do not mix susceptible birds with suspected carriers.
- Sanitation is critical in disease prevention because viral spread within an aviary occurs primarily by contact with contaminated feces and pharyngeal secretions.
- Thoroughly clean water and feed dishes followed by treatment with a disinfectant. Herpesvirus typically is inactivated by desiccation and through contact with most disinfectants.
- Instruct all aviary personnel to practice sound hygiene by washing and disinfecting hands before entering the aviary and after handling individual birds or cages.
- Reduce stress to help prevent shedding and spread of the virus.

Vaccination

Licensed Pacheco's disease virus vaccine is currently available (Biomune, Lenexa, KS). Two vaccinations subcutaneously in the inguinal area 4 to 8 weeks apart followed by yearly boosters are recommended. The vaccine is not effective against all avian herpesvirus serotypes.

Other Herpesviruses

Thirteen different herpesviruses are known to affect birds. The pathogenicity, host spectrum, and relation of these viruses largely are unknown.

- The only herpesvirus of known clinical significance in psittacine birds (besides those that cause Pacheco's disease) is Amazon tracheitis virus.
  - This virus causes a pseudomembranous tracheitis, pharyngitis, and sinusitis.
  - Signs include dyspnea, change or loss of voice, abnormal respiratory signs, and occasionally hemoptysis.
  - Base diagnosis on virus isolation or typical Cowdry type A inclusion bodies in the tracheal mucosa at necropsy.
  - Treatment is similar to that discussed for Pacheco's disease virus.
  - Based on histologic findings, another herpesvirus has been reported as the suspected etiology of wart-like lesions occurring on the feet of cockatoos.
  - Limited success has been reported in these cases with treatment with topical application of acyclovir cream.

Poxviruses

Poxvirus is commonly seen in canaries, pigeons, and wild birds. It is rarely seen in pet psittacine birds due to recent restrictions on importation of these birds.

Two forms of clinical disease caused by avian poxviruses commonly are encountered:

- Dry, or cutaneous, pox is characterized by discrete nodules on unfeathered skin.
- The more common wet, or diphtheritic, pox is characterized by fibronecrotic lesions in the respiratory system, conjunctiva, and pharynx.

The type of disease that develops may depend on the strain of infecting virus, route of infection, and the species, age, and condition of the host.

Etiology

- Avipoxviruses replicate in the cytoplasm of epithelial cells, inducing characteristic intracytoplasmic, lipophilic inclusion bodies called *Bollinger bodies*.
- Host susceptibility and virulence of the virus varies with the strain of avipoxvirus. Most poxvirus strains are relatively host specific.

Transmission

- Poxvirus is incapable of penetrating intact epithelium. Entrance into the host is gained through preexisting traumatic lesions or often is introduced into a flock via mosquito vectors.
- Virus is shed in epithelial crusts and exudates during active infection and in feces, skin, and feather quills during recovery and in latent infections.
- Virus transmission may occur through direct contact with affected birds or through contact with contaminated soil, food, or cages.
- Poxviruses are very resistant to desiccation, humidity, and light and may survive up to 1.5 years in the environment.
- Recurrence of poxvirus lesions has been reported in some species.
- It is postulated that asymptomatic carriers of poxvirus may exist.

Clinical Signs

Diphtheritic (Wet) Pox

- Yellow to gray-brown fibronecrotic plaques may occur on the mucosa of the mouth, choana, beak, esophagus, and trachea.
  - Multiple plaques may coalesce, forming tightly adherent diphtheritic membranes, which, if forcibly removed, leave a raw, hemorrhagic surface.
- Respiratory epithelium may be affected, with resulting dyspnea, rales, serous to purulent naso-ocular discharge, lethargy, and anorexia.
- Death due to secondary bacterial bronchopneumonia is common.

Cutaneous (Dry) Pox

- Signs include papules, pustules, and scabs on the unfeathered portions of the skin.
  - Secondary bacterial and fungal infections are common and may result in swelling or abscessation.
  - If no secondary bacterial infection occurs, the lesions may resolve without scarring in 10 to 14 days.
- In canaries and finches, wart-like lesions are common on unfeathered skin.

Diagnosis

- Clinical lesions suggest the diagnosis.
- Epithelial hyperplasia with ballooning degeneration and intraepithelial vesicles seen on histopathologic examination suggest avian pox.
- Intracytoplasmic lipophilic Bollinger bodies are pathognomonic.

Treatment

- Treatment of secondary fungal or bacterial infections is based on culture and susceptibility testing.
- Birds often have systemic illness, and mortality rates are high.
- Provide supportive care such as supplemental heat, fluid therapy, and assisted alimentation, if mouth lesions are present.
- Prophylactic administration of systemic broad-spectrum antibiotics may prevent secondary bacterial infections.

Prevention

Vaccination

Vaccines are available for canaries, pigeons, and domestic fowl. Use of these vaccines is restricted to high-risk populations, such as recently imported birds or birds exposed to large numbers of mosquitoes. Adverse reactions, including sudden death, have been associated with the vaccine.

Disinfection

Effective disinfectants include 1% potassium hydroxide (KOH), 2% sodium hydroxide (NaOH), and 5% phenol.

- To control an outbreak, replace all wood items in the aviary and clean and disinfect all equipment, nets, cages, and breeding containers.

Reoviruses

There are 11 avian serotypes of reoviruses that are antigenically distinct from each other and from reoviruses isolated from mammals. Of the common pet birds, African grey parrots have historically been the most severely affected.

Etiology

- Avian reoviruses have been isolated or identified by electron microscopy from asymptomatic psittacine and passerine birds.

Transmission

- Both horizontal and egg transmissions of reovirus occur in chickens. However, little is known about transmission in psittacine birds; horizontal transmission through oral and respiratory routes is believed to occur.
- The incubation period in experimental studies is 2 to 15 days. After natural exposure, replication of the virus occurs in the GI mucosa, followed by viremia (24–48 hours) and spread to other organ systems.

Clinical Signs

- Severity of the disease, and thus clinical signs, varies, depending on the age of the host, the virulence of the virus, the route of infection, and the presence or absence of secondary infections.

- Signs include anorexia, depression, yellow-orange urates, diarrhea, dyspnea, and occasionally paresis, hind limb paralysis, and bloody nasal discharge.

Diagnosis

- Gross pathologic changes include hepatosplenomegaly with pale yellow mottling and multifocal gray-white foci.
- The typical histologic lesion is disseminated or focal coagulative, necrotizing hepatopathy.
- A tentative histologic diagnosis may be confirmed by isolating the virus in cell culture from feces, liver, or spleen.

Treatment

- Supportive care is the only treatment currently available.

Prevention

- There currently is no serologic test or commercial vaccine available for reoviruses affecting pet birds.
- Strict quarantine of newly arrived birds, especially birds of African descent, may help prevent flock exposure. However, epidemiologic evidence suggests the existence of an asymptomatic carrier state.
- Viral infectivity can be reduced by prolonged contact with phenols, aldehydes, ethanol, halides, a 0.5% iodine solution, and a temperature of 158°F.

Adenoviridae

Adenovirus infections have been associated with depression, diarrhea, anorexia, and acute death in budgerigars, Amazon parrots, macaws, cockatoos, lovebirds, and parakeets. Adenovirus infections typically produce eosinophilic and basophilic intranuclear inclusion bodies.

Adenovirus infections in psittacines commonly are referred to as *inclusion body hepatitis* or *inclusion body pancreatitis,* depending on the predominant organ system involved.

Clinical Signs

- Signs generally are nonspecific and vary with the organ system affected. Signs include lethargy, depression, fluffed feathers, yellow urates, diarrhea, anorexia, and sudden death.

Diagnosis

- An enlarged, friable liver is the most consistent feature recognized on gross necropsy examination.
- Base definitive diagnosis on histologic examination of affected tissues from necropsy specimens. Histologically, there is diffuse necrosis of parenchymatous organs with eosinophilic and basophilic intranuclear inclusion bodies.

Treatment

- There is no specific treatment.
- General supportive care may be beneficial (warmth, fluids, forced alimentation, and antibiotic therapy for secondary infection).

Prevention

- Disinfect cages and supplies with an aldehyde disinfectant (requires 1 hour of contact) to prevent spread of the disease.
- Quarantine all new birds and strictly isolate affected birds.

Newcastle Disease Virus (Paramyxovirus-1)

Newcastle disease virus (NDV) is of extreme economic importance to the poultry industry. Legally imported birds are placed in USDA quarantine stations for 30 days. These were created to prevent the introduction of virulent forms of this virus into the United States.

▼ ***Key Point*** Smuggling of birds into the United States is the main source of NDV-infected birds. NDV should not be a problem for the serious aviculturist who does not expose an aviary collection to birds of questionable origin. NDV is a reportable disease.

Etiology

- There are nine serotypes of avian paramyxovirus (PMV). The most significant pathogens are virulent serotypes of PMV-1, which has been isolated from most species of domestic, aviary, and wild birds.

Transmission

- The respiratory and oral routes of transmission are equally important.
- Fecal contamination of eggshells may lead to viral spread. The virus infects the red blood cells and then is spread throughout the body.
- The incubation period typically is 4 to 7 days.

Clinical Signs

- Clinical signs depend on the virulence of the strain of virus involved.
- Predominant clinical signs in psittacine birds include fluffed feathers, conjunctivitis, and CNS signs (e.g., ataxia, wing and head tremors, and paralysis of extremities).
- The mortality rate is 22% to 55% of affected birds.
- Chronic NDV infection may develop in survivors. Virus has been isolated from oral and cloacal swabs 84 days to 1 year after exposure.

Diagnosis

- Serologic testing using hemagglutination inhibition, agar-gel immunodiffusion, or enzyme-linked immuno-

sorbent assay can indirectly diagnose avian PMV infection. However, serology is less effective in diagnosing infections than viral isolation. Antibodies typically appear 8 days after infection.
  - Hemagglutination inhibition is not specific for PMV-1 (crossreaction may occur with other PMVs); however, suspect NDV in birds demonstrating high titers.
- Base definitive diagnosis on virus isolation from feces or oral secretions of live birds or from infected organs at necropsy.

Treatment

- No treatment is available. Inform the USDA of any birds positively diagnosed with NDV.

Prevention

All birds legally presented for importation into the United States are placed in a USDA-approved quarantine station for 30 days, at which time samples are taken to detect hemagglutination viruses, including PMV and influenza. Birds with isolates of hemagglutination viruses that are pathogenic to chickens are refused entry.

▼ ***Key Point*** The best prevention against NDV in psittacine birds is avoidance of contact with birds that may have been smuggled into the country.

- No vaccine is available for psittacine birds.

SUSPECTED VIRAL DISEASES

Proventricular Dilatation Disease

Other names for this disease include myenteric ganglioneuritis, infiltrative splanchnic neuropathy, and macaw wasting disease. The disease originally was seen only in macaws but has been reported in almost all psittacine species. Both ultrastructural findings and epidemiologic evidence suggest that proventricular dilatation disease (PDD) has a viral etiology. The disease appears to have a protracted course, with low virulence and extended incubation periods. The potential mode of transmission is unknown at this time.

Clinical Signs

- Signs include intermittent regurgitation, diarrhea, polydipsia or polyuria, depression, passage of undigested food, progressive weight loss, abdominal distension, and central and peripheral neurologic signs.
- In birds with a severely dilated proventriculus, secondary aspiration pneumonia may develop after repeated bouts of regurgitation.

▼ ***Key Point*** Once signs of PDD develop, the disease is usually fatal.

Diagnosis

Antemortem Diagnosis

- A presumptive diagnosis may be based on clinical signs and radiographic identification of an enlarged proventriculus, and it may be made by ruling out all other possible causes of proventricular dilatation.
- Contrast radiography is usually necessary to positively identify a dilated proventriculus.
- Rule out other causes of regurgitation, proventricular dilatation, or passage of undigested food, such as GI foreign bodies, proventricular outflow obstruction (e.g., tumors and granuloma), heavy metal toxicity, proventriculus, enteritis, crop disorders, impaction, pancreatitis, and liver and kidney disease.
- Definitive diagnosis requires the identification of typical histopathologic lesions on biopsy specimens. A biopsy of the crop is relatively non-invasive and may provide a diagnosis. When obtaining a biopsy, be certain to include mucosal blood vessels in the sample. This will increase the likelihood of obtaining a nerve, thus demonstrating histologic lesions. False-negative results are likely if nervous tissue is not obtained or if lesions are absent in the crop but are present in other areas of the GI tract.
- The CBC may demonstrate a leukocytosis and nonregenerative anemia.
- The serum biochemical profile may reveal increased CK and hypoproteinemia.

Postmortem Diagnosis

The diagnosis is made by identification of characteristic lesions on necropsy.

- Gross pathologic changes include proventricular dilatation, ventricular ulcers, and undigested food in the lower GI tract.
- Confirmation of the diagnosis requires identification of accumulated lymphocytes and plasma cells in the nerves of the GI tract, brain, or spinal cord.
  - GI lesions include endoventriculitis, muscle atrophy, lymphocytic leiomyositis, and smooth muscle degeneration.
  - Lesions may be found in the brain and peripheral nerves. Peripheral nervous tissue is affected most often, and lesions include lymphocyte and plasma cell infiltrates in the mesenteric plexus ganglia and in the intrinsic and extrinsic nerves of the proventriculus and ventriculus and intranuclear and intracytoplasmic eosinophilic inclusion bodies in nerve cells of intestinal ganglia.
  - Other, less frequently encountered nervous tissue lesions include multifocal lymphocytic encephalitis with gliosis; neuronophagia and perivascular cuffing in the cerebellum, medulla oblongata, brain stem, cerebrum, spinal cord, and meninges; visceral ganglioneuritis; and lymphocytic poliomyelitis.

Treatment

- There are some reports of prolonged survival with supportive care, a soft gruel diet, and nonsteroidal anti-inflammatory drugs (NSAIDs). In most cases, however, PDD eventually is fatal.
- The use of NSAIDs has alleviated clinical signs and prolonged life in mild to moderately affected birds. Drugs used include meloxicam (Metacam, Merial), 0.1 to 0.5 mg/kg PO q24h, or celecoxib (Celebrex, Pfizer), 10 mg/kg PO q24h, for 6 to 12 weeks.
- It is currently unknown whether, but entirely possible that, birds treated with NSAIDs may continue to be infectious, even after resolution of clinical signs. Continue to isolate birds definitively diagnosed with PDD.

Prevention

- Because an etiologic agent, its transmission mode, and the incubation period have not been identified, prevention is difficult.
- Strictly isolate birds with confirmed PDD from direct or indirect contact with other birds.
- Quarantine birds exposed to confirmed cases for at least 6 months.

▼ ***Key Point*** Do not euthanize birds with radiographic evidence of proventricular dilatation unless a definitive, histologic diagnosis of PDD has been obtained. Rule out other causes of proventricular dilatation.

Papillomatosis

Papillomas are proliferative, wartlike lesions that may occur on mucosal surfaces of the intestinal tract, including the oral cavity, esophagus, crop, proventriculus, and cloaca. Lesions are most commonly identified on the cloacal mucosa. Some birds develop internal papillomatous disease, which results in multiple papillomas throughout the GI tract, and, in some cases, neoplasia of the liver or GI tract. The most common neoplasia associated with internal papillomatous disease is bile duct adenoma or adenocarcinoma. South and Central American birds such as Macaws, Amazon parrots, and conures are the species most frequently affected. Clinical signs have not been reported in South Pacific and African parrots (cockatoos, cockatiels, parakeets, lovebirds, and African grey parrots).

Etiology

- A viral etiology is suspected because papillomas often appear to spread through groups of birds. Currently, evidence suggests that a psittacine herpesvirus similar to that causing Pacheco's disease may be at least in part responsible for this condition. In one study, all birds with cloacal papillomas tested positive for psittacine herpesviruses. Psittacine herpesvirus has also been isolated from hepatic and GI tract neoplasia in birds with papillomas.

Clinical Signs

Clinical signs vary with the location of the lesions. Clinical signs have only been reported in Central and South American parrots.

- Signs of cloacal papillomas include straining to defecate, flatulence, malodorous and bloody stools, persistent enteric bacterial infections, and reduced fertility.
  - Cloacal papillomas may resemble granulation tissue and can be difficult to distinguish from cloacal prolapse.
- Oral papillomas may cause wheezing, dyspnea, excessive salivation, dysphagia, and persistent oral bacterial infections.
- Signs of esophageal, crop, and proventricular papillomas are less common and include vomiting, regurgitation, and weight loss.
- Birds with hepatic or GI tract neoplasia exhibit weight loss, lethargy, or signs referable to the space-occupying effects of the mass.

Diagnosis

- Base the diagnosis on the appearance of the lesions, biopsy, and histopathology.

Treatment

In some cases, the size and appearance of lesions wax and wane without treatment. Treatment is indicated when clinical signs are evident or, in the case of cloacal papillomas, if self-mutilation occurs.

- Cloacal papillomas may be gradually removed with chemical cauterization with silver nitrate sticks. Evert the papilloma from the cloaca, and roll a silver nitrate cautery stick onto the papilloma, taking extreme care not to cauterize normal mucosa. Rinse thoroughly with water. This procedure can be painful; therefore, anesthetize with isoflurane.
- Remove surgically by ligation and resection, electrocautery, or cryosurgery. The technique used depends on the extent of the lesion.
  - Circumferential lesions of the cloaca may require more than one procedure.
  - Take care to avoid the development of postoperative strictures.
- Treat secondary bacterial infections before surgical removal.
- Although a psittacine herpesvirus has been associated with papillomas, treatment with acyclovir is not effective.

Prevention

- Because papillomas may be caused by an infectious agent, carefully examine the cloaca and mouth of all birds being added to a collection for the presence of papillomas. Those with lesions should be denied entry.
- It may be difficult to detect birds that have had papillomas surgically removed. It is likely that a carrier state exists if a herpesvirus is the cause of lesions.
- Until a greater understanding of the relationship between psittacine herpesviruses and papillomas exists, avoid exposure of non-infected birds to birds diagnosed with herpesviruses.

BACTERIAL DISEASES

Gram-Negative Infections

Bacterial infections requiring treatment commonly are encountered in avian medicine, especially in birds that have been stressed, are on a poor nutritional plane, or are housed in unsanitary conditions. Normal intestinal flora in most pet bird species consist primarily of gram-positive bacteria. Although small numbers of gram-negative bacteria may normally be found in healthy birds, many gram-negative bacteria are primary or potentially opportunistic pathogens. Normal psittacine flora includes *Lactobacillus, Bacillus,* non-hemolytic *Streptococcus, Micrococcus, Staphylococcus, Corynebacterium,* and *Streptomyces* species and *Pasteurella gallinarum.*

Etiology

Commonly encountered gram-negative pathogens include *Escherichia coli; Enterobacter, Klebsiella, Pseudomonas, Salmonella, Proteus,* and *Campylobacter* species; and *Pasteurella multocida.*

Clinical Signs

Clinical signs depend on the organ system affected.

- Respiratory, GI, or nonspecific signs such as inappetence, lethargy, and ruffled feathers may be seen alone or concurrently.
- Septicemia, especially from invasion of enteric pathogens, is extremely common in pet birds.
  - Suspect septicemia in any severely depressed bird.

Diagnosis

- If a bacterial cause of illness is suspected, perform a Gram stain and culture on samples collected from sites of infection.
- CBC usually demonstrates leukocytosis, with a relative heterophilia. Toxic heterophils are often seen. With chronic disease, the serum protein electrophoresis may demonstrate a hypergammaglobulinemia. The serum biochemical profile may be helpful in identifying hepatic or renal involvement.

Respiratory System

- The rostral-most portion of the choana is a readily accessible site for collecting specimens from the upper respiratory system.

▼ ***Key Point*** Microbiologic analysis of samples from the choana is only significant if visible pathology is present or if clinical signs of respiratory disease are evident.

- Other techniques for isolation of respiratory microbial agents include aspiration of the sinuses and tracheal washing (see Chapter 168).
- Direct culture of the air sacs or air sac flushing may be performed via laparoscopy.

Gastrointestinal System

- Readily accessible sites for isolation of microbial agents include the crop, cloaca, and fresh feces.
- In large birds, the proventriculus and ventriculus may be cultured directly using a rigid endoscope or small flexible endoscope.

Other Organ Systems

- Organ systems such as the urogenital tract and liver, both common sites of bacterial infection, are accessible only by more invasive techniques, such as laparoscopy or exploratory laparotomy.
- Septicemic birds often are severely depressed and are unable to withstand invasive procedures. Aggressive empirical treatment with antibiotics is often indicated for these birds.

Treatment

Treatment is indicated when potentially pathogenic bacteria are isolated from a bird with system-specific signs or signs of septicemia.

▼ ***Key Point*** Identification of gram-negative organisms on samples taken from clinically healthy birds does not usually warrant treatment. Monitor these birds for clinical signs and shifts in bacterial flora.

Selection of Antibiotics

Whenever possible, select antibiotics based on culture and susceptibility testing.

Kirby Bauer Susceptibility Test

- Bacterial isolates are classified as susceptible based on serum concentrations of antimicrobial agents that are achievable in humans.

Table 169-1. ANTIBIOTICS FOR USE IN AVIAN PATIENTS

Generic Name	Product Name (Manufacturer)	Dosage	Comments
Amikacin (250 mg/ml)	Amiglyde (Bristol)	10–20 mg/kg q12h IM	Potentially nephrotoxic Synergistic with penicillins
Piperacillin (injectable)	Pipracil (Lederle)	100–200 mg/kg q6–8h IM, IV	Effective against most gram-negative bacteria Synergistic with aminoglycosides Freeze after reconstitution until use Good activity against gram-negative bacteria
Cefotaxime	Claforan (Hoechst-Roussel)	75 mg/kg q6–8h IM	Broad-spectrum, low toxicity Good against gentamicin-resistant gram-negative isolates
Ceftiofur	Naxel (Pharmacia & Upjohn)	75–100 mg/kg q6–8h IM, IV	Synergistic with aminoglycosides Reconstituted drug lasts 12 weeks in freezer, 10 days in refrigerator Broad-spectrum, penetrates into CNS
Enrofloxacin	Baytril (Bayer)	10–20 mg/kg q24h IM, PO	Broad-spectrum, little toxicity Irritating when injected IM—do not use for >3–5 days
Metronidazole	Flagyl (Searle)	50 mg/kg q12h	Effective against many anaerobic bacteria
Trimethoprim-sulfamethoxazole (suspension)	Bactrim (Roche)	100 mg/kg q12h PO	Good against many gram-negative and gram-positive isolates Excellent for hand-feeding neonates May cause emesis in some birds, especially macaws

CNS, central nervous system; IM, intramuscularly; IV, intravenously PO, orally (per os).

- Because it may not be possible to achieve these high levels in pet birds, this test may not accurately predict the efficacy of the antibiotic chosen in vivo.
- Determining the minimum inhibitory concentration (MIC) of antibiotics allows a more accurate assessment of antimicrobial efficacy in pet birds; however, this test is not readily available. For this reason, the Kirby Bauer test still is commonly used.
- When choosing an antibiotic based on standard Kirby Bauer testing check the following:
  - The bacterial isolate should be susceptible to the antibiotic.
  - The antibiotic preferably should be bactericidal, known to penetrate into the site of infection, and effective at very low serum concentrations.
- Antibiotics and dosages commonly used in pet birds are listed in Table 169-1.

Route of Administration

Oral Administration

- Direct oral administration of medications often is used in pet birds, especially for palatable solutions or suspension. However, this method is difficult for some owners. Instruct owners on the proper restraint techniques. Even after this, birds sometimes spit out the medication, and aspiration is a possibility.
- Addition of medications to a small amount of favorite food is a stress-free method and generally effective as long as the entire portion is readily consumed.
- Administration of antibiotics via drinking water is the least preferred method because most antibiotics are unpalatable and are not water soluble and because ingestion of the medication is sporadic and effective concentrations at the site of infection are rarely achieved.
- When a bird is hospitalized and the intestinal tract is functioning properly, oral medications may be administered via gavage tube.

Parenteral Administration

- Many antibiotics commonly used in avian medicine are poorly absorbed when given orally, necessitating parenteral administration.
- Use injectable antibiotics in the following cases:
  - When a bird is unwilling to take oral medications
  - When GI motility is altered
  - In critically ill or septicemic birds
- The advantages of this method include precise dosing, rapid development of therapeutic serum concentrations, and relatively stress-free administration.
- Some practitioners teach their clients to administer IM injections to their pets (the technique for IM injection is described in Chapter 168).

Monitoring

Assess antibiotic effectiveness by monitoring the resolution of clinical signs, serial hemograms, cytology, and culture. Serial fecal or cloacal Gram stains during and after antibiotic administration are important because development of secondary infections, especially candidiasis or aspergillosis, are common.

Gram-Positive Infections

Gram-positive infections occur less frequently in pet birds. Pathogens include beta-hemolytic *Streptococcus, Staphylococcus aureus,* and *Clostridium* spp. Follow the same principles for diagnosis and treatment as outlined previously for gram-negative infections.

Avian Tuberculosis

Etiology

Tuberculosis in psittacines, unlike that in mammals, usually is a primarily alimentary disease.

- Although a few cases of *Mycobacterium tuberculosis* and *M. bovis* have been reported in pet birds, the causative agent usually is *M. avium.*
- These gram-positive, acid-fast granulated rods are capable of causing disease in birds, pigs, guinea pigs, rabbits, and humans.
- Brotogeris parakeets (especially gray-checked parakeets) are particularly susceptible, followed by Amazon parrots, budgerigars, and Pionus parrots.

Transmission

- Transmission occurs primarily by ingestion of fecal-contaminated food, water, or soil; an aerosol route or wound contamination also is possible. The organism is capable of surviving in soil for up to 2 years.
- After ingestion, the organisms penetrate the GI mucosa and colonize under the serosa.
- A primary bacteremia occurs (usually without clinical signs), and the organisms are phagocytized (but not killed) by mononuclear phagocyte cells of the liver, spleen, and bone marrow. Multiplication within these cells causes a local reaction by the cell-mediated immune system and the formation of nodules, which may calcify with time.
- Release of the organisms from the liver results in a secondary bacteremia, with localization in lungs, kidneys, gonads, and intestines. Tubercles in the intestinal wall may open into the intestinal lumen, resulting in shedding of large numbers of organisms in the feces.

Clinical Signs

- Clinical signs include chronic weight loss (often despite a good appetite), depression, chronic diarrhea, polyuria, and poor feathering.
- Abdominal distension due to hepatomegaly and dilated, fluid-filled, thickened intestines is common.
- Subcutaneous and periorbital masses may be seen.
- Lameness due to endosteal bone proliferation occasionally is reported.
- Signs often are nonspecific and slowly progressive.

Diagnosis

Hematology and Serum Biochemistry

- Severe leukocytosis (>20,000) with marked heterophilia and monocytosis is common.
- Anemia and polychromasia usually are present.
- AST levels usually are elevated with hepatic involvement.

Histopathologic Lesions

- On postmortem examination, in addition to the grossly visible nodules previously described, diffuse infiltration of epithelioid or giant cells may result in a grossly thickened firm intestine, hepatomegaly, or splenomegaly.
- Histologically, the intestinal villi may be club shaped, swollen, and filled with epithelioid cells containing acid-fast rods.
- Definitive diagnosis is based on identification of acid-fast rods and epithelioid cells on biopsy or postmortem slide preparations. The liver is generally the most reliable source.
- Acid-fast staining or culture of feces also may demonstrate the organism, although false-negative results are common owing to intermittent shedding of organisms.
- Cultures require 3 to 6 weeks for results.
- Indirect diagnosis with intradermal tuberculin and slide agglutination tests also frequently produce false-negative results.

Treatment

- Euthanasia often is recommended because of the potential human health hazard, especially to immunocompromised owners.
- Successful treatment of pet birds with *M. avium,* mimicking human treatment protocols, has been reported.

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Chapter

170 Avian Dermatology

Tia B. Greenberg

Skin and feather disorders are common in companion avian species. Since many of these disorders have a psychological basis, either as the primary cause or as a contributing component, diagnosis and treatment can often be frustrating. A detailed history, physical examination, and assessment of a wide range of diagnostic tests are generally required for diagnosis.

ANATOMY

A basic understanding of normal structure and function of the skin is important.

- The avian skin consists of the epidermis, dermis, and subcutis tissue.
- The epidermis is composed of three layers: the basal or germinative layer, the intermediate layer, and the cornified layer.
- The dermis consists of the superficial layer and the dermal layer.
  - The dermal layer varies in thickness depending on its location on the body. For example, the face is a non-feathered area and therefore is thicker than feathered areas.
  - During breeding season, females and some males will develop dermal thickening and neovascularization in the ventral abdominal area. This area is referred to as the *brood patch* or *incubation patch* since it contributes to egg incubation. The area should not be confused with an area of feather loss and is a normal finding.
- The subcutis is composed of the fascia superficialis, the superficial layer, and the favia profunda.
  - The subcutis is a very thin layer and therefore not amenable to suturing.
  - Because this layer is so thin, it can be difficult to maintain a needle in the subcutaneous space while administering subcutaneous injections.

GUIDELINES FOR HEALTHY SKIN AND FEATHERS

Provide the bird owner with information on proper nutrition and husbandry guidelines to keep the bird's skin and feathers healthy.

- Provide a balanced diet including a wide variety of fresh fruits and vegetables, a pelleted diet, and limited access to seeds.
- Allow exposure to unfiltered natural sunshine daily, if possible.
- Bathe or mist feathers daily with water to help promote healthy skin and feathers.

GENERAL HISTORY AND EXAMINATION

History

A complete, detailed history is essential to the diagnosis of birds presenting with dermatologic disorders. Include questions such as the following:

- How long have you owned the bird, and where was it acquired?
- Are there any new birds in the house? If so, are they sick?
- Has this bird had any contact with other birds?
- Has anything changed in the bird's environment?
- What type of cage is used, and where is it located?
- What diet is normally fed and, of this, what does the bird actually consume? Have there been any changes in the diet?
- Has appetite or water consumption changed?
- Are there any behavioral changes?
- Is there any change in droppings?
- What is the bird's reproductive status?
- Have the bird's feathers changed in the past 6 months?
- Does the bird seem itchy?
- When was the onset of the presenting complaint? Has the problem progressed?
- Has the bird been examined by or treated by another veterinarian?
- Has there been any previous illness?
- Is the bird currently on any medications, including over-the-counter medications?

Physical Examination

Perform a thorough physical exam.

- Notice the distribution and severity of skin or feather lesions.

Table 170-1. COMMON DERMATOLOGIC CONDITIONS IN SPECIFIC SPECIES

Canaries
Knemidokoptes
Feather cysts
Scaly leg syndrome
Genetic baldness
Papilloma virus
Chlamydophila
Mites

Budgerigars
Knemidokoptes
Lipomas
Fibrosarcomas
Feather cysts
Uropygial gland problems
Polyfollicilitis

Cockatiels
Giardia
Genetic baldness
Feather cysts
Conures
Feather picking
Self-mutilation

Amazons
Amazon foot necrosis
Lipomas
Feather picking

Cockatoos
Feather picking
PBFDV
Papillomas

Rose-Breasted Cockatoos
Lipomas

Macaws
PBFDV
Feather picking

Lovebirds
PBFDV
Feather picking
Ulcerative dermatitis

PBFDV, psittacine beak and feather disease virus.

- Determine to which of four categories the problem belongs: lack of feather growth, abnormal feather growth, feather destruction, or pseudoproblems (normal changes presumed by the owner to be a problem) (Table 170-1).

DISORDERS OF THE SKIN AND SUBCUTANEOUS TISSUES

Infectious Diseases

Ectoparasites

Knemidokoptes pilae (Scaly Leg and Face Mites)

Etiology

- These mites are most commonly seen in budgerigars, canaries, and finches. They are occasionally reported in cockatiels, Amazon parrots, and other parakeets.
- Transmission is direct; the entire life cycle is on the bird.
- Infestation can be subclinical until the bird becomes immunosuppressed, similar to demodicosis in mammals.
- Clinical disease is often associated with periods of stress or malnutrition.

Clinical Signs

- Lesions begin on the featherless skin of the face, eyelids, cere, beak, and feet.
- Lesions begin as hyperkeratosis, crusting, and flaking, eventually progressing to characteristic honeycomb-like encrustations.
- If left untreated, infestation can deform the beak and nails.

Diagnosis

- Gross appearance of characteristic honeycomb lesions is usually diagnostic.
- If in doubt, perform a gentle skin scraping to confirm the presence of mites.

Treatment

- Give ivermectin at 0.2 mg/kg SQ, PO, or topically every 2 to 4 weeks for three to four treatments.
- Do not administer ivermectin by an IM route.
- For birds weighing <100 g, applying diluted ivermectin (1 mg/ml) topically to the featherless tract of skin overlying the jugular vein may also be effective.
- If proliferative lesions are excessive, gently debride with a cotton-tipped swab and a small amount of mineral oil.
- Corrective beak or nail trimming may be necessary in birds with chronic infestation.
- Correct underlying nutritional deficiencies, environmental stress, or disease.
- Treat all cage mates.

Dermanyssus gallinae (Red Mites)

Etiology

- Red mites affect canaries and are usually only a problem in large breeding operations.
- The mites feed on blood at night and may cause high mortality rates, especially among nestlings.

Clinical Signs and Diagnosis

- Birds are often uncomfortable, pruritic, and restless at night.
- Sometimes signs of anemia can be seen on physical examination.
- Mites usually feed on the bird during the night and live in the environment during the day. Covering the cage with a white cloth overnight and removing it in the morning may facilitate finding the mite. Mites appear as small red dots or may leave small trails of blood on the cloth.

Treatment

- Lightly dust the environment, including nest boxes, with pyrethrins or carbaryl powders.
- Disinfect the entire cage and eliminate crevices in which the mites can hide.
- Provide supportive care for anemic birds.

Biting Lice

- Biting lice that rarely infest pet birds include *Neopsittaconirmus, Psittaconirmus, Eomenopon,* and *Pacifimenopon*.
- These lice can cause a mild to moderate pruritus and hyperkeratosis.
- Identification of lice or eggs on the feathers is diagnostic.
- Pyrethrin sprays and powders can be used but have little residual effect.
- Repeat treatments every 2 weeks to kill newly hatched lice.

Viral Diseases

Herpesvirus

- Hyperkeratotic, papilloma-like lesions on the surface of the feet are relatively common in cockatoos and macaws. Lesions are believed to be caused by a herpesvirus, based on histologic evidence of characteristic inclusion bodies or identification of virus on electromicroscopy.
- Affected birds are clinically normal except for wart-like lesions on their feet.
- The diagnosis is based on physical examination and histologic examination of biopsy specimens.
- Lesions are usually self-limiting. Rubbing a small amount of a gentle moisturizing agent, such as aloe vera, into the feet daily helps loosen and remove hyperkeratotic tissue.

Avian Poxvirus

- Avian pox can cause lesions on the unfeathered skin that can appear ulcerative or as crusts, scabs, or proliferative lesions.
- Systemic or respiratory signs are usually more clinically significant than cutaneous lesions. A detailed description of diagnosis and management of avian poxviruses is discussed in Chapter 169.

Papillomavirus

- Wart-like lesions on unfeathered areas of the skin have occasionally been reported. Histologically, these lesions resemble those caused by papillomaviruses in other species. However, papillomavirus has only rarely been demonstrated to be the causative agent, and other viruses, such as herpesviruses, can cause similar lesions.
- Diagnosis is based on histologic examination and identification of the virus when possible.
- Lesions are benign but may become large or widespread in non-feathered areas. Surgical excision is indicated when possible.

Bacterial Diseases

Primary bacterial skin infections are uncommon. Most infections are secondary to trauma, including self-mutilation or other disease processes. The low incidence of primary pyoderma is thought to be due to high body temperatures and keratinocyte-derived lipids that inhibit bacteria growth.

Bacterial Folliculitis

Etiology

- Primary bacterial folliculitis is unusual in pet bird species. Folliculitis secondary to the trauma caused to the follicle by feather picking may be more common.
- Bacterial pathogens reported include *Staphylococcus* spp and *Aeromonas* spp.

Clinical Signs

- Clinical signs include erythema and swelling around feather follicles.
- If secondary to feather picking, feather loss and occasionally feather malformation may be seen.
- With severe, generalized infection, lesions may progress to erosions with scab formation.
- Pruritus may occur and occasionally may be severe enough to cause self-mutilation.
- Bacterial folliculitis is a rare cause of feather picking but may exacerbate picking if the bird is pruritic.

▼ ***Key Point*** Folliculitis generally does *not* cause feather picking and only rarely occurs as a consequence of feather picking.

Diagnosis

- Examine the skin underlying the feathers for lesions.
- Obtain one or more small skin biopsy specimens that include an affected follicle. When obtaining a biopsy specimen, keep in mind that avian skin and subcutis are extremely thin as compared with that of mammals. Submit biopsy specimens for histologic examination and culture and susceptibility testing.
- In some cases, samples for culture can be obtained via sterile aspiration of perifollicular swelling.
- If the feather pulp is infected, plucking an affected feather and expressing the pulp for cytologic examination and culture may sometimes reveal the causative agent.

Treatment

- Administer antimicrobial therapy based on culture and susceptibility results.
- Correct the underlying cause in birds with secondary folliculitis.

▼ ***Key Point*** Do not use topical antibiotic ointments, especially combination products containing corticosteroids, in birds. Oils from these products will be spread onto the feathers during preening, interfering with normal feather function. Birds can be extremely susceptible to the immunosuppressive effects of corticosteroids, even when applied topically.

Chronic Ulcerative Dermatitis

This syndrome is characterized by ulceration, hyperemia, feather loss, and self-mutilation in a localized area of the dermis. Lesions may be seen alone or may be associated with other diseases.

Etiology

- The cause is unknown but has been anecdotally associated with giardiasis in cockatiels, an unidentified virus in lovebirds, and hypovitaminosis E in other species. Environmental, behavioral, and hormonal factors may also play a role.
- *Staphylococcus* species are usually isolated on culture of lesions but are likely a secondary infection. Many other potential bacterial pathogens, including *Pseudomonas* species, may be cultured.

Clinical Signs

- Disease is most commonly seen lovebirds, cockatiels, grey-cheeked parakeets, Quaker parrots, Amazons, and cockatoos.
- Lesions usually are found in the ventral wing web area and lateral body wall underneath the wing or around the neck, but they can be seen in any area.
- The disease is usually associated with extreme pruritus; self-mutilation may occur.
- Skin may appear thickened, ulcerated, exudative, and hyperemic. Scabs and crusts may form over healing ulcers.

Diagnosis

- Base the diagnosis on clinical signs and the location of lesions.
- Obtain a complete blood count (CBC) and plasma chemical profile to rule out underlying disease.
- Obtain a skin biopsy for histologic examination.
- Perform bacterial and mycotic culture and susceptibility testing to direct antimicrobial therapy.
- Obtain a fresh fecal sample to rule out *Giardia* or other intestinal parasites.

Treatment

- Aggressive systemic antibiotic treatment is usually warranted. Sepsis may occur in untreated birds. Base selection on results of culture when possible. Pending culture, administer broad spectrum antibiotics that are effective against *Staphylococcus* spp., such as enrofloxacin (Baytril, Bayer), 7.5 to 15 mg/kg PO or IM q12h, or ceftazidime (Fortaz, Glaxo), 75 to 100 mg/kg IM q6–8h. Treatment for 4 to 6 weeks may be necessary.
- In some birds, especially cockatiels, lesions respond well to empirical treatment with metronidazole (Flagyl, Searle), 10 to 30 mg/kg PO q12h for 10 days. Treatment success may be due to underlying giardiasis or may be the result of the antimicrobial or anti-inflammatory effects of metronidazole.
- Apply topical silver sulfadiazine 1% cream (Silvadene, Marion Merrell Dow) or mild topical astringent such as Domeboro solution.
- Prevent self-mutilation. In severe cases, application of an Elizabethan collar may be necessary. With milder cases, control self-mutilation by administering antihistamines such as hydroxyzine (Atarax, Roerig), 2.2 mg/kg PO q8h, or anti-compulsive medications.

Avian Tuberculosis

- Cutaneous mycobacteriosis is unusual in pet birds. Lesions are usually caused by mycobacterium avium and can be an extension of systemic disease.
- Lesions usually appear around the head and neck. Most appear as subcutaneous swellings but may appear wart-like or ulcerated.
- Perform a skin biopsy or cytologic examination with acid-fast staining or polymerase chain reaction to identify mycobacterium.
- Inform owners of zoonotic potential.
- See Chapter 169 for a discussion of the diagnosis and treatment.

Fungal Diseases

- *Trichophyton flavis, Microsporum gypseum,* and *Malassezia* spp. are rare causes of dermatitis.
- Diagnosis is based on repeated isolation on culture and identification of organisms on histopathologic examination.
- Treat with appropriate antifungals.
- Warn owners about zoonotic potential.

Neoplasia

Cutaneous neoplasms occur with relative frequency in companion birds. Most diagnostic and treatment protocols have been extrapolated from mammalian medicine. Refer to the corresponding chapters on mammalian neoplasia for details (see Section 3).

Squamous Cell Carcinoma

This is the most common malignant tumor found on pet birds and has been reported in a variety of species.

Clinical Signs

- The most common sites affected include the back, uropygial gland, and wings. Oral mucosa, including the crop and esophagus, can also be affected.
- Tumors are locally invasive and readily metastasize.
- Tumors appear raised, irregular, and proliferative, and they may or may not ulcerate.

Diagnosis

- Perform an exfoliative cytologic exam, fine-needle aspirate, or excisional biopsy to diagnose.

Treatment

- Excise the mass with complete margins, when possible. Consider radiation therapy.
- Intralesional carboplatin and cisplatin, and cryotherapy, have also been attempted.

Lipoma

Lipomas are benign tumors of lipocytes that may grow rapidly over time. They are a common occurrence in budgerigars but can be seen in any pet species.

Etiology

- A diet high in fat and limited exercise seems to contribute to formation of lipomas. Tumors are most commonly found on obese birds. Hypothyroidism may play a role.
- There may be a genetic predisposition in budgerigars.

Clinical Signs

- Common areas affected include the ventral thoracoabdominal area, wings, back, neck, and legs.
- They may be single or multiple.
- Large tumors may interfere with movement.

Diagnosis

- Palpate for one or more well-delineated, soft, fluctuant masses. Masses may appear white or yellow through the skin.
- Perform a fine-needle aspirate or biopsy to confirm the diagnosis.

Treatment

- Many lipomas will respond to dietary changes. Place the bird on a low-fat diet, restrict the amount of food offered, and increase exercise.
- Surgery may be indicated if the masses interfere with movement, become ulcerated, or become infected or if the bird is picking at the mass. Complete excision can be difficult if the masses are large.
- Masses can be vascular, and risk of hemorrhagic can be significant.
- Do not use levothyroxine unless a diagnosis of hypothyroidism has been confirmed.

Liposarcomas

Etiology

- Malignant tumors are composed of immature adipocytes and lipoblasts.

Clinical Signs

- Liposarcomas usually appear as firm, multilobulated, poorly encapsulated, and highly vascular subcutaneous masses.
- They are usually found on the sternum or uropygial gland.
- Occasionally, they are found in the liver, skeletal muscle, and thoracoabdominal area.
- Tumors have the potential to metastasis and can be locally invasive.
- Liposarcomas have been reported in budgerigars, cockatiels, Quakers, and green-cheeked conures.

Diagnosis

- Perform a biopsy with histologic examination to confirm the diagnosis.

Treatment

- Compete excision is often difficult due to the invasiveness of the tumor.

Fibrosarcomas

Etiology

- Malignant tumors arise from mesenchymal cells and fibroblasts.
- Fibrosarcomas are commonly seen in budgerigars, cockatiels, and macaws but can occur in any species.

Clinical Signs

- Fibrosarcomas can occur anywhere on the body but usually are found on the head or limbs.
- They are locally invasive and rarely metastasize.
- Tumors appear as firm, irregular, non-movable subcutaneous masses that may ulcerate.

Diagnosis

- Perform biopsy and histopathology for diagnosis.

Treatment

- Surgery can be performed, but recurrence is common. Limb amputation may be indicated to prevent recurrence or metastasis.

- Intratumoral cisplatin and radiation have not been successful.

Xanthomas

- Xanthoma is not a true neoplasm but an accumulation of macrophages containing lipid, multinucleated giant cells and cholesterol in the dermis.
- Xanthomas are commonly seen in cockatiels, rose-breasted cockatoos, grey-cheeked parakeets, green-winged macaws, and budgerigars.

Etiology

- The etiology is unknown but may be related to high-fat diets and diets containing aromatic hydrocarbons.
- Most affected birds are obese and have been maintained on a high-fat, seed-containing diet.

Clinical Signs

- These tumors usually only become a problem if the bird picks at the area, the lesions become traumatized, or they become extremely large.
- Lesions can be diffuse or localized.
- Masses appear as areas of thickened, yellow-orange, friable skin.
- They commonly occur on the wing tips, abdomen, and thighs but may occur anywhere.

Diagnosis

- Characteristic gross appearance is often diagnostic.
- Perform a biopsy and histologic examination to confirm the diagnosis.

Treatment

- Small masses that are not traumatized may not require treatment.
- Dietary correction may prevent future occurrence.
- Attempt surgical excision. Some masses are difficult to excise due to their large size and difficulty in closing the defect. Affected dermis is very friable and does not hold suture well.
- Irradiation with low-energy x-rays or hyperthermia has been suggested for lesions not amenable to surgical excision.

Follicular Cysts

Etiology

- These are commonly referred to as feather cysts and consist of an accumulation of keratinaceous debris within a follicle. Cysts may be acquired or congenital.
- Acquired cysts may form secondary to trauma, malnutrition, or bacterial or viral infection of the follicle.
- Congenital cysts are usually seen in canaries, especially in Norwich and Gloucester. These birds are genetically bred for soft feathering, which may predisposes them to cyst formation.
- Folliculomas, benign tumors of the feather follicles, may resemble or contribute to follicular cyst formation. Differentiation is based on histologic examination following surgical excision of the cyst.

Clinical Signs

- Lesions most commonly appear on the wing or back.
- Raised yellow to beige subcutaneous masses, often freely movable, can become quite large.
- Birds may pick at these areas.
- Incision of lesions may reveal caseous keratinaceous debris or may contain an entire feather (ingrown feather).

Diagnosis

- Perform an excisional biopsy with histologic examination.
- Location and appearance of the gross lesions may be diagnostic.

Treatment

- Complete surgical excision of the entire follicle is the treatment of choice.
- Fulguration with an electrosurgery or lancing and curettage of the follicle may also be successful.
- In canaries with congenital cysts, removing the entire affected feather tract may be required.

Other Diseases of the Skin

Allergic Dermatitis

- Birds develop dermal lesions that are histologically similar to those seen in mammals with allergic dermatitis. However, little information exists on allergic response in birds.
- Anecdotal reports suggest that pruritic birds with lesions compatible with allergic dermatitis may improve when the suspected allergen is removed or antihistamines are administered.
- Intradermal skin testing has been examined in psittacine species; however, results have not been conclusive and testing cannot yet be recommended to confidently diagnose allergies in these species.
- Antihistamines reported to be effective in birds include hydroxyzine HCl (Atarax, Roerig), 2.0 to 2.2 mg/kg PO q8h, and diphenhydramine, 2 to 4 mg/kg PO q12h.
- Some birds have anecdotally improved on oral essential fatty acid therapy.

Amazon Foot Necrosis

This syndrome has been reported in all species of Amazon parrots but is most commonly seen in yellow-naped and yellow-headed Amazon parrots. Affected birds will chew on the scaled portion of their feet and hocks, sometimes to the point of tearing scales and

underlying tissue. Reappearance of lesions is often cyclic.

Etiology

- The cause of this condition is unknown.
- Proposed causes include contact hypersensitivity, poor nutrition, seasonal sexual frustration, high-fat diets, and bacterial, viral, and immune-mediated infection.
- *Staphylococcus* has been isolated from many of these birds but may represent a secondary infection.

Clinical Signs

- Birds often appear pruritic or painful around the hocks and feet. Sometimes this is a promontory sign.
- There may be areas of black and brown patching of the scales on the feet and legs prior to gross necrosis or self-mutilation.
- Lesions range from areas of dark brown or black swelling to scaling and peeling of the superficial scales to erythremia, necrosis, and sloughing or mutilation of the scales, skin, and deeper tissues.
- Secondary bacterial or mycotic infections may be present.

Diagnosis

- Obtain a detailed history, including environmental and dietary history.
- Perform a CBC, plasma biochemistry, bile acid concentration, and plasma protein electrophoresis to look for underlying disease.
- Diagnosis is usually based on the gross characteristics and distribution of lesions.
- Due to the limited amount of skin over these areas, skin biopsy is difficult to perform.
- Perform deep culture and susceptibility testing on samples from the lesions.

Treatment

- Long-term management is often required.
- Maintain strict sanitation of the environment.
- Try to eliminate contact allergens if identified.
- Administer antibiotics based on cultures and susceptibility testing.
- Administer antifungal therapy if indicated.
- Administration of hydroxyzine HCl (Atarax, Roerig) at a dosage of 2.0 to 2.2 mg/kg PO q8h may diminish pruritus and mutilation.
- Topical treatments include chlorhexidine solution or povidone-iodine solution diluted 1:10 and applied daily to the areas. Apply silver sulfadiazine 1% cream (Silvadene, Marion Merrell Dow) or topical antibiotic creams when indicated.
- Apply bandages or an Elizabethan collar as needed to prevent further mutilation.

Nutritional Disorders

Hypovitaminosis A

- This is one of the most common nutritional deficiencies seen in pet birds.
- Squamous metaplasia of epithelial cells in the oral and respiratory mucosa often progress to the formation of white, keratin-filled plaques.
- Signs are usually confined to the respiratory or oral mucosa, but occasionally white plaques are found in the subcutaneous tissues around the beak, submandibular, or periorbital regions.
- See Chapter 171 for details on diagnosis and treatment.

DISORDERS OF THE CUTANEOUS GLANDS

- Birds do not have sweat glands.
- There are four major types of cutaneous glands found in bird skin: glands of the external ear canal, meibomian eyelid glands, pericloacal glands, and the uropygial gland.

Uropygial Gland

Normal Anatomy and Function

- The uropygial gland is a bilobed gland found at the tail base of most psittacine birds. It drains into a single papilla at the base of the tail.
- Normally, the gland is easily expressed and secretes a clear, oily fluid.
- This gland is absent in Amazon parrots, some pigeons, and doves.
- The uropygial gland produces a sebaceous material containing vitamin D precursors, which are converted to the active form of vitamin D_3 when exposed to ultraviolet light. During preening, the active form of vitamin D_3 is ingested.
- Exposure to unfiltered ultraviolet light is necessary for this metabolic process to take place.
- Material produced by the uropygial gland is very important for waterproofing feathers.
- Material produced by the gland also produces antibacterial and antifungal components, which help maintain the integrity of the skin.

Disorders

There are three common uropygial gland disorders: impaction, abscessation, and neoplasia.

Impaction and Abscessation of the Uropygial Gland

- An impacted gland is a gland that does not express easily; fluid generally remains clear unless a bacterial infection is present.
- A gland that is abscessed may or may not express normally. Fluid within the gland contains purulent exudate.

- Obtain fluid from the gland via expression or fine-needle aspirate for cytologic examination and culture.
- Remove dried exudates or other debris blocking the papilla to drain an impacted gland.
- Administer antimicrobial therapy as indicated from culture and susceptibility testing.
- Surgical extirpation may be necessary for abscesses not responsive to medical therapy or for neoplastic conditions.

Uropygial Gland Tumors

- Tumors of this gland include squamous cell carcinoma, adenoma, adenocarcinoma, and fibrosarcoma.
- The most common tumor found is fibrosarcoma.
- Adenomas and adenocarcinomas are commonly found in budgerigars and canaries.
- Perform a fine-needle aspirate for cytologic examination or biopsy with histologic examination.
- Obtain radiographs to determine if metastasis has occurred and to evaluate the invasiveness of the tumor.
- Attempt complete surgical excisions if an adenoma is diagnosed.
- Adenocarcinomas and fibrosarcomas carry a poorer prognosis, especially if the tumor has invaded the pelvic bones, since complete excision is rarely possible.
- If the invasion into the pygostyle has occurred, amputation can be attempted.

DISORDERS OF THE FEATHERS

Anatomy and Function

- Feathers serve three primary functions: flight, insulation, and waterproofing.
- In addition, feathers are used to demonstrate territorial behaviors, courtship, and defense.
- Feathers are similar to hair in that they are derived from epithelium and dermal layers of the skin.
- Stress, nutrition, hormones, and diseases can affect feather growth.
- In most birds, the body surface is divided into non-feathered portions called apteria and feathered portions called pterylae.
- There are 10 major feather types:
  - Contour (vaned) feathers consist of major flight feathers of the wing and tail.
  - Semiplume feathers provide insulation.
  - Filoplume feathers are proprioceptive.
  - Powder down feathers produce powder (keratin).
  - Bristles are found around the mouth, nostrils, and eyes.
  - Coverts are arranged in rows on the wings and tail.
  - Remiges are found in the wing and are responsible for flight.
  - Retrices are the tail feathers.
  - Down feathers are small fluffy feathers used for insulation.
  - Hypopnea feathers are attached to the underside of other feathers.

Molting

- Molting is the shedding and replacement of the stratum corneum and feathers. New feathers erupting trigger the shedding of the old feather.
- This process depends on neurohormonal factors, which are regulated by stress, thyroid, gonads, photoperiod, and breeding state.
- Environmental heat and humidity promote molting; usually 60% humidity is adequate for proper molting.
- Most birds will molt once a year, but budgerigars can sometimes molt 2 to 3 times a year.
- Some psittacine birds may take up to 2 years to complete a single molt cycle.
- African grey parrots, cockatiels, and cockatoos constantly shed powder down, and this should not be considered abnormal.
- Lack of normal molting can be the cause or the result of disease.
- During the molting process, the metabolic demand on the bird is increased. A well-balanced diet should not be overlooked.
- A diet lacking protein can contribute to an improper molt.

Coloration

- A variety of pigments and structural adaptations are responsible for the colors seen in bird plumage.
- There are three principle pigments found in bird feathers: Melanin is the most common pigment and is responsible for black, grays, and browns. Carotenoids are responsible for the intense reds and yellows. Porphyrins produce a range of reds, browns, and greens.
- Birds lacking sources of dietary carotenoids (orange or dark green fruits and vegetables) may be able to maintain bright orange or yellow plumage.
- Any color abnormalities of feathers can be caused by deficiencies of one or more nutrients such as lysine; choline; protein; essential fatty and amino acids; vitamins A, D, and E; copper; zinc; and iron.

Disorders of the Feathers

Common feathering problems include broken blood feathers, abnormal-appearing feathers, lack of feather growth or regrowth resulting in feather loss, and feather picking.

Pseudoproblems

- Pseudoproblems are conditions that inexperienced owners perceive to be a problem but that are normal behavioral or physiologic changes. These problems include molting, dandruff, and bare areas.
- Molting (see the discussion above) is often confused by the owner as feather picking.
- Birds spend a significant amount of time preening their feathers, and shed feathers may be found in or around the cage. Considering a complete molt may take up to a year to complete, an owner may consider this excessive.
- New, emerging feathers, called *pin feathers* because they are partially or completely enclosed in a keratin sheath, can be found in areas where the old feathers were shed. These are often readily visible on the head, an area that solitary birds cannot easily reach to preen.
- Dandruff on the cage bottom is a common owner misperception. What are mistaken for dandruff are small pieces of the keratinaceous sheath that surrounds newly emerging feathers. Pieces of the sheath are picked off and dropped to the cage floor during normal preening; the amount of "dandruff" on the cage bottom can be considerable during a heavy molt but is normal.
- Bare areas called apteria (see above) are normal featherless areas between feather tracts. Some owners become concerned that these areas are abnormal.
- Some color mutations of cockatiels normally have a featherless area under the feather crest on the head.

Broken Blood Feathers

- Newly emerging feathers, especially large feathers on the tail and wings, contain a rich blood supply within the developing sheath. This blood supply gradually recedes as the feather grows. If the feather is broken, significant hemorrhage can occur.
- The broken feather will usually continue to bleed until action is taken. Continued hemorrhage can be fatal.
- To control hemorrhage, the feather can be carefully pulled from its base.
  - For removal, the feather should be isolated from surrounding feathers.
  - Place a hemostat around the base of the feather.
  - Firmly stabilize the wing or tail at the feather's origin.
  - Apply gentle traction until the feather is removed.
  - Apply direct pressure to the skin where the feather originated until the bleeding stops.
  - If bleeding continues, a small amount of surgical glue can be applied to the skin or a small absorbable suture can be placed.
  - Avoid applying chemical or electrical cautery on the skin where the feather was pulled. Cautery can damage the feather follicle and cause abnormal feather growth and feather cysts.
- Pulling very large tail or wing feathers on large birds such as macaws and cockatoos can sometime cause significant tearing of the skin. For these feathers, ligate the blood feather with suture material slightly proximal to the break. Monitor these birds to ensure that hemorrhage does not recur.
- Avoid applying chemical cautery to the bleeding feather shaft, since the bird can ingest it during preening.

▼ ***Key Point*** Broken blood feathers can cause significant, even fatal, hemorrhage. Treat breakage as an emergency situation.

Feather Loss without Plucking

Spontaneous feather loss or lack of feather regrowth occurs much less commonly than feather picking in pet birds.

Etiology

Feather loss without plucking can be caused by the following:

- Genetic baldness under the crest feathers in color mutation cockatiels
- Ectoparasites, especially Knemidokoptes
- Damaged follicles
- Malnutrition
- Viral diseases, especially psittacine beak and feather disease virus (PBFDV) (circovirus) or avian polyomavirus
- Hypothyroidism
- Excessive or irregular molt pattern
- Genetic factors (especially in Lutino cockatiels)
- Obesity
- Systemic disease (septicemia alopecia)

Clinical Signs

- Feather loss can occur anywhere on the body, including the head region.
- The surrounding skin may or may not appear normal.
- The owner denies ever observing the bird picking itself.

Diagnosis

- Obtain a detailed history including diet, housing, management, initial appearance of lesions, lesion progression, lesion duration, pattern of feather loss, previous treatments, and response.
- Perform a thorough physical examination; look specifically for abnormalities in emerging feathers.
- Perform a CBC, plasma chemical analysis, bile acid concentration, plasma protein electrophoresis, and possibly whole body radiographs to look for underlying disease resulting in poor feathering.

- Test for PBFDV and polyomavirus. See Chapter 169 for details on diagnosis.
- Consider obtaining a skin biopsy that contains abnormal feather follicles for histologic examination.

Treatment

- Treatment consists of correcting any underlying disease or nutritional deficiencies.
- See the discussion of infectious disease above, nutritional and endocrine diseases below, or Chapter 169 for details on treatment.

Nutritional Diseases

Nutritional excesses, deficiencies, and imbalances are common in avian patients.

Etiology

- Birds are often fed an all-seed diet, which is inadequate in essential fatty acids, zinc, copper, protein, and vitamins A, E, and B.
- Protein and amino acids are essential for hormone, enzyme, muscle, bone, and normal feather production.

Clinical Signs

- Delayed or abnormal molt
- Prolonged retention of old feathers, resulting in ragged, frayed feathering
- Dull coloration
- "Bronzing" or brown or black appearance to the tips of feathers
- "Stress bars" or lines of depigmentation on contour feathers
- Excessively scale or thickened skin on the face and feet
- Overgrowth or abnormal consistency of the beak and nails
- Signs of respiratory, hepatic, or renal disease secondary to malnutrition

Diagnosis

- Obtain a complete dietary history.
- Birds with dermatologic signs of malnutrition often have systemic manifestations as well, such as hepatic, respiratory, or renal disease.
- Perform a CBC, plasma biochemical analysis, bile acid concentration, and plasma protein electrophoresis to look for systemic disease.
- Obtain radiographs to rule out systemic disease.

Treatment

Advise owners to convert the bird to a nutritionally complete, well-balanced diet. Although species variation exists and information on what constitutes a balanced diet is incomplete, general guidelines include the following:

- Add fresh fruits and vegetables
- Add whole grains and legumes
- Feed a commercial pelleted diet
- Supplement seeds with a balanced vitamin and mineral supplement while converting to a new diet

Endocrine Causes of Feather Abnormalities

Hypothyroidism

Etiology

- Hypothyroidism can lead to symmetrical feather loss without pruritus. Many anecdotal reports exist in pet birds, especially Amazon parrots. However, only one published report, in a scarlet macaw, exists. Lack of confirmed cases may be due to the unavailability of thyroid-stimulating hormone (TSH) for stimulation testing and due to the lack of established normal T4 values for avian species.
- Budgerigars with iodine-deficiency goiter may become hypothyroid. However, the most common clinical manifestation of goiter in these species is related to the space-occupying effects of the enlarged thyroid gland.

Clinical Signs

- The plumage may appear dull, fringed, and have black tinting.
- Hyperkeratosis and thickening of the skin may occur.
- Mild to diffuse loss of contour feathers may be seen over the head and body.
- Primary feathers may be tattered and show bronzing.
- No evidence exists of molting or newly emerging feathers in bald areas.
- Affected birds may be obese.
- Poor reproductive performance may be seen.
- There may be a mild anemia and elevated serum cholesterol concentration.

Diagnosis

- In budgerigars with goiter, a positive response to supplementation may be diagnostic.
- In other species, clinical signs, history, skin biopsy, and basal T4 may be suggestive.
- Decreased basal T4 concentration alone is not diagnostic, as many factors can influence T4 concentration and normal values have not been well established.
- A positive response to exogenous L-thyroxine supplementation alone is not diagnostic. Most euthyroid birds will undergo a molt or lose weight with supplementation.
- Perform a CBC and plasma biochemical analysis.
- Obtain radiographs to rule out systemic causes for disease.
- If available, perform a TSH response test by administering 1 IU of TSH per kg IM. Obtain a presample and a 6-hour post-sample.

- A normal TSH response is a twofold increase from basal T4 concentration; failure to reach this increase is diagnostic.
- Since TSH may not be widely available, it may be necessary to base a presumptive diagnosis on clinical signs, results of the CBC and chemistry profile, basal T4 concentration, and skin biopsy and on ruling out other causes of feather loss.

Treatment

- Provide supplemental oral iodine to budgerigars.
- Administer L-thyroxine at a dosage of 0.01 to 0.02 mg/kg PO q12h. This dosage is empirically based on treatment in small animals; pharmacologic data on appropriate administration in birds does not exist. Supplement the hormone with caution and carefully monitor the bird for response to treatment and toxicity.
- Do not administer L-thyroxine in drinking water.
- Obtain a periodic serum T4 concentration to monitor response to therapy and potential toxicity.
- Serious side effects include anorexia, cardiotoxicity, hyperactivity, and death.

▼ ***Key Point*** Hypothyroidism is an unusual cause of feather loss in pet birds. Empirical supplementation of L-thyroxine in birds can have serious, life-threatening side effects. The proper dosage in birds has not been well established. Monitor carefully for signs of thyroid toxicosis such as hyperactivity, weight loss, poor feathering, anorexia, or increased appetite, and discontinue use if observed. Sudden death has also been reported.

Other Endocrine Abnormalities

- Spontaneous hypoadrenocorticism (Cushing's disease) has not been reported in pet birds. Iatrogenic hypoadrenocorticism due to exogenous steroid administration is common; however, dermatologic signs have not been observed.
- Baldness in male canaries is believed to be caused by a testosterone deficiency. An incidence of up to 60% has been anecdotally reported. Treatment with testosterone, 2.5 mg/kg IM or PO once weekly for 6 weeks, may induce feather regrowth in some affected birds.

Feather Picking and Self-mutilation (Non-behavioral)

- Feather picking and self-mutilation of feathers are extremely common problems in pet birds. Some birds pull the feathers out, whereas others will shred or mutilate existing feathers without removing them. Occasionally, mutilation of the skin and/or underlying muscle may accompany feather mutilation or may be seen alone.
- Although any species of psittacine bird can be affected, feather picking is most common in African grey parrots, cockatoos, Eclectus parrots, conures, and macaws. In these species, psychological or behavioral disorders are the most common cause of feather picking (see the discussion later in this chapter). In small birds such as budgerigars and cockatiels, an underlying disease process is more likely to cause in feather picking than psychological causes.
- Feather picking can be extremely frustrating to diagnose and treat. A wide variety of disease processes can cause or contribute to feather picking, and extensive diagnostic testing is usually required to identify the cause. In many cases, the cause appears to be behavioral. Successful treatment of behavioral feather picking varies considerably and, in some cases, remains nonresponsive to environmental, behavioral, or pharmacologic treatment.

Etiology

- Nearly every infectious and metabolic disease in birds has been reported to initiate or exacerbate feather picking in pet birds. In most cases, the mechanism of this response is unknown. Feather picking has been most commonly associated with the following:
- Endoparasitism—Especially pruritic picking in the wing web area in cockatiels with giardiasis.
- Hepatic disease
- Renal disease
- Air sac disorders or coelomic cavity granulomas—These may cause focal feather picking.
- Ingluvitis—Occasionally, this causes focal picking over the crop.
- Enteric bacterial or mycotic infection
- Allergic dermatitis—Food, contact, or environmental allergens; birds may appear pruritic or agitated.
- Neoplasia of any type
- Follicular dermatitis—This is rarely a primary cause but may occur secondary to feather picking and may exacerbate the behavior. Dermatitis may be bacterial, viral, or mycotic. Birds often appear pruritic or agitated.
- Heavy metal toxicity—Zinc or lead toxicosis has been anecdotally associated with feather picking.
- Nutritional deficiencies—Such deficiencies may cause pica and feather picking.
- Topical sprays—Many over-the-counter or homemade "remedies" for ectoparasites or for the prevention or treatment of feather picking are irritating to birds and can cause feather picking.
- Soap, shampoos, or other products used for bathing birds.
- Hypothyroidism—This does not usually cause feather picking.
- Ectoparasitism—Although rare, red mites, lice, and Knemidokoptes can contribute to feather picking.

Diagnosis

- Obtain a complete history, including duration and progression of feather picking, areas of feather loss, and any previous treatment.
- Perform a complete physical examination.
- Obtain blood for a CBC, plasma biochemical analysis, and plasma protein electrophoresis to look for underlying disease.
- Perform diagnostic testing to rule out infectious diseases such as *Chlamydophila,* PBFDV, and polyomavirus (see Chapter 169).
- Measure blood concentrations of heavy metal.
- Perform skin and feather scrapes to rule out ectoparasites when indicated.
- Perform a fecal direct smear, float, and Gram stain.
- Perform a skin biopsy, including affected feathers for histologic examination and culture.
- Obtain whole body radiographs to investigate systemic disease.
- Consider performing laparoscopy to investigate metabolic disease and determine if the bird is reproductively normal. Obtain biopsy samples of abnormal organs where indicated.

Treatment

- Identify and treat any underlying medical problems.
- Consider administration of metronidazole (50–60 mg/kg q12 PO for 7–10 days) to treat *Giardia* in any pruritic, feather-picking cockatiel, even if the fecal examination is normal, since organisms are shed intermittently. Many feather-picking cockatiels will improve with metronidazole therapy, regardless of the cause. The reasons for this positive response are not clear. Other species of birds rarely respond.
- Antihistamines may be effective if the bird appears pruritic. Administer hydroxyzine HCl (Atarax, Roerig) at 2 mg/kg orally twice daily. Some birds may become drowsy.
- Correct any dietary deficiencies.
- Apply a physical barrier to plucking, such as an Elizabethan collar or tube collar, *only* if the bird is in danger of inflicting serious harm to itself. Birds that are mutilating to the point of removing skin and underlying tissues may need a temporary barrier while the underlying disorder is treated. Applying a collar alone does not treat the cause of feather picking and causes significant stress.
- If a collar is necessary, hospitalize the bird for 24 to 48 hours for observation, and provide supportive care if needed. Some birds become severely lethargic and will not eat or drink when collared.
- Keep the bird in a space free of objects capable of entangling the collar. Birds have become seriously injured or asphyxiated due to Elizabethan collar entanglement.
- Use collars commercially manufactured for birds (Veterinary Specialty Products, Boca Raton, FL).
- New feathers will not emerge normally from their keratin sheaths if not preened regularly. Long-term collaring does not allow normal preening.
- Do not apply topical sprays, homemade or sold over the counter, to deter feather picking (such as bitter-tasting solutions). Birds are very meticulous about their feathers, and these solutions often exacerbate picking.

▼ ***Key Point*** Every attempt should be made to rule out underlying disease as a cause of feather picking before diagnosing psychological feather picking. Feather picking can sometimes be the only or most prominent sign of serious underlying disease. A thorough diagnostic evaluation, including CBC, plasma biochemical analysis, fecal testing for parasites and microflora, whole body radiography, testing for infectious diseases, skin biopsy, and exploratory laparoscopy may all be required to rule out systemic disease.

Behavioral or Psychological Causes of Feather Picking

Psittacine birds are extremely intelligent, gregarious, and social animals. Unlike pet dogs and cats, they have not had the advantage of centuries of selective breeding for a domestic temperament. Instead, most captive-bred parrots are only a few generations removed from wild birds. Captivity in most households cannot provide the exercise, free flight, mental stimulation, or complex social flock behaviors that exist in the wild. Preening and mutual grooming are important psychosocial activities and would normally occupy a significant portion of the day. Exaggeration of these activities, progressing to mutilation of feathers or skin, is the most common and disconcerting aberrant behavior seen in captive psittacine birds. Mutilation is often accompanied by other stereotypic behaviors such as repeated movements of the body or toys or screaming.

Reasons for this aberrant behavior may sometimes become clear with a careful history—for example, lack of mental or social stimulation, a change in the household routine, or other stressful events. However, even birds that are obviously well cared for, are in a stimulating environment, and are treated as a family member may feather pick or self-mutilate. In these cases, the cause is often elusive. Advise the owners that this can be a very frustrating disorder to deal with and that, in some cases, the behavior may not improve despite treatment.

Etiology

- Proposed contributing factors include boredom, frustration, nervousness, anxiety, social isolation, separation anxiety, overcrowding, environmental changes, lack of stimulation, and inappropriate housing.
- Birds spend a large portion of their time foraging for food. In captivity, food is supplied spontaneously,

denying birds the opportunity to exercise this vital mentally stimulating activity.
- Flocks in the wild are well structured with routine. Picking may result if the bird's environment has no daily routine or if the normal routine is disrupted.
- Birds are gregarious flock creatures; many do not cope well with the social isolation that occurs when left alone for prolonged periods during the day. Some birds will feather pick even if left alone at night.
- Attention-seeking behavior may contribute to feather picking. Owners often scold the bird or attempt to distract it, inadvertently providing the bird with attention and reinforcing the behavior.
- Reproductive frustration may contribute to feather picking. Affected birds often exhibit other signs of reproductive interest such as masturbation and regurgitation.
- Too many birds kept in a small area can lead to overcrowding and stress.
- Once some birds begin picking, the behavior can become a vicious cycle similar to obsessive-compulsive disorders in humans.
- Neurochemical abnormalities or inherited factors may contribute to feather picking. There appears to be a greater predilection for feather picking in species such as cockatoos, African grey parrots, Eclectus parrots, and conures. Some birds respond well to treatment with psychopharmacologic agents.

Diagnosis

- Rule out any possible underlying medical causes of feather picking.
- Obtain a detailed history, including area of feather loss, duration, progression of picking, daily routine, changes in the environment, breeding behavior, and other abnormal behaviors, if present.
- Have the owner keep a log of when and under what circumstances the bird feather picks.
- Obtain a detailed dietary history.
- Perform a careful physical examination.
- If evidence of pyoderma exists, obtain samples for cytologic exam and culture (see previous discussion in this chapter).

Treatment

▼ ***Key Point*** Attempt to identify and correct any environmental stressors or deficiencies. Often several changes in surroundings and numerous activity trials are needed before a positive response is seen. The addition of pharmacologic agents is effective in only some cases. Advise the owners that the solution is rarely simple and generally requires dedication and long-term treatment. Some birds fail to respond to any treatment.

- Provide mental and physical activity to occupy the bird during the day.
- Birds have a strong need to chew. Provide materials for the bird to shred such as perches of soft non-toxic wood, branches, paper (magazines, books), toys with multiple textures, or coconut shells.
- Provide toys that stimulate thinking and foraging behavior.
- Dedicate playtime at the same time every day.
- Move the cage to an area in which there is a lot of activity.
- Leave the television or radio on during the day.
- Continuous loop videos are commercially available containing film of birds engaging in natural behaviors. Playing these videos during the hours that the bird is alone has been beneficial in many cases.
- Advise owners to buy the largest cage possible for the bird. If possible, a large flight cage with outdoor access is most effective.
- Provide a safe hide box for the bird for security and "quiet time."
- Allow the bird 8 to 12 hours of sleep a night.
- The addition of a cage mate is helpful in some cases. However, not all birds will stop picking with the addition of a mate and may actually feather pick the mate or teach the new bird to feather pick. Addition of a mate may make the original bird less interactive with people, or the original bird may not accept the new bird and may harm it.
- Quarantine all new birds for 60 days.
- Psychopharmacologic drugs have been used with varying success; however, there is no one panacea for feather-picking birds. A therapeutic trial may be necessary with several different agents before results are achieved. Some birds do not respond to pharmacologic treatment. Suggested therapeutic agents include the following:
  - Haloperidol (Haldol, DuPont) at a dosage of 0.1 to 0.4 mg/kg PO q24h. Begin at a low dose and increase gradually every 5 to 7 days, to effect, if well tolerated. Drowsiness is the most common side effect.
  - Tricyclic antidepressants, such as clomipramine HCl (Clomicalm, Novartis) at 1.0 mg/kg PO q24h. Up to 2.0 mg/kg q24h has been tolerated and effective in some birds. Rare anecdotal reports of sudden death exist, possibly due to an underlying arrhythmia. Alternatively, try doxepin (Sinequan, Roerig) at a dosage of 0.5 to 1.0 mg/kg q12h.
  - Naltrexone (Trexan, DuPont) at a dosage of 1.5 mg/kg PO q8–12h. Naltrexone is an opioid antagonist used to counteract the release of endogenous opioids that may occur during picking or self-mutilation. Do not use in birds with liver disease.
- Serotonin-specific reuptake inhibitors (SSRIs) are rarely effective.
- Some female birds displaying sexual behaviors respond to leuprolide acetate (Lupron, TAP Pharmaceuticals) depot injection at 800 µg/kg IM every 14 days. Three doses are usually sufficient to inhibit

further egg laying. Repeat treatment may be needed if signs return. Lupron is believed to act by inhibiting the release of follicle-stimulating hormone and luteinizing hormone. The owner must also discourage all sexual behavior by removing toys or any other objects to which the bird is directing sexual behavior.
- Other treatments include the use of human chorionic gonadotropin (hCG) at 1500 IU/kg IM every 14 days to inhibit reproductive activity in female birds.
- Megestrol acetate, testosterone, and medroxyprogesterone have all been used, but due to their serious and possible lethal side effects they are strongly discouraged.
- Apply a physical barrier to plucking, such as an Elizabethan collar or tube collar, *only* if the bird is in danger of inflicting serious harm to itself. Birds that are mutilating to the point of removing skin and underlying tissues may need a temporary barrier while the underlying disorder is treated. Applying a collar alone does not treat the cause of feather picking and causes significant stress. See the discussion of Elizabethan collars above.
- Do not apply topical sprays, homemade or sold over the counter, to deter feather picking (such as bitter-tasting solutions). Birds are very meticulous about their feathers, and these solutions often exacerbate picking.
- Do not perform radical beak grinding to inhibit picking.

Oiled Birds

- In most cases, the owner has applied an oily substance to prevent the bird from picking, to attempt treatment of a dermatologic condition, or as accidental contact with oil.
- The most serious consequence is hypothermia. Oils interfere with the insulation and waterproofing functions of the feathers.
- Ingestion may cause gastritis or gastric ulceration.
- Crude oils can be toxic if ingested. Birds will vigorously preen when something is applied to their feathers.
- Administer activated charcoal to prevent further absorption.
- Wash the bird in commercial dishwashing soap such as Dawn (Procter & Gamble) to remove topical oil.
- Dry the bird well and keep it warm.
- Provide supportive care as needed.

Glue Traps

- Birds occasionally become entrapped in glue traps used for rodent pests.
- Advise the owner to leave the bird attached to the trap and bring the bird into the hospital.
- Try to manually remove small parts from the trap; if this is not possible, use Armor All Protectant (Armor All Products) automobile cleaner to assist removal.
- Once the bird is removed, wash the bird with warm water to remove any residue.
- Give supportive care as needed.

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Chapter

171 Avian Respiratory System Disorders

Matthew S. Johnston

Disorders of the respiratory system are very common in birds. The unique anatomy and physiology of the avian respiratory system can make the diagnosis and treatment of disorders of the respiratory system difficult for the veterinary clinician. This chapter will focus mainly on anatomy, physiology, and clinical management of disorders of the respiratory system of pet parrots. For ease of use, the respiratory system will be discussed based on anatomy, with separation of the upper respiratory tract and lower respiratory tract. Clinical signs of many different disorders are very similar depending on the anatomic location of the disease process.

ANATOMY AND PHYSIOLOGY

Upper Respiratory Tract

- The upper respiratory tract begins at the nares, which are usually located on a fleshy mound at the base of the rhinotheca (upper beak keratin) called the cere.
- The cere may be feathered or unfeathered, depending on the species.
- The nares open on the dorsal aspect of the cere into the nasal cavity. An operculum is present just within the nasal opening in Amazon parrots (*Amazona* species) that probably functions in filtering out particulate matter.
- The nasal cavity is divided by a septum and is composed of three fairly distinct and well-vascularized conchae—rostral, middle, and caudal. The middle concha is the largest of the three in most parrots.
- The nasal cavity opens into the dorsal aspect of the oral cavity via the choanal slit. The choanal slit is normally lined by a respiratory epithelium and, grossly, sharp papillae can be seen extending into the lumen of the slit from the lateral margins. Absence of these choanal papillae is a sign of respiratory pathology.
- During breathing, the larynx abuts the choanal slit to allow close-mouthed nasal breathing in a normal parrot.
- The infraorbital sinus is the only sinus in birds, but it is quite large and convoluted, with six diverticula that can be found anatomically throughout the head and beak.
- The dorsal aspect of the infraorbital diverticulum opens into the middle and caudal nasal conchae. This dorsal opening makes drainage of the sinus difficult in a clinical setting.
- The infraorbital sinus communicates with the cervicocephalic air sacs at the base of the skull.
- The rima glottidis is not covered by an epiglottis, as is the case in mammals. Paired arytenoids cartilages form the walls of the rima glottidis.
- Compared with that of mammals, the avian trachea and rima glottidis are quite wide in diameter relative to the size of the bird. In addition, the trachea is long and often convoluted as it tracks down the neck. This convolution allows the bird full range of flexibility in the neck.
- Because of the large diameter and length of the trachea, there is a larger physiologic dead space in birds compared with in mammals. To compensate for this, birds tend to have a slower respiratory rate but a larger tidal volume.
- The tracheal rings are complete, and tracheal expansion capacity is very limited.
- At the bifurcation of the trachea (at the thoracic inlet in most parrots), the syrinx can be found. The syrinx is the sound-production organ of the bird, and it is an important anatomic structure as it is a common location of many disease processes, including inhaled foreign bodies and fungal granulomas. The syrinx is composed of a number of complex cartilages, muscles, and membranes that work together to create vibrations that can be amplified to create loud sounds.

▼ ***Key Point*** The infraorbital sinus is very complex and convoluted. It is only open to the nasal cavity dorsally, making drainage of the sinus very difficult.

▼ ***Key Point*** The trachea is formed by complete tracheal rings, which restrict expansion of the trachea, so be very cautious when using cuffed endotracheal tubes. The syrinx is the "voice box" of a parrot and is situated at the bifurcation of the trachea, an anatomic location of many disease processes.

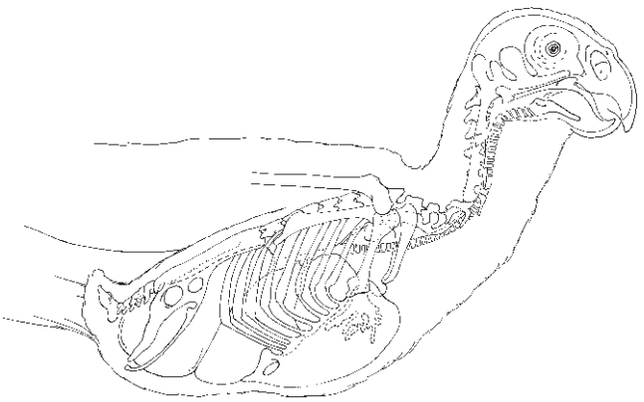

Figure 171-1. Anatomy of the air sacs.

Lower Respiratory Tract

- The lower respiratory tract consists of the lungs and air sacs (Fig. 171-1).
- The lungs are paired, non-expansible, and located against the dorsal body wall in the thoracic region of the coelom.
- The parabronchi travel throughout each lung and have extensive anastomoses with each other. The parabronchi have outpocketings throughout their length, termed atria, which further open into infundibula. The infundibula narrow in size into air capillaries, the functional equivalent of the mammalian alveoli. Gas exchange occurs throughout the anastomosing meshwork of the air capillaries, which course in immediate proximity to the blood capillaries.
- To complete a respiratory cycle, birds require two breaths. On the first inhalation, the majority of inhaled air moves into the caudal air sacs. On the first exhalation, this air then moves through the lungs, where gas exchange occurs. On the second inhalation, the air in the lungs moves to the cranial air sacs, and on the second expiration, this air is then expelled through the trachea. This unidirectional flow of air makes up the majority of respiration in pet parrots.
- Bidirectional flow also occurs in parrots, wherein a small percentage of inhaled air goes directly to the lungs and is then expelled on expiration. Because of these two systems, birds exchange gas on both inspiration and expiration.
- Birds lack a diaphragm; they rely on a system of bellows, the air sacs, to propel air throughout the respiratory tract. Pressure changes in the air sacs are a result of muscle-controlled volume changes within the thoracoabdominal coelom (see Fig. 171-1).
- Parrots have nine air sacs: paired cervicocephalic, single clavicular, paired cranial thoracic, paired caudal thoracic, and paired abdominal. The latter four sets of air sacs have connections to the lungs (termed ostia), so they are considered part of the lower respiratory tract. As discussed above, the cervicocephalic air sacs have connections to the infraorbital sinus but not the lungs.
- Histologically, air sacs are similar to peritoneum: one to two cell layers thick, relatively avascular, and composed of connective tissue stroma.
- In some species, the air sacs extend into the bones. In parrots, the only consistently pneumatic bone is the humerus, which is aerated by the clavicular air sac.

▼ ***Key Point*** Birds exchange gas on both inspiration and expiration. A complete respiratory cycle in a parrot takes two complete breaths to cycle air unidirectionally through the air sacs and lungs. The air sacs are very thin and relatively avascular, and they do not function in gas exchange.

CLINICAL SIGNS OF RESPIRATORY DISORDERS

Upper Respiratory Tract

Signs of upper respiratory tract disorders can be divided into nasal, sinus, or choanal disorders and tracheal or syringeal disorders. In many instances, diseases that affect one of these anatomic sites also affect another.

- Common historical and physical examination findings in parrots with nasal, sinus, or choanal disorders include the following:
  - Sneezing
  - Picking at the nares
  - Rubbing of the head on perches
  - Nasal discharge
  - Ocular discharge
  - Periorbital swelling
  - Facial asymmetry or focal subcutaneous facial swellings
  - Blunting of choanal papillae
  - Hyperemia of the cere
  - Lack of airflow through one or both nostrils
  - "Wet" respiratory noises auscultated over the sinuses
  - Plaque-like lesions around the choana or within the oral cavity
  - Discharge or swelling at the choanal slit
  - Inflation of the infraorbital sinus during expiration
- Common historical and physical examination findings in parrots with tracheal or syringeal disorders include the following:
  - "Coughing" (birds cannot technically cough since they lack a diaphragm)
  - Voice change
  - Stridorous breathing
  - Deep and slow respiratory pattern

- Clicking respiratory noises
- History of recent anesthesia and intubation
- Traumatic wounds to the neck
- Exercise intolerance
- Cyanosis of beak or nail beds (in parrots with unpigmented beak and skin)
- Collapse

Lower Respiratory Tract

Common historical and physical examination findings in parrots with lung or air sac disorders include the following:

- Dyspnea
- Tachypnea
- Tail bob
- Lethargy
- Decreased appetite
- Exercise intolerance
- Respiratory noise
- Cyanosis of beak or nail beds (in parrots with unpigmented beak and skin)
- Shock
- Coelomic distention

▼ ***Key Point*** Many different diseases can present with similar clinical signs based on their location within the respiratory tract.

DISORDERS OF THE UPPER RESPIRATORY TRACT

Hypovitaminosis A

This condition is seen most frequently in Amazon parrots but can occur in any species. A thorough dietary history is the most important diagnostic tool.

Etiology

- Most birds with clinical signs from hypovitaminosis A are adult birds that have been fed an unsupplemented seed diet. Hypovitaminosis A causes squamous metaplasia of epithelial cells.

Clinical Signs

- Most commonly, parrots present with chronic sinusitis due to secondary infections and blunted choanal papillae.
- In addition to upper respiratory signs, parrots may have reproductive, gastrointestinal, or urinary tract problems due to the squamous metaplasia of all epithelial cell types.

Diagnosis

- Obtain a specific dietary history of what the parrot eats, not just what it is offered.
- Perform sinus aspirates for cytology and perform culture and sensitivity (including fungal cultures) as secondary infections are common (see Chapter 169).

Treatment

- Correct the diet by recommending a formulated pelleted diet, fresh food diet, or some combination of the two. Seeds should be fed in a minute quantity if at all.
- Treat secondary infections with appropriate antimicrobials; trimethoprim-sulfa (25 mg/kg PO q12h) or enrofloxacin (20 mg/kg PO q24h) are good first-line choices until culture results are obtained.
- Give a single injection of vitamin A (10,000 IU/kg IM). Vitamin A is often available combined with vitamins D and E. Dosing should be made on the vitamin A component of this mixture. No more than two injections given 1 week apart should be recommended, as oversupplementation of vitamin A can have serious deleterious effects.
- Supplement the diet with beta carotene (one to two drops per parrot) while the bird is being converted to a healthier diet. Beta carotene is a precursor to formed vitamin A and overdosage is unlikely, as parrots will excrete what they do not need. Owners can monitor for orange or yellow discoloration of the urine, which occurs when beta carotene is being supplemented in excess. Supplementation with formed vitamin A is not recommended due to the likelihood of overdosage. Signs of hypervitaminosis A are similar to those of hypovitaminosis A.

Prognosis

- The prognosis is generally good, although some parrots are left with permanent damage to the epithelium and may need chronic treatments.

Rhinitis

Etiology

- This condition can occur in any species of parrot and is often associated with hypovitaminosis A or environmental irritants such as dust, scented cleaning products, aerosol sprays, or tobacco smoke.

Clinical Signs

- Parrots most commonly present with nasal discharge, sneezing, picking at the nares, and scratching of their beak on perches.

Diagnosis

- Obtain a thorough dietary and environmental history, paying particular attention to airborne irritants.
- Perform a nasal flush using sterile saline and collect a sample for cytologic examination and culture (see

Chapter 168). With rhinitis, cytology should demonstrate inflammatory cells and possibly bacterial or fungal agents.

Treatment

- See the section on hypovitaminosis A for good first-choice antimicrobials or a base choice on cytologic findings.
- If the diet is deficient in vitamin A, correction of the diet should be part of the therapeutic plan.
- Control environmental irritants by use of air filtration, humidification, and adequate ventilation.
- In dry climates, owners can be taught to perform nasal flushes to moisturize the upper airway.

Prognosis

- Prognosis is generally good.

Rhinoliths and Nasal Foreign Bodies

Etiology

- Rhinoliths occur most commonly in African grey parrots, while foreign bodies can occur in any species. Rhinoliths are concretions of mucous and debris that form within the nasal cavity. Any small airborne particles can become nasal foreign bodies when inhaled.

Clinical Signs

- Parrots most often present with acute onset of nasal discharge, facial discomfort, and sneezing.

Diagnosis

- Obtain a thorough environmental history, paying particular attention to humidity and inhaled particulate matter.
- Use a penlight or small fiber-optic endoscope or transilluminator to look into the nares. Rhinoliths are usually easily identifiable as mass-like, hard concretions just within the nares. Foreign objects may or may not be seen depending on how deep within the nasal cavity they are lodged. If a foreign body is suspected but not seen, the bird should be anesthetized for rigid rhinoscopy.

Treatment

- Perform a nasal flush to remove debris and moisturize the airway. Perform the flush over a container so that foreign objects can be easily identified (see Chapter 168).
- Use a hypodermic needle or cotton-tipped applicator to remove rhinoliths by gently teasing the rhinolith off of the mucous membranes. Some bleeding may occur with this technique. Significant hemorrhage can be controlled with an ice pack of the nose or topical diluted (1:100) epinephrine nasal drops.

Prognosis

- Prognosis is generally good.
- Humidification and air purification may help prevent recurrence.

Sinusitis

Etiology

- This condition can occur in any species but is seen most commonly in New World parrots. It is associated with hypovitaminosis A and environmental irritants, but it can also occur as a primary disease process.

Clinical Signs

- The most common clinical signs are asymmetrical facial swelling(s), facial discomfort, and sneezing.

Diagnosis

- Perform sinus aspirates for cytology and culture and sensitivity (including fungal culture).
- Consider testing for psittacosis (*Chlamydophila psittaci* infection) in high-risk birds. See below and Chapter 169 for details on chlamydiosis.
- Perform cranial imaging such as skull radiographs, computed tomography (CT), or magnetic resonance imaging (MRI) in advanced or recurrent cases to assess the presence of granulomatous or caseated masses (see Chapter 4). Skull radiographs are less sensitive for picking up small lesions but are more readily available than CT or MRI.

Treatment

- Some cases respond favorably to antimicrobial treatment based on culture and sensitivity, nebulization, and correction of dietary or environmental causes. Nebulization with saline is usually effective; however, some clinicians prefer to add medications to their nebulization. Commonly used nebulized medications include acetylcysteine to moisturize airways (200 mg/9 ml in sterile water), enrofloxacin for gram-negative sinusitis (10 mg/ml in sterile saline), gentamicin for gram-negative sinusitis (50 mg/10 ml in sterile saline), and clotrimazole for fungal sinusitis (10 mg/ml in polyethylene glycol). Nebulization is best performed with a nebulizer unit in a sealed cage.
- Many birds with sinusitis will not completely respond to antimicrobial medications and correction of husbandry. In recurrent cases, suspicion should be raised of caseated or granulomatous masses that may require surgical removal.

Prognosis

- The prognosis is guarded with advanced or chronic, recurrent disease.

Psittacosis

Etiology

- Caused by the organism *Chlamydophila psittaci,* psittacosis is a very important zoonotic disease of pet birds. In humans, it may cause generalized malaise and flu-like symptoms. In addition to its respiratory signs, it usually causes hepatic pathology.
- Psittacosis seems to be most prevalent in the small parrots such as cockatiels *(Nymphicus hollandicus)* and budgerigars *(Melopsittacus undulatus).* See Chapter 169.

Clinical Signs

- Clinical signs attributable to the respiratory system include sneezing, oculonasal discharge, facial discomfort, and hyperemia of mucous membranes. Other clinical signs include lethargy, biliverdinuria (green discolored urates), and anorexia.

Diagnosis

- Obtain a thorough history of exposure to other birds (boarding, pet stores, bird shows, wild birds).
- Perform a complete blood count (CBC), plasma biochemistry panel, and plasma protein electrophoresis (EPH) to check for leukocytosis characterized by a monocytosis, elevated aspartate aminotransferase and/or bile acids, or hyperglobulinemia.
- Perform polymerase chain reaction (PCR) testing of a choanal and cloacal swab.
- In larger parrots, elementary body antibody titers, complement fixation, or immunofluorescent antibody may be useful.

Treatment

- Isolate parrots with clinical signs of psittacosis from other parrots until treatment has been initiated. Research has demonstrated a cessation of shedding after 1 week of treatment with tetracycline antibiotics.
- Treat with doxycycline for a minimum of 45 days. Doxycycline can be given orally, weekly by depot intramuscular injection, in medicated water, or in medicated feed depending on the circumstances. The oral dosage for doxycycline is 25 to 50 mg/kg q24h in most parrots.
- Psittacosis is a reportable disease in most states, and you should check with your local health department in confirmed or suspected cases.

Prognosis

- Prognosis is generally good if treatment is initiated early in the course of the disease.
- Recurrence is more likely in cockatiels, budgerigars, and lovebirds.

Choanal Atresia

- Choanal atresia has been reported to occur in African grey parrots.
- Typical historical presentation is a young bird that is unable to nose-breathe and has copious mucoid nasal discharge. In some cases, the choanal slit may appear to be open, but endoscopic examination reveals a soft-tissue membrane occluding the nasal passage just dorsal to the choanal slit.
- Several treatment modalities have been attempted. The two most successful surgical corrections include stenting and laser surgical ablation of the membrane. Fatal hemorrhage is a potential complication of these surgical procedures, and some cases will reclose and require multiple surgical procedures.

Aspergillosis

Etiology

- Although traditionally thought of as a disease of the lower respiratory tract, aspergillosis (caused by *Aspergillus* species) commonly occurs in the infraorbital sinus and trachea. *Aspergillus* granulomas can form at the syrinx, leading to upper airway obstruction.
- Aspergillosis is more common in immunosuppressed parrots or in parrots that obtain a heavy burden of organisms in a short period of time.

Clinical Signs

- Clinical signs in parrots can be those of a chronic sinusitis or tracheal obstruction, including voice changes historically.

Diagnosis

- Perform a CBC and an EPH to look for a leukocytosis and/or hyperglobulinemia. Research suggests that aspergillosis should be considered a differential if the albumin-to-globulin ratio, as measured by an EPH, is markedly decreased.
- *Aspergillus* antibody and antigen testing are neither sensitive nor specific in pet parrots, so their utility as a diagnostic tool is questionable.
- Radiographs are generally not sensitive for defining tracheal granulomas, although if a soft tissue mass is seen within the trachea, aspergillosis should be suspected.
- Place an air sac cannula if tracheal obstruction is suspected to stabilize the patient prior to further diagnostics (see Chapter 168).
- Under anesthesia, perform tracheoscopy or tracheal washes to obtain samples for cytology, histopathology, and fungal culture. *Aspergillus* species are easily identified cytologically or histologically because of their

characteristic pseudohyphae and septate branching. *Aspergillus* species are common environmental contaminants and the most common contaminant of culture plates. So, interpretation of a positive culture in the face of negative cytology or histopathology should be made with caution.

Treatment

- Surgical or endoscopic removal or ablation of granulomas is necessary before medical therapy will be effective.
- Most parrots require hospitalization for several days of inpatient treatment followed by a very extensive and long-term outpatient treatment. During treatment, monitor the CBC or EPH to assess progression. Periodic tracheoscopy may be beneficial to assess the presence of granulomatous or plaque lesions. Duration of therapy ranges from 1 month to lifelong, and determining an end point of therapy can be extremely difficult if classic clinicopathologic findings are not present.
- Treat medically with nebulization and systemic antifungals. Commonly used nebulized antifungals include clotrimazole (10 mg/ml in polyethylene glycol) and amphotericin B (7 mg/ml in saline). The most commonly used systemic antifungal is itraconazole (10 mg/kg PO q24h), but this drug should be used with great caution in Africa grey patients due to their apparent sensitivity to its hepatotoxic effects. In African grey parrots, use ketoconazole (30 mg/kg PO q12h) or fluconazole (15 mg/kg PO q12h).

Prognosis

- Prognosis is generally poor, and recurrence is common.

Mycoplasmosis

- *Mycoplasma* species uncommonly cause sinusitis and blepharoconjunctivitis in pet parrots. Mycoplasmosis should be suspected in cases of sinusitis that partially respond to antibiotics but never completely resolve.
- Unfortunately, definitive diagnosis is very difficult, as culturing *Mycoplasma* species is a time-consuming and not clinically useful practice.
- Long-term, combination antimicrobial treatment is usually necessary to eradicate the organism from the host.

Tracheal Foreign Bodies

Etiology

- Parrots with tracheal foreign bodies usually present as emergencies due to upper airway obstruction.
- Cockatiels seem predisposed to aspiration of seeds, although tracheal foreign bodies can occur in any species.

Clinical Signs

- Parrots usually present with acute dyspnea attributable to the upper airway; often, a seed is aspirated during vigorous feeding, so feeding practices should be questioned when obtaining a history.

Treatment

- Place an air sac cannula to provide an open airway until definitive therapy can be provided (see Chapter 168).
- Tracheal lavage can be attempted but carries an inherent risk of drowning or forcing the foreign object further down the respiratory tract, so it is not recommended unless other treatments are not feasible. This should be performed with the bird under general anesthesia and an air sac cannula in place.
- Perform a tracheoscopy to remove the foreign body (usually a seed) in larger parrots.
- If you are unable to perform a tracheoscopy, perform a tracheotomy to allow surgical removal of the foreign object. A tracheotomy is performed at the level of the thoracic inlet unless radiographs or a tracheoscopy determine that the foreign object is further cranially.
- Begin nonsteroidal anti-inflammatory drugs (NSAIDs) and antibiotics to reduce the chance of tracheal stricture.

Prognosis

- Prognosis is good if the foreign object can be removed.

Tracheitis and Tracheal Strictures

Tracheitis and tracheal strictures appear to occur more commonly in macaws and cockatoos, possibly because in these genera the trachea narrows as it courses toward its bifurcation.

Etiology

- Most tracheitis and tracheal strictures occur as a result of a malpositioned, oversized, rigid, or cuffed endotracheal tube. Tracheal intubation is important during anesthesia, but it is very important to not inflate cuffed tubes and to make sure uncuffed tubes are not positioned so as to put pressure on the tracheal mucosa.

Clinical Signs

- Most cases have a history of recent endotracheal intubation.
- "Coughing," upper airway obstruction, and voice change are the most common clinical signs.

Diagnosis

- Take radiographs to assess for tracheal stricture as demonstrated by acute narrowing of the tracheal lumen.
- Perform tracheoscopy to confirm stricture or diagnose tracheitis.

Treatment

- Place an air sac cannula to provide a patent airway if the patient is dyspneic (see Chapter 168).
- Tracheitis will sometimes respond favorably to NSAIDs and antibiotics if diagnosed early in the course of disease, but it may lead to tracheal stricture if not addressed.
- Tracheal strictures usually require surgical removal of the strictured site, as the complete tracheal rings prevent effective bougienage or ballooning procedures.

Prognosis

- Prognosis is generally good if the stricture is treated early or if the tracheal stricture can be removed.

Extramural Tracheal Obstructions

Any mass that compresses the trachea can lead to signs of upper airway obstruction. The most common cause of this is goiter in budgerigars, but any extraluminal neoplasia can have a similar presentation.

DISORDERS OF THE LOWER RESPIRATORY TRACT

Aspiration Pneumonia and Air Sacculitis

Etiology

- This condition occurs most commonly in neonates or hand-fed chicks that are accidentally fed directly into the trachea and is almost always fatal. However, it can also occur in parrots that are regurgitating for any reason or iatrogenically in parrots that are administered fluids via crop gavage.

Clinical Signs

- The most common clinical sign is severe dyspnea.

Diagnosis

- Take radiographs to confirm lung and air sac opacities. In minor cases, thickened air sac membranes will appear as radio-opaque lines on the radiograph.

Treatment

- Most cases require hospitalization for inpatient treatment with broad spectrum antimicrobials, nebulization, and supportive care.

Prognosis

- The prognosis is guarded.

Hypersensitivity Syndrome

Etiology

- Seen most commonly in macaws, this condition is characterized by an intense inflammatory reaction within the lungs (pneumonitis) to an airborne irritant.
- Common irritants include feather dust from other parrots that produce powder down, aerosolized disinfectants and deodorizers, tobacco smoke, or dust.

Clinical Signs

- The most common clinical signs are wheezing, tail bob, and exercise intolerance.

Diagnosis

- Perform a CBC to assess the presence of polycythemia and eosinophilia. In some cases, the polycythemia can be quite severe (as high as 85%) owing to chronic hypoxia. Eosinophilia is not always present.
- Perform radiographs to assess the lung field for increased radio-opacity of the normal reticulated pattern. The avian lungs are evaluated on a lateral projection, and the normal lung has a fine reticular pattern throughout its parenchyma. Birds with hypersensitivity pneumonitis will have thickenings of the reticular pattern that appear similar to bronchial lung patterns of cats or dogs.

Treatment

- Antihistamines and NSAIDs have been used with limited success. Commonly used antihistamines include diphenhydramine (4 mg/kg PO q8h) and hydroxyzine (2.2 mg/kg PO q8h). Commonly used NSAIDs include meloxicam (0.5 mg/kg PO q12h) and carprofen (2 mg/kg PO q12h).
- Bronchodilators have been used with mixed success. Commonly used bronchodilators include terbutaline (0.1 mg/kg PO q12h) and aminophylline (4 mg/kg PO q6–12h).
- Avoid corticosteroids due to severe side effects, including immunosuppression and gastric ulceration.
- Resolution will only occur if irritants can be removed from the bird's environment by physical removal, air purification, and excellent ventilation. In some cases, even with removal of the source of irritation, birds are left with some degree of pneumonitis, although it may be easier to manage.

Prognosis

- The prognosis is guarded.

Polytetrafluoroethylene Toxicosis

Etiology

- Polytetrafluoroethylene (PTFE) (Teflon and other non-stick coatings) causes severe pulmonary hemorrhage in parrots when pans containing these non-stick coatings are overheated.

Clinical Signs

- Parrots are presented severely dyspneic or often dead; some may be coughing up blood-tinged sputum.

Treatment

- Treat immediately with oxygen, furosemide (2 mg/kg IM), and terbutaline (0.01 mg/kg IM). Minimize handling of these severely dyspneic birds or consider anesthesia and mechanical ventilation to maintain oxygenation.
- Advise owners to keep parrots as far from the kitchen as possible if the owners use non-stick cookware. Ideally, parrot owners should not use cookware coated with PTFE.

Prognosis

- Prognosis is very guarded.

Inhaled Irritants

Any inhaled irritant can cause signs of respiratory distress in pet parrots. Treatment of any of these consists of removal of the source of irritation and supportive care of the parrot. Some of the more common irritants include the following:

- Potpourri and other strongly scented deodorizers
- Tobacco smoke
- Dust or pollution
- Aerosolized sprays
- Concentrated cleaning agents (undiluted bleach or vinegar)
- Perfumes or colognes
- Oven cleaner

Aspergillosis

Etiology

- As discussed above, aspergillosis occurs mainly in immunocompromised parrots.
- Aspergillosis can occur as discrete granulomas within the air sacs or lungs or as a disseminated, fulminant air sacculitis and pneumonia.

Clinical Signs

- Clinical signs include lethargy, exercise intolerance, and dyspnea.

Diagnosis

- Perform a CBC to look for leukocytosis characterized by a heterophilia and monocytosis.
- Perform an EPH to look for a hyperglobulinemia. As discussed above, one of the more common findings in parrots with aspergillosis is a markedly decreased albumin-to-globulin ratio.
- Antibody or antigen serology is neither sensitive nor specific in parrots, so its diagnostic value is limited.
- Take radiographs to assess for granulomatous masses or air sac lines. Air sac lines are most commonly seen on the lateral projection in the normally radiolucent air sac triangle that sits just cranial to the pelvis. On the ventrodorsal projection, air sac lines may be apparent just cranial to the femurs.
- Obtain biopsies of air sacs and/or granulomas for cytology, histopathology, and fungal culture using endoscopic guidance. As discussed above, cytology or histopathology is more sensitive and specific than fungal cultures, as *Aspergillus* species are common culture plate contaminants.

Treatment

- If possible, remove granulomas surgically or with endoscopic assistance using a diode laser.
- Treat medically with nebulization and systemic antifungal agents for at least 6 weeks. See above discussion on upper airway aspergillosis for commonly used antifungal drugs.

Prognosis

- Prognosis for complete remission is poor, although some cases can be managed long term. Determination of the end point of therapy is difficult, as radiographic changes may be permanent because of scarring of the air sac membranes, and not all cases will have classic clinicopathologic findings.

Bacterial Pneumonia and Air Sacculitis

Etiology

- Although rare in parrots, primary bacterial pneumonia and air sacculitis can occur, usually as a result of gram-negative colonization of the respiratory tract.
- Bacterial pneumonia and air sacculitis occur most frequently in parrots that are immunosuppressed from concurrent diseases, poor husbandry, or chronic stress.

Diagnosis

- Perform a CBC to assess for a leukocytosis characterized by a heterophilia.

- Perform an EPH to assess for hyperglobulinemia, usually characterized by elevations of the alpha or beta globulins.
- A tracheal wash can be performed under anesthesia, or laparoscopy may be performed to obtain samples for cytology and culture and sensitivity.

Treatment

- Hospitalize for inpatient treatment with antibiotics (enrofloxacin at 20 mg/kg IM as a single dose followed by oral administration q24h pending culture and sensitivity results), oxygen therapy, nebulization, and supportive care.

Prognosis

- Prognosis is guarded.

Focal Subcutaneous Emphysema

Etiology

- Often called *air sac rupture,* this condition occurs for unknown reasons, most commonly in Amazon parrots.

Clinical Signs

- It is characterized by a focal, air-filled swelling usually around the shoulders or neck. It is caused by a ruptured cervicocephalic or clavicular air sac. Usually birds have no clinical signs except for the swelling.

Diagnosis

- Perform an aspirate of the swelling to confirm that it is air filled.

Treatment

- Treatment is often unrewarding, but stenting has showed some promise.
- Some cases will resolve without treatment.

Prognosis

- Prognosis is good for life, although some birds are left with permanent swelling.

Neoplasia

Etiology

- Neoplasia of the lungs is uncommon and appears to occur more frequently in cockatoos. Primary bronchial carcinomas are the most common tumor type.

Clinical Signs

- Frequently, the presenting complaint is a pathologic fracture or swelling of a long bone, as boney metastases are common in this disease. Many birds have no signs attributable to the respiratory system, but primary tumors are found on postmortem examination.

Treatment

- Thus far, treatment attempts have been unrewarding, but chemotherapy may be attempted.

Newcastle Disease (Exotic Newcastle Disease)

- This important agricultural disease has recently been found in pet parrots. It is a highly contagious, usually fatal disease caused by a paramyxovirus, which affects the respiratory, gastrointestinal, and neurologic systems.
- Most recently, it has been diagnosed in flocks of parrots that were illegally smuggled into the United States.
- Any birds that die with premonitory signs attributable to these systems should receive a full necropsy examination.
- This disease is reportable in all states.

Psittacosis

- Diagnostics for psittacosis and an overview of the disease have been given above and in Chapter 169.
- Be aware that psittacosis can also cause pneumonia and air sacculitis, although these presentations are unusual in pet parrots.

Sarcocystosis

Etiology

- Disease attributable to infection with *Sarcocystis falcatula* occurs most commonly in the southeastern United States. Most commonly, it affects Old World parrots, although New World species have been reported to be infected.

Clinical Signs

- Clinical signs are those of an acute pneumonitis, usually resulting in high mortality.

Diagnosis

- Diagnosis is made by the demonstration of oocysts within the lung tissue. Oocysts may also be found in striated and cardiac muscle.

Treatment

- This disease can be controlled by limiting exposure of parrots to flies and cockroaches, which serve as the transport host for the organism.

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Chapter

172 Avian Digestive System Disorders

Barbara L. Oglesbee

DISORDERS OF THE BEAK

General Principles

Normal Structure and Function

- The beak includes the bones of the upper and lower jaws and their keratinized sheaths or rhamphotheca. This horny covering functionally replaces the lips and teeth of mammals.
- The shape of the beak varies, depending on how the species feed and live.
  - In psittacines, the upper beak is massive and curved, and the lower beak is small and horseshoe shaped (this is why psittacines are called hookbills).
- The beak is adapted to cracking large nuts and seeds, as well as tearing and shredding wood from trees to provide nest sites.
- Histologically, the horny beak resembles skin and consists of dermis and modified epidermis. The stratum corneum of the epidermis is very thick.
- The horny tissue of the beak is continuously replaced during normal wear and tear.

Normal Beak Growth

- Many bird owners erroneously believe that the upper beak grows only from the cere and continues to the tip (or edges), where it is then worn off (and that the process is similar in the lower beak). On the contrary, beak tissue grows continuously outward (toward the surface) over much of the beak.
- As the keratinized epithelium reaches the surface, it is worn off or may move distally a short distance before it is shed.
- Beak tissue truly moves rostrally only toward the edges and tip.

Beak Overgrowth

Many pathologic conditions can change the normal outward appearance of the beak, adversely affecting its primary functions of food gathering, prehension, preening, and protection. Regardless of the etiology, overgrowth may take various forms, the most common of which are listed here.

- The tip of the upper beak, lower beak, or both may be overgrown.
- Elongation of the upper beak, usually accompanied by subcorneal petechia and increased malleability, is commonly seen in budgerigars with underlying metabolic disease (most commonly hepatic disease).
- Malocclusion of the beak causing the upper beak to angle off to one side, while the lower beak angles in the opposite direction, is referred to as *scissors beak*. The tips and outer edges usually are overgrown owing to a lack of occlusal wear.
- The upper beak is shortened and does not extend out over the tip of the lower beak (prognathism).
- An area of the beak may appear bulged or thickened because of buildup of covering horn. This commonly is seen in birds lacking access to rough surfaces but may also been seen in birds with systemic disease or malnutrition.

Beak Trimming

- Severe malocclusions, such as scissors beak, require surgical correction. See “Supplemental Reading” at the end of this chapter.
- When the underlying condition has been identified and treated, corrective beak trimming may be necessary.
  - Mild overgrowth or a buildup of covering horn may be trimmed if it is interfering with the function of the beak. Depending on the size of the bird, use human fingernail trimmers, cuticle nippers, Roscoe nail trimmers, or an electric hobby tool (Dremel) with a coarse sanding bit.
  - Anesthesia usually is not required; however, be aware that some birds stress easily during this procedure, especially when a hobby tool is used, and deaths have been reported.

▼ ***Key Point*** Knowledge of the normal anatomy and conformation of the beak for each individual species is necessary for proper trimming. Inaccurate trimming, and especially overtrimming, can cause malocclusion, pain and potentially severe hemorrhage.

Nutritional Disorders

An *all-seed diet* is deficient in many nutrients, especially vitamin A, essential in maintaining the health and integrity of epithelial tissues. Hypovitaminosis A may cause hyperkeratosis of epithelial surfaces.

Clinical Signs

Signs include beak thickening and overgrowth. The surface of the beak is hard and thickened, and it appears flaky and chipped instead of smooth.

Diagnosis

Base the diagnosis on clinical signs and a history of a seed-based diet.

Treatment

▼ ***Key Point*** Place pet birds on a commercial pelleted diet whenever possible.

- Supplement a commercial diet with fruits, vegetables, legumes, wholegrain cereals or rice, and small amounts of lean-cooked meats or eggs.
- If the bird will not convert to a commercial diet, then use a commercial avian vitamin supplement.
- Perform beak trims as necessary.

Bacterial and Mycotic Infection

Superficial or deep bacterial and mycotic infections occasionally are seen. These usually are secondary to trauma, chronic rhinitis, or other systemic diseases. Gram-negative enteric organisms (e.g., *Pseudomonas, Escherichia coli,* and *Klebsiella* species) are the most common bacteria isolated. *Aspergillus fumigatus* is the mycotic agent most commonly identified. In budgerigars, *Knemidokoptes* mite infestation is the most common infectious cause of beak deformity.

Clinical Signs

- The surface of the beak appears brittle and crumbly instead of smooth and hard. This may involve the entire beak or may be localized. Lesions may occur externally or within the oral cavity.
- The bird is reluctant to eat, crack seeds, or play with toys. The beak may seem painful.
- Areas of localized necrosis may be found on the beak surface or on the underside of the upper beak.

Diagnosis

- Examine stained specimens from affected areas for inflammatory cells, bacteria, or fungi.
- Obtain bacterial and fungal cultures of lesions.

Treatment

▼ ***Key Point*** Bacterial and mycotic infections of the beak usually are secondary to trauma, systemic disease, or nutritional deficiencies. Whenever possible, identify and treat the primary disease.

- Debride localized necrotic areas with the bird under anesthesia.
- Base antibiotic therapy on culture and sensitivity testing. Pending culture results, begin antibiotic therapy with a broad-spectrum antibiotic such as trimethoprim-sulfa or enrofloxacin (Baytril, Haver/Diamond) (see Chapter 169 for dosages). Long-term systemic therapy usually is required in addition to local debridement.
- For localized *Aspergillus* infection, see Chapter 169 for diagnosis and treatment. Treatment for months may be required.
- The prognosis is guarded if the fungal disease is systemic.

Trauma

Beak damage from trauma can occur in all species and often is the result of aggressive behavior among individual birds housed together, flying into walls or windows, struggling after beak entrapment, or improper beak trimming. A split lower beak may result from a fall, injury from another bird, biting with excessive force, or beak trimming.

Clinical Signs

- An inability to eat and manipulate food or toys may be the only presenting signs. Thoroughly inspect the beak to identify trauma because some injuries are not obvious.
- The beak may seem painful.
- Look for hemorrhage, cracks, punctures, avulsions, or complete amputation.

Treatment

Treatment varies with the type of injury. If the bird is reluctant to eat, forced alimentation may be necessary until the beak has healed sufficiently.

Cracked Upper Beak Tip

- Remove the tip with nail clippers or grind it with a hobby tool.
- Apply ammonium sulfate or ferric subsulfate powder to control hemorrhage.

Split Lower Beak

- If the crack extends the entire length of the beak, dividing it into two movable segments, nothing can

be done to permanently fuse the pieces back together. However, most birds eventually adapt to this condition.
- Wire and dental acrylics can only temporarily repair the crack.
- Birds can eat a normal diet with this condition; cracking seed or pellets is usually not a problem.
- Occasional trimming of the lower beak segments may be necessary because of inadequate occlusion with the upper beak.

Puncture Injury Penetrating the Horny Layer

- Initially treat as an open wound and debride damaged and necrotic areas with the bird under general anesthesia.
- Administer topical and systemic antifungal or antibiotic agents, based on culture and sensitivity testing.
- Defects in the horny layer may be filled or patched with acrylic compounds once a healthy granulation bed has been established.

Beak Avulsions

- If avulsion of the distal one-third occurs, treat as follows:
  - Treat initially as an open wound (as described previously).
  - Cover the open end with acrylics as a temporary patch if necessary (see "Supplemental Reading").
  - Regeneration of the beak is possible, but the beak may never appear totally normal.
- Damage to the proximal one-third of the beak usually is not reversible.
- If the injured birds can be kept alive with forced alimentation, the damaged beak may scar over and the bird may adapt to a soft-food diet.
- Avulsion of the entire upper or lower beak is not reversible. Affected birds usually die of starvation or secondary infection, or they require euthanasia.
- Successful use of beak prosthetic devices has been reported but is rare.

Prevention

- Do not leave birds uncaged unless they are closely supervised.
- Keep apart birds that exhibit obvious aggressive tendencies toward each other. This is a common problem in breeding pairs of cockatoos. Sexually active males may attack females that are not sexually receptive, and beaks commonly are bitten. Preventive measures include the following:
  - Large flight cages
  - Clipping wings of the male but not the female bird
  - Nest boxes with two separate entrances

Neoplasia

Neoplasia of the beak is encountered infrequently, usually in older birds. Fibrosarcoma, fibroma, and squamous cell carcinoma are the most common types.

Clinical Signs

- *Fibrosarcoma* usually appears as a well-demarcated, fleshy protrusion from the horny layer.
- *Squamous cell carcinoma* appears as a focal area of hemorrhage or ulceration.
- Common signs include weight loss and inability to eat.

Diagnosis

Base the diagnosis on histologic examination of excised tissues.

Treatment

- Surgical excision or debulking of beak tumors is rarely successful.
- Cryosurgery or radiation therapy may be beneficial, but the prognosis is generally guarded.

Environmental Factors

- To maintain a normal appearance of the beak, chewing on hard objects and rasping of the outer horny layer of the beak is necessary.
- Lack of access to materials necessary for normal beak wear can result in beak overgrowth or a flaky, chipped surface.
- Provide ample amounts of wood for the bird to chew on. This may be in the form of perches, nest boxes, or wood toys.
- Other items suitable for chewing include rawhide, concrete perches, lava stones, mineral blocks, and leather.

Growth and Developmental Abnormalities

- These conditions usually are seen in preweaned or recently weaned birds. The exact causes are unknown.
- The most common presentations are as follows:
  - *Scissors beak,* a lateral deviation of the upper beak seen most often in macaws
  - *Prognathism,* which affects the architecture of the upper beak and is seen most often in cockatoos
- Treatment by construction and application of a simple, durable prosthesis allows the redirection of beak growth (see "Supplemental Reading").

DISORDERS OF THE ORAL CAVITY

Normal Structure and Function

- Because birds lack a soft palate, which separates the nasal and oral parts of the pharynx in mammals, the oral cavity and pharynx of birds form a single cavity called the *oropharynx*.
- The roof of the mouth, or hard palate, is located immediately behind the upper beak.
  - Rostrally, the palate resembles a hard, fleshy cushion against which the tongue can manipulate objects.
  - Caudally, the palate is divided into two folds containing numerous caudally directed papillae, which are referred to as the *choana*. The choana communicate directly with the nasal passageway.
- The floor of the oropharynx is occupied by the tongue and the glottis.
  - The psittacine tongue is thick, blunt, and dexterous.
  - The glottis lies on the midline directly behind the tongue.
  - Papillae are distributed over the laryngeal prominence and posterior floor of the pharynx. Birds do not have an epiglottis.
- The surface of the oropharynx is lined by stratified squamous epithelium that is keratinized in regions subject to abrasion, such as the papillae.
- *Salivary glands* are not visible grossly and are distributed over the palatine folds, base of the tongue, laryngeal prominence, and pharynx. These glands primarily produce mucus and thus often are referred to as *mucous glands*.
- Psittacine birds do not produce the large amount of watery saliva seen in mammals. Therefore, the oral mucosa is normally only slightly moist, and the tongue is dry.

▼ ***Key Point*** Diseases of the oral cavity are common in pet birds. Routinely inspect the mouth during examination.

Hypovitaminosis A

Hypovitaminosis A, which is generally the result of an unsupplemented, all-seed diet, causes squamous metaplasia of the oral epithelium and subsequent hyperkeratosis of the mucous glands. Keratin-filled cystic structures may be found on the palatine folds, base of the tongue, laryngeal prominence, and pharynx. These lesions may coalesce and become secondarily infected to form large abscesses.

Lesions are more likely to be seen in large psittacine birds (e.g., Amazon and African grey parrots, macaws, and cockatoos) than in small species (e.g., budgerigars and cockatiels).

Clinical Signs

- Signs include white or yellow cysts and abscesses in the oral mucosa.
- If the lesions become secondarily infected, anorexia, general malaise, and weight loss may be present.
- Accompanying signs include blepharitis, conjunctivitis, uveitis, rhinitis, sinusitis, and dyspnea.

Diagnosis

- The diagnosis usually is based on the history and physical examination.
- Obtain biopsy specimens to confirm the diagnosis.

Treatment

- Change the diet as previously described under "Nutritional Disorders."
- Under isoflurane anesthesia, lance and curette oral abscesses; perform a Gram stain and bacterial and fungal culture on the abscess contents.
- Administer systemic antibiotic or antifungal agents, as indicated by culture.
- Provide supportive therapy, such as forced alimentation and fluid therapy, as needed.

Prevention

- Provide a diet adequate in vitamin A or add vitamin supplementation, as described under "Nutritional Disorders."
- Dark green and yellow vegetables are good sources of vitamin A.

Psittacine Pox

See Chapter 169 in this section for discussion of this disorder.

Oral Candidiasis

Candida albicans is a secondary invader that affects the mouth, esophagus, and crop. Factors predisposing to oral candidiasis include poor sanitation, malnutrition, coexisting disease, and prolonged antibiotic therapy. Cockatiels and macaws are affected most commonly.

Clinical Signs

Clinical signs vary with the severity of the disease and include the following:

- Anorexia, general malaise, and weight loss
- Vomiting, regurgitation, and mucus evident on the feathers of the head
- Wet feathers surrounding the mouth, halitosis, and oral hemorrhage
- Poor feeding response in hand-fed baby birds

Diagnosis

- Examine the oral mucosa for lesions that typically appear as a thickening of the oral mucosa associated with a mucoid exudate.
- Lesions may progress to focal or widespread mucosal necrosis, forming diphtheritic membranes or white caseated plugs.
- Perform a Gram or Diff-Quik stain on exudate from oral lesions; look for budding yeasts.
- Perform a fungal culture of oral lesions.

Treatment

▼ ***Key Point*** Candidiasis is usually a secondary invader. Correct predisposing factors in conjunction with specific antifungal treatment.

- In mild cases, birds may respond to nystatin (Mycostatin, Bristol-Myers Squibb), 1 ml/300 g q8h, PO.
- More often, systemic therapy with one of the azole antifungal agents is necessary. Administer ketoconazole (Nizoral, Janssen), 20 to 30 mg/kg q12h, PO, or fluconazole (Diflucan, Roerig), 20 mg/kg q48h, PO.
- Continue treatment until all lesions are healed (usually 1 month or longer).

Prevention

- Provide a clean environment, including food and water. Do not leave moist foods in the cage longer than 2 hours.
- Thoroughly disinfect utensils when feeding baby birds. Soak utensils in chlorhexidine solution (Nolvasan, Fort Dodge), 2 oz per gallon of water.
- Do not save powdered baby foods once they are reconstituted beyond one feeding or overgrowth of yeast and bacterial occurs.
- If long-term antibiotic therapy is indicated (e.g., to treat chlamydiosis), give antifungal agents such as nystatin and ketoconazole prophylactically.

Bacterial Infections

Bacterial infections of the mouth are unusual and are usually caused by similar conditions that encourage the growth of *C. albicans*. Common pathogens include *E. coli* and *Salmonella, Proteus, Pseudomonas, Enterobacter,* and *Citrobacter* species.

Clinical Signs

Lesions are variable but can appear similar to those of candidiasis (e.g., mucoid exudate or abscess formation).

Diagnosis and Treatment

Perform a Gram stain and bacterial culture on any exudate found in the mouth.

- Large numbers of enteric bacteria present in clinically ill psittacines with accompanying oral lesions are significant.
- Administer systemic antibiotic therapy, based on susceptibility testing.

Prevention

- Treat underlying systemic disease.
- Provide a clean environment and offer fresh food, as described previously under "Oral Candidiasis."

Oral Papillomas

See the discussion of oral papillomas in Chapter 169 in this section.

Trichomoniasis

Trichomonas gallinae is a flagellated protozoan parasite. Trichomoniasis usually occurs in aviaries with many birds housed together and rarely is seen in individual pet birds. Infection may extend into the esophagus, crop, lungs, and oral cavity. The budgerigar is the most commonly affected pet bird. Outbreaks have been reported in neonatal Amazon parrots, conures, and cockatiels.

Clinical Signs

- White, sticky plaques may coalesce to form yellow, caseated masses on the choana, tongue, or pharyngeal mucosa.
- Common signs include anorexia and weight loss.
- Moisture around the beak and halitosis may occur.

Diagnosis

- Perform a saline wet mount of oral exudate for microscopic examination.
- Organisms are flagellated and pear shaped, and they move in a spiral motion. Thousands may be seen on one slide.
- In psittacine birds, organisms often are not present on wet mounts of oral exudates, especially in the early stages.
- High numbers of organisms are sometimes found on wet mount smears from lungs of recently deceased birds.

Treatment

Give metronidazole (Flagyl-Searle), 30 mg/kg q12h PO, for 10 days. Crush the tablets and mix with a palatable liquid.

▼ ***Key Point*** Treat birds with oral lesions that suggest trichomoniasis with metronidazole, even when this organism is not positively identified.

Prevention

In an aviary, quarantine and examine all new budgerigars for organisms in the pharynx and crop before introduction to the flock.

Trauma

Trauma to the mouth is rare, but when it occurs, lacerations or bite wounds to the tongue are most common. The next most common injury is laceration or crushing injury to the intermandibular space as a result of the bird being hooked or caught on items such as chains or toys.

▼ ***Key Point*** Hemorrhage in tongue lacerations can be profuse and life threatening. Immediate treatment is required.

Treatment

- Anesthesia may be required; use isoflurane via an endotracheal tube.
- Control hemorrhage via direct pressure or cauterization.
- Clean, debride, and suture injuries, as required.
- Administer systemic broad-spectrum antibiotics prophylactically.

DISORDERS OF THE ESOPHAGUS AND CROP

Normal Structure and Function

Esophagus

- The avian esophagus is thin walled and highly distensible. It courses down the right side of the neck, the opposite of the placement in mammals.
- The esophagus is lined by incompletely keratinized, stratified squamous epithelium, with numerous subepithelial mucous glands.

Crop

- The crop is a dilatation of the esophagus found in many (but not all) species of birds. It is prominent in psittacines birds.
- The crop is located just cranial to the thoracic inlet. It is firmly attached to the underlying skin and thus can easily be seen and palpated externally.
- The crop in parrots is oriented transversely across the neck. Food enters from the right side and exits caudally on the midline.
- When the proventriculus and ventriculus are full, food may be stored in the crop. Stored food undergoes softening and swelling, but no chemical digestion takes place.
- Food eventually is moved caudally from the crop by powerful smooth muscle contractions of the crop and the esophageal wall.
- The crop (and proventriculus) is much larger in preweaned psittacine birds than in adults to accommodate large volumes of food required for rapid growth.
- As a bird is weaned, it is not uncommon for it to lose 10% to 15% of its body weight because of shrinkage of these organs and change in diet.

Crop Stasis

Many environmental, dietary, and systemic conditions can lead to crop stasis.

- Management factors include dehydration, low ambient temperature, change in the formula or in the consistency or amounts being fed, and unsanitary feeding methods.
- Medical conditions that cause crop stasis include bacterial or fungal ingluvitis (inflammation of the crop), heavy metal toxicity, foreign bodies, tumors (including papillomas), obstruction within the alimentary tract distal to the crop, and ileus due to generalized systemic disease (e.g., polyomavirus infection or proventricular dilatation disease).
- *Sour crop* refers to crop stasis in baby birds with bacterial or yeast overgrowth.

Clinical Signs

Hand-Fed Chicks

- The crop may be enlarged and pendulous and may fail to empty or may do so extremely slowly.
- Feeding response varies from normal to absent.
- Vomiting or regurgitation may occur.
- Initially, birds are alert and active, but depression and listlessness occur as the disease progresses.
- There is failure to gain weight, or there is loss of body weight.
- The number of droppings decreases.
- There may be discoloration or necrosis of the skin overlying the crop.

Adult Birds

- The enlarged crop fails to empty or does so slowly.
- Varying degrees of weight loss, weakness, depression, and anorexia are seen.
- Vomiting may occur; expelled food may collect on feathers of the head and neck.

Diagnosis

- Question the owner regarding husbandry practices (housing, ambient temperature, humidity, and diet) and possible exposure to infectious diseases.
- Palpate the crop to determine the amount and consistency of its contents, degree of thickness, muscle tone, fibrous or necrotic areas, and abscesses.
- Examine the skin over the crop for discoloration and necrosis.

- Transillumination of the crop may reveal its contents.
- The lower esophagus extends through the thoracic inlet and cannot be examined externally.
- Examine the mouth for oral lesions, which, if present, often extend into the esophagus and crop. This is often the case with bacterial and yeast infections, trichomoniasis, and occasionally papillomas.
- Endoscopic examination of the interior of the crop and esophagus or proventriculus requires general anesthesia. Examination may be useful to identify inflammation, tumors, and foreign bodies that can cause crop stasis.
- Perform a Gram stain and culture of exudate or food material from the esophageal or crop wall. Large numbers of gram-negative bacteria and budding yeasts are abnormal, but they may represent overgrowth within putrefying food in the stagnant crop only and may not be the primary cause of crop stasis. Be sure to look for the underlying cause of crop stasis and not overinterpret Gram stains.
- Perform a complete blood count (CBC) and serum chemistry profile to rule out systemic disease.
- Obtain blood samples for determination of blood lead concentrations to rule out heavy metal toxicity.
- Radiographs (plain films or contrast studies) may reveal obstruction caused by foreign bodies, tumors, or the presence of heavy metals.
- Histopathologic examination of tissues from chicks at necropsy can be important in the management and treatment of outbreaks of disease in aviaries.

Treatment

The primary goal of therapy is to alleviate crop stasis, which, if not corrected, leads to dehydration, starvation, secondary infections, and eventually death. Treatment and management in neonates can be extremely labor intensive and time consuming. If possible, evaluate and stabilize these birds in the hospital, and then instruct the client in home treatment. Most clinics simply do not have the personnel, housing, or time to provide 24-hour nursing care.

▼ ***Key Point*** Regardless of the cause of crop stasis, do not feed affected birds solid food (adults) or formula (chicks) until crop motility returns.

Measures to Restore Crop Motility

- Add warm water or lactated Ringer's solution to the crop to break down impacted food. This may stimulate emptying of the crop.
- If crop motility does not return, manually empty the crop contents. Insert a large catheter (metal or rubber) into the crop via the mouth and aspirate the contents (see Chapter 168). Be careful not to aspirate the mucosal lining of the crop during this procedure.
- Save samples of aspirated material for cytologic examination and bacterial or fungal culture.
- Rinse the crop with several flushes of normal saline or warm water after emptying contents.
- To treat dehydration, administer subcutaneous, intravenous, or intraosseous fluids daily until crop motility returns.
- Administer oral fluids such as lactated Ringer's solution and Pedialyte (Ross Products) in place of solid food or formula until motility begins to return. Frequent dosing in small amounts is recommended so as not to stretch the crop.
  - If the crop fails to empty adequately during this time, remove the solution contents once daily to prevent putrefaction.
  - If gastrointestinal (GI) obstruction has been ruled out, administer metoclopramide (Reglan, Robins) at 0.5 mg/kg q12h, IM or IV, or cisapride (available through veterinary compounding pharmacies) at 0.5 mg/kg q8h, PO.
- As motility begins to return, add formula to the oral fluids. Begin with a very diluted solution and gradually increase the concentration until a normal consistency is achieved.
- Administer parenteral broad-spectrum antibiotic and antifungal agents as indicated by Gram staining or to prevent secondary infections. Oral preparations may be administered once crop motility returns.

Environmental Factors

- House well-hydrated birds in an incubator or brooder (95–98°F for hatchlings, 94–97°F for neonates up to 7 days old, 90–94°F for neonates up to 14 days old, and 85–90°F for chicks more than 14 days old).
- Maintain relative humidity above 50%.
- Feed birds a consistent formula type or brand. Formula temperature should be approximately 98°F to 100°F.

▼ ***Key Point*** Identification and treatment of any underlying disorders are essential in the treatment of crop stasis.

Prolonged Crop Stasis

- Overfeeding or prolonged stasis in neonates can result in a pendulous, atonic crop.
- Use a crop supporter to provide support for the crop and to facilitate emptying (see Chapter 168).

Prevention

- To prevent crop stasis in hand-fed neonates, provide a clean, warm brooder; feed a good hand-feeding formula; and practice sanitary handling techniques:
  - Clean the brooder daily; follow ambient temperature guides as previously described.
  - Use a commercial hand-feeding formula or a proven home recipe. Do not switch arbitrarily from one formula to another.
  - Feed birds on a regular schedule.

  - Feed amounts appropriate for the size of the bird; do not overfill the crop.
  - Maintain consistent formula viscosity and temperature.
  - Make fresh formula for each feeding.
  - Disinfect utensils and bowls used for food preparation and delivery after each feeding.
  - Use separate feeding syringes for each bird.
  - Instruct caretakers to wash their hands before handling each bird.
- If there is a history of candidiasis in the aviary or for an individual bird, administer nystatin prophylactically until weaning.
- Correct other predisposing factors for bacterial and fungal infections, as previously described.

Foreign Bodies

The powerful beaks and persistent chewing habits of psittacine birds can lead to ingestion of foreign bodies, which may lodge in the crop.

Clinical Signs

- Crop stasis or delayed crop emptying may be seen.
- Regurgitation or repeated attempts at regurgitation may occur.

Diagnosis

- Palpate the crop. Many rigid objects large enough to lodge in the crop are palpable externally.
- Transillumination of the crop may reveal its contents.
- A small, rigid endoscope may be used to examine the crop and remove foreign bodies.
- Radiograph the cervical area. In some cases, contrast (barium or air) radiography may be necessary to visualize the object.

Treatment

- Retrieve smaller foreign bodies by passing a forceps into the crop through the mouth or by percutaneously manipulating the object into the esophagus for removal through the mouth.
- General anesthesia with isoflurane usually is required in all birds except neonates.
- Surgical removal via *ingluviotomy* (incision into the crop) may be required to remove the object.
- Close the crop wall with 4-0 to 6-0 polydioxanone (PDS) sutures in an inverting, interrupted suture pattern.
- Close the skin using a simple interrupted suture pattern.

Goiter

Etiology

Iodine-deficient thyroid dysplasia may develop in budgerigars fed a seed diet without vitamin or mineral supplementation.

Clinical Signs

All clinical signs are attributed to the space-occupying effects of the enlarged glands; thyroid hormone concentrations are usually normal. Signs include the following:

- Regurgitation
- Crop stasis or delayed crop emptying
- Clicking noise with respiration

Diagnosis

- Base the diagnosis on the clinical signs and history.
- Enlarged thyroid glands are usually not palpable because they are contained within the thoracic cavity.

Treatment

- Inject sodium iodide (Butler), 0.02 ml/30 g, IM, if birds are severely dyspneic.
- Maintain budgerigars on oral Lugol's iodine (Strong Iodine solution, Humco) in the drinking water. Mix 2 ml of Lugol's with 20 ml of water, then add 1 drop/oz of water daily for 1 week and once weekly thereafter.

Prevention

For budgerigars, switch to a commercial pelleted diet or supplement the existing diet with a commercial avian vitamin and mineral preparation.

Thermal Burns

Crop burns in neonates are caused by feeding hand-rearing formula at a temperature greater than 105°F. History usually reveals that the formula was heated in a microwave oven and not sufficiently stirred or tested for temperature.

Clinical Signs

- Birds usually remain bright and alert and maintain a normal feeding response despite full-thickness necrosis of portions of the crop and overlying skin. Therefore, these birds usually are not presented for evaluation until the caretaker notices formula leaking from the crop fistula onto the chest feathers.
- Necrosis and fistula formation does not occur until several days after the burn occurs.

Diagnosis

Base the diagnosis on the clinical signs and history.

Treatment

▼ ***Key Point*** Do not attempt surgical debridement or removal of scabs until wound contracture is complete and the crop begins to leak. Premature debridement may cause excessive loss of viable tissue.

- After anesthetizing the bird with isoflurane, debride all necrotic edges of the skin and crop.
- Close the crop wall and skin as described for ingluviotomy under "Foreign Bodies."
- Administer prophylactic antibiotic therapy using enrofloxacin, trimethoprim-sulfa, or cefotaxime.

DISORDERS OF THE PROVENTRICULUS AND VENTRICULUS

Normal Structure and Function

Proventriculus

- The proventriculus, or glandular stomach, is continuous with the esophagus at the level of the base of the heart and contains digestive (pepsinogen-secreting) and mucous glands.
- A strong muscular sphincter separates the proventriculus from the ventriculus.

Ventriculus

- The ventriculus, or muscular stomach (also known as the "gizzard"), contains two opposing sets of muscles used for grinding food.
- The epithelium secretes keratinous fluid that hardens to provide a surface against which food may be ground. Grit within the proventriculus aids this grinding action; however, in most psittacine birds, grit is not essential for digestion of food.
- Contractions of the proventriculus and ventriculus are coordinated to provide adequate mixing and grinding of gastric contents and digestive enzymes.

Foreign Body Impaction

Ingested objects small enough to bypass the thoracic inlet may lodge in the proventriculus or ventriculus. The pyloric sphincter, a valve-like structure separating the ventriculus from the duodenum, helps restrict larger solid objects from leaving the ventriculus. Small objects tend to collect in the ventriculus owing to its blind, pouch-like relationship to the remainder of the digestive tract.

Etiology

- Unweaned chicks typically are presented for ingestion of nesting substrates such as wood chips and shavings (especially young macaws) or for accidental swallowing of feeding instruments (e.g., tubes, spoons, or gavage needles).
- In weaning-age chicks, there may be impaction of seed hulls and other food objects that have been swallowed whole.
- Adults commonly present with a history of ingesting toys, cage parts, wood from perches, or carpet fibers. Shredded wood from perches or nest boxes and commercially available braided rope toys are the most common GI foreign bodies.
- Overconsumption of grit can cause impaction. If grit is provided, a small amount (10–20 pieces) given every few months is adequate.

▼ ***Key Point*** Do not offer gravel or grit free choice to pet birds. Ill or otherwise stressed birds may overeat grit, causing impaction of the ventriculus. Do not offer whole seeds or other hard foods to weaning birds.

Clinical Signs

- Early signs include crop stasis, decreased fecal output, and regurgitation.
- If the impaction is partial, chronic regurgitation, weight loss in adults, and decreased weight gain in neonates may be seen.
- Anorexia, lethargy, depression, seizures, and death occur with complete obstruction, erosion of mucosa, perforation, and septicemia.

Diagnosis

- Rule out crop impaction and foreign bodies (described previously).
- Obtain abdominal radiographs. Some objects may be visible on plain radiographs, but contrast radiography often is necessary. Use a mixture of 72% barium sulfate suspension diluted 1:1 with water at 25 ml/kg into the crop via a gavage tube. The entire GI tract should be delineated by the barium within 2.5 hours.
- It may be possible to identify and retrieve the object via endoscopy. An incision into the crop may be needed to access the proventriculus. Insert the endoscope through the crop via an ingluviotomy at the level of the thoracic inlet and direct it through the esophagus into the proventriculus.
- In larger birds, a flexible endoscope can be inserted through the oral cavity.

Treatment

- Small, non-toxic objects lodged in but not obstructing the ventriculus may be ground down and enzymatically digested by natural processes. Limited amounts of fine gravel grit can expedite the process.
- If the object is visible via endoscopy, it usually can be removed using blunt-jawed grasping forceps.
- Gastric lavage has been used to flush out objects lodged in the proventriculus.
- Proventriculotomy may be necessary to remove larger foreign bodies.

Prevention

- In neonates, use only large, non-ingestible or, alternatively, easily digestible nesting substrates. Also, use

only long, flexible feeding tubes to allow easy retrieval if syringe disconnection should occur.
- Monitor parent-reared chicks for signs of nest box substrate ingestion.
- When chicks begin feeding on their own, do not feed them seeds. Offer only small particles of fresh, soft foods.
- Restrict adult birds from access to toys that are easily broken apart, rope toys, and soft woods if the bird has been observed swallowing these objects or has a history of GI foreign bodies.
- Avoid feeding chitinous insects to pet birds.

Proventricular Dilatation Syndrome

See Chapter 169 in this section for a discussion of proventricular dilatation syndrome.

Papillomatosis

See Chapter 169 in this section for a description of this disorder.

Candidiasis

Etiology

C. albicans is a secondary invader, primarily of the mouth, esophagus, and crop, and has been discussed previously as a cause of oral lesions and crop stasis. Overgrowth of *Candida* may also occur in the lower digestive tract, particularly in the proventriculus. Lesions usually are not found in the lower digestive tract alone but are an extension of esophageal or crop candidiasis.

Clinical Signs

Common signs include delayed crop emptying, vomiting, diarrhea, and weight loss.

Diagnosis

- Endoscopic examination of the proventriculus (described previously) may reveal rough, thickened, white mucosa characteristic of candidiasis. Similar gross lesions usually are visible in the crop.
- Perform a Gram stain and fungal culture on samples obtained from the crop and fresh feces or from the proventriculus during endoscopic examination.
  - Although *C. albicans* may be part of the normal intestinal flora, large numbers of budding yeasts on Gram stains of these samples are abnormal and warrant treatment.
- Differentiate *Candida* organisms from brewer's yeast, which is commonly seen on Gram-stained fecal samples from birds fed bread products or some pellets. Brewer's yeast is non-budding, and fungal culture results will yield no growth.

Treatment

See "Treatment" under "Oral Candidiasis."

Bacterial Proventriculitis

Common pathogens of bacterial proventriculitis include *E. coli* and *Klebsiella, Enterobacter,* and *Salmonella* species.

Clinical Signs

Signs include vomiting, regurgitation, delayed crop emptying, and weight loss.

Diagnosis

- Perform the diagnostic procedures outlined under "Oral Candidiasis."
- The CBC may demonstrate leukocytosis with heterophilia.

For further discussion of bacterial infections, see Chapter 169 in this section.

DISORDERS OF THE INTESTINES

Infectious Diseases

Bacterial enteritis, *Mycobacterium avium,* and viral enteritis are common causes of diarrhea, vomiting, and weight loss in pet birds (see Chapter 169).

Giardiasis

Etiology

The trophozoite and cyst forms of the flagellated protozoan parasite *Giardia* are found in the crop and duodenum.

- The incidence is estimated to be as high as 20% to 50% in cockatiels, budgerigars, and lovebirds in some regions of North America.
- Giardiasis occurs less frequently in conures, Amazon parrots, cockatoos, and macaws.

Clinical Signs

- Malabsorptive diarrhea, characterized by voluminous, mucus-covered feces, or the passing of undigested food may be seen.
- Weight loss may be gradual or sudden, with losses of 20% to 30% of body weight.
- In cockatiels, pruritus—especially along the wing webs, axillary region, and back—has been anecdotally associated with intestinal giardiasis. This often is manifested by feather picking and occasionally is manifested by self-mutilation.

- Although the exact relationship is unknown, a hypersensitivity reaction is believed to be responsible.
- Paresis or lameness has been reported in birds with heavy *Giardia* infections. Malabsorption of vitamin E and selenium is the suspected cause.

Diagnosis

- Perform a direct saline smear assay on fresh feces immediately after collection to identify *Giardia* trophozoites and cysts. Staining with carbolfuchsin or iodine may aid visualization of organisms.
- Zinc sulfate centrifugation may reveal trophozoites in fecal samples.

▼ ***Key Point*** Because *Giardia* organisms are shed intermittently, false-negative test results are common.

- If a direct fecal examination cannot be performed immediately, submit the feces to a laboratory specializing in avian clinical pathology for trichrome staining.
- Fecal enzyme-linked immunosorbent assay and florescent antibody testing can also be performed by laboratories specializing in avian clinical pathology. The sensitivity and specificity of these tests have not been completely evaluated.
- The CBC may demonstrate a peripheral eosinophilia.
- Hypoproteinemia may be noted on the serum biochemical profile as a result of intestinal malabsorption.

Treatment

- Give metronidazole (Flagyl, Searle), 30 mg/kg q12h, PO, for 7 to 10 days. Crush the tablets and mix with a palatable liquid.
- If lameness or paresis is present, give vitamin E or selenium (Seletoc, Schering-Plough), 0.1 mg of selenium per kilogram, IM, every 14 days.

Helminthiasis

Intestinal helminths are most frequently a problem in newly imported birds or birds in captive breeding colonies.

Etiology

- Ascarids commonly are found in cockatiels, cockatoos, budgerigars, and other Australian parakeets. Ascaridiasis can be a persistent problem in captive breeding colonies, particularly if the birds have access to a wood or concrete floor. The life cycle is direct, as in mammals.
- *Capillaria* species (intestinal threadworm) can be found in all species of pet birds but is most common in macaws, conures, and Australian birds. The worms may be found in the mouth, esophagus, and small intestines. The life cycle is direct.
- Cestodes are found primarily in Old World psittacines (e.g., cockatoos and African grey parrots). They may be responsible for hemorrhagic enteritis and chronic wasting in African grey parrots. They have an indirect life cycle, with arthropod or annelid worms as intermediate hosts.

Clinical Signs

Clinical signs are generally nonspecific, with weight loss, diarrhea, and general unthriftiness predominating.

Diagnosis

Avian helminth eggs are detected by routine salt or sugar fecal flotation, as for dogs and cats.

Treatment

- Ivermectin (Ivomec 1% solution, Merck) is effective against intestinal nematodes when given at a dose of 200 µg/kg, IM, or diluted 1:9 with water in propylene glycol and given at 0.2 mg/kg, PO, every 2 weeks.
- Levamisole (Tramisol, American Cyanamid) is effective against most intestinal nematodes when given at a dosage of 10 to 20 mg/kg, SQ, every 2 weeks or as a solution of 10 ml/gallon drinking water if treating an entire flock (use as the only source of drinking water for 1 to 3 days).
- For cestodes, give praziquantel (Droncit, Haver/Diamond) at a dosage of 10 to 20 mg/kg, PO, and repeat in 10 to 14 days.

DISORDERS OF THE LIVER

Infectious Diseases

Etiology

Infectious disorders such as chlamydiosis, viral disease, bacterial hepatitis, and occasionally *Mycobacterium avium* are common causes of liver diseases in pet birds. This is especially true in larger psittacines such as parrots, macaws, and cockatoos, although cockatiels and budgerigars also may be affected.

Diagnosis

- Indicators of liver disease include green-yellow urates (biliverdinuria), hepatomegaly (palpable or radiographically evident), and serum biochemical profile indicators such as increased levels of serum bile acids and aspartate aminotransferase (AST). AST values may be elevated with either liver or muscle damage. Concurrent elevation in serum AST and creatine kinase (CK) values indicates muscle damage. Decreased serum albumin levels often are seen with liver disease.

- Liver biopsy often is necessary for definitive diagnosis with identification of a specific etiologic agent.
- See Chapter 169 for specific diagnostic tests, treatment, and prevention of infectious disease.

Fatty Liver Syndrome

Fatty liver syndrome (FLS), or hepatic lipidosis, commonly is seen in budgerigars, cockatiels, Amazon parrots, or any bird on a high-fat (especially all-seed) diet. Accumulation of fat in the liver is usually gradual, and with severity it will cause the destruction of normal liver cells and may progress to fibrosis.

Etiology

- The etiology of FLS is unknown; however, malnutrition appears to play a major role.
- Most birds with FLS are obese and on a high-fat diet consisting primarily of seeds.
- Unlike FLS in cats, anorexia does not appear to play a role in the development of this disorder.

Clinical Signs

- Most affect birds are obese, although with chronicity significant weight loss may occur.
- The most common clinical signs are lethargy, anorexia, depression, biliverdinuria, and poor feathering. Diarrhea and/or vomiting may also be seen.
- Budgerigars frequently have overgrown, soft, friable beaks, with focal areas of hemorrhage.
- Sudden death has been reported in budgerigars, cockatiels, and Amazon parrots, with hepatic lipidosis as the only identifiable lesion on necropsy.

Diagnosis

- Obtain radiographs of the abdomen to detect hepatomegaly.
- Increased AST, bile acid, and cholesterol concentrations are usually present on the serum biochemistry profile.
- Liver biopsy is necessary to confirm the diagnosis. Grossly, the liver is enlarged, yellowish, and friable.

Treatment

- Administer intravenous or interosseous fluids to critically ill birds. If anorexic, forced alimentation with low-fat gruel is indicated (see Chapter 168).
- Place the bird on a strict low-fat diet containing at least 12% protein. Eliminate seeds from the diet.
- Ideally, a commercial avian pellet formula should make up at least 40% of the diet, with the remainder consisting of vegetables, fruits, and grains or legumes.

Hepatic Fibrosis

Etiology

- Hepatic fibrosis is a common sequela to chronic liver disease.
- The primary insult can be infectious (e.g., bacterial, viral, or chlamydial) or non-infectious (e.g., FLS). Fibrosis can persist after elimination of the primary insult.

Diagnosis

- Radiographs usually reveal a normal-sized or small liver shadow.
- Increase in serum AST concentration is variable. With severe disease, AST may be normal. Bile acid concentrations are increased.
- Liver biopsy is required for definitive diagnosis of hepatic fibrosis.
- Ascites is seen in severe (end stage) disease. Clinical signs of ascites include abdominal distention and dyspnea due to compression of air sacs.

Treatment

- Supportive care in the form of fluid therapy, nursing care, and appropriate diet are essential in the treatment of hepatic disease.
- If significant ascites is present, perform abdominocentesis.
- Colchicine has been reported to be beneficial in the treatment of chronic liver disease by interfering with collagen precursor synthesis. Doses have been extrapolated from those used in cats.
- Ursodeoxycholic acid has been used anecdotally for its immune-modulating effects, induction of choleresis, and effect on the circulating bile pool. Doses have been extrapolated from those used in cats.
- Antibiotic therapy may be indicated if bacterial hepatitis is suspected to limit inflammation and subsequent fibrosis. Common choices include doxycycline (Vibramycin, Pfizer), 25 to 50 mg/kg PO q24h, or a combination of enrofloxacin (Baytril, Bayer), 10 to 20 mg/kg PO q24h, and metronidazole (Flagyl, Searle), 50 mg/kg PO q12h.
- If hepatic encephalopathy is suspected, administer lactulose at a dosage of 0.3 to 1.0 ml/kg PO q12h; decrease the dose if diarrhea develops. Metronidazole may be added to alter colonic flora.

Aflatoxicosis

Etiology

- Avian aflatoxicosis is caused by the ingestion of toxic metabolites from molds such as *Aspergillus flavus* and *Aspergillus parasiticus*. Foods in which these molds may be found include peanuts and peanut products, cereals, breads, cheeses, beans, and meat.
- Aflatoxins frequently are hepatoxic and may be carcinogenic.

Clinical Signs

Signs generally are nonspecific and include anorexia, weight loss, and depression.

Diagnosis

- Base the diagnosis on history, clinical signs, and fungus isolation from feed or the GI tract.
- Gross and histopathologic lesions from postmortem or liver biopsy confirm the diagnosis.
  - Chronic lesions include biliary hyperplasia, cirrhosis, generalized fatty degeneration, and portal fibrosis.
  - Acute lesions include massive hepatocyte necrosis and hepatic hemorrhage.

Treatment

- No specific therapy is available. Supportive care, antibiotic, antifibrotic and Ursodeoxycholic acid may be helpful (see treatment of hepatic fibrosis above).
- Oral selenium may act as a competitive inhibitor of aflatoxins in the liver.

Hemochromatosis

Etiology

Hemochromatosis, defined as excessive deposition of iron in hepatic parenchymal cells with resultant cellular damage, is common in mynahs and toucans. Iron normally is absorbed from the intestines at a rate dependent on the body's needs and then recycled with minimal excretion from the body.

- In hemochromatosis, there is excessive uncontrolled absorption and storage of iron.
- The mechanism of this defect in iron metabolism is not understood, but affected birds absorb and store even small amounts of iron in the diet.

Clinical Signs

Signs include weight loss, dyspnea, and abdominal swelling from severe hepatomegaly and ascites.

Diagnosis

Diagnosis is based on clinical signs and confirmation on hepatic biopsy. Radiographs demonstrate hepatomegaly, sometimes with splenomegaly and cardiomegaly. Elevation in serum AST and bile acid concentrations is inconsistent.

Treatment

- For symptomatic control of ascites, periodically remove abdominal fluid and administer diuretics.
- Successful long-term treatment has been reported with weekly phlebotomies.
- Iron chelation therapy with deferoxamine mesylate, 100 mg/kg SC q24h, may help reduce serum and hepatic iron concentration.
- Change the diet to a low-iron commercial ration (20–40 ppm).
- Chronic disease may lead to fibrosis or cirrhosis. Treat as described under fibrosis above.

Prevention

- Many commercial mynah pellets contain excessively high levels of iron. Place mynahs and toucans on low-iron (20 to 40 ppm) commercial pelleted food.

Neoplasia

Primary and metastatic neoplasms have been reported in all psittacine birds; they are particularly prevalent in budgerigars and Amazon parrots.

- An increased incidence of hepatic neoplasia has been noted in birds with papillomas.
- Primary tumors seen include bile duct carcinoma, hepatocellular carcinoma, hepatoma, fibrosarcoma, and hemangiosarcoma.
- Hepatomegaly usually is palpable or visible on radiographs.
- Diagnosis is confirmed by biopsy.
- Treatment is ineffective.

DISORDERS OF THE PANCREAS

Etiology

- As in liver disease, many infectious agents (e.g., bacteria, *Chlamydia,* and viruses) may target the pancreas alone (e.g., many viral infections) or concurrently with other organ systems (see Chapter 169).
- Non-infectious causes of pancreatitis include nutritional factors; pancreatitis may be seen secondary to egg yolk peritonitis (see Chapter 173).
- In some cases, pancreatitis diagnosed at necropsy showed an intense inflammatory process without infectious etiology, especially in birds on high-fat (seed) diets.
- There is a possible correlation between hypercalcemia occurring in hens in breeding condition (serum calcium levels usually are 20 times normal before ovulation) and onset of pancreatitis (hypercalcemia is known to be a cause of pancreatitis in humans).

Clinical Signs

- Signs include anorexia, polyuria or polydipsia, diarrhea, and listlessness.

Diagnosis

- Serum amylase levels are sometimes elevated, and lipemia, hypercalcemia, and hyperglycemia may be present.
- Radiography may reveal decreased abdominal detail.
- Definitive diagnosis is based on pancreatic biopsy, obtained via laparoscopy.

Treatment

- Treatment is similar to that for dogs and cats and includes fluid therapy (nothing per os), antibiotic therapy, and maintenance on a low-fat diet (see Chapter 73).

I would like to acknowledge Scott McDonald for his contribution of this chapter to the first edition.

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Chapter

173 Avian Reproductive Tract Disorders

Heather L. Bowles

Avian reproductive disorders are a result of complex combinations of hormonal, physiologic, and behavioral actions reacting to photoperiods, food availability, and availability of nest sites. Environmental influences unique to captivity may induce reproductive and hormonal activity in several ways. For instance, artificial lighting may interfere with the normal photoperiod and annual light cycles, resulting in inappropriate cycling. Food is typically available ad libitum in captivity, and it often is high-fat, calorically dense seed or foods high in simple carbohydrates, such as corn and fruit. These foods may actually stimulate reproduction. A lack of an appropriate mate may also cause reproductive problems. Most pet birds are not intended for breeding and do not have mates. As a result, some of these birds select an abnormal mate such as their human cohabitants or cage furniture. Along with all of these common environmental influences, there may be genetic factors that contribute to a lack of normal reproductive hormonal balance.

Reproductively driven birds may display instinctual territorial and mate-related behaviors. These behaviors may include but are not limited to aggression, biting, and excessive vocalization. These "undesirable" behaviors may jeopardize their value as pets, diminishing the pet-human relationship, and even result in these birds losing their homes.

Reproduction often is not desired in pet birds. Egg production and hormonal cycling may lead to diseases of the reproductive system or systemic, endocrine, and metabolic disorders. Therefore, avian practitioners have sought medical and surgical methods to limit reproductive drive and hormone production.

FEMALE REPRODUCTIVE DISORDERS

See Figure 173-1 for reproductive anatomy of the female bird.

Chronic or Excessive Egg Laying

Etiology

- Chronic egg laying in pet birds occurs when a hen lays repeated clutches or a larger-than-normal number of eggs per clutch without regard to the presence of a mate or accurate breeding season. This process often physically exhausts the reproductive tract and is a serious metabolic drain, particularly on calcium stores. These factors may predispose the hen to egg binding, yolk peritonitis, and osteoporosis.
- Commonly affected species include cockatiels, finches, and lovebirds; however, any species may be affected.

Diagnosis

Diagnosis of chronic egg laying is based on history and physical examination.

History

- Affected hens lay large numbers of eggs with or without a pause period between clutches.
- A thorough history of the environment will often reveal several reproductive stimuli and a "mate relationship" with the owner, another member of the household, or an inanimate object.

Physical Examination

- This examination may be unremarkable.
- Palpate the abdomen. An egg is sometimes palpable in the coelom. The abdomen often has a doughy consistency due to uterine distension.
- Look for other, secondary disease conditions such as a pathologic fracture secondary to osteoporosis.

Laboratory Evaluation

- Serum chemistries may reveal hypercalcemia, hypercholesterolemia, and hyperglobulinemia supportive of an ovulating hen.
- In some cases, hypocalcemia is seen if the hen's calcium stores are depleted, particularly if she is consuming a low-calcium seed diet.

Treatment

Medical therapy for chronic egg laying focuses on stopping egg production while removing predisposing stimuli and correcting any secondary diseases that may be present. Pharmacologic, behavioral, nutritional,

Table 173-1. MEDICAL THERAPY FOR REPRODUCTIVE DISORDERS

Drug	Dosage	Comments
Leuprolide acetate	150–800 µg/kg IM	Administered every 14 days; three doses are usually adequate
Human chorionic gonadotropin	250–500 IU/kg IM on days 1, 3, and 7 500–1000 IU/kg IM	Stable in refrigerator 60 days If a second egg is laid, repeat dose on day 3; if a third egg is laid, repeat dose on day 7
Levonorgestrel		Not recommended
Medroxyprogesterone		Not recommended
Arginine vasotocin	0.01–1.0 mg/kg IM	Stable in standard freezer
Prostaglandin E (Prepidil Gel)	0.1 ml/100 g 0.002–0.1 mg/kg	May freeze into aliquots and thaw Applied topically prior to administration; relaxes uterovaginal sphincter while inducing uterine contractions
Prostaglandin F-2-alpha (Lutalyse)	0.02–0.1 mg/kg IM	May not relax uterovaginal sphincter when inducing uterine contractions Topically applied to prolapsed uterine tissue to stop hemorrhage and shrink tissues

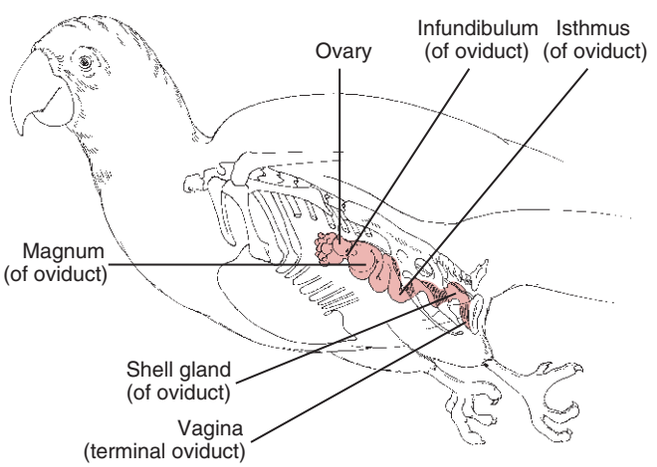

Figure 173-1. Reproductive anatomy of the female bird. The shell gland is equivalent to the uterus.

environmental, and surgical options are used alone or in combination, depending on the needs of the individual patient. Pharmacologic options have included medroxyprogesterone acetate, levonorgestrel, human chorionic gonadotropin, testosterone, and leuprolide acetate.

Pharmacologic Therapy (Table 173-1)

Leuprolide Acetate

- Leuprolide acetate (Lupron Depot, TAP Pharmaceuticals) is a long-acting gonadotropin-releasing hormone (GnRH) analogue. Principles for use of Lupron have been extrapolated from use in humans and other species and are often effective in controlling ovulation in birds.
- Administer 150 to 800 µg/kg IM every 14 days. Three doses are usually sufficient to inhibit further egg laying. Repeat treatment may be needed if signs return.

Human Chorionic Gonadotropin

- Human chorionic gonadotropin (hCG) (Pregnyl, Organon) has been used successful to inhibit egg laying with few side effects; however, it has not been consistently effective and patients may become refractory to treatment.
- Reported dosage regimens vary. Administration of 250 to 500 IU/kg IM on days 1, 3, and 7 has been effective to prevent laying. Alternatively, administer 500 to 1000 IU/kg IM after the first egg is laid. If another egg is laid, repeat the injection on day 3; if a third egg is laid, repeat the injection on day 7.

Other Hormonal Treatments

- Medroxyprogesterone acetate, although often effective, may cause serious side effects such as polyuria and polydipsia, obesity, lethargy, hepatic lipidosis, diabetes mellitus, hepatic cirrhosis, and death. Therefore, it is not recommended.
- Testosterone therapy interrupts the ovulatory cycle, but it has inconsistent results and is contraindicated in patients with liver disease.
- Norethindrone or mestranol, and tamoxifen, have been also used in a limited number of species with unreliable results.

Environmental Modification

- Decrease the photoperiod to 8 to 10 hours of daylight per day.
- Remove from the enclosure nest sites, toys, and other items toward which the bird has a sexual affinity. Pro-

hibit access to the nesting environment or materials such as a box, other dark cavities, or shredded papers.
- If the bird is showing nesting behavior and laying eggs in a designated site, leave the eggs in the "nest" for the duration of the normal incubation period for each species. Removal of the eggs may stimulate the hen to lay more eggs to replace those removed.
- Remove any perceived or actual mate from the cage or room. In some species, such as the cockatiel, both visual and auditory separation from an actual or perceived mate may be necessary.
- A "one-person bird," which has a single household person who exclusively or primarily handles and cares for it, should potentially be viewed as having a "mate relationship" with that person. This may serve as a trigger for reproductively driven behaviors. Advise this person to avoid stimulatory petting such as rubbing the pelvis, dorsum, and cloacal regions.
- Avoid feeding calorically dense diets, as mentioned previously.
- Encourage interactive behaviors that simulate a "flock relationship," such as the bird being handled by several people in the household.
- Periodically change or rotate the cage location and furniture (toys, perches, food dishes) to discourage territorial behavior and limit reproductive drive in response to a perceived "nest site."
- Correct any nutritional problems to improve the hen's overall dietary plane and reduce the severity of metabolic drain. Dietary alteration and reduction of caloric intake appears to anecdotally reduce or stop egg production. This nutritional effect often is achieved by converting the pet bird from a seed-based diet to a formulated one. The exact reason for this effect is unknown, but it is common practice in poultry to reduce feed intake to stop egg production and induce molting.

▼ ***Key Point*** Removal of environmental stimuli is essential to inhibiting ovulation in birds. Pharmacologic therapy will sometimes fail if even seemingly minor stimuli (such as access to cage papers to shred as nest material) are present.

Surgical Treatment

Salpingohysterectomy may be elected or necessary if medical therapy is not successful and if there is no intent to breed the affected hen. Laparoscopic salpingohysterectomy may be performed as a preemptive measure on juvenile birds to prevent egg production and its associated diseases.

Other Treatment

Any secondary disease conditions also should be appropriately treated.

Polyostotic Hyperostosis

Etiology

- Physiologic osteomyelosclerosis is the deposition of calcium stores in medullary bone for future use in egg production.
- Polyostotic hyperostosis differs from physiologic osteomyelosclerosis in that this condition occurs in non-laying hens and cocks as a result of pathologic conditions.
- The pathogenesis of polyostotic hyperostosis still is unclear. Many affected birds exhibit concurrent reproductive-associated activity or may suffer from reproductive-associated disease conditions.
- Hepatic disease may play a role in this condition due to the liver's role in the inactivation of estrogen. However, a recent study does not support this theory, stating that budgerigars affected by polyostotic hyperostosis had no evidence of estrogen secretion or other endocrine disease.

Diagnosis

- History and physical exam may reveal lethargy, depression, reduced appetite, and reproductively driven behaviors.
- Serum chemistries typically demonstrate hypercalcemia. The bird may be normocalcemic or hypocalcemic if on a calcium-deficient diet.
- Radiographs reveal significantly increased bone density of the long bones and occasionally the vertebrae.

Treatment

- Pharmacologic therapy and environmental manipulation to inhibit ovulation (listed above under treatment of excessive egg laying) may reduce reproductive hormone production and the subsequent effect on bone metabolism.
- Increased medullary bone density appears to resolve radiographically with resolution of reproductive drive or underlying reproductive disease.

Egg Binding and Dystocia

Definition

- Egg binding is defined as the failure of an egg to pass through the oviduct within a normal period of time.
- Most companion birds lay eggs at intervals of greater than 24 hours, and individuals may vary further.
- This variability may make it difficult to determine if there is a problem in the early stages of this disease.
- Dystocia involves the mechanical obstruction of oviposition.

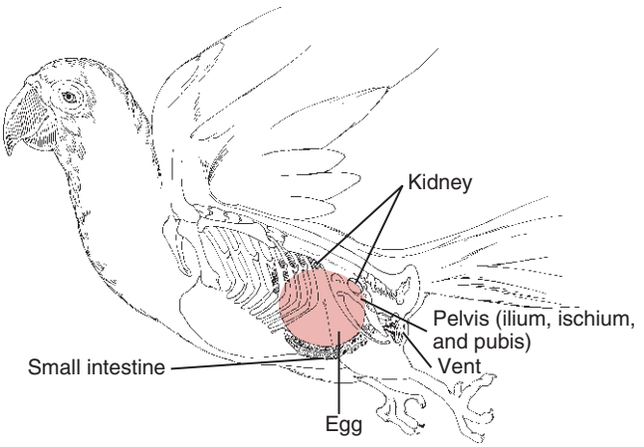

Figure 173-2. Anatomic landmarks associated with egg binding.

- The most common anatomic areas for this obstruction to occur are the distal uterus, vagina, and vaginal-cloacal junction. See Figure 173-2 for other anatomic landmarks associated with egg binding.

Etiology

- Causes of egg binding may include chronic egg laying, oviductal muscle dysfunction secondary to excessive egg laying, disorders of calcium metabolism, vitamin E and selenium deficiencies, malnutrition, obesity, inadequate exercise and muscle strength, malformed eggs, mechanical tears or damage to the oviduct, oviductal infections, systemic disease, genetic predisposition, and environmental stressors.
- Dystocia also may result when a developing egg in the distal oviduct obstructs the cloaca or causes oviductal tissue to prolapse.
- Oviductal torsion and oviductal or abdominal masses compressing the oviduct also may obstruct passage of an egg and result in dystocia. Breeding birds out of their natural season, egg-producing virginal hens, and hens with a persistent right oviduct may be predisposed to egg binding or dystocia.

Clinical Signs

- Cockatiels, canaries, and finches are most commonly affected and usually present with more severe clinical signs, possibly due to their small size.
- Clinical signs associated with egg binding and dystocia vary according to severity, size of the bird affected, and degree of secondary complications.
- Common signs include acute depression, abdominal straining, persistent tail wagging, a wide stance, pelvic limb paresis or paralysis, failure to perch, abdominal distension, urine or urate retention, dyspnea, and sudden death.

Secondary Disorders

- An egg lodged in the pelvic canal may compress the pelvic blood vessels, ureters, ischiatic nerves, and cloaca, causing pelvic limb paresis, paralysis, cyanosis, circulatory disorders, or urine or urate retention.
- Pressure necrosis of the oviductal wall may occur.
- Dystocia may cause metabolic disturbances by interfering with normal defecation and micturition, and cause ileus and renal disease, respectively.

Diagnosis

History

Diagnosis of egg binding or dystocia in a severely compromised patient may be made based on history and physical examination alone, and the patient may not be stable enough to survive other diagnostic procedures. Rapid diagnosis and therapy are crucial for a successful outcome.

▼ ***Key Point*** The severity of the patient's condition can be estimated by the degree of depression and the length of time clinical signs have been present.

Physical Examination

- Palpate the abdomen for the presence of an egg. Palpable eggs may be located within the oviduct or ectopically within the coelom. A combination of abdominal palpation, cloacal examination, radiographs, coelomic ultrasound, laparoscopy, and/or laparotomy may be required to determine the egg's position.
- Cranially located, soft-shelled, and non-shelled eggs may not be palpable.

Diagnostic Imaging

- Obtain abdominal radiographs. Shelled eggs are visible radiographically. Eggs are typically located in the distal oviduct, in the region of the uterus.
- Osteomyelosclerosis of the femurs, tibiotarsi, radii, ulnas, and/or spine may be visible. A soft tissue density suggestive of an enlarged ovary in the region of the ovary may be noted, supportive of a reproductively active hen.
- Coelomic ultrasound often will reveal an egg and may identify soft-shelled or non-shelled egg(s) that may not have been identifiable on radiographs. Again, there may be several eggs visible within the coelom. Follicles may be visible on the ovary, indicating the potential for further ovulation and egg formation.

Laboratory Evaluation

- A hematologic analysis and serum chemistries are useful to identify any predisposing and secondary diseases.

- A complete blood count may reveal a leukocytosis with a relative heterophilia if there is a concurrent inflammatory or infectious process.
- Serum chemistries may demonstrate elevated aminotransferase and creatinine phosphokinase due to skeletal muscle enzyme leakage from tissue damage or as a result of reduced food consumption and a hypermetabolic state.
- Hypercholesterolemia and hyperglobulinemia are supportive of an ovulating hen.
- Elevated total and ionized calcium and may be indicative of a cycling hen. Hypocalcemia may be observed if the hen has been consuming a calcium-poor diet or has been laying excessive numbers of eggs, resulting in depletion of her calcium stores.

Treatment

Therapy varies with history, severity of clinical signs, and diagnostic test results.

Supportive Care

- Provide supportive care, including a warm and humid environment, parenteral calcium, fluid therapy, and nutritional support.
- Administer broad-spectrum antibiotics if an infectious etiology is suspected or if the integrity of the oviduct may be compromised.
- Administer analgesics if the patient appears to be in pain or if clinical knowledge of the patient's condition suggests that pain may be a part of the pathologic state.

▼ ***Key Point*** In birds that are not severely compromised, supportive care alone often is enough to allow oviposition, although the hen should be monitored closely for deterioration of her condition, which may require further intervention.

Pharmacologic Therapy (See Table 173-1)

- Prostaglandin and hormonal therapy may be used to induce oviductal contractions. This may result in expulsion of the egg if the contractility of the oviduct is sufficient to expel the egg, the uterus is intact, the egg is within the oviduct, and there is no obstruction such as a neoplastic mass, granuloma, or egg adhered to the oviduct.
- Prostaglandin and hormonal therapy requires exogenous calcium to be effective. Because many of these patients are severely hypocalcemic due to either malnutrition or chronic egg laying, supplemental calcium may be required prior to administration of these medications.

Prostaglandin E-2

- Apply prostaglandin E-2 (PGE_2) (dinoprostone) gel (Prepidil Gel, Upjohn) topically, per cloaca, to the uterovaginal sphincter, at a dose of 0.1 ml per 100-g bird.
- PGE_2 causes relaxation of the uterovaginal sphincter while inducing oviductal contractions. These contractions usually expel the egg within 15 minutes.
- After the egg is expelled, flush the cloaca with warm water or saline to remove remaining gel, prevent further discomfort from continued uterine contractions, and minimize systemic side effects.

▼ ***Key Point*** Contact with PGE_2 gel may cause altered menses and induce spontaneous abortion in women. Therefore, it is important to flush any excess from the cloaca after egg expulsion and precaution staff and clients regarding contact with any stool and/or urine produced.

Prostaglandin F-2-alpha and Other Hormonal Therapy

- Administration of prostaglandin F-2-alpha (PGF_{2a}), oxytocin, or arginine vasotocin (AVT) will also cause powerful uterine contractions.
- These treatments are administered parenterally, rather than topically, and are more likely to cause systemic side effects such as hypertension, bronchoconstriction, and general smooth-muscle stimulation.

▼ ***Key Point*** PGF_{2a}, oxytocin, and AVT do not cause relaxation of the uterovaginal sphincter while inducing powerful oviductal contractions. This may result in reverse peristalsis, severe pain, and/or rupture of the uterus. Therefore, prior to their use determine if the uterovaginal sphincter is open.

Manual Manipulation

- If supportive care and medical therapy fail to induce oviposition, then manual manipulation may be necessary.
- Massage the abdomen and vaginal opening, which may relax the vaginal sphincter and allow passage of the egg in mildly affected birds. It may be helpful to infuse lubricants into the cloaca to moisten the urodeum and vagina.
- Apply careful digital pressure to the cranial portion of the egg, directing pressure caudally to encourage movement through the distal oviduct and cloaca. Using a cloacal speculum, dilate the vaginal opening of the oviduct by inserting a blunt probe (e.g., a lubricated cotton-tipped swab), gently advancing in a twirling motion.
- Potential complications of manual manipulation may include retroperistalsis of the egg out of the oviduct into an ectopic position within the coelom, rupture of the egg, oviductal trauma, oviductal laceration, and displacement of the egg or fragments into an ectopic position.

Ovocentesis

- Ovocentesis may be performed to facilitate passage of an egg. Aspiration may be performed through the cloacal opening if the egg is distally located or transabdominally if the egg is more cranially positioned.
- Manipulate the egg so that the shell is visible through the cloaca and insert an 18-gauge needle with syringe attached into the egg. Aspirate the contents of the egg into the syringe, while manually collapsing the shell and expelling the pieces through the cloaca.
- If the egg cannot be seen through the cloaca due to a more cranial location, perform transabdominal ovocentesis. Manually position the egg directly against the abdominal wall so that other abdominal organs are displaced and not damaged during aspiration. Insert a needle with a syringe attached through the skin and abdominal wall into the egg. Aspirate the egg contents into the syringe while manually collapsing the egg. The eggshell remnants can then be expelled through the cloaca, either naturally or with clinical assistance.
- Confirm radiographically that these eggshell pieces have been completely expelled. If these pieces are not expelled within a reasonable amount of time, approximately 36 hours, it may be necessary to irrigate the oviduct through the cloaca or laparotomy approach.
- Use medical therapy to reduce reproductive activity (as described under excessive laying above) to temporarily prevent further egg production.
- Salpingohysterectomy may be indicated if egg remnants are retained and the hen is not required for breeding. Some clinicians advocate flushing the postoviposition uterus with saline, chlorhexidine, or iodine to remove any shell fragments and decrease the incidence of metritis. Oviductal rupture, resulting in an ectopic egg, shell fragments, or yolk coelomitis, is a possible complication of ovocentesis.

Surgical Treatment

- Prostaglandin treatment, manual delivery, and ovocentesis are contraindicated in cases of ectopic eggs, oviductal rupture, oviductal torsion, and mechanical obstruction.
- Surgical intervention is indicated in birds with oviductal rupture with or without an ectopic egg, oviductal necrosis, oviductal torsion, abdominal hernia, or conditions interfering with defecation and/or micturition.
- Surgical removal of an egg may be elected as an initial treatment or if medical treatment is not successful.
- If surgical intervention is necessary, perform bacterial culture and sensitivity and histopathologic analysis on oviductal tissue samples.
- Salpingohysterectomy may be considered to prevent further reproductive complications after medical therapy, and any predisposing and secondary diseases should be corrected.

Oviductal Prolapse

Etiology

- Oviductal prolapse may occur secondary to any condition that causes chronic, excessive abdominal straining, such as physiologic uterine hyperplasia, egg laying, or dystocia. An intracoelomic, space-occupying mass also may induce prolapse of the oviduct.
- Predisposing factors may include abnormal or soft-shelled eggs, malnutrition, obesity, salpingitis, and cloacitis.

Clinical Signs

Typically, the uterus protrudes through the cloaca, often with a partial prolapse of the vagina and cloaca.

Diagnosis

- Complete blood count, serum chemistries, radiographs, ultrasonography, and laparoscopy should be included in a complete diagnostic evaluation to identify predisposing or secondary disease conditions.
- Bacterial culture and sensitivity of the prolapsed tissue should be performed to aid appropriate antibiotic therapy.

Treatment

- Rapid treatment is necessary to prevent necrosis of prolapsed tissues.
- Remove any egg, egg remnants, or debris and irrigate all exposed tissues.
- Keep tissues well moistened to prevent desiccation.
- Topical anti-inflammatories, such as dimethyl sulfoxide (DMSO) at 1 ml/kg to the affected area once, may be of benefit.
- Repair any lacerations and gently replace all tissues.
- Temporary stay sutures placed in the vent opening may be indicated to aid in preventing recurrence. Recurrence is common, and repeated replacement often is required.
- Administer broad-spectrum antibiotics and antifungals while bacterial and fungal cultures are pending.
- Administer hormonal treatment to decrease reproductive activity (described under excessive laying above) to prevent further prolapse, prevent egg formation, decrease the size of oviductal tissue, and allow the reproductive tract to rest.
- Salpingohysterectomy may be considered to prevent recurrence. Predisposing factors should be corrected to prevent recurrence and secondary diseases should be addressed.

Uterine Torsion

- Uterine torsion usually is diagnosed in the later stages of the disease.

- Birds typically present with abdominal distension secondary to coelomitis.
- Early clinical signs may include depression and anorexia following recent oviposition.
- A complete blood count often demonstrates a leukocytosis with a relative heterophilia, and serum chemistries show an elevated aspartate transferase and creatinine kinase.
- Diagnosis usually is made at exploratory laparotomy or laparoscopy. Many times, severe vascular compromise and necrosis of the oviduct is found, which requires salpingohysterectomy.

Oviductal Impaction

Etiology

- Oviductal impaction may occur following salpingitis, metritis, or cystic hyperplasia of the oviduct or dystocia.
- Substances causing impaction include excess mucin, albumin, or inspissated egg material.

Clinical Signs

Clinical signs may be vague and can include cessation of egg production, broody behavior without egg production, weight loss, anorexia, depression, constipation, diarrhea, abdominal distension, and reluctance to walk or fly.

Diagnosis

- Usually there is a history of reproductive activity.
- A leukocytosis with or without a relative heterophilia may be noted.
- Serum chemistries may be supportive of an ovulating hen.
- Radiographs and coelomic ultrasound may demonstrate a soft tissue density in the region of the oviduct, displacement of other coelomic viscera, loss of coelomic visceral detail, or coelomic fluid if there is a concurrent coelomitis.
- Definitive diagnosis of oviductal impaction often is made during laparoscopy or celiotomy, revealing an abnormal-appearing, enlarged oviduct with or without coelomitis and adhesions.
- Bacterial culture and sensitivity should be performed on specimens from the affected oviduct, and histopathologic examination should be performed on biopsy samples.

Treatment

- Provide supportive care, including parenteral fluids, nutritional support, warmth, and broad-spectrum antibiotics, pending culture and sensitivity results.
- In most cases, it is necessary to clean and repair or surgically remove the oviduct. Surgery may be complicated if coelomic fluid and/or adhesions are present.
- To prevent recurrence, begin medical therapy to reduce reproductive hormone production and reproductive activity and reduce environmental stimuli altered as discussed with chronic egg laying above.

Salpingitis and Metritis

Etiology

- Salpingitis is inflammation of the oviduct either by an infectious or non-infectious etiology, the latter being far less common. It is usually associated with air sacculitis, liver disease, pneumonia, systemic infections, and ascending infections of the oviduct from the uterus or cloaca.
- Salpingitis is most common in adult hens but occasionally may occur in young birds.
- Commonly identified pathogens include *Escherichia coli, Salmonella, Mycoplasma, Pasteurella,* and *Streptococcus* species. Newcastle disease virus also has been associated with salpingitis. In ground-nesting species such as *Anseriformes* and emus, non–lactose-fermenting, gram-negative bacteria such as *Pseudomonas aeruginosa, Proteus mirabilis,* and *Proteus vulgaris* commonly are identified.
- Non-infectious causes of salpingitis include trauma and inflammation secondary to oviposition disorders, malnutrition, and foreign bodies.
- Metritis is a localized infection or inflammatory process within the uterine portion of the oviduct. Metritis may occur secondary to dystocia, egg binding, oviductal impaction, systemic bacterial infection, and ascending infection. Salpingitis and metritis may cause abnormal shell formation and impaired uterine contractions, and it may cause infections in chicks and embryos, including embryonic death.
- Fatalities are often associated with ovulation, egg binding or dystocia, oviductal rupture, coelomitis, and septicemia.

Clinical Signs

Clinical signs of salpingitis and metritis may be vague and difficult to detect initially, and they include decreased egg production, infertility, abnormally shaped eggs, and mild depression. More advanced cases may exhibit anorexia, lethargy, abdominal distension, oviductal rupture, coelomitis, and septicemia.

Diagnosis

- Hemogram often reveals leukocytosis with a relative heterophilia. Serum chemistries may or may not be supportive of an ovulating hen.
- Radiographs and ultrasonography may reveal an enlarged oviduct. Laparoscopy may or may not identify inflammation of the serosal surface of the oviduct. The oviduct may be thin walled, be decreased in length, or have vascular congestion. The lumen may contain fluid or fibrinous exudates.

- Definitive diagnosis of salpingitis and metritis is based on cytology, bacterial and fungal culture and sensitivity, and biopsy with histopathologic analysis of a specimen from the oviduct.

Treatment

- Correct any underlying or contributing causes.
- Administer antibiotic therapy for identified or suspected bacterial organisms, pending results of bacterial culture and sensitivity.
- Initiate pharmacologic treatment and husbandry-related intervention, as discussed with chronic egg laying, to prevent further hormonal stimulation with subsequent egg production, which may perpetuate or contribute to this disease.
- Monitor patients closely, including oviductal bacterial culture and sensitivity and fertility monitoring after treatment, as many cases are difficult to resolve completely. It is important to note that bacteria isolates from the cloaca are not equivalent to oviductal infectants, and cloacal bacterial cultures should be interpreted carefully.
- Severe, refractory cases may require laparotomy to remove necrotic tissue and flushing of the oviduct with fluids and antibiotics.
- Patients suffering from severe salpingitis may require salpingohysterectomy, or this may be elected in milder cases to resolve disease and prevent recurrence if the hen is not intended for breeding.

Cystic Hyperplasia of the Oviduct

Etiology

Cystic hyperplasia of the oviduct may occur from improper formation of the left oviduct or secondary to an endocrine abnormality. In addition, the vestigial right oviduct may become cystic, and the associated ovary often has cystic changes. Cystic hyperplasia often contributes to salpingitis and egg binding.

Clinical Signs

Clinical signs may include depression, anorexia, abdominal distension, ascites, and dyspnea. A tentative diagnosis is made through history, physical examination, and supporting laboratory tests, similarly to that of salpingitis and metritis.

Diagnosis

- Radiographs may demonstrate an enlarged soft tissue density in the region of the oviduct.
- Ultrasonography may reveal an enlarged oviduct that may be filled with fluid or have obvious cysts present, with or without concurrent ovarian follicles or cysts.
- Laparoscopy may show a dilated oviduct filled with a white or brown mucoid fluid.
- Definitive diagnosis requires laparotomy with biopsy, cytology, histopathology, and bacterial culture and sensitivity.

Treatment

- Initiate therapy to stop ovulation, as outlined under excessive egg laying above, due to increased risk of rupture during ovulation and oviposition.
- If bacterial infection is suspected or documented by cytology and bacterial culture and sensitivity, begin appropriate antibiotic treatment.
- Salpingohysterectomy may be required to resolve the current problem or prevent future recurrences and should be considered if the hen is not intended for breeding, as complete resolution with medical therapy alone may be difficult.

Oviductal Rupture

Etiology

- Oviductal rupture may occur secondary to dystocia or oviductal disease.
- Administration of prostaglandins, oxytocin, vasotocin, and ovocentesis may cause traumatic rupture of the oviduct.

Clinical Signs

Clinical signs may include depression, anorexia, and abdominal distension secondary to coelomitis or deposition of egg or oviductal contents.

Diagnosis

- Radiographs and ultrasonography may reveal polyostotic hyperostosis, a soft tissue density in the region of the ovary, ovarian follicles, an enlarged or cystic oviduct, a shelled or non-shelled egg, and coelomic fluid if a concurrent coelomitis is present.
- Diagnosis is confirmed at laparoscopy or laparotomy.

Treatment

The laceration may be repaired, depending on the integrity of the tissue, or salpingohysterectomy may be performed as a therapeutic and preventative technique.

Ectopic Ovulation

Etiology

- Ectopic ovulation may result from failure of the infundibulum to retrieve an ovulated ovum, reverse peristalsis of the oviduct, or oviductal rupture.
- Ectopic ovulation does not necessarily result in coelomitis. Internal laying actually is a common occurrence in many avian species, and the ova usually are resorbed without any problems.
- Reverse peristalsis may be triggered by obstruction of the oviduct, cystic hyperplasia, neoplasia, malnutrition, trauma, and stress.

- The ectopic ova may be resorbed without incident or may induce a severe coelomitis.

Clinical Signs

Clinical signs of ectopic ovulation may include transient or persistent depression, inappetence, and abdominal distension, especially if there is an associated coelomitis.

Diagnosis

- There may be a leukocytosis with a mature heterophilia. Serum chemistries may demonstrate an ovulating hen.
- Radiographs may reveal polyostotic hyperostosis and one or multiple eggs in the abdomen.
- It may be difficult or impossible to determine if an egg is located within the oviduct or is ectopic without laparoscopy or laparotomy, depending on its location within the coelom.

▼ ***Key Point*** Incidental detection of ectopic ova by ultrasound in the absence of clinical signs may resolve on its own with no treatment, and any medical or surgical intervention may be contraindicated.

Treatment

- If an egg is not laid within a reasonable time period and/or the patient's condition is declining, an exploratory laparotomy is indicated.
- Ectopic eggs are removed by laparotomy, and any oviductal tear should be surgically repaired or a salpingohysterectomy should be performed.
- Cytology, bacterial culture and sensitivity, and histopathology should be performed in cases of oviductal rupture, cystic hyperplasia, and neoplasia.

Cystic Ovarian Disease

Etiology

Cyst development may be caused by endocrine disorders, anatomic abnormalities on the ovary itself, and neoplasia.

Clinical Signs

Clinical signs include abdominal distension and associated dyspnea, usually due to secondary coelomitis. Advanced cystic ovarian disease may cause depression, inappetence, and weight loss.

Diagnosis

- A thorough history may reveal current or previous egg production, with an abrupt halt. Owners may report chronic reproductive behavior without egg production or impaired reproductive performance in breeding hens.
- A leukocytosis with a relative heterophilia commonly is seen, as well as a peripheral hypercalcemia, hyperglobulinemia, and hypercholesterolemia.
- Radiographs may demonstrate polyostotic hyperostosis, a soft tissue density in the area of the ovary and/or oviduct, coelomic fluid, and displacement of coelomic viscera.
- Ultrasonography may reveal fluid-filled cyst(s) in the area of the ovary or simply coelomic fluid of an undetermined source. An ovarian cyst may be quite large and may actually fold onto itself as it grows. There may be normal ovarian follicles present as well.
- In birds with associated coelomitis, perform abdominocentesis to collect fluid for cytologic exam and bacterial culture and sensitivity. Abdominocentesis is often both diagnostic and therapeutic.
- Perform a laparoscopic examination to identify the ovary, and obtain biopsy specimens for histologic examination and for culture and susceptibility testing. Aspirate the contents of the cysts. Fluid is typically clear to straw colored and of low cellularity.

▼ ***Key Point*** Exercise extreme caution during a laparoscopic exam and aspiration, as fluid from the cyst or coelom may gain access to the respiratory system through the entry hole in the abdominal air sac.

- A laparoscopic exam with ovarian biopsy is especially important in the diagnosis of ovarian disease in those patients with cysts that do not resolve with medical therapy, as it is not uncommon for hens to develop ovarian cysts secondary to neoplasia and oophoritis.

Treatment

- Treatment goals include resolution of cyst(s) and associated disease conditions such as coelomitis, oophoritis, ovarian granuloma, and neoplasia.
- Perform abdominocentesis in dyspneic hens with coelomic fluid to relieve dyspnea caused by fluid compressing the air sacs.
- Initiate pharmacologic, behavioral, environmental, and dietary intervention (as described under treatment of excessive laying above) to reduce ovarian activity with production of reproductive hormones that may perpetuate ovarian cysts.
- Aspiration of cysts, salpingohysterectomy, and partial ovariectomy may be beneficial for complete resolution.
- Regularly monitor treated hens for recurrence, since long-term resolution may be difficult.

Reproductive-Associated Coelomitis

Etiology

- Reproductive-associated coelomitis includes sterile egg yolk coelomitis, ectopic ovulation-associated coelomitis, and septic coelomitis.

- Coelomitis may be found in association with other diseases such as malnutrition, metabolic disorders, and systemic infections. Cystic ovarian disease, salpingitis, metritis, cystic hyperplasia, oviductal rupture, oviductal and ovarian granulomas, oviductal rupture, septicemia, intestinal rupture, and neoplasia may cause associated coelomitis as well.

Clinical Signs

Clinical signs may include transient or persistent depression, lethargy, and inappetence. Patients with more advanced disease may suffer from weight loss, abdominal distension, and dyspnea associated with coelomic fluid and air sac compression.

Diagnosis

- Tentative diagnosis of reproductive-associated coelomitis is made through history, physical examination, and supporting laboratory tests.
- The hen may have a history of egg production, which often has abruptly stopped.
- It is important to note that not all patients with coelomitis will have identifiable fluid present.
- Leukocytosis with a relative heterophilia is usually seen, along with hypercalcemia, hyperglobulinemia, and hypercholesterolemia compatible with preovulation and immediate post-ovulation. Many birds will be hypocalcemic due to calcium depletion subsequent to malnutrition or chronic egg laying.
- Some birds may have egg yolk visible in their peripheral blood smears, as well as above the buffy coat, in separated blood samples.
- Radiographs may demonstrate polyostotic hyperostosis, soft tissue density in the region of the ovary and/or oviduct, coelomic fluid, abdominal and caudal thoracic air sac compression, or even an obvious shelled or non-shelled egg. Contrast radiography may be helpful to illustrate organ displacement and locate any suspected space-occupying mass.
- Ultrasound may reveal coelomic fluid, ovarian follicle(s), ovarian cyst(s), an ovarian mass, and oviductal masses such as granuloma or neoplasia.
- Perform abdominocentesis on hens with coelomic fluid. Cytology of coelomic fluid may demonstrate a septic or non-septic exudate, a transudate, or yolk or fat globules if such material is present. Perform bacterial culture and sensitivity on samples of coelomic fluid.
- Laparoscopy and/or laparotomy may be necessary to identify the causative etiology of coelomitis.

Treatment

- Treatment of reproductive-associated coelomitis varies with type and severity of clinical signs. Many birds respond well to supportive care alone.
- Perform abdominocentesis in dyspneic hens with coelomic fluid to relieve dyspnea caused by fluid compressing the air sacs.
- Administer broad-spectrum antibiotics to hens with suspected or confirmed septic coelomitis while waiting for sensitivity results on fluid obtained from abdominocentesis.
- Corticosteroids may be indicated in cases in which an infectious etiology has been excluded, but they should be used judiciously due to potential serious side effects.
- Initiate pharmacologic, behavioral, environmental, and dietary intervention (as described under treatment of excessive laying above) to reduce ovarian activity with production of reproductive hormones that may perpetuate this condition.
- Once the coelomic fluid has decreased and the patient is stable, it may be beneficial to perform a laparoscopic examination. This allows direct visualization of the ovary, oviduct, and other organs to help confirm underlying conditions such as a cyst, granuloma, and/or tumor.
- Obtain a biopsy on abnormal tissue for cytologic or histopathologic examination and bacterial culture and sensitivity.
- A laparotomy with or without a salpingohysterectomy may be necessary to remove a mass, cystic oviduct, or inflammatory debris from the abdomen, particularly if medical therapy alone is not effective.
- During laparoscopy or laparotomy there is a risk of fluid gaining access to the respiratory system via the incision through the abdominal air sacs, and often there are significant adhesions between the oviduct and the neighboring viscera due to chronic inflammation.

Oophoritis

Etiology

Inflammation of the ovary results from neoplastic, mechanical, or infectious causes. Infectious oophoritis often occurs as a result of spread from adjacent organs or septicemia and is frequently bacterial in origin.

Clinical Signs

Clinical signs may be vague and include anorexia, weight loss, depression, cessation of egg production, egg binding, and sudden death.

Diagnosis

- A diagnosis of oophoritis is made through history, physical examination, radiography, ultrasonography, abdominocentesis with coelomic fluid analysis, laparoscopy, laparotomy, and biopsy of the ovary with bacterial culture and sensitivity and with histopathologic analysis.

- Hematology may demonstrate a leukocytosis with a relative heterophilia.
- Radiographs and ultrasound may demonstrate an enlarged soft tissue density in the region of the ovary, ovarian follicle(s), and ovarian cyst(s), and there may be coelomic fluid present if there is a concurrent coelomitis.
- If coelomic fluid is present, abdominocentesis is beneficial both therapeutically and diagnostically. Perform cytologic analysis and bacterial culture and sensitivity on fluid recovered. Laparoscopy may demonstrate an enlarged, abnormal-appearing ovary, which may have associated hypervascularization.
- Persistent or chronic oophoritis may progress to granulomatous disease, which may be evident on ultrasound, laparoscopy, and laparotomy.
- Definitive diagnosis is based on ovarian biopsy with histopathologic examination, along with bacterial culture and sensitivity.

Treatment

- Administer broad-spectrum antibiotics, pending sensitivity results.
- Initiate pharmacologic, behavioral, environmental, and dietary intervention (as described under treatment of excessive laying above) to reduce ovarian activity with production of reproductive hormones that may perpetuate this condition.
- Repeat the laparoscopic exam, bacterial culture and sensitivity, and complete blood count until culture results are negative and any leukocytosis has resolved.
- Carefully monitor reproductive performance and general condition, as complete resolution may be difficult.
- Partial ovariectomy, usually performed with salpingohysterectomy, may be beneficial in refractory cases if the hen is not intended for breeding.

Ovarian and Oviductal Neoplasia

Etiology

- Ovarian and oviductal neoplasia most commonly is seen in the budgerigar *(Melopsittacus undulates)* and gallinaceous species.
- Lymphomatosis, adenocarcinoma, leiomyosarcoma, leiomyomas, adenomas, and granulosa cell tumors have been reported.

Clinical Signs

Clinical signs usually include abdominal distension, coelomic fluid, lameness, dyspnea, depression, inappetence, and chronic reproductive-associated behavior.

Diagnosis

- Alteration of secondary sex characteristics such as a cere color change may occur.
- Perform a complete diagnostic workup in all hens with egg binding, oviductal impaction, ovarian cysts, abdominal hernia, and coelomic fluid, since neoplasia is a common underlying cause of these conditions.
- Diagnosis is supported by history, physical examination, demonstration of enlargement in the area of the ovary or oviduct on radiographs, and ultrasound. Definitive diagnosis is based on biopsy with histopathologic examination of abnormal tissues.

Treatment

- There have been anecdotal reports of treatment with chemotherapeutic drugs such as carboplatin; however, no consistent results have been documented to date.
- Prognosis for long-term recovery is grave with no refereed reports of successful treatment.
- Salpingohysterectomy with partial or complete ovariectomy may have value in select patients.

Parasites

Etiology

- Ascarids and flukes have been reported to infect the oviduct from the cloaca by reverse peristalsis.
- Heavy infestation may cause soft-shelled and shell-less eggs and may result in salpingitis. *Anseriformes* are most commonly affected. Ascarids and small flukes reportedly have been passed in eggs.

Diagnosis

- Diagnosis is made by finding adult worms in the oviduct on laparotomy or necropsy or by finding adult worms in eggs laid by affected hens.
- Perform a fecal floatation, especially on ground-dwelling species.

Treatment

- Prophylactic anthelmintic programs may be helpful in preventing severe infestations.
- If these worms obstruct the oviduct, they require surgical removal or salpingohysterectomy.

Overproduction of Eggs

- Safe numbers of egg production for different species is not definitively documented.
- Nutrition and environmental conditions affect safe production levels. Free-ranging psittacines typically produce one to two clutches per year; however, many captive psittacines produce far more chicks than this.
- While many birds show no obvious side effects, chronically overproducing hens may develop reproductive tract disorders, as well as poor body condition and feather quality.
- To improve long-term health in producing birds, egg production should be limited to two clutches per year

in birds that show any signs of poor health secondary to overproduction.
- It also is recommended that all birds receive some rest period each year to prevent reproductive disorders from developing.

MALE REPRODUCTIVE DISORDERS

Orchitis

Etiology

Infectious orchitis may occur from ascending infections, hematogenous spread, or infected adjacent organs. Rarely, non-infectious causes are associated with inflammation of the testicles.

Clinical Signs

Early clinical signs are vague and difficult to detect, and they may include infertility, mild depression, and decreased appetite. As the disease progresses, the patient may develop lethargy, inappetence, and abdominal distension if a secondary coelomitis develops.

Diagnosis

- Leukocytosis with a relative heterophilia may be noted.
- The testicles may be enlarged on radiographs and ultrasound. There also may be notable enlargement, inflammation, and hypervascularization on laparoscopy.
- Definitive diagnosis is made by cytology, bacterial culture and sensitivity, and histopathologic examination of samples from affected testicles.

Treatment

Therapy includes broad-spectrum antibiotics, pending sensitivity results.

Testicular Neoplasia

Etiology

- Neoplasms reported include Sertoli cell tumors, seminomas, interstitial cell tumors, and lymphosarcomas. Leiomyosarcoma and carcinoma have been reported to arise from the epididymis and ductus deferens.
- Testicular neoplasia commonly has been documented in the budgerigar *(Melopsittacus undulates)* and often is unilateral.

Clinical Signs

Clinical signs include abdominal distension and one-sided paresis, paralysis, or cyanosis of the pelvic limb due to compression of the ischiatic nerve and blood vessels. Alterations of secondary sex characteristics such as cere color change from blue to brown may occur.

Diagnosis

- Often the disease is advanced once clinical signs are evident.
- Definitive diagnosis is made by testicular biopsy and histopathologic examination.
- Radiographs may reveal a soft tissue mass in the region of the testicles, air sac compression, and secondary sex changes such as polyostotic hyperostosis, even in male birds.

Treatment

Treatment includes orchiectomy. Chemotherapy has been reported if the tumor is deemed incompletely or non-resectable or if the patient is not a good surgical candidate. However, no conclusive data is available regarding the efficacy of chemotherapy to date.

DISORDERS OF THE CLOACA

Cloacal Papillomas

Cloacal papillomas have been noted in New World psittacine species. To date the cause is unknown, but a herpesvirus is strongly suspected. See Chapter 169 for a complete discussion.

Cloacal Prolapse

Etiology

Cloacal prolapse may occur secondary to chronic straining from masturbation, egg laying, space-occupying abdominal masses, and inappropriate weaning and social behavior.

Diagnosis

- History includes straining and observation of intermittent or persistent prolapsed mucosa through the vent opening. Physical examination will reveal prolapsed tissue through the vent that may be intermittent or persistent.
- Obtain samples from prolapsed tissue for cytologic examination and bacterial culture and sensitivity to aid antibiotic therapy.
- Perform a complete blood count, serum chemistries, radiographs, ultrasound, and endoscopic exam of the coelom and cloaca to determine any other predisposing cause.

Treatment

- Thoroughly clean, irrigate, and lubricate prolapsed tissue. Examine affected tissue for necrosis, and remove any adhered egg remnants.
- In birds with chronic reproductive-associated behavior and straining secondary to masturbation, initiate pharmacologic therapy and environmental manipulation (as described under excessive laying above) to decrease reproductive stimuli.
- Cloacopexy and the use of temporary stay sutures may be helpful in temporary or permanent reduction. However, those procedures interfere with movement of the cloaca and may alter defecation and micturition.
- Ventplasty may decrease the vent opening and prevent further prolapse if the vent has become flaccid.
- Clomipramine hydrochloride and phenylpropanolamine hydrochloride administration have anecdotally been reported to contract the vent orifice and assist in the resolution of prolapse of the cloaca.
- Salpingohysterectomy with partial ovariectomy or orchiectomy may be beneficial in those patients refractory to medical therapy.
- Administer broad-spectrum antibiotics pending bacterial culture and sensitivity, because primary and secondary bacterial infections are common.

Cloacitis

Etiology

- Cloacitis may result from both infectious and noninfectious processes.
- Cloacal prolapse, cloacal papillomas, cloacoliths, and bacterial infections may cause inflammation of these tissues. This may result in secondary urogenital and/or gastrointestinal disease due to their anatomic relationship to the cloaca.

Diagnosis

Obtain samples from the cloaca for cytologic examination and bacterial culture and sensitivity testing.

Treatment

- Initiate appropriate antibiotic therapy as directed by culture and sensitivity testing.
- Dimethyl sulfoxide may be used to reduce inflammation with no systemic side effects, and swabbing the cloaca with petroleum jelly will prevent fecal and urate accumulation on the cloacal surface with subsequent irritation.

Cloacolithiasis

Etiology

Cloacolithiasis is infrequently noted in pet birds. It may result from previous egg binding, infectious cloacitis, malnutrition, or neurologic disease of the cloaca.

Diagnosis

Perform cloacal cytology with bacterial culture and sensitivity.

Treatment

- Manually or surgically remove cloacoliths.
- Administer broad-spectrum antibiotics, pending culture results.
- Change the diet to improved nutrition when indicated.
- Monitor patients closely for recurrence; prognosis for return to normal breeding performance is poor.

Cloacal Neoplasia

Etiology

Cloacal carcinomas are infrequently reported in pet birds.

Diagnosis

- Perform a laparoscopic examination of the cloaca, noting patency of openings into the urodeum, proctodeum, and coprodeum.
- Definitive diagnosis is based on histopathologic analysis of biopsy samples.

Treatment

Surgically remove neoplastic masses, with caution not to damage the openings to the gastrointestinal, urinary, and reproductive tract.

Other Cloacal Diseases

- Cloacal strictures may occur due to associated cloacal disease or secondary to surgical procedures such as biopsy or cauterization of papillomas.
- These strictures may be gently manually dilated with the use of a speculum.
- Excessive feathering around the vent may cause infertility; these feathers should be removed by trimming or pulling prior to breeding season.

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Chapter

174 Avian Neurologic Disorders

Anthony Pilny / Katherine E. Quesenberry

Companion and aviary birds frequently develop clinical signs associated with the peripheral or central nervous system. Although many possible causes of neurologic disease exist, certain syndromes and diseases occur commonly. Diagnosis of these syndromes is based on history, clinical signs, results of diagnostic tests, and response to therapy.

PRINCIPLES OF DIAGNOSIS

History

Several important points should be included in the general history of a bird with neurologic disease.

- Dietary history is important because nutritional deficiencies are factors in many diseases. Ask for specific details, such as the following:
  - What is the regular diet? Does the bird have dietary preferences?
  - What vitamin and mineral supplements are being given?
  - Is adequate calcium provided for egg-laying females?
- What is the home environment of the bird, especially as related to exposure to trauma or toxins?
- Is the bird always caged or is it allowed free flight in the house?
- Does the bird chew on any painted surfaces, metal objects, or plants?
- What types of toys are kept in the cage?
- Is the bird a recent purchase or a long-term pet? Is there exposure to other birds? Was the bird boarded recently with exposure to other birds?
- When was the onset of the disorder, and what has been the duration and progression of clinical signs?

Clinical Signs

Clinical signs associated with neurologic disease in birds are similar to those seen in mammals.

- The most common clinical signs are seizures, ataxia, paresis, paralysis, head tilt, circling, abnormal mentation, nystagmus, intention tremors, and visual deficits. Weakness and ataxia can be manifested as falling off the perch.
- It may be difficult to distinguish weakness secondary to severe systemic disease from that associated with neurologic disease.
- The presence or absence of other neurologic deficits may be helpful in determining which body system is involved.
- Unilateral or bilateral lameness or wing droop may indicate a peripheral nerve deficit. Rule out fractures and other musculoskeletal abnormalities as a cause.

Neurologic Evaluation

The goal of the examination is to determine if the neuropathy is focal or diffuse and to localize lesions.

- Cranial nerve function should be assessed in addition to peripheral nerve function.
  - Assess vision in each eye by slowly moving a hand or an object toward the bird from behind on each side. A bird with visual deficits does not react until the object is very close or its face is touched.
  - The pupillary light reflex is difficult to evaluate because of the presence of striated muscle in the iris. A widely dilated pupil that reacts minimally to changes in light intensity may indicate a visual deficit.
  - Check facial sensation by touching various parts of the face with hemostats. Assess the palpebral reflex as in mammals.
- Neurologic evaluation of neonates can be difficult, and comparison with clutchmates may be the best way to detect abnormalities. Useful tests include feeding responses, vocalization, use of wings for balance, and perching ability.

Diagnostic Tests

Methods of diagnosis and treatment in birds are limited by anatomic variations, patient size, and lack of reference values to interpret test results. Diagnostic test options that may be helpful in diagnosing neurologic disease are a complete blood count, biochemical profile, bile acid concentration, plasma protein electrophoresis, viral and *Chlamydophila* screening tests,

blood lead levels, radiographs, computed tomography, and magnetic resonance imaging. Neurologic tests can include electroencephalograms and auditory-evoked potentials.

PRINCIPLES OF TREATMENT

▼ ***Key Point*** Birds with neurologic disease need special nursing care in the hospital and at home.

- Keep ataxic birds or birds having seizures in cages without perches. Provide soft bedding.
- Use small, shallow, or covered water bowls to prevent accidental drowning, especially with small birds.
- Remove sharp objects, chains, and potentially dangerous toys from the cage.
- Make food easily accessible by spreading it on the floor or by providing several containers in the cage.
- *Supplemental fluids* and *gavage feeding* are necessary for anorectic birds (see Chapter 168) and birds that are unable to eat because of tremors or ataxia.
- Give *antibiotics* if bacterial disease is suspected or if a risk of secondary bacterial infection exists. If possible, use antimicrobials that cross the blood-brain barrier (e.g., trimethoprim-sulfa at 100 mg/kg PO q12h or chloramphenicol at 50 mg/kg PO q8–12h).
- Administer *antifungal* agents if fungal infection of the central nervous system (CNS) is a differential diagnosis. Fluconazole (5–15 mg/kg PO q12h) reaches therapeutic concentrations in the brain parenchyma and the cerebral spinal fluid.
- *Anti-inflammatory drugs* (corticosteroids) may be beneficial in the treatment of acute head trauma. Be conservative in administration because of the potential for adrenal suppression and immune compromise. For long-term anti-inflammatory treatment, nonsteroidal anti-inflammatory drugs (NSAIDs) (e.g., carprofen at a dosage of 2–5 mg/kg PO q12h or meloxicam at 0.2 mg/kg PO q24h) are safer.
- Give *supplemental calcium* if blood calcium concentrations are abnormally low.
- Administer *chelating agents* such as calcium ethylenediaminetetraacetic acid (Calcium EDTA, or CaEDTA) (35 mg/kg IM q12h for 5 days, off 3 days, then as needed), dimercaptosuccinic acid (DMSA) (25–35 mg/kg PO q12h for 5 days a week for 3–5 weeks), or both to birds with suspected heavy metal toxicosis, such as lead. With lead toxicosis, birds often improve clinically within 24 to 48 hours. Side effects of treatment are rare, and birds can be treated with CaEDTA and/or DMSA on an emergency basis until results of tests for blood lead concentrations are known.
- *Anticonvulsants* such as diazepam (0.5–2.0 mg/kg IV) or midazolam (1–2 mg/kg IM) are helpful in controlling seizures.
- Give parenteral *vitamins* to birds with suspected vitamin deficiencies. Vitamin D_3 is especially important in African grey parrots and birds with hypocalcemia. Give multivitamin B-complex and thiamine if birds are anorectic or thiamine deficiency is suspected. Supplement with vitamin E or selenium if muscular weakness is present.

METABOLIC OR NUTRITIONAL DISORDERS

Hypocalcemia

▼ ***Key Point*** African grey parrots on unsupplemented seed diets are predisposed to a hypocalcemic syndrome.

Hypocalcemia is associated with neurologic abnormalities, especially in African grey parrots. This syndrome is less common than in previous years, probably because more bird owners are better educated about avian nutrition and feed pelleted diets.

Etiology

- The exact cause of this syndrome is unknown. A common history in African grey parrots with hypocalcemia is an all-seed diet with little or no vitamin supplementation, suggesting that a lack of vitamin D_3 may be a factor. Abnormal parathyroid function is also possible.

Clinical Signs

- Common neurologic signs include seizures, opisthotonus, tonic extension of the limbs, incoordination, dilated pupils, and convulsions.
- Seizures are the most common clinical sign and may be triggered by sudden noise and excitement. The seizure lasts several seconds and can occur as an acute onset of tetanic spasms with extensor rigidity, wing flapping, vocalizations, focal facial seizures, and occasionally nystagmus.
- Skeletal abnormalities, including pathologic fractures and nutritional bone disease, that are usually associated with dietary calcium deficiency are rarely seen in African grey parrots.

Diagnosis

Base the diagnosis on the history, clinical signs, results of plasma biochemical analysis, and response to therapy.

- To determine proper treatment, measurement of blood calcium concentration is necessary.
  - The total plasma calcium concentration is usually low in affected birds (1.5–6.0 mg/dl).
- Obtain whole-body survey radiographs to identify soft tissue or bone abnormalities and to detect any metal

objects in the gastrointestinal (GI) tract or soft tissues that may indicate lead toxicosis.
  - The proventriculus and intestinal loops may appear dilated on radiographs. Hypocalcemia may cause decreased smooth muscle contraction and motility of the GI tract.
- Consider and investigate other potential causes for the clinical signs (e.g., lead toxicosis and systemic fungal infection).

Treatment

- Give supplemental calcium orally or parenterally.
  - In severely debilitated birds, start treatment with calcium gluconate, 50 to 100 mg/kg IM q12–24h.
  - If seizures are infrequent and the danger of aspiration during seizures is minimal, give calcium supplements orally, such as Neo-calglucon, 25 mg/kg PO q24h).
- During initial therapy, give supplemental vitamin D_3 (1000 IU of D_3 per 300 g IM) of compounded emulsion; repeat in 7 days as needed.
- Provide general supportive care and control continuous or severe seizures with diazepam or midazolam as needed.
- Correct the diet to provide adequate calcium and vitamins. Encourage use of pelleted diets. Add a liquid calcium supplement, or crush Tums or hard-boiled eggshells over food.

Prognosis

- The prognosis is good in most birds; however, African grey parrots with blood calcium concentrations less than 2.0 mg/dl may not improve with treatment. Improvement in some birds is gradual.

NEOPLASIA

Central Nervous System Neoplasia

Primary tumors of neural tissue origin are rare in psittacine birds. Meningiomas, pituitary adenomas, and glioblastomas are a few of the neoplasms that have been reported, most commonly in budgerigars and cockatiels.

Clinical Signs

- Common signs include ataxia, weakness, wide-based stance, and postural abnormalities.
- Depression, nystagmus, abnormal mentation, and visual deficits often are present.

Diagnosis

- Clinical diagnosis of a CNS tumor is extremely difficult. Static or progressive clinical signs indicating CNS involvement with failure to respond to therapy suggests neoplasia.
- Computed tomography or magnetic resonance imaging of the brain can be diagnostic.
- Diagnosis is usually determined by results of necropsy.

Treatment and Prognosis

- Anti-inflammatory therapy may be helpful in the short term. The prognosis is poor.

Paresis Secondary to Renal or Gonadal Neoplasia

▼ ***Key Point*** Tumors of renal tissue origin are common in budgerigars 4 years of age and older and are associated with progressive unilateral limb paresis.

Gonadal tumors are less common than renal tumors; clinical signs may resemble those of renal neoplasia.

Etiology

- The ischiatic nerves pass through the renal parenchyma; renal neoplasia that compresses the nerve will result in paresis.

Clinical Signs

- Progressive paresis or paralysis of the leg on the ipsilateral side develops from pressure of the tumor on the sciatic nerve.
- Muscle atrophy may be severe in the affected leg.
- Polyuria may be present.

Diagnosis

Base the diagnosis on history, clinical signs, physical examination, and radiographic or ultrasonographic findings.

- Palpate the abdomen carefully on the affected side to detect the presence of a mass.
- Obtain radiographs to identify a soft tissue mass in the area of the kidney.
  - Barium contrast radiography may reveal ventral or lateral displacement of bowel loops in the dorsal-sacral area of the kidney or gonad, suggestive of a mass.

Treatment and Prognosis

- No treatment is available.
- Budgies usually die within several months of the onset of clinical signs.

INFECTIOUS DISEASES

Viruses

Several viruses affect the avian nervous system (see Chapter 169).

- *Paramyxovirus* (PMV) causes neurologic disease in many species of wild and domestic birds.
- *Newcastle disease* (PMV-1) and other strains (PMV-3) can cause CNS disease in psittaciformes. Clinical signs can include torticollis, trembling, paresis, and opisthotonus. PMV-1 is common in pigeons in which the virus spreads to the kidneys and CNS. PMV causes torticollis, depression, and weight loss in finches. A number of PMV serotypes have been seen in mynahs and toucans. PMV-3 infections are particularly common in the *Neophema* genus of Australian grass parakeets. Head tilt, subclinical pancreatic disease, and/or CNS disease are seen with this virus infection. Diagnosis is based on symptoms, virus isolation, and serology. A vaccine is available.
- *Proventricular dilatation disease* (PDD) is suspected to be viral cause of neurologic signs in psittacine species. (See Chapter 169 for details.)
- Neurologic deficits are sometimes seen in birds with *polyomavirus*. Diagnosis is by polymerase chain reaction testing and a vaccine is available.
- *West Nile virus* is a cause of neurologic disease in many species of wild and captive birds, including psittacine and passerine species. Birds housed outdoors during mosquito season are at highest risk. West Nile virus has been identified in more than *100 species of birds* found dead in the United States. Most of these birds were identified through reporting of dead wild birds by the public.
- Other suspected viral causes of neurologic disease have been reported but are uncommon.

Bacteria and Fungi

Neurologic disease resulting from bacterial or fungal infection is sometimes seen.

- Bacterial encephalitis secondary to systemic infection can result in multifocal neurologic disease.
  - Neurologic signs are seen with fungal infections affecting the CNS or peripheral nervous system. Clinical signs vary from paralysis or paresis to generalized weakness, ataxia, or seizures. *Aspergillus* spp. are implicated most commonly, but infections with other fungi do occur (e.g., *Mucormycosis*).
- *Chlamydophila psittaci* (psittacosis) can cause CNS lesions and neurologic signs. Typical signs of psittacosis (see Chapter 169) may be present.
- Infection with *Mycobacterium* spp. can result in neurologic signs, either as a result of direct involvement of the nervous system or secondary to weakness associated with systemic disease.
- Neurologic signs secondary to salmonellosis are seen in pigeons.

Parasites

Parasitic causes of neurologic diseases are rare in birds.

- Possible causes include microfilaria, protozoa (e.g., *Plasmodium* and *Atoxoplasma* spp.), sporozoa (*Sarcocystis* and *Toxoplasma* spp.), and nematode migration.
- Diagnosis usually is based on results of necropsy and histologic examination of tissue samples.

TOXICOSES

Lead Toxicosis

Lead toxicosis is a common cause of neurologic disease in pet birds. Other aspects of lead toxicosis, as pertaining to dogs and cats, are discussed elsewhere.

▼ ***Key Point*** Sources of lead include surfaces or objects painted with lead-based paint, stained glass, mirror backing, champagne bottle foil, lead-weighted objects (curtain weights), and some ceramic or glazed dishes.

Clinical Signs

- Signs of acute lead ingestion include depression, anorexia, gastroenteritis (usually hemorrhagic), crop stasis, regurgitation, dehydration, and hemoglobinuria.
- Neurologic signs may be latent in onset. Latent signs include seizures, ataxia, weakness, paresis, and leg paralysis.

Diagnosis

Establish the diagnosis based on the history, clinical signs, diagnostic tests, and response to therapy.

- Measure blood lead concentration. Lead concentrations of 10 µg/dl or greater suggest lead toxicosis.
- Obtain radiographs to screen for metal objects in the GI tract (or soft tissues). The presence of metal in a bird with typical clinical signs suggests lead toxicosis.
  - The absence of metal in the GI tract does not exclude a diagnosis of plumbism. Small amounts of lead are often completely absorbed from the GI tract, and therefore no longer visible, prior to the onset of clinical signs.
- Birds with lead toxicosis maybe mildly or severely anemic. Measure packed cell volume (PCV) in birds that appear anemic before collecting blood samples for routine tests. Basophilic stippling of red blood cells is uncommon.

Treatment

- Chelation therapy is indicated in any bird with suspected lead toxicosis. CaEDTA is effective and is the most commonly used chelating agent.
  - Give CaEDTA at a dosage of 35 mg/kg IM q12h for 5 days, off 3 days, then as needed.

- DMSA (25–35 mg/kg PO q12h for 5 days a week for 3–5 weeks) chelates lead in soft tissues more quickly than CaEDTA.
  - D-penicillamine, another chelating drug administered orally can be used for chelation therapy. However, GI side effects (e.g., vomiting) sometimes occur and therapy must be discontinued.
- Magnesium sulfate (Epsom salts) given orally may help bind lead particles in the GI tract and inhibit further absorption. Dosage is empirical (e.g., a pinch dissolved in dextrose or added to food given every 12 hours).
- Supportive therapy includes supplemental fluids, antibiotics, iron supplementation, vitamins, and tube feeding.
- Anticonvulsants are occasionally necessary to control seizures.
- Laxatives or lubricants may help speed passage of metal from the GI tract.
- Persistence of a high blood lead level or clinical signs indicate that a second or third course of therapy is needed.
- Lead stores in bones may be released during calcium mobilization in reproductively active hens.

Prognosis

- Birds with lead toxicosis usually respond quickly to chelation therapy. Clinical signs may diminish significantly after 1 to 2 days of therapy. Birds with leg paralysis from chronic lead toxicosis have a more guarded prognosis.
- Monitor progress by repeating tests for blood lead concentration. If results remain high, repeat chelation treatment for another 5 days and recheck the blood lead concentration.

Other Toxicoses

- Other heavy metals are occasionally associated with neurologic disease in pet birds.
- Exposure to organophosphates and other pesticides may cause incoordination, severe depression, and diarrhea.
- Toxicoses from exposure to marijuana, alcohol, and other drugs have been reported.
- Neurologic abnormalities followed by acute death may be seen in birds exposed to polytetrafluoroethylene (Teflon) (see Chapter 171).

TRAUMATIC INJURY

Head Trauma

- Head trauma can cause mild to severe neurologic signs.
- Treatment depends on the severity of clinical signs.
- Shock or anti-inflammatory doses of short-acting corticosteroids may be indicated in birds with acute trauma.
- Provide general supportive therapy as needed.
- The prognosis depends on the severity of the injury and the response to therapy.

Peripheral Nerve Trauma

- Musculoskeletal injury can result in peripheral nerve damage.
- Treatment and prognosis depend on the extent of tissue damage.

Miscellaneous Disorders

Gout

Gout can cause peripheral gait abnormalities that may appear as neurologic deficits. Gout is most common in old budgerigars but also occurs in other species.

- Ataxia, weakness, and a stiff gait are common signs. Clinical signs usually develop before uric acid deposits (tophi) are visible as subcutaneous deposits in the joints and legs.
- The plasma uric acid concentration may range from normal to significantly high.

Liver Disease

Weakness, ataxia, and abnormal mentation are seen occasionally with severe liver disease (see Chapter 172).

Hypoglycemia

Hypoglycemia can cause weakness, lethargy, and neurologic signs.

▼ ***Key Point*** Measure whole-blood glucose concentration in any bird that is collapsed, weak, having seizures, or comatose. Seizures usually occur at blood glucose levels less than 100 mg/dl. Recently weaned and young birds are most susceptible.

Lipemia

- Signs of central neurologic abnormalities can occur in birds with severe lipemia. Birds with highly lipemic blood may have sludging and resultant anoxic episodes.
  - The cause of the hyperlipidemia is not known, but this syndrome is seen most frequently in reproductive hens and obese birds. In hens, it may be related to high levels of circulating lipoproteins and cholesterol during the egg-laying cycle.
- Treatment with niacin (50 mg/kg q8h) and gemfibrozil (Lopid, Parke-Davis) (30 mg/kg q8h) is sometimes effective in controlling clinical signs in birds with high triglyceride levels. Statins may be effective in birds with high cholesterol levels.

- Atherosclerosis is suspected to cause neurologic clinical signs in birds. These signs can include falls, collapse, and ataxia.

Yolk Emboli

- Yolk emboli to the CNS may result in neurologic abnormalities (see Chapter 173).
- Hens usually remain alert but are ataxic and have a head tilt.
- Treatment is similar to that for birds with lipemia. Hens gradually improve over weeks to several months.

Other Nutritional Factors

- Deficiencies in vitamins A, B_2, B_6, B_{12}, C, and E and in selenium are related to neurologic disorders.
- Because specific vitamin deficiencies are difficult to confirm, give supplemental multivitamins if a deficiency is suspected.

Lorikeet Tetraparesis

- A progressive tetraparetic syndrome has been described in lorikeets.
- The exact etiology is unknown, but a virus or protozoa is suspected.

IDIOPATHIC EPILEPSY

Idiopathic epilepsy has been described as a clinical syndrome in pet birds, most commonly in lovebirds and red-lored Amazon parrots.

- Phenobarbital may be effective in controlling clinical signs.
- The typical dosage range is 4.5 to 6 mg/kg PO q12h, titrated based on blood levels.

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Chapter

175 Ferrets

Christine Ellis

Clinical Techniques

RESTRAINT

- Most pet ferrets are gentle, tractable, and are easy to restrain without assistance. Often only minimal restraint is needed when performing a physical examination. Some ferrets may be lightly restrained on the examination table. Others will need to be restrained in a firmer manner.
- Tractable ferrets can be lightly restrained on an examination or treatment table by placing one hand under the chest and lifting slightly.
- Energetic ferrets may be restrained by scruffing (Fig. 175-1). Use one hand to grasp the skin over the back of the neck and lift the ferret up, suspending all the limbs. Stroke the abdomen with a downward motion to relax the ferret. The ferret's back may be supported with the other hand, or the ferret may then be reclined along the forearm of the arm used to scruff the ferret. Most ferrets will become very relaxed, although some young ferrets and some females may resist.
- Firm restraint is often required when administering vaccinations or when performing treatment procedures. Control the head by scruffing, or by cupping the back of the ferret's neck and placing the thumb and fingers along the caudal border of the mandibles. Place the other hand over the pelvis to restrain the hindquarters on the table top with the hind legs underneath the body; do not pull the legs back.
- Aggressive ferrets, such as nursing females, kits, or ferrets raised with little human contact, are uncommon. Restrain these ferrets by the scruff of the neck, using the techniques previously described. Avoid using leather gloves, which are awkward. Use sedation if necessary.

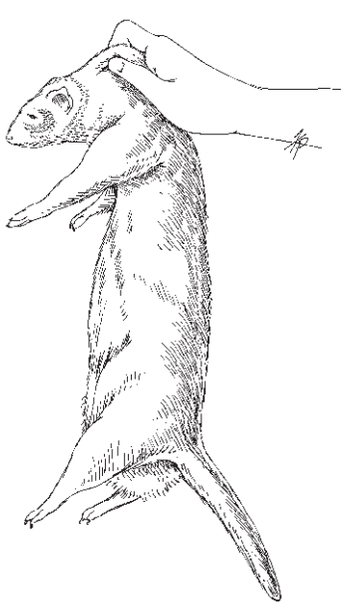

Figure 175–1. "Scruffing" a ferret for restraint.

DIAGNOSTICS

Blood Collection

There are several suitable sites for blood collection in ferrets:

- Cephalic vein
- Lateral saphenous vein
- Jugular vein
- Cranial vena cava
- Ventral tail artery

▼ ***Key Point*** Do not perform cardiac puncture or retro-orbital bleeding.

Indications

- Cephalic or lateral saphenous venipuncture may be used to obtain small amounts of blood (<1.0 ml) for a packed cell volume (PCV), blood glucose, complete blood cell count (CBC), or serum biochemistry analysis.
- The jugular vein, cranial vena cava, cephalic vein, or ventral tail artery may be used to collect larger volumes of blood.
- Use the jugular vein to collect blood for transfusion.

Table 175-1. REFERENCE RANGES FOR HEMATOLOGIC VALUES IN FERRETS

		Fitch Ferrets*		Albino Ferrets†	
Value	Sex	Range	Mean	Range	Mean
Hematocrit (%)	♂	46–57	49.1	44–61	55.4
	♀	47–51	48.4	42–55	49.2
Hemoglobin (g/dl)	♂	15.2–17.7	16.1	16.3–18.2	17.8
	♀	15.2–17.4	15.9	14.8–17.4	16.2
Red blood cells ($\times 10^6$/µl)	♂			7.30–12.18	10.23
	♀			6.77–9.76	8.11
Reticulocytes (%)	♂			1–12	4.0
	♀			2–14	5.3
White blood cells ($\times 10^3$/µl)	♂	5.6–10.8	7.3	4.4–19.1‡	9.7
	♀	2.5–8.6	5.9	4.0–18.2‡	10.5
Neutrophils	♂	616–7020/µl	2659/µl	11–82%	57.0%
	♀	725–2409/µl	1825/µl	43–84%	59.5%
Lymphocytes	♂	1728–4704/µl	3791/µl	12–54%	35.6%
	♀	1475–5590/µ	3426/µl	12–50%	33.4%
Monocytes	♂	0–432/µl	176/µl	0–9%	4.4%
	♀	100–372/µl	263/µl	2–8%	4.4%
Eosinophils	♂	112–768/µl	378/µl	0–7%	2.4%
	♀	50–516/µl	214/µl	0–5%	2.6%
Basophils	♂	0–112/µl	50/µl	0–2%	0.1%
	♀	0–172/µl	48/µl	0–1%	0.2%
Bands	♂	0–972/µl	233/µl		
	♀	0–248/µl	99/µl		
Platelets ($\times 10^3$/µl)	♂			297–730	453
	♀			310–910	545
Mean corpuscular volume (μm^3)	♂				54
	♀				61
Mean corpuscular hemoglobin (pg)	♂				17.6
	♀				19.9
Mean corpuscular hemoglobin concentration (%)	♂				32.2
	♀				32.8

*Males all castrated.
†Males all intact.
‡These white blood cell counts are higher than those currently seen in clinical practice. At our laboratories, the normal white blood cell count is $3–8 \times 10^3$/µl, and most are $4–6 \times 10^3$/µl.
Adapted with permission from Lee EJ, Moore WE, Fryer HC, Minocha HC: Hematological and serum chemistry profiles of ferrets *(Mustela putorius furo)*. Lab Anim 16:133–137, 1982; and Thornton PC, Wright PA, Sacra PJ, Goodier TEW: The ferret, *Mustela putorius furo,* as a new species in toxicology. Lab Anim 13:119–124, 1979. Copyrights 1979 and 1982, Macmillan Magazines Limited.

Other Considerations

- Sedation: Collection of blood from the jugular veins, cranial vena cava, or ventral tail artery may require sedation and/or the assistance of two people for restraint. Sedation is rarely required for venipuncture of cephalic, lateral saphenous, or jugular veins.
- If necessary, clip the hair over the venipuncture site to see the vein.
- The normal hematocrit of ferrets is high; draw three times as much blood as the volume of plasma or serum required. (See Tables 175-1 and 175-2 for blood values reported in normal ferrets.)
- The PCV, red blood cell count (RBC), hemoglobin, white blood cell count (WBC), and plasma proteins often rapidly decrease after induction of isoflurane anesthesia.

Techniques

Cephalic Vein

- Collect blood from the cephalic vein in ferrets using the same restraint technique described for dogs and cats.
- Use an insulin syringe with a 28-gauge needle or a 1cc tuberculin syringe with a 25-gauge needle to collect volumes of blood up to 1.0 ml. Larger volumes of blood may be collected with a 3cc syringe and a 25-gauge needle.
- Alternatively, place a 25-gauge needle in the vein and collect blood directly from the hub into small blood collection tubes.

Table 175-2. REFERENCE RANGES FOR SERUM BIOCHEMISTRY VALUES IN FERRETS

Value	Albino*	Fitch†
Total protein (g/dl)	5.1–7.4	5.3–7.2
Albumin (g/dl)	2.6–3.8	3.3–4.1
Glucose (mg/dl)	94–207	62.5–134
Fasting glucose (mg/dl)		90–125‡
Blood urea nitrogen (mg/dl)	10–45	12–43
Creatinine (mg/dl)	0.4–0.9	0.2–0.6
Sodium (mmol/L)	137–162	146–160
Potassium (mmol/L)	4.5–7.7	4.3–5.3
Chloride (mmol/L)	106–125	102–121
Calcium (mg/dl)	8.0–11.8	8.6–10.5
Phosphorus (mg/dl)	4.0–9.1	5.6–8.7
Alanine aminotransferase (U/L)		82–289
		78–149§
Aspartate aminotransferases (U/L)	28–120	57–248§
Alkaline phosphatase (U/L)	9–84	30–120
		31–66§
Bilirubin (mg/dl)	<1.0	0–0.1§
Cholesterol (mg/dl)	64–296	119–209§
Carbon dioxide (mmol/L)	16.5–28	16–28§

*Combined values of male (N = 40) and female (N = 24) ferrets from Thornton PC, Wright PA, Sacra PJ, Goodier TEW: The ferret, *Mustela putorius furo,* as a new species in toxicology. Lab Anim 13:119–124, 1979.
†Combined values of intact male, female, and castrated male ferrets (total N = 13, aged 4–8 mo) from Lee EJ, Moore WE, Fryer HC, Minocha HC: Haematological and serum chemistry profiles of ferrets *(Mustela putorius furo).* Lab Anim. 16:133–137, 1982, except where noted.
‡From Brown S: Personal communication, 1995.
§Combined values from cardiac and orbital venipuncture of male ferrets (N = 16) from Fox JG: Normal clinical and biologic parameters. In: Fox JG (ed): Biology and Diseases of the Ferret. Philadelphia: Lea & Febiger, 1988, pp 159–173.

Lateral Saphenous Vein

- The lateral saphenous vein runs diagonally across the lateral surface of the hindleg, just proximal to the hock.
- Use an insulin syringe with a 28-gauge needle or a 1-ml syringe with a 25-gauge needle to collect small blood samples (<1.0 ml).

Jugular Vein

- Several methods are described for jugular venipuncture:
  - The ferret may be placed in sternal recumbency at the edge of the table. Extend the head dorsally with the front legs held down, out of the path of the venipuncturist.
  - Alternatively, wrap the ferret in a towel with the front legs drawn back along the thorax, leaving the head and neck extended from the towel. Position the ferret in dorsal recumbency, and extend the head and neck by scruffing.
  - Restrain the ferret in the same manner described for the cranial vena cava (see below).
  - Ferrets that struggle should be sedated for this procedure.
  - Use a 1-ml or 3-ml syringe with a 25- to 22-gauge needle for sample collection.

Cranial Vena Cava

- This procedure is referred to as cranial vena cava venipuncture, but, in reality, blood is collected from the jugular vein as it passes into the thoracic cavity at the thoracic inlet.

▼ ***Key Point*** Blood collection from the cranial vena cava requires complete immobilization of the ferret; otherwise, do not attempt the procedure. Use sedation or the help of two assistants for restraint.

- Do not use this site if intrathoracic disease (e.g., mediastinal mass, mega-esophagus) or coagulopathy is suspected.

Technique

1. Place the ferret in dorsal recumbency. One assistant restrains the head and neck in extension while holding the forelegs alongside the thorax. A second assistant restrains the hindquarters without pulling the rear legs back. Precise positioning facilitates the procedure.
2. Palpate the manubrium and locate the "notch" on either side where the manubrium and the first rib meet.
3. Insert a 3-ml syringe with a 25-gauge, $^{5}/_{8}$-inch needle at either notch and direct the needle at a shallow angle (<45 degrees) along an imaginary line running from the notch toward the opposite rear leg.
4. Insert the needle to the hub and gently aspirate while withdrawing the needle.
5. If the ferret struggles, abort the procedure, and do not make a second attempt until the ferret is quiet. Ferrets that struggle persistently should be sedated for this procedure.

Ventral Tail Artery

- Venipuncture at this site may be painful.

Technique

1. Scruff the ferret and place it in dorsal recumbency (wrapping it in a towel may help with restraint), or anesthetize the ferret and place it in dorsal recumbency.
2. Prepare the site aseptically.
3. Use a 1- or 3-cc syringe and a 22- to 25-gauge needle for sample collection.
4. Insert the needle on the ventral midline of the tail at 30-degree angle toward the body approximately 2 to 3 cm from the anus.
5. Advance the needle to the bone; withdraw it slowly while applying a slight vacuum to the syringe.

6. Apply direct pressure to the site for several minutes after the needle is withdrawn.

Collection of Blood for Transfusion

A detailed discussion of the techniques used for blood collection for transfusion and blood transfusion is presented in the Hematopoietic System section in this chapter.

Diagnostic Imaging

Radiography

- Use standard radiographic techniques (see Chapter 4), including sedation for correct positioning and to limit exposure of the technician, as well as high detail radiographic film and cassettes.
- When interpreting films, it helps to think of the ferret as an elongated cat.
- The kidneys are relatively short (about two lumbar vertebrae in length).
- Splenomegaly is a common radiographic finding.
- For barium-contrast radiography of the gastrointestinal (GI) tract, give 15 ml/kg of 20% barium solution PO via syringe feeding or lavage tube. Most ferrets will accept syringe feeding of barium. Normal GI transit time is about 3 to 4 hours.

Ultrasound

- Echocardiography may be used to evaluate the heart in ferrets with suspected cardiac disease (see "Cardiovascular Disease").
- Other uses of ultrasound in ferrets include investigation of intra-abdominal or intra-thoracic masses, organomegaly, paraurethral cysts, or prostatic cysts.

Bone Marrow Aspiration

- The indications, guidelines, and techniques for bone marrow sampling are the same as those described for dogs and cats. (see Chapter 22)
- Preferred sites include the proximal femur and humerus. The iliac crest may be used for sample collection as well, but can be a difficult site to access.
- Sedation is required for bone marrow aspiration. Use a 20- or 22-gauge spinal needle with stylet for sample collection.

Splenic Aspiration

Fine-needle aspiration of the spleen has been performed successfully in ferrets and is a rapid means of evaluating splenic cytology. In ferrets, the only contraindication is suspected hemangiosarcoma of the spleen. Sedation is rarely necessary, but is recommended if the ferret persistently struggles.

Technique

1. Two assistants are recommended for restraint. Place the ferret in dorsal recumbency. One assistant should restrain the head and neck by scruffing the ferret with one hand. The other hand is used to restrain the forelimbs. A second assistant restrains the hind limbs by placing one hand around the pelvis.
2. Palpate the spleen and position it against the left lateral or ventral body wall.
3. Clip and prepare the site aseptically.
4. Insert a 25-gauge needle attached to a 3-ml syringe to the hub at a perpendicular angle to the skin and aspirate from the spleen.
5. When a small amount of bloody fluid is visualized in the needle hub, withdraw the needle and prepare slides routinely for cytology.

Cystocentesis

- Urine may be collected by cystocentesis using the same technique described for the cat.
- A 22- or 25-gauge needle on a 1- or 3-cc syringe may be used for sample collection.
- Anesthesia is recommended if the ferret is difficult to restrain.

THERAPEUTIC TECHNIQUES

Intravenous Therapy

▼ ***Key Point*** Sedation is often required for placement of a butterfly or indwelling intravenous (IV) catheter, or for small-volume IV therapy.

- For small-volume IV therapy (0.3–0.4 ml), use an insulin syringe. The cephalic or lateral saphenous veins are the preferred sites for injection. Sedation may not always be required for a single injection.
- A 25-gauge butterfly catheter may be used to administer larger, single-dose volumes into the cephalic vein.
- An indwelling catheter can be placed in the cephalic, lateral saphenous, or jugular vein. Sedation is usually required.
- Flush indwelling catheters with small volumes of heparinized saline solution to maintain catheter patency.
- Peripheral indwelling catheters can be placed rapidly and are useful in emergency situations and for surgery.

Cephalic or Saphenous IV Catheter Placement

Technique

1. Clip and prepare the site aseptically.
2. Tent the skin over the vein and make a small cut-down incision in the skin with a 22-gauge needle, taking care to avoid the vein.
3. Introduce a $^1/_4$–$^1/_2$ inch indwelling catheter (20–24 gauge) through the cut-down incision and into the vein.

4. When catheterizing small or debilitated ferrets it is often helpful to attach a tuberculin syringe containing heparinized saline to the catheter hub after removing the stylet. The heparinized saline may then be flushed through the catheter, dilating the vein while the catheter is advanced. The person holding off the vein must release the vein if this technique is used.
5. Cap the catheter and tape it in place routinely.

Jugular Catheter Placement

Technique

1. Sedation is required for placement.
2. Place the anesthetized ferret in dorsal recumbency. Clip and prepare the site aseptically. Make a small cut-down incision over the jugular vein as described previously.
3. Introduce a 20-gauge or smaller catheter into the vein. Suture in place and place a tape bandage around the neck.
4. Ferrets often do not tolerate jugular catheters. Jugular catheters are not used very often unless venous access is required for treatment purposes.

Intraosseous Catheter Placement

- Sedation is required for placement.
- The femur is the preferred site for IO catheter placement.

Technique

1. Place the anesthetized ferret in lateral recumbency. Clip and prepare the site aseptically.
2. Wearing a sterile surgical glove, palpate the top of the greater trochanter, and locate the trochanteric fossa.
3. Introduce the tip of a 20- or 22-gauge spinal needle with stylet in place into the trochanteric fossa, and advance the needle parallel to the long axis of the femur through the cortical bone and into the medullary cavity. Flush with heparinized saline.
4. Suture into place.

Subcutaneous and Intramuscular Injections

- Restrain the ferret by scruffing. Some ferrets may require two people for restraint.
- SC injections may be given in the loose skin over the shoulders.
- IM injections may be given in the quadriceps, the semimembranosus-semitendonosus muscles of the hind limbs, or in the expaxial muscles of the lower back.
- Limit the volume of the IM injections, due to the small muscle mass of the ferret.

Fluid Therapy

- Fluids may be administered SC, IV, or IO, depending on the needs of the patient.
- The daily fluid requirement for ferrets has not been reported but can be estimated at 70 to 100 ml/kg/day. Adjust for dehydration and fluid loss.
- Administer SC fluids over the dorsal shoulder and thoracic region.
- IV or IO fluid therapy is used for a wide range of medical and surgical situations, and is recommended for ferrets that are >5% dehydrated.
- IV or IO fluids must be administered with an infusion pump. Fluids may be given as a continuous infusion, may be administered by continuous infusion, or may be given in 2 to 3 bolus doses over a 24-hour period.
- Ferrets may require the addition of dextrose to fluids because hypoglycemia is common.

Oral Therapy

- Oral medications are most easily given to ferrets in liquid form.
- If possible, compound medications formulated in tablet or capsule form into liquid suspensions, or crush and mix them with a sweet-tasting substance such as Nutri-Cal (Evsco Pharmaceuticals) feline hairball laxative, or fruit-flavored syrup, and administer by syringe.
- Ferrets suffering from insulinoma should not be given sugar-based treats or medications if at all possible. Hide medications in fatty acid supplements, vegetable oil, whipping cream, or meat baby food.

Nutritional Support

- Supplemental feeding is important in the management of anorectic or critically ill ferrets, and in the treatment and prevention of hypoglycemic episodes associated with insulinoma.
- Most ferrets can be force-fed dietary supplements by syringe. Once they acquire a taste for a given supplement, it may be possible to offer it in a bowl.
- Feed ferrets as much food as they will take comfortably (12–25 ml) 2 to 4 times daily.
- Foods useful for force-feeding include the following: meat baby foods, slurried cat or ferret food, and Science Diet A/Dliquid soy-based formulas (e.g. Deliver 2.0, Mead Johnson Nutritionals) may be added to the mixture to increase the calorie content and improve palatability.

Drug-Dosing Guidelines

- Use of all medications is considered off-label for the ferret; there are no approved drugs available for ferrets in the United States.

- Several exotic animal formularies are commercially available that include drug dosage information on ferrets.
- When dosing information is not available, use feline dosages with the following exceptions:
  - *Chloramphenicol*: (50 mg/kg) bid, IV, SC, IM, or PO.
  - *Aspirin*: (10–25 mg/kg) bid–tid PO (canine dosage).
- Many ferrets become lethargic when placed on enalapril (Enacard, Merck Agvet) for cardiac disease. Start with a very low dose (0.25–0.5 mg/kg) q48h PO. Some ferrets cannot tolerate more than every-other-day therapy.
- *Ivermectin* (0.06 mg/kg) q30d PO for heartworm prevention; (0.05 mg/kg) once 3 to 4 weeks after adulticide treatment as a heartworm microfilaricide; (0.50–1.0 mg/kg) PO, SC, repeat in 14 days for sarcoptic mites; (1mg/kg) instill half the calculated dose into each ear and repeat in 14 days for ear mites.

Blood Transfusions

A detailed discussion of the techniques used for blood collection for transfusion and blood transfusionis presented in the Hematopoietic System section in this chapter.

Urinary Catheterization

- Sedation or isoflurane anesthesia facilitates urinary catheterization. The procedure may be difficult in ferrets with urethral disease or urethral calculi.

Males

1. Position in dorsal recumbency and prolapse the penis from the prepuce.
2. Identify the urethral opening, which lies ventral to the tip of the penis. It is helpful to place a 24-gauge IV catheter (with stylet removed) into the urethral opening as a guide.
3. Use a ferret urinary catheter (Slippery Sam ferret urinary catheter, Cook Veterinary Products) an open-ended tomcat catheter, or a #3.5-Fr. feeding catheter. A wire stylet may be useful.
4. Suture into place.

Females

1. Position in ventral recumbency with the hindquarters elevated and use a tomcat catheter or a 3.5-Fr. feeding tube with or without a stylet.
2. The urethral orifice is located on the ventral floor of the vaginal vault. Catheterize the urethra blindly or after identification using a vaginal speculum.

Ferrets with urethral disease

- The catheter may only pass part way into the urethra (often to the pelvic flexure). This may be sufficient to allow retrograde flushing of urethral calculi into the bladder, or to empty the bladder of a ferret with urethral obstruction secondary to prostatic enlargement.

Sedation

▼ ***Key Point*** Isoflurane administered by face mask is the most convenient method to immobilize a ferret for procedures such as venipuncture and radiography. Induction and recovery are rapid.

Doses for parenteral agents used in ferrets are listed in Table 175-3.

- Acepromazine is useful for sedation.
- Butorphanol tartrate has been used at SC, IM, IV, but can cause very profound sedation in some ferrets.
- Ketamine alone does not produce effective muscle relaxation. Use in combination with acepromazine for minor surgical procedures, or with diazepam for more complicated procedures.
- Medetomidine is not analgesic; animals will respond to painful stimuli. Use with an analgesic agent. This agent is reversible (atapamazol).
- Tiletamine-zolazepam (Telazol, Fort Dodge) gives variable muscle relaxation but is useful for immobilization for procedures such as venipuncture, radiography, and electrocardiography. Recovery may be prolonged.
- Xylazine may cause bradycardia or vomiting, and is not recommended for use.

Anesthesia and Analgesia

- Premedicate with parenteral agents followed by facemask induction. Alternatively ferrets may be given

Table 175-3. DRUGS RECOMMENDED FOR CHEMICAL RESTRAINT AND ANALGESIA OF FERRETS

Drug	Dosage (mg/kg)	Route
Chemical Restraint		
Acepromazine	0.1–0.3	IM, SC
Ketamine	25–35	IM, SC
plus acepromazine*	0.2–0.3	
Ketamine	25–35	IM
plus diazepam	2–3	
Ketamine	10–25	IM
plus xylazine	1–2	
Analgesics		
Buprenorphene	0.01–0.03 mg/kg q8–12h	SC, IM, IV
Butorphanol tartrate	0.05–0.5 mg/kg q8–12h	SC, IM
Carprofen	1 mg/kg q12–24h	PO
Flunixin meglumine	0.5–2.0 mg/kg q12–24h	IM, IV

*Use this combination for minor surgery.
IM, intramuscular; SC, subcutaneous.

inhalant agents without premedication via chamber or face-mask induction.
- Isoflurane is the inhalant anesthetic most commonly used in small mammal practice. Sevoflurane is used in some practices as well. Pharmacokinetic and pharmacologic isoflurane and sevoflurane are very similar; sevoflurane smells better and is better tolerated during face-mask induction.
- Isoflurane does not provide analgesia. Administer an analgesic pre- or intra-anesthesia if a painful procedure is to be performed. Analgesic agents commonly used in ferrets include Buprenorphene (0.01–0.03 mg/kg q8–12h SC, IM, IV), Butorphanol (0.05–0.5 mg/kg q8–12h SC, IM), Carprofen (1 mg/kg q12–24 PO), and Flunixin meglumine (0.5–2.0 mg/kg q12–24h IM, IV).
- Intubate ferrets to facilitate intermittent positive pressure ventilation (IPPV). A 2.5 to 3.5 mm endotracheal tube usually is suitable.
- The same planes of anesthetic depth reported for dogs and cats occur in the ferret.
- Follow basic principles of anesthesia for small animals, (see Chapter 2) and provide supplemental heat during surgery; administer IV fluids (isotonic electrolyte solutions supplemented with 2.5–5% dextrose) during long procedures and for insulinoma surgery.

Infectious Diseases of the Ferret

VIRAL DISEASES

Canine distemper and influenza are the two most common viral diseases of the ferret. Influenza is zoonotic between humans and ferrets, and is typically passed from humans to ferrets. Canine distemper is 100% fatal in the ferret, making distemper vaccination imperative.

Canine Distemper

Etiology

- The canine distemper virus (CDV) is a paramyxovirus. Transmission occurs through direct contact with infected animals of any species, and through contact with fomites such as in shoes or clothing.
- The incubation period for CDV in the ferret is typically 7 to 10 days; however, incubation for some strains of CDV may take up to 21 days. (For discussion of CDV in dogs, see Chapter 13).

Clinical Signs

- Early in the disease the only clinical sign may be a mild unilateral or bilateral conjunctivitis.
- Pyrexia (>40°C), anorexia, and profuse mucopurulent naso-ocular discharge develop as the disease progresses.

▼ ***Key Point*** Ferrets develop a distinct pattern of hyperkeratosis of the integument of the chin, lips, and footpads. Lesions may occur in the rectal and inguinal areas as well.

- Other clinical signs include central nervous system (CNS) abnormalities, diarrhea, and severe depression.

Diagnosis

▼ ***Key Point*** Preliminary diagnosis of CDV may be based primarily on the history, physical examination, and clinical signs, which are unlike those of any other disease in the ferret.

- The history often reveals that the animal is unvaccinated, overdue for booster vaccination, or is improperly vaccinated. There is often no evidence of direct exposure to an infected animal because fomite transmission can occur.
- Differential diagnoses early in the disease include influenza and bacterial conjunctivitis. As the disease progresses, development of the integumentary lesions around the chin, lips, and footpads are pathognomonic.
- A fluorescent antibody test can be performed on blood smears, conjunctival scrapings, or mucous membrane scrapings. This test is only useful in the first days of disease onset; false-negative results are common. Modified live vaccine strains of canine distemper will not affect this test.
- Plasma samples can be submitted to measure antibody titer. A positive result is not always diagnostic of disease because both infected and vaccinated ferrets can have a positive titer. Unvaccinated ferrets with a positive titer are likely infected with CDV.
- Fluorescent antibody staining may be performed on imprints of the lymph nodes, bladder epithelium, and cerebellum postmortem.
- Histopathologic diagnosis may be possible via identification of inclusion bodies in the cytoplasm or nucleus of epithelial cells of the trachea, urinary bladder, skin, gastrointestinal tract, lymph nodes, spleen, and salivary glands.

Treatment

▼ ***Key Point*** Treatment for canine distemper is rarely effective, and is limited to supportive care only. Most affected animals must be euthanized.

- Disinfect the household thoroughly using 0.2% Roccal (Upjohn), 0.75% phenol, or 2% to 5% sodium hydroxide.
- In multiple animal households, remove all clinically affected animals. Vaccinate the remaining animals immediately.

Prevention

▼ ***Key Point*** Preventing infection by vaccination is crucial in pet ferrets, since treatment is not effective.

- Vaccinate all ferrets in the household or facility. Currently only two vaccines are approved for use in ferrets: PureVax (Merial, Athens, GA), and Fervac-D (United Vaccines, Inc., Madison, WI). Give 1 ml SC, using the following schedule:
- If the dam is vaccinated: Vaccinate kits at 8 weeks of age and repeat vaccination every 3 to 4 weeks until the kits are 16 weeks of age.
- If the dam is unvaccinated: Vaccinate the kits at 6 weeks of age and repeat every 3 to 4 weeks until the kits are 16 weeks of age.
- Revaccinate annually. Sources claim that immunity lasts for 3 years; however, outbreaks have been known to occur 18 months after vaccination.
- Use of serum titers as a method to evaluate an animal's current immunological status is unsubstantiated.
- Quarantine new ferrets and canines for 4 weeks before exposure to other resident animals. Vaccinate new animals immediately after acquisition at the beginning of the quarantine period.
- Use of Galaxy D (Schering-Plough Animal Health Co., Omaha, NE) for distemper vaccination has been described. Use of this product in ferrets is extra-label. This product has proved effective in preventing canine distemper in young ferrets; however, duration of immunity is unknown.
- Do not use CDV vaccines that contain canine parvovirus, adenovirus, or other viruses. It is not necessary to vaccinate for leptospirosis unless there is exposure to wild rodents.

Influenza

Etiology

The influenza virus is an orthomyxovirus. Ferrets are susceptible to influenza A and B; this is the only documented zoonotic disease of the ferret. Human-to-ferret transmission is more common than ferret-to-human transmission. Transmission occurs by direct contact with naso-ocular discharges, and via inhalation of aerosolized droplets.

- The incubation period is typically 2 to 10 days post-exposure.
- The clinical course of the disease is typically 7 to 14 days.

Clinical Signs

▼ ***Key Point*** Influenza typically causes only mild illness and discomfort, and is usually self-limiting in an otherwise healthy animal.

- Clinical signs may include any combination of the following:
  - Sneezing with a clear, serous nasal discharge.
  - Mild conjunctivitis with serous ocular discharge. Crusting around the eyes may occur rarely.
  - A nonproductive cough that may be loud and paroxysmal, and often occurs more frequently at night.
  - Diarrhea. Vomiting may occur in rare cases.
  - Partial to total anorexia, listlessness, and fever.
  - Pneumonia, severe illness, or death may occur in neonates, geriatric patients, and in ferrets with concurrent diseases such as lymphosarcoma or insulinoma.
- Ferrets with underlying immunosuppressive disorders, especially lymphosarcoma, may develop repeated or cyclic episodes of influenza. Rule out lymphosarcoma by performing a complete blood cell count (CBC), bone marrow biopsy/cytology, or a peripheral lymph node biopsy (see Lymphoma in this chapter).

Diagnosis

Diagnosis is based primarily on the clinical signs, history, and physical examination.

- The history often indicates recent exposure to a human or another ferret with influenza or signs of upper respiratory tract disease.
- The overall physical condition often remains good, although slight or moderate dehydration may be present if the animal is not eating or drinking normal amounts.
- Differential diagnoses include the very early stages of canine distemper, GI rotavirus infection, and lymphosarcoma. If mucopurulent nasal or ocular discharge is noted, consider early CDV or a secondary bacterial infection.

Treatment

- Supportive care generally is sufficient.
  - Encourage the ferret to eat and drink. Offer 1 to 3 tablespoonfuls of Hill's Science Diet A/D or strained meat baby food bid–qid if the animal refuses the regular diet.
  - If indicated, give an oral electrolyte solution that is palatable to ferrets.
- If sneezing or coughing is excessive and interferes with eating or sleeping, give an antihistamine such as chlorpheniramine (1.0–2.0 mg/kg) bid–tid PO, or diphenhydramine (0.5–2.0 mg/kg) bid–tid PO. Nasal solutions containing phenylephrine may be used to relieve nasal congestion.
- Antibiotics are not necessary unless secondary bacterial infection is present.
- Antiviral medications such as amantadine (6mg/kg) bid PO (Symmetrel, ENDO Pharmaceuticals, Chadds

Ford, PA) may be useful in the treatment of ferrets with influenza. Zanamivir (12.5 mg/kg) once intranasally (Relenza, GlaxoSmithKline, Research Triangle Park, NC) has been shown experimentally to prevent influenza infection.

Prevention

Good hygiene is the key to prevention.

- Discuss the zoonotic potential with the client. Advise clients to wash their hands frequently, and to avoid holding the ferret near the face.
- In the veterinary hospital, do not allow influenza-infected personnel to handle ferrets, especially if the animal is a neonate, a geriatric patient, or a patient debilitated by serious disease.
- Vaccination is not recommended; only short-term immunity results, and the wide variation of the influenza virus makes appropriate vaccination difficult.

Rabies

Etiology

Rabies is caused by a rhabdovirus that results in fatal disease in ferrets. It is transmitted via contact with an infected animal's saliva (see Chapter 15). This is a zoonotic disease; however, there has never been a report of ferret-to-human rabies transmission. Experimentally, the incubation period is 28 to 33 days.

Clinical Signs

▼ ***Key Point*** Very little is known about rabies in naturally infected ferrets.

- It is known that ferrets may become naturally infected; however, there is some question as to how easily they can contract the disease and the length of the incubation period. Information about clinical signs is derived primarily from literature associated with laboratory-infected ferrets. Signs are variable and include:
  - Behavioral abnormalities that range from anxiety and hyperactivity to lethargy.
  - Neurologic signs such as ascending paralysis, ataxia, hyperparesthesia, and posterior paresis.

Diagnosis

Diagnosis is based on clinical signs, and/or a history of known or potential exposure to rabies.

- History may include a recent bite wound or exposure to a rabid animal.
- The ferret may be unvaccinated; however, development of rabies in vaccinated individuals has occurred in other animal species.
- Differential diagnoses include Aleutian disease, botulism, brain hypoxia from severe seizures, CNS neoplasia, insulinoma, intervertebral disc disease, and viral or bacterial encephalitis.
- Postmortem laboratory testing of brain tissue (fluorescent antibody staining [FAS] or virus isolation) confirms the diagnosis (see Chapter 15).

Treatment

- There is no treatment for rabies.
- Euthanize the suspect animal to protect humans and other animals in its environment. Submit animal for postmortem FAS testing of brain tissue.

▼ ***Key Point*** It has not been demonstrated that ferrets are carriers of rabies. Many public health facilities now recognize and accept the 10-day quarantine period for ferrets; however, in some states, unvaccinated ferrets involved in biting incidents will be euthanized and submitted for rabies testing. It is important to be familiar with state and local laws regarding vaccination requirements and the laws following a biting incident.

▼ ***Key Point*** The Compendium of Animal Rabies Prevention and Control recommends that ferrets be confined and observed for 10 days following human exposure. If signs compatible with rabies develop, the animal should be euthanized and protocols for rabies testing should be followed. Vaccinated ferrets exposed to a potentially rabid animal should be revaccinated and quarantined for 45 days. Euthanize any unvaccinated ferret exposed to a rabid animal.

Prevention

- Vaccination is the only prevention, and is mandatory in some states.
- Imrab 3 (Rhone Merieux) is an inactivated rabies vaccine that is currently the only rabies vaccine approved for use in ferrets. Administer at a dose of 1 ml SC.
- Vaccinate initially at 3 months of age. Revaccinate annually.

Aleutian Disease

Etiology

Aleutian disease (ADV) is caused by a parvovirus that affects both mink and ferrets. Transmission occurs by direct contact or via contact with fomites contaminated with any infected body fluid, including blood.

ADV produces a progressive immune-mediated disease accompanied by the deposition of antigen-antibody complexes in multiple organs of the body. The virus is prevalent in the ferret population, but the percentage of ferrets that develop clinical illness is low. In

one survey of 700 ferrets, 10% were serologically positive, but only two animals developed clinically active disease. Some ferrets may be asymptomatic carriers, while others may have natural immunity to the disease.

Clinical Signs

▼ ***Key Point*** The clinical signs of Aleutian disease are extremely variable, and the incubation period can be as short as 1 day or as long as 90 to 200 days.

- Ataxia, mild incoordination, posterior paresis, or tremors may be the initial presenting signs. Initially ferrets often continue to eat, and appear bright and alert. As the disease progresses, paresis progresses to the forelimbs, and wasting develops that may continue for weeks or months.
- Anorexia, lethargy, melena, and urinary incontinence are seen in later stages of the disease.
- A slow wasting disease existing without neurologic signs may also occur.

Diagnosis

- Diagnosis may based on the history, clinical signs, physical examination findings, the presence of high serum total protein and hypergammaglobulinemia, and a positive ADV test. Diagnosis is confirmed with histopathology.
- Differential diagnoses include bacterial or viral encephalitis, CNS neoplasia, canine distemper, lymphosarcoma, gastric foreign body, tuberculosis, intervertebral disc disease, systemic mycoses, and rabies (in cases with behavioral changes and sudden paralysis).
- Exposure history is often not helpful because of the prevalence of asymptomatic carriers.
- High serum total protein may be present. Serum protein electrophoresis may demonstrate hypergammaglobulinemia (>20% of the total serum protein).
- Blood samples may be submitted for counterimmunoelectrophoresis testing (United Vaccines, Inc., Madison, WE) or enzyme-linked immunosorbent assay (ELISA) testing (Avecon Diagnostics, Bath, PA). An in-house saliva sample kit is available as well (Avecon Diagnostics, Bath, PA).
- Histopathology demonstrates lymphocytic plasmacytic infiltration and perivascular cuffing in many organ systems. The kidneys, liver, lymph nodes, and spleen are often affected.

Treatment

▼ ***Key Point*** There is no effective treatment for Aleutian disease. Provide supportive care and do not allow contact between clinically ill animals and healthy ferrets. Euthanasia is usually indicated only for clinically affected animals.

- Asymptomatic ferrets that test FAS-positive for ADV should not be euthanized because they may never become clinically ill. Infected ferrets may remain asymptomatic for life, but can remain persistently infected. Other ferrets may develop nonpersistent, self-limiting disease and fully recover.
- Administration of corticosteroid therapy and supportive care may prolong the life of some ferrets with clinically active disease.

Prevention

Breeding colonies

- Breeding colonies should be closed. New animals should be ADV tested and quarantined prior to introduction.
- Test all resident ferrets and remove serologically positive animals from the population.
- ADV-negative animals should be retested in 6 months, before adding them to the colony, due to the potentially long incubation period.

Pets

- It is not necessary to test a pet ferret unless it has been exposed to a clinically ill animal.
- It is not necessary to euthanize a clinically normal, non-breeding ADV-positive ferret or remove it from contact with other pet ferrets. Advise the client, however, that there is a slight possibility that the pet may develop clinical illness.
- Do not house ferrets in close proximity to mink.
- Retest ADV-positive animals in 6 months since some animals may eventually eliminate the virus and become negative.

Rotavirus

Rotavirus causes gastrointestinal infection and a bright green or yellowish-green diarrhea. Rotavirus is described in the "Gastrointestinal System" section in this chapter.

Lymphosarcoma

Lymphosarcoma is common in the ferret, and is discussed in the "Neoplasia" section in this chapter.

BACTERIAL DISEASES

Common Bacterial Infections

Etiology

Staphylococcus, Streptococcus, Escherichia coli, and other common bacteria from the environment can be introduced through penetrating wounds, punctures, abrasions, contact with mucous membranes, and by inhalation or ingestion.

- Abscessation is an uncommon form of bacterial infection in ferrets.

Clinical Signs

- An abscess may occur in any part of the body, including the anal glands, mammary tissue, mouth, mucous membranes, reproductive tract, respiratory tract, subcutis, and prostatic tissue.
- Body temperature may be ≤40°C if bacterial sepsis is present.
- Bacterial dermatitis causes thickened, irritated areas of skin. Affected ferrets may lick and chew these areas until they become denuded and ulcerated.
- Bacterial conjunctivitis causes a thick mucopurulent ocular discharge and swelling of the conjunctiva; corneal ulcerations may be present.
- Bacterial pneumonia causes lethargy, fever, anorexia, and dyspnea, and is often accompanied by mucopurulent nasal discharge and coughing.
- Bacterial mastitis occurs primarily in the lactating jill, and is accompanied by depression, fever, and anorexia. One or more mammary glands are swollen, discolored, and warm to the touch.
- Bacterial metritis may or may not cause a vaginal discharge; depression, fever, and partial or total anorexia are often present.
- Bacterial vaginitis causes a thick mucopurulent yellow-to-green vaginal discharge with little odor. Fever is usually absent, and the animal does not appear clinically ill.

Diagnosis

- Presumptive diagnosis is based on clinical signs, physical examination, demonstration of bacteria on routine cytology, results of bacterial culture, and sensitivity of the affected sites. The total WBC may demonstrate a marked leukocytosis (>10,000).

Treatment

- Treatment should consist of appropriate antibiotic therapy based on culture and sensitivity results, and surgical drainage or excision of the affected tissue when appropriate.
- Begin treatment with a broad spectrum antibiotic pending the results of culture and sensitivity testing, or when obtaining a culture is not feasible.
- Provide supportive treatment as needed, such as fluid therapy and nutritional support.

Specific Treatment

Cutaneous Abscesses

- Lance and thoroughly flush with an antiseptic solution. Keep the area open and flush twice daily until healing occurs by second intention.
- Administer oral antibiotics until signs of infection are gone and a healthy bed of granulation tissue is present.

Mastitis

See Mastitis in the Reproductive Disease section in this chapter.

Uterine Infection (Metritis, Pyometria)

See Uterine Infection in the Reproductive Disease section in this chapter.

Respiratory Tract (Pneumonia)

- If possible, perform a tracheal wash and submit samples for cytology, bacterial culture, and sensitivity testing.
- If pleural effusion is evident on radiography, perform thoracocentesis. Submit samples for cytology, bacterial culture, and sensitivity testing.
- Start oral broad-spectrum antibiotic therapy immediately, pending culture and sensitivity results. If pleural effusion is present, consider treating with a combination of clindamycin and cephalosporins (use cat dosages).
- Use of bronchodilating agents and/or nebulization therapy may be beneficial treatment modalities as well.

Conjunctivitis

- Treat conjunctivitis with a broad-spectrum ophthalmic ointment.
- Perform a fluorescent corneal staining test to rule out corneal ulcers. (see Chapter 133)

Anal Gland Infection

- Submit samples for bacterial culture and sensitivity testing.
- Begin treatment with broad-spectrum oral antibiotics. Modify treatment based on culture sensitivity results.
- Instruct owners to hot pack the affected area 5 to 10 minutes bid–tid.
- Treat until infection and swelling resolve, then perform anal sacculectomy.
- Continue antibiotic treatment 10 to 14 days postoperatively.

Campylobacteriosis Infection

- *Campylobacter* spp. typically causes GI disease (see "Gastrointestinal System").

Salmonellosis

- *Salmonella* spp. may rarely cause gastroenteritis in ferrets (see "Salmonella" within "Gastrointestinal System").

Botulism

- Botulism is a rarely encountered disease in the domestic ferret caused by the ingestion of food contaminated with the *Clostridium botulinum* toxin. *C. botulinum* is commonly found in the soil.
- Uncooked food or food contaminated with soil can be the source of the infection.

Tuberculosis

- Clinical cases of tuberculosis in the ferret are reported infrequently; however, ferrets are susceptible to bovine, avian, and human *Mycobacterium* spp. infections.
- The disease can be transmitted by ingestion of contaminated meat (poultry or meat), unpasteurized milk, or food contaminated by the droppings of infected wild or pet birds (see Chapter 19 for information about tuberculosis in dogs and cats).
- Clinical signs include chronic weight loss, and diarrhea that is unresponsive to treatment. Vomiting may occur as well in some cases.
- Diagnosis is based on history, clinical signs, and the exclusion of other diseases; it is confirmed by intestinal biopsy. Histopathologically granulomatous inflammation and acid-fast bacteria are identified. Infection may also be confirmed by culturing the organism, and with polymerase chain reaction (PCR) testing.
- Because of the zoonotic potential of this disease, treatment is not recommended. Affected animals should be euthanized.

FUNGAL INFECTIONS

Dermatophytosis

Etiology

Dermatophytosis is rare in the ferret and is typically caused by *Microsporum canis* and *Trichophyton mentagrophytes*. Dermatophytes are transmitted by direct contact with infected animals or contaminated bedding, caging, and fomites.

▼ ***Key Point*** Ferrets are usually not carriers of these organisms. Clinical disease is typically self-limiting. The most common source of infection of the pet ferret is the household cat.

Clinical Signs

- Young, debilitated, or geriatric ferrets are the most commonly affected.
- Lesions are consistent with those described in other species (see Chapter 42). Alopecia with erythema, inflammation, hyperkeratosis, superficial crusting, lichenification, and erythema are present. Pruritis is common and may lead to self-trauma and secondary pyoderma.

Diagnosis

- Diagnosis is based on the identification of the fungal agent on skin scrapings, fungal culture, or a positive Wood's light examination (*M. canis*). (see Chapter 42).

Treatment

- Dermatophytosis is often self-limiting and may resolve without therapy. However, due to the zoonotic potential, treatment is recommended.
- Topical treatment includes the use of keratolytic shampoos, and/or lime sulfur dips. (see Chapter 42).
- Oral therapy consists of the administration of griseofulvin (25 mg/kg) PO sid for 21 to 30 days. Perform a CBC every 14 days while the ferret is receiving treatment.
- Disinfect the home by steam cleaning, the application of dilute (1:10) bleach or chlorhexidine solutions, and vacuuming thoroughly to remove infectious spores. Dispose of the vacuum cleaner bag after vacuuming is complete. A thorough cleaning of the heat ducts and air conditioner/heater filters is also recommended.

Other Fungal Infections

Systemic mycoses are rare in the ferret; however blastomycosis, histoplasmosis, cryptococcosis, coccidioidomycosis, and aspergillosis have been reported.

- Consider these infections in the differential diagnosis of any systemic disease that is refractory to treatment and involves wasting, granulomatous lesions, persistent or recurring draining wound tracts, and respiratory tract disease.
- Diagnosis is based on the histopathological or cytological demonstration of the fungal organism in biopsies or aspirates (see Chapter 20).
- Complement fixation and precipitation tests have been used with variable success.
- Treatment is the same as described for the dog and cat (see Chapter 20).

Hematopoietic System

SPLENOMEGALY

Primary disease of the spleen is uncommon. Splenomegaly is often a common incidental finding in a healthy adult ferret, or it may occur in association with

a wide variety of disease conditions. Perform a complete medical evaluation in all splenomegaly cases.

Etiology

- Splenomegaly may be a normal or incidental finding in some patients.
- Pathological causes of splenomegaly may include chronic immune stimulation, erythroid bone marrow insufficiency, extra-medullary hematopoiesis (EMH), hypersplenism, heart disease, and neoplasia.
- Splenomegaly can occur concurrently with adrenal gland disease and insulinoma, but it is usually an incidental finding.
- *Extramedulllary hematopoiesis (EMH)* may cause enlargement of the spleen. The etiology of EMH is unclear; compensation for myeloid insufficiency and chronic immune stimulation have been suggested as causes. Ferrets with EMH typically do not show evidence of hematological abnormalities. Grossly the spleen has a normal shape and color, but it appears enlarged.
- *Hypersplenism* may cause enlargement of the spleen, but is rare in the ferret.
  - Destruction of one or more blood cell lines by the splenic reticuloendothelial system occurs; affected ferrets will have anemia, leukopenia, thrombocytopenia, or pancytopenia.
  - Bone marrow may be normal or hyperplastic in affected patients.
- *Lymphoma* is the most common neoplasia of the ferret spleen. Hemangioma or hemangiosarcoma may occur as well.
  - When splenic lymphoma is present the spleen typically has irregular borders and a nodular texture. White or tan nodules may be noted grossly on the surface of the spleen and in the parenchyma. Metastasis may be present.
- *Splenic torsion* and *abscessation* are rare in the ferret.

Clinical Signs

- The normal ferret spleen measures approximately 5 cm × 2 cm × 1 cm, and may be palpated in the left cranial abdominal quadrant. The texture of the spleen should be slightly firm, smooth, and the edges should be sharp.
- An enlarged spleen is often noted on abdominal palpation as a firm, elongated smooth mass extending down the left side of the ferret abdomen, or crossing diagonally across the ventral abdomen from the left cranial abdominal quadrant to the caudal right abdominal quadrant.
- Abdominal distention may occur.
- Occasionally the spleen is so large and pendulous that the ferret can barely lift its abdomen off the ground.
- Abdominal discomfort due to splenomegaly appears to be uncommon in ferrets.

Diagnosis

- Perform a CBC, platelet count, serum biochemical analysis, bone marrow cytology, and whole body radiography.
- Diagnosis of hypersplenism is based on the presence of one or more cytopenias, normal to hypercellular bone marrow cytology/biopsy, and the absence of blood loss, infection, or neoplasia.
- Obtain whole body radiographs to delineate the borders of the spleen and to rule out other abnormalities such as cardiomegaly or hepatomegaly that may contribute to splenomegaly.
- Splenic aspiration or biopsy may be performed. Perform fine-needle aspiration of the spleen using a 25-gauge needle (see "Clinical Techniques"). Do not perform splenic aspiration if hemangiosarcoma is suspected.
- Perform an abdominal ultrasound to evaluate the spleen. When the splenic parenchyma appears irregular, an ultrasound-guided biopsy or fine-needle aspiration may be performed.
- Perform a splenic biopsy during abdominal exploratory surgery, particularly if the spleen is irregular or discolored.

Treatment

Treatment depends on the primary disease condition. Usually splenectomy is not necessary.

▼ ***Key Point*** Indications for splenectomy are the same as for other species and include hypersplenism, splenitis, splenic abscess, torsion, rupture, neoplasia, and discomfort caused by excessive splenomegaly.

- To perform a splenectomy, follow the surgical guidelines for splenectomy in dogs and cats (see Chapter 25).
- Anemia may result after splenectomy; the decision to perform splenectomy should be made cautiously, and with consideration to the health of the ferret as a whole.
- Administer antibiotics and fluid therapy pre- and postoperatively.
- Monitor asymptomatic ferrets with splenomegaly with periodic physical examination, CBC evaluation, imaging, and splenic aspiration.

ANEMIA

The clinical approach to anemia in ferrets is the same as for other species. Anemias are classified as regenera-

tive or nonregenerative; treatment is directed at the specific cause.

Etiology

There are many causes of anemia in ferrets; decreased erythropoiesis, destruction of red blood cells, and blood loss contribute to anemia.

- *Nonregenerative anemia* (normocytic, normochromic, nonregenerative anemia) occurs when bone marrow hematopoiesis is disrupted. Bone marrow cytology of affected ferrets may appear normal.
  - Decreased erythropoiesis may be caused by chronic metabolic disease (renal, hepatic), chronic inflammation, hyperestrogenism, bone marrow suppression, and neoplasia.
  - Anemia of chronic disease can occur whenever long-term illness is present and is caused by decreased erythrocyte survival, decreased availability of iron, or a decreased response to the anemia treatment.
  - Anemia associated with chronic inflammation is mediated by sustained inflammatory cytokine release.
  - Hyperestrogenism may cause nonregenerative anemia due to estrogen-induced bone marrow suppression. Unspayed female ferrets, female ferrets with ovarian remnants, or hyperestrogenism associated with chronic adrenal disease may contribute to this syndrome.
  - Myeloid and leukemic neoplasias can cause suppression of bone marrow erythropoiesis due to replacement of normal bone marrow by neoplastic or fibrotic changes.
- *Erythrocyte destruction* may cause anemia; causes include immune-mediated disease, toxins, parasitism, or septicemia.
  - Idiopathic immune-mediated hemolytic anemia, and immune-mediated hemolysis secondary to viral disease or blood parasites have not been reported in the ferret.
  - Drug-induced hemolysis and heavy metal toxicosis (including zinc) are potential causes of hemolytic anemia.
- *Anemia secondary to blood loss* may be secondary to trauma, hemostatic disorders, bleeding lesions, and parasitism.
  - Bleeding lesions may be internal or external.
  - Bleeding ulcers may lead to anemia, and may be associated with *H. mustelae* gastritis, gastrointestinal foreign body, or chronic use of ulcerogenic drugs.
  - Parasitism is uncommon in the ferret. Coccidiosis in the young ferret or severe flea infestation may cause anemia.
  - Hemostatic disorders include thrombocytopenia associated with estrogen toxicity, rodenticide poisoning, and liver disease.

Clinical Signs

- Clinical signs include weakness, pallor, lethargy, and inappetence. Jaundice may be seen if hemolysis is present.
- A soft systolic murmur is common in anemic ferrets.
- A swollen vulva is present in ferrets with persistent estrus, an ovarian remnant, and in some cases of adrenal gland disease. Hair loss may also be present on the shoulders and flanks.
- Ferrets with estrogen toxicity may have signs of thrombocytopenia such as petechiae, ecchymoses, and melena.
- Melena may be noted if GI bleeding is present.
- Palpate the spleen. Splenomegaly may be caused by hypersplenism and subsequent anemia.
- Check carefully for fleas. Perform a fecal examination.

Diagnosis

- Diagnosis is based on the medical history, the physical examination findings, and a complete diagnostic work-up that includes a CBC, reticulocyte count, serum biochemical analysis, whole-body radiographs, and bone marrow cytology if indicated.

History

- Obtain a careful history regarding possible blood loss, toxicity, and foreign body ingestion. Determine the duration of vulvar swelling (if present).

Laboratory Tests

- Characterize the anemia based on RBC parameters and hemoglobin concentration.
  - The normal hematocrit for the ferret is 46% to 61%, higher than that of other animals. The erythrocyte count is higher as well; erythrocyte counts as high as 17.0×10^6 cells/µl have been reported.
  - The normal reticulocyte count may be as high as 10%. Reticulocyte counts greater than 12% are indicative of a regenerative bone marrow response.
  - Regenerative anemia is often the result of blood loss or hemolysis.
- Perform bone marrow aspiration (see Clinical Techniques), particularly if the anemia is nonregenerative, to identify infiltrative processes and assess the morphology of RBC precursors. Bone marrow cytology from animals affected with anemia of chronic disease may be normal. Bone marrow cytology is also indicated in ferrets with nonregenerative anemia that is unresponsive to treatment after 6 to 10 days.
- Obtain blood for blood lead concentration if lead poisoning is suspected.

Diagnostic Imaging

- Whole-body radiographs are indicated to rule out abdominal neoplasia, GI foreign body, and thoracic neoplasia. A GI contrast study may be helpful to rule out the presence of GI ulcers. Ultrasound may be helpful based on the rule outs established.

▼ ***Key Point*** Anemia in an intact female ferret with a swollen vulva for more than 4 weeks most likely is due to estrogen toxicity.

Treatment

The objectives of treatment are to treat both the anemia and the underlying cause.

- General supportive care includes oxygen therapy, subcutaneous fluids, and nutritional supplementation.

Treatment of the Anemia

- Specific supportive care includes whole blood transfusion, iron dextran therapy, and the administration of erythropoietin.
- Oral iron supplements may be administered to replenish whole-body iron stores.
- Erythropoietin may be used to treat ferrets with nonregenerative anemia. Administer 100 U/kg three times per week until the PCV is stable, then administer 1 to 2 times a week. Continue to monitor the PCV, and titrate the dose as needed.

Blood Transfusion

- Indications for blood transfusion include the clinical status of the patient, a low packed-cell volume (PCV) of <12%, the specific cause of the anemia, and the potential for continued blood loss.
- Ferrets lack specific blood types; transfusion reactions are rare in the ferret; up to three transfusions from the same donor and transfusions from multiple donors are considered safe.
- The normal blood volume of an adult ferret may be calculated as 8% of the body weight.
- The ideal value of the PCV post-transfusion would be within the normal reference range; a more likely goal is 5% to 10% higher than the pre-transfusion PCV. For dosage guidelines, see Chapter 22.
- Before transfusion, administer a rapid-acting corticosteroid, such as dexamethasone sodium phosphate (6–8 mg/kg once IV) or prednisolone sodium succinate (22 mg/kg once IV), as a slow bolus infusion, and administer an antihistamine such as diphenhydramine (0.5–1 mg/kg IV, IM, SC) to the recipient ferret.

Collection of Blood for Transfusion

- The normal blood volume of ferrets has not been reported, but is estimated to be 5% to 6% of the total body weight (approximately 60 ml/kg). Twenty percent of the estimated blood volume (approximately 12 ml) may be collected from healthy ferrets.
- The jugular vein is the preferred site for the collection of large volumes of blood for transfusion.
- Sedate the donor ferret and place it in dorsal recumbency.
- Use a butterfly catheter to collect the blood into a syringe containing an anticoagulant such as sodium citrate (0.1 ml citrate per 0.9 ml blood) or acid-citrate-dextran (ACD) (1 ml per 6 ml blood collected).
- Transfer the blood immediately to the recipient. Blood should be filtered as it is transfused to the recipient.
- Administer fresh blood transfusions through an indwelling catheter or via a butterfly catheter into the cephalic or jugular vein. If a vein is inaccessible, administer into the peritoneal cavity or via the intraosseous route into the proximal femur.
- Whole blood is commercially available from Marshall Farms (Marshall Pet Products Inc., Wolcott, NY).
- Hemoglobin substitutes such as Oxyglobin (Bioprure Corporation, Cambridge, MA) (11–15 ml/kg) IV or IO over 4 hours may be used if whole blood is unavailable.
- Administer Oxyglobin slowly in normovolemic patients and in patients with renal disease, heart disease, or when the risk of pulmonary edema is present.

Treatment of the Cause of Anemia

- Stop bleeding (internal or external).
- Correct the underlying cause of GI bleeding, including medical therapy for GI ulceration (see "Gastrointestinal System"), surgery to remove GI foreign body, and antibiotics and supportive care for enteritis/colitis.
- For anemia of chronic disease, treat the underlying primary disease process.
- Address metabolic disease (renal, hepatic) if present.
- To correct estrogen toxicity in the intact female, terminate estrus (see below) and provide supportive care until the bone marrow is functional. Broad-spectrum antibiotic therapy is important for the control of sepsis in leukopenic patients. Estrogen toxicity associated with ovarian remnants is treated by surgical removal of the remnants when the ferret is stable enough for surgery. Estrogen toxicity associated with adrenal gland disease is treated by adrenalectomy. Preoperative care is the same as that described for the intact female (see below). (For diagnosis and treatment of adrenal tumors see "Adrenal Gland Disease.")
- Treat fleas with any product that is safe for use in cats (see Chapter 45).
- Treat lead poisoning following the same protocols recommended for cats (see Chapter 22).

- Anemia secondary to neoplasia is associated with a poor prognosis. Some cases of lymphoma may respond to treatment (see "Neoplasia").

Termination of Estrus

- Administer human chorionic gonadotropin (HCG) in a single injection of 100 IU (or 1000 USP) IM. Repeat this dose in 1 to 2 weeks if vulvar swelling has not diminished.
- Alternatively, give gonadotropin-releasing hormone (GnRH) at a dose of 20 µg IM or SC; repeat in 2 weeks if necessary.
- GnRH and HCG are effective only after the 10th day of estrus. Bone marrow toxicity is not immediately reversible with termination of estrus; the PCV continues to fall for days to weeks.
- Monitor the PCV as a useful guide to therapy and prognosis:
  - PCV > 25%—the prognosis is good and termination of estrus is the only therapy required.
  - PCV 15% to 25%—the prognosis is guarded because the PCV level can decrease further after termination of estrus.
  - PCV < 15%—the prognosis is poor and aggressive supportive care is indicated, including multiple blood transfusions until bone marrow function is restored.

Prevention

- Some causes of anemia in ferrets can be prevented. Educate owners about proper husbandry techniques to avoid flea infestation, foreign body ingestion, and trauma.

▼ ***Key Point*** To prevent estrogen toxicity, spay all female ferrets not used for breeding.

Neoplasia

INSULINOMA

Insulinoma (pancreatic beta-cell tumor) is one of the most common neoplasias of the ferret. Disease is most common in ferrets over 2 years of age, and results in progressive, cyclic, or persistent hypoglycemia.

Etiology

- The incidence of insulinoma is typically higher in ferrets in the United States than in ferrets in other countries. The cause(s) are unknown.
- Possible etiologies include a limited genetic pool and diet. Ferrets in the United States are typically fed processed foods containing large amounts of cereal grains. Ferrets in other countries are typically fed a more natural diet consisting of meats and whole prey items.

Clinical Signs

- Early signs may be subtle and transient. Cyclic or progressive episodes of profuse hypersalivation and pawing at the mouth (which is indicative of nausea), lethargy, depression, "stargazing," and posterior paresis may be seen during periods of hypoglycemia.
- As the disease progresses, or during periods of inadequate food intake, symptoms become more pronounced and may progress to stupor or coma. Seizures may occur.
- Splenomegaly is a common, unassociated finding on physical examination (see "Splenomegaly" under "Hematopoietic System" in this chapter).
- Adrenal disease is often identified concurrently in many ferrets with insulinoma (see "Adrenal Neoplasia" in this chapter).

Diagnosis

▼ ***Key Point*** Base a presumptive diagnosis of insulinoma on the history, clinical signs, and repeated evidence of hypoglycemia in the presence of normal or elevated blood insulin levels. Make a definitive diagnosis via surgical removal and histopathology of a pancreatic tumor or biopsy.

- Differential diagnoses include hepatic disease, sepsis, starvation, and laboratory error.

Fasting Serum Glucose

- A carefully monitored fast of 4 to 6 hours is sufficient.
- If necessary, obtain several samples over a period of several days.
- Normal fasting serum glucose concentration is 90 to 110 mg/dl. Ferrets with insulinoma often have a fasting serum glucose of 20 to 75 mg/dl. Ferrets with fasting serum glucose between 75 to 90 mg/dl are considered suspect and should be monitored.
- Do not fast the animal for more than 6 hours. Discontinue fast if signs of hypoglycemia occur. Prolonged fasting may lead to collapse, coma, or seizures. Feed the ferret a high-protein and high-fat meal as soon as possible after collection of blood.

Blood Insulin Values

- Measurement of blood insulin concentration is not consistently reliable in the ferret.
- False positive results may occur if liver disease, non-islet cell tumors, or sepsis are present.
- Blood insulin concentrations greater than 275 pmol/liter (or 38 µU/ml) are considered elevated in ferrets. However, if the ferret is severely hypoglycemic at the time of sample collection, the blood insulin

value may be normal because insulin and glucose are in a constant dynamic state.

Serum Biochemical Profile and Complete Blood Cell Count

- The serum biochemical profile is typically normal except for the presence of hypoglycemia.
- The CBC is typically normal.
- A slight elevation in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) may be noted. The cause is unknown and may incidental, or may indicate hepatic lipidosis due to chronic hypoglycemia or some hepatic pathology.

Treatment

▼ ***Key Point*** Insulinoma is a progressive disease in ferrets. Educate owners how to recognize the signs of hypoglycemia and how to manage hypoglycemia at home (see "Medical Therapy" and "Hypoglycemia Episodes").

- Treatment options include medial therapy and/or surgical therapy.
- Medical therapy will need to be adjusted as the disease progresses.
- Surgery is used as a management tool and is not curative.

Medical Therapy

Insulinoma is a progressive disease, even after surgical intervention. Medial therapy is often effective in controlling symptoms associated with insulinoma for 6 to 18 months. Frequent feeding is the first step in treatment. Add prednisone and diazoxide as clinical signs and hypoglycemia worsens.

- Feed high-quality protein and high-fat meals frequently, especially after exercise or a long sleep. Avoid foods containing sugar or excessive carbohydrates (except to treat hypoglycemic episodes); these foods cause short term hyperglycemia followed by a period of hypoglycemia 1 to 2 hours later.
- 1 to 3 tablespoons of Hill's Science Diet A/D or meat-based baby foods may be given twice daily and as needed.
- Chromium has been anecdotally reported to stabilize blood glucose and insulin levels in humans. Brewer's yeast, which is a rich source of chromium, has been beneficial in some ferrets with insulinoma. Give $^1/_8$ to $^1/_4$ tsp of Brewer's yeast q12h in the high-quality protein, high-fat meal.
- When frequent feedings no longer control clinical signs, begin corticosteroid therapy. Administer a prednisone or prednisolone suspension at a starting dosage of 0.1 to 0.25 mg/kg bid PO. As clinical signs worsen, increase the dosage gradually as needed to control signs. When the dosage approaches (0.75–1.0 mg/kg) bid PO consider the addition of diazoxide.
- Corticosteroids promote hepatic gluconeogenesis and antagonize the effects of insulin at the cellular level. Ferrets appear to tolerate corticosteroids well; side effects are minimal at lower dosages. Corticosteroids are usually the first treatment of choice because they are inexpensive and cause few side effects in the ferret.
- Add diazoxide (Proglycem, Baker Norton Pharmaceuticals) (10 mg/kg/day) PO divided bid–tid when frequent feedings and corticosteroids no longer control clinical signs. The diazoxide dosage may be gradually increased up to 60 mg/kg/day PO divided bid–tid as needed. Diazoxide is expensive, and is not palatable for some ferrets. Potential side effects at high doses include hypertension, lethargy, depression, anorexia, and nausea.

Treatment of Acute Hypoglycemic Episodes

- Hypoglycemic episodes require specific therapy.
- Mild to moderately severe hypoglycemic episodes often can be treated successfully at home. Instruct the client to give the ferret honey or corn syrup.
  - Owners should be taught how to identify hypoglycemic episodes and how to administer medications with a syringe.
  - If the ferret has collapsed, rub honey or corn syrup on the gingiva (taking care not to be bitten).
  - Once the animal is stabilized, owners should feed a high-protein meal, and make arrangements to bring the ferret in for a blood glucose test.
- Severe hypoglycemic episodes that do not respond to home therapy or that result in seizures require treatment in a veterinary hospital (see Chapter 35).
  - Administer a slow IV bolus of 50% dextrose (0.5–2 ml) until the ferret responds. Give no more than necessary to stop signs of hypoglycemia. If the ferret continues to have seizures or remains comatose, place an IV catheter and administer fluids containing 5% dextrose. Also administer a corticosteroid.
  - Anticonvulsant therapy (diazepam 1–2 mg IV to effect) may be necessary if the ferret is in status epilepticus. Follow anticonvulsant protocols for dogs and cats (see Chapter 127) while correcting the hypoglycemia.
  - Modify the medical treatment as necessary, and consider surgical intervention.

Surgical Therapy

Surgical therapy is the treatment of choice even though surgical removal or debulking of pancreatic tumors or partial pancreatectomy is palliative and provides only temporary remission of signs (6 to 24 months).

- Follow canine preoperative protocols (see Chapter 35). Fast the ferret for only 4 to 6 hours preoperatively to avoid hypoglycemia.
- Administer IV or IO isotonic fluids containing dextrose (2.5–5.0%) 1 to 2 hours preoperatively if possible, during surgery, and continue postoperatively until the ferret is stable and is eating and drinking.
- Evaluate the blood glucose concentration pre-, intra-, and postoperatively if possible.
- See Chapter 35 for information about the surgical removal of insulinoma.

▼ ***Key Point*** Perform a complete abdominal exploratory; insulinomas can metastasize to the regional lymph nodes, liver, and spleen (uncommon). Concurrent adrenal tumors (see Adrenal Gland Disease) are common.

- If the spleen is enlarged and appears irregular or mottled, consider performing a complete or partial splenectomy and submit for histopathology.

Postoperative Care and Complications

- Postoperatively monitor the blood glucose concentration bid–tid until the ferret is discharged from the hospital. Many ferrets become euglycemic immediately after surgery. Some ferrets may remain hypoglycemic. Rarely, ferrets may become transiently hyperglycemic after surgery.
- Most ferrets will require resumption of medical therapy 2 to 6 months after surgery. Some ferrets will need medical therapy immediately postoperatively.
- Monitor blood glucose levels for 10 to 14 days after surgery and at 60 to 90 day intervals.
- *Iatrogenic pancreatitis* is rarely a problem in ferrets; however, as a precaution, withhold food and water for 12 hours postoperatively; give 2.5% to 5.0% dextrose IV during this period. Monitor blood glucose 1 to 4 times daily.
- *Transient diabetes mellitus* may occur postoperatively. Hyperglycemia and glucosuria may be present for 1 to 21 days postoperatively; generally no treatment is required.
- Histopathologic examination of the pancreatic mass may reveal hyperplasia, adenoma, and/or adenocarcinoma of the pancreatic beta cells, even within a single tissue specimen.

Prognosis

- The prognosis is guarded, but with surgery and medical treatment, ferrets have had a good quality of life for more than 1 year after diagnosis of insulinoma. The median survival time was 17 months (range, 0.5–40 months) in one study of 53 ferrets treated with surgery, medical management, or both.

ADRENAL GLAND DISEASE/ADRENAL NEOPLASIA

Adrenal tumors are common in ferrets, and occur with approximately the same frequency as insulinomas. Adrenal neoplasia and insulinomas often appear concurrently. Adrenal tumors have been identified in ferrets as young as 1 year of age, although they typically occur in ferrets >2 years of age.

- Adrenal gland disease in ferrets is not Cushing's disease. Excessive sex steroids, not corticosteroids, are produced by a hyperplastic or neoplastic adrenal gland.

Etiology

- The etiology is unknown. Possible causes of adrenal disease in ferrets include early neutering, genetic factors, and lack of exposure to normal seasonal photoperiods. The incidence of adrenal neoplasia is higher in ferrets in the United States. In the U.S., ferrets are typically neutered at 6 weeks of age, and are housed indoors under artificial light cycles. Ferrets in Europe and Australia are typically housed outside, and are not neutered until 6 months of age.
- Adrenal neoplasia in ferrets causes a variety of clinical signs, and appears to be the result of excessive secretion of estrogens and androgens, not cortisol. Pituitary-dependent hyperadrenocorticism has not been documented in ferrets.
- Adrenal tumors most commonly arise from the adrenocortical tissue. Common histopathological findings include hyperplasia, adenoma, and adenocarcinoma.

Clinical Signs

- Signs include progressive, bilaterally symmetric alopecia, usually starting at the tail base and progressing cranially. Hair loss often starts in the early spring or fall. There may be a history of alopecia and spontaneous hair regrowth as well.
- Pruritis often is reported, along with excessive dryness of the skin and small excoriations. Thinning of the skin is common.
- An enlarged vulva, mimicking estrus, may be the only clinical sign in spayed females. Mucoid or mucopurulent vulvar discharge may be noted. Castrated males may exhibit territorial marking and sexual behaviors, and may develop the strong body odor and oily hair coats of intact males. Mammary hyperplasia can occur in either sex.
- Male ferrets may present with partial to complete urinary obstruction. Persistent elevation of adrenal-derived androgenic hormones may cause development of prostatic hypertrophy, prostatic cysts, or periurethral cysts, which cause narrowing of the

urethra. Affected ferrets may present with stranguria, dysuria, azotemia, and severe metabolic derangement. Male ferrets that are described as straining to urinate should be treated as an emergency (see "Urinary System").

- Atrophy of abdominal musculature and mobilization of fat to the ventral abdomen, leading to a pendulous appearance, may be seen.
- Atrophy of hind limb musculature and rear limb paresis can occur.
- Polyuria/polydipsia is uncommon but has been reported.
- Collapse, anemia, and petechiation resembling estrogen toxicity have been described in male and female ferrets with chronic or advanced adrenal disease (see Hematopoietic System).
- Enlarged adrenal glands may occasionally be noted on the physical examination. The left adrenal gland is easier to palpate than the right.
- Radiographs are not typically helpful in confirming this disease. Ultrasonography may be useful for identification of adrenalmegaly.
- CBC is typically unremarkable unless estrogen toxicity-like anemia is present. The serum chemistry profile is typically within normal limits unless insulinoma is present.

Diagnosis

▼ ***Key Point*** A history of symmetric truncal hair loss suggests the diagnosis. Differential diagnosis includes seasonal alopecia, which typically appears in the spring or fall, affects only the tail, and resolves after several weeks.

- Female ferrets often present with a swollen vulva. Differential diagnoses include an intact female ferret, a female ferret with an ovarian remnant, and seasonal alopecia. Perform a serum steroid panel or administer human chorionic gonadotropin (100 IU) IM to determine if a female ferret is unspayed or has an ovarian remnant.
- A plasma steroid hormone assay may be used to support the diagnosis. Elevated plasma concentration of estradiol, androstenedione, and/or 17-hydroxyprogesterone is a reliable indicator of adrenal gland disease (see Table 174-4). A hormone panel is commercially available through the Clinical Endocrinology Laboratory of the Department of Comparative Medicine at the University of Tennessee.
- The adrenocorticotropic hormone (ACTH) stimulation test and the low-dose dexa-methasone suppression test are not useful in ferrets. Ferrets with adrenal gland disease do not produce abnormal concentrations of cortisol, and adrenal gland disease in the ferret appears to be independent of ACTH. Urine cortisol/creatinine ratio does not appear to be a specific indicator of adrenal gland disease.

Table 175-4. STEROID HORMONE CONCENTRATIONS IN FERRETS

Steroid	Range
Androstenedione (nmol/L)	0–15
Estradiol (pmol/L)	30–180
17-hydroxyprogesterone (nmol/L)	0–0.8

From Clinical Endocrinology Laboratory, University of Tennessee College of Veterinary Medicine.

- Perform exploratory surgery to confirm the diagnosis.

Treatment

- Adrenal tumors can be managed medically or surgically. Surgical management is preferred and recommended.
- Medical treatment may cause clinical signs to regress, but will not stop growth of the adrenal tumor.

Medical Therapy

The goal of medical treatment is to decrease or eliminate the clinical signs of adrenal gland disease. Medical therapy will not stop or prevent the growth of an existing tumor, and should be reserved for ferrets that are poor surgical candidates, ferrets with inoperable bilateral adrenal tumors, or ferrets with recurrent adrenal gland disease.

- Medical treatments described in the literature include mitotane, ketoconazole, androgen receptor blockers, aromatase inhibitors, and gonadotropin-releasing hormone analogs.
- *Gonadotropin-releasing hormone analogs.* There are two general types of GnRH analogs: GnRH agonists and GnRH antagonists. To date only GnRH agonists such as leuprolide acetate (Lupron Depot, TAP Pharmaceuticals Inc., Lake Forest, IL) have been used to control the signs of adrenal disease in the ferret. Of the medical treatments described, anecdotal reports suggest that leuprolide acetate has been most effective in alleviating dermal and urogenital signs of adrenal disease. Administer the 1 month depot formulation of leuprolide acetate at a dose of (250 µg/kg) IM every 30 days.
- *Androgen receptor blockers* theoretically block the actions of androgens at the receptor site, and decrease or reverse the signs of adrenal gland disease. In human medicine these drugs are used to treat men with prostatic carcinoma or prostatic hyperplasia. Flutamide (Eulexin, Schering Corporation, Kenilworth, NJ) and bicalutamide (Casodex, AstraZeneca Pharmaceuticals LP, Wilmington, DE) have been used, primarily in male ferrets. Results are variable.

- *Aromatase inhibitors* such as anastraozole (Arimidex, AstraZeneca Pharmaceuticals LP) inhibit aromatase, an enzyme involved in estrogen production. Some ferrets show decreased evidence of adrenal gland disease symptoms when treated with this drug.
- *Mitotane* (0,p'-DDD) (Lysodren, Bristol-Myers Squibb Oncology, Princeton, NJ) is *rarely effective* in ferrets with adrenal gland disease, presumably because ferrets do not develop pituitary-dependent hyperadrenocorticism. If clinical signs do resolve, they will often recur as soon as the mitotane therapy is withdrawn.

▼ ***Key Point*** Perform a fasting blood glucose test before starting mitotane therapy. Do not use mitotane if blood glucose is low (indicative of concomitant insulinoma). Mitotane causes a decrease in endogenous cortisol production; if insulinoma is present, serum glucose levels also may fall, causing a hypoglycemic crisis.

- Give mitotane (50 mg/kg) PO q24h for 7 days, then q48h until clinical signs start to resolve. At that time decrease to q72h until signs are fully resolved, then maintain the ferret on 50 mg/kg once q7–30d as necessary.
- Mitotane must be compounded in 50-mg aliquots in #1 capsules. Capsules must be administered intact. Have owners coat the capsules with vegetable oil, push into the back of the throat, and follow with a palatable liquid or blenderized cat food to promote swallowing.
- The most common side effect of mitotane is hypoglycemia. Teach owners to recognize the signs of hypoglycemia, and have prednisone available at home. If side effects occur, discontinue mitotane and administer prednisone (1.0–1.25 mg) PO.
- If continuation of mitotane therapy is desired after a hypoglycemic crisis, administer concomitantly with prednisone (see Insulinoma).
- *Ketoconazole* is not effective in the treatment of adrenal disease in the ferret.

Surgical Therapy

Follow the adrenalectomy preoperative protocol described for dogs (see Chapter 33).

- Fast the ferret 4 to 6 hours preoperatively. Place an indwelling IV or IO catheter preoperatively, and administer fluids pre-, intra-, and postoperatively. If insulinoma is present concurrently treat and monitor appropriately.
- Perform a ventral midline laparotomy. Palpate and visualize both adrenal glands carefully. Normal adrenal glands are 5 to 8 mm × 2–3 mm in size, are pale pink in color, and are typically surrounded by fat.
- The left adrenal gland lies in a fat pad cranial to the left kidney. The right adrenal gland is located craniomedial to the right kidney under the caudate liver lobe adjacent to the vena cava. It may be necessary to transect the hepatorenal ligament to fully visualize and palpate this gland.
- Adrenal changes may be subtle, especially in younger ferrets and because the adrenal glands are surrounded by fat. Visual changes, such as dark circular lesions and small raised cysts, may be present instead of gross enlargement.
- One or both adrenal glands may be affected. If only the left adrenal gland is affected, removal is relatively straightforward. If the right adrenal gland is affected, removal can be difficult because of the gland's proximity to the vena cava and liver (see Chapter 33).
- If both adrenal glands are affected, remove the left adrenal gland and debulk the right adrenal gland. Bilateral adrenalectomy has been described in the ferret, but should be done with caution. Monitor postoperatively for development of acute adrenal hypocorticism. If acute AHC develops, treat as described for dogs (see Chapter 33).

▼ ***Key Point*** Always perform a complete abdominal exploratory. Observe and palpate the pancreas at surgery for insulinomas, which often are found concurrently with adrenal neoplasia.

Postoperative Care and Complications

- Monitor fasting serum glucose levels every 60 to 90 days during mitotane therapy and after adrenalectomy, even if no pancreatic nodules were evident during surgery.

Prognosis

- The prognosis following successful surgery is good. A full resolution of clinical signs can be expected in many cases.
- Recurrent or continued symptoms of adrenal gland disease may be associated with development of a tumor on the remaining adrenal gland, or recurrence of an adrenal tumor due to metastasis (which is rare).
- Even without treatment, ferrets may survive up to 2 years or longer after diagnosis, although the hair loss is generally progressive.
- Potential sequelae to chronic adrenal gland disease include prostatic disease, bone marrow suppression, or mechanical interference with the vena cava (right adrenal gland).

Pheochromocytoma

Pheochromocytomas are adrenal tumors that arise from the adrenal medulla and produce excessive amounts of catecholamines. Pheochromocytomas have been reported in ferrets, but are rare. Treatment of choice is surgical removal of the affected gland.

LYMPHOSARCOMA

Lymphosarcoma (lymphoma) is common in ferrets of all ages, and is similar in presentation to the disease in cats and dogs (see Chapter 27). Three presentations may occur in the ferret and include lymphosarcoma, lymphocytic, and lymphoblastic forms.

Etiology

- A viral etiology has been hypothesized.

Clinical Signs

Clinical signs are variable, depending on the form of lymphoma present and the organ system involved.

- *Lymphosarcoma*: Solid tissue tumors are present in the organs or lymph nodes.
- *Lymphocytic lymphoma*: Adult ferrets are most commonly affected. The course and survival time can be long. Peripheral lymphadenopathy is typically present and metastasis to visceral organs may occur. The neoplastic cell identified on cytology or histopathology is a mature, well-differentiated lymphocyte.
- *Lymphoblastic lymphoma*: Young ferrets are most commonly affected. Leukemia and neoplasia in visceral organs occur early in the course of this form of the disease. Large immature lymphocytes are noted on cytology or histopathology.
- *Other forms*: Cutaneous lymphoma may occur in the ferret.
- Clinical signs that may accompany any form of lymphoma include:
  - Inappetence, lethargy, splenomegaly, and weight loss despite a normal appetite
  - Dyspnea, tachypnea, and exercise intolerance
  - Peripheral lymphadenopathy and/or abnormal CBC
  - Acute collapse, often with pyrexia
  - Fever of unknown origin
  - Cutaneous masses
  - Chronic diarrhea and/or rectal prolapse
- Some ferrets are asymptomatic; lymphoma may be an incidental finding during evaluation for another medical problem.
- Lymphoma tends to be a more acute, fulminant disease in younger animals.

Diagnosis

The method of diagnosis depends on the organ system involved.

- Obtain a thorough history and physical examination.
- Perform a CBC, platelet count, and a serum biochemistry profile. If the ferret is anemic, perform a reticulocyte count.
- Often the CBC and differential WBC counts are not diagnostic for lymphoma. The CBC may be normal or may reveal an absolute or relative lymphocytosis. Anemia, leukopenia, and thrombocytopenia may be seen. Abnormal lymphocytes may occasionally appear in the differential count.
- Persistent absolute lymphocyte counts greater than 3500 or a relative lymphocytosis (>60%) are considered suspicious; repeat the CBC in 4 to 6 weeks and perform a bone marrow biopsy and/or lymph node biopsy if the CBC results are repeatable or if lymphadenopathy is present.
- The serum chemistry profile may disclose elevated liver enzymes if the liver is involved; paraneoplastic syndromes are uncommon in the ferret.
- Perform thoracic and abdominal radiography and ultrasonography to evaluate for intra-thoracic and intra-abdominal masses.
- Perform fine-needle aspiration or biopsy of affected tissues for histological and cytological examination. Fine-needle aspiration of the spleen is usually inconclusive.
- Lymph node biopsy is often the most helpful diagnostic tool for diagnosis of lymphoma. If possible, biopsy an enlarged lymph node. When lymphadenopathy is not present, biopsy the popliteal lymphnode. The popliteal lymph node is the most accessible peripheral node for biopsy. Avoid biopsy of intra-abdominal lymph nodes if possible.
- Perform bone marrow aspiration to identify infiltration by neoplastic cells and the disease (see "Clinical Techniques").

Treatment

Splenectomy

- If the spleen is involved, perform a splenectomy (see Chapter 25) to reduce the overall tumor load.

Chemotherapy

Chemotherapy for lymphoma may be successful (approximately 10% remission rate). In general, protocols have been adapted from feline medicine (see Chapters 26 and 27).

- Success of chemotherapy may be affected by the age of the ferret, concurrent disease (e.g., adrenal gland disease, insulinoma), concurrent medication, inappropriate use of and resistance to chemotherapeutic agents (ferrets treated with prednisone prior to chemotherapy), and the type of lymphoma present.
- Ferrets with bone marrow involvement or with solid tumors involving organs typically have a poor prognosis.
- Longer periods of remission tend to occur in individuals with adult onset or lymphocytic lymphoma.
- IV chemotherapeutic agents are given via butterfly catheter or small-gauge needle with the ferret under

Table 175-5. CHEMOTHERAPY PROTOCOL II FOR LYMPHOMA*

Week	Drug	Dose
1	Vincristine	0.07 mg/kg, IV
	Asparaginase	400 IU/kg, IP
	Prednisone	1 mg/kg, PO, q24h and continued throughout therapy
2	Cyclophosphamide	10 mg/kg, SC
3	Doxorubicin	1 mg/kg, IV
4–6	As weeks 1–3 above but discontinue asparaginase	
8	Vincristine	0.07 mg/kg, IV
10	Cyclophosphamide	10 mg/kg, SC
12	Vincristine	0.07 mg/kg, IV
14	Methotrexate	0.5 mg/kg, IV

IV, intravenously; IP, intraperitoneally; PO, per os; SC, subcutaneously.
*Protocol is continued in sequence biweekly after week 14.
From Rosenthal KE: Ferrets. Vet Clin North Am 24:19–20, 1994.

sedation; face-mask administration of isoflurane is the most convenient and rapid method of sedation.
- One chemotherapy protocol is outlined in Table 175-5.

▼ ***Key Point*** Monitor the CBC weekly. If the WBC falls below 2000 WBC/µl, or the RBC falls below 4 × 10^6/µl discontinue vincristine for 1 week or more until the WBC count increases to at least 3000 WBC/µl.

- Palliative therapy may be attempted by administering oral prednisone (2.2 mg/kg) PO q24h.
- Supportive care is important (see "Nutritional Support for Insulinoma").
- Consider referral to an oncologist if experience with chemotherapeutic agents is limited.

OTHER TYPES OF NEOPLASIA

- *Chordoma:* Chordomas are tumors that arise from notochord remnants. Tumors occur most often at the tip of the tail, but may occur in the cervical region as well.
- *GIT:* Gastric adenocarcinoma.
- *Reproductive tract:* Tumors include granulosa cell tumors, luteomas, and leiomyomas in intact females and in remnant tissue in spayed females. Sertoli cell tumors have been reported in intact males.
- *Skin and Subcutis:* See Dermatologic Diseases in this chapter.
- Other tumors reported in ferrets include chondroma, chondrosarcoma, fibroma, fibrosarcoma, hepatic adenocarcinoma, hemangioma, hemangiosarcoma, mast cell tumor, mesothelioma, osteoma, osteosarcoma, schwannoma, squamous cell carcinoma, thymoma, and renal and pancreatic carcinomas.

Dermatologic Diseases

SEASONAL CHANGES IN THE SKIN AND HAIRCOAT

Ferrets may experience dramatic seasonal changes in the haircoat triggered by photoperiod changes. This change is most apparent in the intact animal. If one is unfamiliar with these changes, normal coat changes may be interpreted incorrectly as a medical problem.

▼ ***Key Point*** Individual animals may exhibit different patterns of coat change each successive year.

Haircoat

- A normal, diffuse, gradual thinning of the coat typically occurs in the spring when the photoperiod is increasing and continues through the summer. The coat typically becomes shorter and darker at this time, and the face mask may appear or disappear. Focal alopecia should not be present.
- Some ferrets may experience a dramatic 1-day loss of the undercoat.
- A normal, but dramatic, loss of body weight (up to 40%) may occur at this time as well.
- Hair growth will reverse in the fall and winter. Coats typically become longer, thicker, and lighter. Body weight may change (up to 40%) as well.
- Females in estrus and males "in season" may show an even more marked hair loss but should not have areas of alopecia.
- Males typically lose hair in the inguinal area because of constant rubbing to mark territory; the mid- and caudal abdomen is often wet with urine.
- Neutered ferrets or ferrets kept under artificial lighting conditions often experience no coat changes.
- Neutering or spaying may cause temporary, diffuse alopecia hair thinning postoperatively, particularly if the animal was reproductively active at the time of surgery. The preoperative color pattern may not return.
- At any time of the year, regrowth of hair that has been shaved for medical procedures is slow. This is particularly true in the winter and summer when no active hair growth is occurring.

Skin

- Hair regrowth (regardless of the cause of alopecia) is often preceded by a blue to purple discoloration of the skin that can alarm the owner. This discoloration

is caused by new hairs growing through the dermis, and is most noticeable on the abdomen and face.
- Intact jills may exhibit a bluish discoloration of the skin during estrus. If ovariohysterectomy is performed while a jill is in estrus, this discoloration may occur approximately 10 days postoperatively.
- Pseudonails associated with hyperkeratosis of the footpads may occur in ferrets older than 2 years of age that are housed on carpet or linoleum surfaces. Trim pseudonails as necessary. Rub a small amount of petroleum jelly or vitamin E oil into the pads daily to help prevent lesions.

INFECTIOUS DISEASES

Bacterial Infections

Cutaneous bacterial infections in ferrets are typically manifested as abscesses or as a diffuse, ulcerative pyoderma.

Abscesses

- Abscesses may develop secondary to puncture wounds, bites, or may develop in the inguinal fat after traumatic injury (e.g., being stepped on). For diagnosis and treatment of abscesses, see "Infectious Diseases."

Ulcerative Pyoderma

Ulcerative pyoderma is the second most commonly encountered form of bacterial dermatitis in the ferret.

Etiology

- Various bacteria can cause ulcerative pyoderma. The most common agents are *Staphylococcus* and *Streptococcus* spp.

Clinical Signs

- Focal alopecia with diffusely hyperemic, thickened, ulcerated skin may occur over any area of the body.

Diagnosis

- Perform a cutaneous punch biopsy (see Chapter 37) to rule out diffuse cutaneous mast cell tumor, which may have a similar gross appearance.
- Perform bacterial culture and sensitivity testing.

Treatment

- Administer systemic antibiotics based on culture and sensitivity testing. Antibiotics effective in the treatment of pyoderma in ferrets often include amoxicillin-clavulanate (Clavamox, SmithKline) (13–25 mg/kg) q12h PO and cephalosporins (use feline dosages).
- Topical treatments include twice-weekly cleansing with an antibacterial shampoo containing chlorhexidine or benzoyl peroxide. Daily application of an antibacterial cream may be beneficial if the lesion is small and localized.

Canine Distemper Virus Infection

Dermatologic lesions are quite prominent with CDV infection in ferrets.

- Dermatologic signs typically begin with hyperemia around the lips, chin, eyes, and sometimes the inguinal area. With time, crusts and skin thickening may appear.
- Hyperkeratosis of the foot pads occurs as the disease progresses.
- See Infectious Diseases in this chapter for a detailed discussion of CDV in ferrets; also see Chapter 13 for a discussion of CDV in dogs.

Dermatophytosis

- *Microsporum canis* and *Trichophyton mentagrophytes* are the most common causes of superficial mycotic infections in the ferret.
- See "Infectious Diseases" in this chapter for diagnosis and treatment.

EXTERNAL PARASITES

Fleas

- Flea infestation may be encountered in pet ferrets. Clinical signs are similar to those seen in cats (see Chapter 45).

Treatment

- Flea shampoos, dips, or powders containing pyrethrin may be used. Products containing lindane or organophosphates are not recommended for use in the ferret.
- Imidacloprid (Advantage, Bayer Corporation, Shawnee Mission, KS) (0.4ml) topically every 3 weeks has been reported to be effective. No adverse effects have been noted. This drug may be used in conjunction with lufenuron.
- Lufenuron (Program, Norvartis Animal Health, Greensboro, NC) (45 mg) PO every 4 weeks has been anecdotally reported to be effective. Advise clients that there is a 6- to 8–week period before flea numbers are observed to decline.
- Fipronil (Frontline, Merial LTD., Iselin, NJ). Half the cat dose has been anecdotally reported to be effective. This drug may be used in conjunction with lufenuron.
- Selamectin (Revolution, Pfizer, New York, NY). Administration of the cat dosage has been anecdotally reported to be effective.

- Flea collars are not recommended because they come off easily and small pieces can be ingested.
- Treat the environment for fleas.

Ear Mites

Ear mite infection in ferrets is caused by *Otodectes cyanotis,* the same parasite that infects cats and dogs.

Clinical Signs

- Ferrets rarely exhibit pruritis, even with heavy mite infestation.
- Ferrets normally have large volumes of dark reddish-brown ear wax present in the ear canal, which resembles the debris present with *O. cyanotis* infestation. If ear mite infestation is present, wax production may become excessive and cause occlusion of the external ear canal.
- *O. cyanotis* infestation may be accompanied by secondary bacterial infection, leading to otitis media or otitis interna. Neurological signs such as head tilt and circling may occur (see Chapter 61 for techniques for the management of otitis media in cats).
- When chronic ear mite infestation is present, lichenification and a bluish pigment may appear on the inner surface of the pinnae. These changes are caused by a response to chronic irritation, and usually regress after treatment.
- Rarely, *O. cyanotis* may colonize other parts of the body.

Diagnosis

- Examine all ferrets for ear mites; the incidence of infestation is high in some populations.
- Mites in the ear canal can often be visualized using an otoscope; however, otoscopic examination is often difficult because of the uncooperative nature of the patient and small size of the ear canal.
- Confirm the diagnosis by microscopic examination of ear debris.

Treatment

- Thoroughly clean the ears.
- Administer ivermectin (Ivomec, Merck-Sharp & Dohme Agvet), (1 mg/kg) divided into two doses. Instill one dose into each ear. Repeat in 2 weeks.
- Tresaderm (Merck Agvet, Rahway, NJ) may be used to treat ear mites in ferrets. Administer 2 drops in each ear q24h for 7 days, stop for 7 days, then repeat. This medication has been reported to be effective in treatment of ear mites in the ferret.
- Selamectin may be used for treatment of ear mites in the ferret. Use at the dose described for treatment of fleas.
- Bathe the ferret within 24 to 48 hours after treatment. Wash all bedding and treat all other potential hosts in the household (see Chapter 59).
- Topical treatments may not be effective due to the narrow size of the ear canal, and patient resistance to treatment.
- Persistent infections may be due to the presence of ear mites on the body, or failure to deliver the topical agent effectively. In such cases, parenteral administration of ivermectin (0.5 mg/kg) SC every 7 to 10 days for 2 treatments may be necessary. Do not use topical and parenteral ivermectin together.

Sarcoptic Mange

Etiology

Sarcoptes scabiei mites are transmissible between dogs and ferrets via contact with the infected hosts or their bedding. (See Chapter 44 for discussion about sarcoptic mange in dogs and cats.)

Clinical Signs

- Lesions are typically confined to the feet, which become hyperemic, swollen, and intensely pruritic. Crusting often occurs around the nails, and in severe cases the nails may slough.
- Generalized alopecia, accompanied by intense pruritis, occurs rarely.

Diagnosis

- A positive diagnosis is based on clinical signs, exclusion of differential diagnoses, and positive skin scrapings obtained from several sites (false negative results do occur).
- A common differential diagnosis is contact allergy. Similar lesions have been observed in ferrets housed on plastic-floor cages. These lesions resolve when the cage bottom is changed to wire or wood.

Treatment

- Advise clients of the zoonotic potential of this parasite.
- Treatment may need to be based on differential diagnoses; mites may be difficult to identify on skin scrapings.
- Administer ivermectin (0.5 mg/kg) SC every 2 weeks for three treatments.
- Lime sulfur dips may be used instead of ivermectin. Dip ferrets in 2% lime sulfur every 7 days until signs have resolved for 2 weeks.
- Wash all bedding and treat all potential contact hosts in the household.

Demodectic Mange

Etiology

Demodicosis is rare in the ferret.

Clinical Signs

- Otitis externa has been associated with demodicosis. This may be the only presenting sign.
- Localized alopecia accompanied by pruritis may occur.

Diagnosis

- Mites may be identified on routine skin scrapings and examination of ear canal debris.

Treatment

- Treatment can be difficult. Use ivermectin at the daily dose described for dogs (see Chapter 43).
- Do not use mitotane.

ENDOCRINE ALOPECIA

Tail Alopecia

Etiology

The etiology of tail alopecia in the ferret is unknown but is suspected to be caused by hormonal fluctuations because the disease responds to changes in the photoperiod. Hair loss occurs most commonly at the time of the fall molt, when the photoperiod is becoming shorter, but may be seen any time of year under artificial lighting conditions. Hair regrowth usually occurs in 2–8 weeks. The same pattern of alopecia is not always repeated annually.

Clinical Signs

- Hair loss, ranging from diffuse hair thinning to complete alopecia, occurs from the base of the tail to the tip.

▼ ***Key Point*** Alopecia occurs only on the tail. If alopecia extends to the body, suspect another form of endocrine disease, such as adrenal gland disease.

- Comedones and a brown, waxy scale may accompany the alopecia.

Diagnosis

- Diagnosis is based on clinical signs.
- Differential diagnoses include the early stages of adrenal gland disease; however, hair loss on the body typically occurs as well when this condition is present.

Treatment

- No treatment is necessary. Hair regrowth will occur when the photoperiod changes.
- Artificially lengthening the photoperiod may speed hair regrowth, although not reliably.
- If the tail exhibits excessive amounts of waxy scaling or comedones, clean the tail weekly with a mild shampoo.

Estrus Alopecia

Alopecia may be seen in intact females that have been in estrus for 1 month or longer.

Clinical Signs

- Bilaterally symmetrical hair loss over the shoulders and flanks, which eventually progresses to involve the entire body. Hairs epilate easily, and the underlying skin appears normal.
- A grossly enlarged vulva indicates a state of estrus. Be aware that the ferret also may be anemic and thrombocytopenic (see "Anemia").

Diagnosis

- Diagnosis is based on clinical signs in an intact female.

Treatment

- Perform an ovariohysterectomy (see Chapter 91) if the ferret is stable enough for the procedure, or induce ovulation with HCG (see "Termination of Estrus"; "Anemia").
- Hair regrowth will recur rapidly after surgery or ovulation; however, changes in hair length, color, or thickness are common.

Adrenal Gland Disease

- Bilateral, symmetrical alopecia is a common sign of adrenal disease in the ferret (see "Adrenal Gland Disease").

Hypothyroidism

- Hypothyroidism has not been documented in ferrets.

NEOPLASIA

Neoplasia of the skin is the third most common neoplasia reported in the ferret and commonly occurs in ferrets 1 year of age and older. Complete removal of skin masses using wide surgical excision followed by histopathology is recommended.

Mast Cell Tumors

Mast cell tumors are the most common skin masses encountered and are typically benign in the ferret.

- Individual tumors typically appear as slightly raised, flat, button-like cutaneous masses ranging in size from 2 to 10 mm. The tumors are often tan in color or may be hyperemic with a dark flaky crust. Tumors may also appear as raised, ulcerated areas, or as diffuse areas of erythema and crusting. Pruritis may be present at the site.
- Mast cell tumors have occasionally been associated with diffuse or generalized areas of alopecia that resolve with surgical removal of the tumor.
- Metastasis is rare but has been reported in the lung and gallbladder (see Chapter 28 for information about mast cell tumors in dogs and cats).

Sebaceous Epitheliomas

- These tumors may also be referred to as haral cell tumors or sebaceous adenomas and are common in the ferret.
- Tumors may appear as wart-like, ulcerated, or cystic masses ranging in size from 0.5 to 2 cm.
- Excision is usually curative. Recurrence is rare, and metastasis is not reported.

Other Neoplasms

- Other, less common neoplasms of the skin and subcutaneous tissues include: basal cell carcinoma, basi-squamo-sebaceous carcinoma, hemangioma, histiocytoma, leiomyosarcoma, lymphoma, myxosarcoma, neurofibrosarcoma, perianal gland adenocarcinoma, sebaceous gland adenocarcinoma, and squamous cell carcinoma.
- Adenocarcinomas often metastasize to regional lymph nodes, liver, and lungs.
- Diagnosis, treatment, and prognosis for these tumors in ferrets are the same as for dogs and cats (see Chapter 30).

Cardiovascular Diseases

CHARACTERISTICS OF THE NORMAL FERRET HEART

- Cardiac auscultation is centered more caudally in the thorax than are auscultations in cats.
- The heart extends from the sixth rib to the caudal border of the seventh or eighth rib (compared with cats, where it extends from the second to the sixth rib).
- The heart rate averages 180 to 250 beats per minute.
- A pronounced sinus arrhythmia and pronounced bradycardia are common during auscultation.
- Cardiac disease is relatively common in the ferret. Quality of life and long-term prognosis for ferrets with cardiac disease depends on the type and severity of cardiac disease present, and the initial response to treatment. Many ferrets do well for months on the appropriate medications.

Congestive Heart Failure

Clinical Signs

- Ferrets appear to compensate well for early cardiac insufficiency, perhaps because a slight decrease in activity is not readily apparent to owners.
- Ferrets with congestive heart failure (CHF) may present with clinical signs that resemble symptoms associated with other disease entities, such as anorexia, ascites, coughing, dehydration, dyspnea, exercise intolerance, generalized weakness, hindlimb weakness, hypothermia, lethargy, tachypnea, and weight loss.
- Pale or cyanotic mucus membranes and a prolonged capillary refill time (CRT) may be noted on physical examination.
- Jugular pulses may be present when right-sided CHF is present.
- Femoral pulses may be weak, irregular, or normal.
- Ascites, hepatomegaly, or splenomegaly may be noted on abdominal palpation.
- Murmurs may be noted on auscultation, and are typically associated with valvular insufficiency.

Diagnosis

- History and physical examination findings are important in the diagnosis of heart disease.
- Perform a complete physical examination, including auscultation of the heart, and evaluation of the capillary refill time. Observe for tachypnea or dyspnea and auscult the lungs. Palpate the abdomen and examine for ascites.

▼ ***Key Point*** Proceed with further testing only if the ferret is stable. Otherwise, administer furosemide and oxygen therapy.

- Diagnosis requires information obtained by radiography, ECG, and echocardiography.
- Obtain whole-body radiographs. The cardiac silhouette typically appears enlarged and globoid in shape with rounded right and left ventricles. Ascites, hepatomegaly, pleural effusion, and pulmonary edema may be present as well.
- Evaluate a CBC, serum biochemical profile, and urinalysis to determine if azotemia, electrolyte abnormalities, or other systemic diseases are present. Perform a heartworm test if the history is supportive for potential exposure.
- If thoracic or abdominal effusion is present, perform thoraco- or abdominocentesis and submit fluid for

Table 175-6. ELECTROCARDIOGRAPHIC DATA FOR 52 CLINICALLY NORMAL FERRETS*

Parameter	Mean ± SD (Range)† (n = 25)	Value‡ (n = 27)
Age (mo)	10–20	Average, 5.2
Male:female ratio	All male	1.25
Body weight (kg)	1.4 ± 0.2	NA
Heart rate (beats/min)	196 ± 26.5 (140–240)	233 ± 22
Rhythm		
Normal sinus	NA	67%
Sinus arrhythmia	NA	33%
Frontal plane MEA (degrees)	86.13 ± 2.5 (79.6–90)	77.22 ± 12
Lead II		
P amplitude (mV)	NA	0.122 ± 0.007
P duration(s)	NA	0.024 ± 0.004
PR interval(s)	0.056 ± 0.0086 (0.04–0.08)	0.047 ± 0.003
QRS duration(s)	0.044 ± 0.0079 (0.035–0.06)	0.043 ± 0.003
R amplitude (mV)	2.21 ± 0.42 (1.4–3)	1.46 ± 0.84
QT interval(s)	0.109 ± 0.018 (0.08–0.14)	0.12 ± 0.04

NA, not available; MEA, mean electrical axis.
*All ferrets were sedated with ketamine-xylazine.
†Data from Bone L, Battles AH, Goldfarb RD, et al: Electrocardiographic values from clinically normal, anesthetized ferrets *(Mustela putorius furo)*. Am J Vet Res 49:1884–1887, 1988.
‡Data adapted from Fox JG: Biology and diseases of the ferret. Philadelphia, Lea & Febiger, 1988, p 170; and Edwards J: Unpublished data, 1987.

cytologic examination. Perform centesis as described for cats; take into consideration the relatively caudal position of the heart in ferrets. Sedation is usually necessary. A modified transudate is typically associated with CHF.

- Perform standard six-lead electrocardiography (ECG) if possible (Table 175-6 lists normal ferret ECG parameters). Sedation may be necessary. Electrocardiography may reveal atrial premature contractions, atrial tachycardia, atrial fibrillation, ventricular premature contractions, and ventricular tachycardia.

▼ ***Key Point*** Sedation with isoflurane is recommended when necessary. Sedation with ketamine or a ketamine-diazepam combination raises the heart rate. The heart rate tends to decrease with ketamine-xylazine sedation; therefore, avoid using xylazine in ferrets with suspected cardiac disease.

- Echocardiography is the most useful diagnostic tool in the ferret. The same echocardiographic changes observed in the dog and cat are seen in the ferret. (Table 175-7).

Table 175-7. MEAN ECHOCARDIOGRAPHIC VALUES FOR 34 NORMAL ADULT FERRETS

Parameter	Mean Value
Left ventricle, end-diastolic	11.0 mm
Left ventricle, end-systolic	6.4 mm
Left ventricular posterior or free wall	3.3 mm
Fractional shortening	42%
End-point septal separation	None

From Sitinas N, Beeber N, Skeels M: Unpublished data, 1992.

Treatment

▼ ***Key Point*** Treatment of acute CHF should focus on improving oxygenation and reducing cardiac preload and afterload.

- Place the ferret in an oxygen-rich environment. Administer supportive care such as subcutaneous fluids (e.g. 0.45% saline and 2.5% dextrose), and provide nutritional support for ferrets that are anorexic.
- Administer diuretics such as furosemide (1–4 mg/kg) IM or IV bid–tid.
- Nitroglycerin 2% ointment may be applied to the skin in the axilla, inguinal area, or on a hairless body surface.
- Angiotensin-converting enzyme (ACE) inhibitors may be given to reduce afterload and preload. Give enalapril (Enacard, Merck Agvet Division) (0.5 mg/kg) PO q48h, then titrate up to q24h if possible. ACE inhibitors may cause hypotension in ferrets, titrate to effect.

- When diuretics and ACE inhibitors are used together it is important to monitor for azotemia.
- Perform thoracocentesis or abdominocentesis when indicated.
- Monitor body weight, CRT, heart rate and rhythm, hydration status, mucous membrane color, respiratory rate, respiratory effort, BUN, creatinine, and serum electrolytes.

▼ ***Key Point*** Chronic therapy typically includes the use of ACE inhibitors, and diuretics with the addition of digoxin in ferrets with dilated cardiomyopathy. Whenever possible, try to titrate the diuretic dose to the lowest possible dose without recurrence of pleural effusion or pulmonary edema.

- Administer digoxin elixir (0.01 mg/kg) PO sid–bid to ferrets with dilated cardiomyopathy.
- Side effects associated with digoxin include anorexia, arrhythmias, diarrhea, lethargy, and vomiting.
- Serum digoxin levels should be monitored every 4 to 8 weeks. Normal values have not been published for the ferret; reference values for dogs and cats are used for interpretation.
- Use of antiarrhythmic drugs such as atenolol or diltiazem is not well documented in the ferrets, but may be useful in the treatment of ferrets with hypertrophic cardiomyopathy.
- Salt-free diets may be beneficial; however, they are often unpalatable to ferrets. Instruct the owner to avoid feeding snacks, treats, or food items with a high-salt content.
- Management includes periodic reevaluation of heart rate and rhythm, serum electrolytes, and renal values. Radiographs should be used to monitor for the development of pulmonary edema or changes in the cardiac silhouette. ECG and echocardiography should be repeated periodically as well.

Cardiomyopathy

Cardiomyopathy may occur in ferrets 2 years of age or older. Dilated (congestive) and hypertrophic forms can occur; the dilated form is more common.

Dilated Cardiomyopathy

Etiology

The cause of dilated cardiomyopathy (DCM) in the ferret is unknown.

Clinical Signs

- Abdominal enlargement secondary to ascites, anorexia, dyspnea, lethargy, and weight loss are often noted.
- Ascites, heart murmur, pale mucous membranes, tachycardia, and weakness may be noted on physical examination.
- Moist rales and increased respiratory sounds may be noted when pulmonary edema is present.
- Pleural effusion may be present, and may cause an increased inspiratory effort. The heart may sound muffled on auscultation.
- Coughing generally is not noted.

Diagnosis

- See the CHF section in this chapter.

Treatment

- Treatment is the same as that described for CHF.
- Taurine supplementation does not appear to have any effect on DCM in the ferret.

Follow-Up Care

- See the CHF section in this chapter.

Hypertrophic Cardiomyopathy

Etiology

The cause of hypertrophic cardiomyopathy (HCM) is unknown.

Clinical Signs

- Clinical signs may be compatible with those described for CHF or DCM (see above).
- Other clinical signs are similar to those described for the cat, and include acute onset of congestive heart failure and/or sudden death.

Diagnosis

- Follow the same guidelines described for DCM.
- Include HCM on the rule-out list when evidence of cardiac disease is noted on the physical examination or diagnostic evaluation.
- Radiographs may not be beneficial in the diagnosis of HCM.
- Echocardiography should be used for definitive diagnosis.

Treatment

- Treatment should be aimed toward alleviating signs of CHF and improving the diastolic efficiency of the left ventricle.
- Administer beta-adrenergic blocking drugs such as atenolol (3.125–6.25 mg) PO sid. Titrate to effect.
- Administer calcium channel blockers such as diltiazem (3.75–7.5 mg) PO bid. Titrate to effect.
- Diuretics are indicated if symptoms of CHF are present (see above).

Follow-Up Care

- Follow-up is the same as that described for CHF and DCM.

Heartworm Disease

Natural and experimental heartworm infections have been reported in ferrets (see Chapter 152). The clinical presentation of heartworm disease typically resembles that of cats; however, the life cycle of *Dirofilaria immitis* in ferrets is similar to the life cycle present in the dog. Reported adult worm burdens range from 1 to 10. The presence of only one adult worm in the heart can be lethal.

Etiology

- Heartworm disease is caused by the canine heartworm *Dirofilaria immitis,* a filarial nematode that is transmitted via mosquitoes.
- Ferrets that are housed outdoors in endemic areas are at greatest risk of infection; however, ferrets kept indoors also can become infected.

Clinical Signs

- Clinical signs include coughing, dyspnea, hepatomegaly, inappetence, lethargy, melena, weakness, and symptoms associated with right-sided CHF (pulmonary edema, pleural effusion, ascites). Sudden death due to pulmonary artery obstruction may also occur.
- Microfilaria may be present in the blood of approximately 50% of infected ferrets.

Diagnosis

- Diagnosis is based on the history, clinical signs, heartworm test results, radiographs, and echocardiography.
- If the history is compatible with cardiac failure, inquire about possible mosquito exposure.
- Physical examination findings resemble those of heart failure (see above).

▼ ***Key Point*** Minimize stress in ferrets suspected of heartworm disease. If symptoms of congestive heart failure are present, delay further diagnostic evaluation until the patient is stabilized (see "Treatment of Congestive Heart Failure").

- Obtain whole body radiographs. Thoracic changes may include cardiomegaly with enlargement of the right atrium, caudal vena cava, and right ventricle. Pleural edema and pleural effusion may be present as well. Radiographic changes in the peripheral pulmonary arteries are not typically noted because the worms tend to reside in the right side of the heart and in the main pulmonary artery. Abdominal changes often include hepatomegaly, splenomegaly, and ascites.
- If possible, draw blood for the modified Knott's test for microfilaria. Microfilaria are identified in approximately 50% of infected ferrets.
- Submit blood for an enzyme-linked immunosorbent assay (ELISA) for *Dirofilaria* antigen. Antigen is produced by adult female heartworms; there is a potential for false negative test results in ferrets with low worm burdens. A commercial assay (Snap Heartworm Antigen Test Kit; IDEXX Laboratories Inc., Portland, ME) has been used to detect heartworm infection in the ferret.
- Perform a CBC, serum biochemical profile, and urinalysis to rule out the presence of other systemic diseases.
- If pleural or abdominal effusion is present, submit fluid for cytology. A modified transudate is typically noted when CHF is present.
- Echocardiography may be used to visualize heartworm(s) in the pulmonary artery, right ventricle, and right atrium; dilation of the right ventricle and right atrium may be assessed as well. Doppler echocardiography may be used to evaluate the patient for the presence of pulmonary hypertension.

Treatment

- Treatment of heartworm disease in ferrets is difficult. Success is dependent on early diagnosis, diligent supportive care, and long-term antithrombotic therapy in conjunction with adulticide therapy.
- If signs of CHF are present, treat this first, and stabilize the patient (see the CHF section).
- If the patient is symptomatic and microfilaremia positive:
  - Administer microfilaricidal therapy: Ivermectin (50 µg/kg) SC every 30 days until clinical signs and microfilaremia resolve.
  - Follow with adulticide therapy: melarsomine (Immiticide, Rhone Merieux, Athens, GA) using a two-stage protocol:
    Stage 1: Administer a single dose of melarsomine (2.5 mg/kg) IM.
    Stage 2: 1 month later, administer two injections of melarsomine (2.5 mg/kg) IM given 24 hours apart.
- Transient swelling at the site of injection is common.
- Administer prednisone (0.5 mg/kg) PO sid–tid during adulticide treatment and for as long as clinical signs persist.
- If pleural effusion is present administer diuretics (see the CHF section).
- Cage confinement is important for 4 to 6 weeks after treatment.
- Perform a post-treatment ELISA for heartworm antigen 3 months after adulticide therapy. Repeat every 30 days if results are positive. Most ferrets become seronegative 4 months after treatment.
- Begin heartworm prevention 1 month after adulticide treatment.
- If ferrets are microfilaria negative, administer adulticide therapy as described above.

Prevention

▼ *Key Point* Because of the high mortality associated with heartworm disease, recommend preventive therapy for all ferrets in heartworm-endemic areas.

- Ivermectin may be given as preventive therapy beginning 1 month before and continuing 2 months after mosquito season. Liquid ivermectin 1% may be diluted in propylene glycol (0.3 ml ivermectin in 30 ml propylene glycol) and administered at a dose of (0.2 ml/kg) PO every month. This solution must be stored in an amber glass bottle out of sunlight. Feline Heartguard (Merck Agvet) may be administered using the dose appropriate for a 1- to 5-lb cat.
- If possible, house all ferrets in endemic areas within structures with mosquito-proof screening.
- Follow the same recommended guidelines for heartworm prevention in dogs and cats.

Valvular Heart Disease

Valvular heart disease may occur in ferrets >3 years of age.

Clinical Signs

- Clinical signs depend on the severity of the underlying disease process.
- Mitral regurgitation may be ausculted as a systolic murmur in the left apical region.
- Tricuspid regurgitation is ausculted in the right parasternal region.
- Dyspnea and moist rales may be noted on auscultation of the lungs if CHF is present.

Diagnosis

- Obtain thoracic radiographs to evaluate the size of the heart and to determine if CHF is present. Pulmonary edema typically appears as a mixed alveolar and interstitial pattern in the caudodorsal lung lobes.
- Electrocardiography (ECG) may be normal or may demonstrate evidence of atrial arrhythmias.
- Echocardiography typically demonstrates thickening of affected valves and atrial enlargement.
- Doppler echocardiography may be used to identify and quantify the degree of regurgitation present. Aortic regurgitation is often noted in ferrets and is considered an incidental finding.

Treatment

- Treatment is recommended if CHF is present, or if cardiac enlargement is significant (see the CHF section).

Myocarditis

Myocarditis occurs when the myocardium is infiltrated with inflammatory cells, resulting in the development of reduced myocardial function, arrhythmias, and replacement of the normal myocardial tissue with fibrous tissue.

Etiology

- Causes include sepsis, systemic vasculitis, parasitic, bacterial or viral infection, and autoimmune disorders.
- Aleutian disease can cause fibrinoid necrosis and mononuclear cell infiltration of the arterioles of the heart.

Clinical Signs

- Antemortem diagnosis is difficult.
- Suspect myocarditis if arrhythmia and/or acute myocardial dysfunction is noted in association with multisystemic illness.
- Definitive diagnosis is made by histopathological evaluation of affected myocardial tissue.

Treatment

- Treatment should be directed at identifying and treating the underlying systemic disease.
- Cardiovascular support should be provided and may include the use of diuretics or antiarrhythmic drugs (see the CHF section).

Other Cardiac Diseases

As clinical experience with pet ferrets increases, other types of cardiac disease are likely to be recognized. Third-degree heart block (of unknown etiology) and various forms of valvular disease, including mitral and tricuspid insufficiency and endocarditis, have been seen in ferrets.

- The approach to these conditions in ferrets is the same as for other companion animals; use the drug dosages given previously for cardiac myopathies.

Gastrointestinal System

CHARACTERISTICS OF THE NORMAL FERRET DIGESTIVE TRACT

Teeth

- The permanent teeth erupt between 50 and 74 days of age.
- The dental formula is 2 (I3/3, C1/1, Pm3/3, M1/2).
- The third upper premolar (carnassial tooth) has three roots. The second lower molar has one root. All other premolars and molars have two roots.

Gastrointestinal Tract

- The ferret is an obligate carnivore with a simple stomach, short intestinal tract, no cecum or ileocolic valve, and a short colon.

- The duodenum terminates at the jejunoileum; there is no gross anatomic distinction between the jejunum and the ileum.
- The junction of the jejunoileum and the colon is determined by evaluating the pattern of anastomosis between the jejunal artery and the ileocolic artery.
- GI transit time is approximately 3 to 4 hours.

Anal Sacs

- The anal sacs are located between the external and internal anal sphincter muscles at 4 and 8 o'clock. The ducts are located near the mucocutaneous junction.

Diet

- The exact nutritional requirements of the ferret have not been determined.
- The diet of the ferret must contain predominantly animal protein and fat.
- Due to the short digestive tract and rapid GI transit time, the ferret requires a concentrated maintenance diet high in protein (30–35%) and fat (15–18%), and low in fiber. The protein quality should be 85% to 90% digestible.
- Breeding ferrets and kits may require diets higher in protein and fat.
- Meat, poultry, meat and poultry meals, and other animal-based proteins should appear first, then several more times on the food ingredient list.
- Complex carbohydrates (starch, fiber) are not readily digested by the ferret. High–fiber diets can induce a relative protein-calorie deficiency; the ferret cannot eat enough of a low-density food to meet its high maintenance requirements.
- Premium cat foods and ferret diets typically meet the ferret's nutritional requirements for growth and reproduction.
- Treats and supplements should not exceed more than 10% of the daily diet. Acceptable treats include meat baby foods, and moist cat or ferret diets. High–sugar or carbohydrate treats should be limited, especially if insulinoma is present.
- Fatty acid supplements should be given in measured amounts (a few drops per day). Administration of large quantities of fatty acid supplements may reduce the intake of the balanced diet.
- Canine diets should not be fed to ferrets; the protein, fat, and carbohydrate content is not appropriate, and the diets often contain high percentages of grain and vegetable matter.
- The long–term effect of formulated dry and canned diets on the long–term health of ferrets is controversial among some practitioners.
- Some practitioners feel that feeding commercial diets containing large quantities of plant-based ingredients contributes to the development of eosinophilic gastroenteritis, inflammatory bowel disease, insulinoma, urolithiasis, and general untriftiness. For example, most ferrets in the United States are fed dry kibbled diets, and the incidence of insulinoma is high. Many ferrets in Europe and Australia are fed whole prey items (e.g., a "natural diet), and the incidence of insulinoma is low.
- A correlation between diet and the development of certain diseases in ferrets is hypothetical at this time; however, this controversy demonstrates the need for longer–term diet studies in the ferret.

DENTAL DISEASE

- The canine teeth are often worn or broken at the tips due to biting and gnawing.
- Broken canine teeth typically are not painful unless the dental pulp is exposed.
- Dental tartar and periodontal disease are common in ferrets over 2 years of age.
- Soft, moist diets may predispose ferrets to the development of dental disease.
- Tartar typically accumulates first on the second and third upper premolars.
- Dental abscesses are not common, but may be noted, even in young ferrets.
- Follow the basic medical and surgical treatment principles described for dental diseases in dogs and cats (see Chapter 64).

SALIVARY MUCOCELE

- Ferrets have five major pairs of salivary glands: the parotid, submandibular, sublingual, molar, and zygomatic.
- Salivary mucocele occurs secondary to trauma or infection of a salivary gland.
- Salivary mucocele typically presents as a soft to firm swelling in the region of the orbit, oral commissure, or mandibular lymph node. Aspiration of the swelling often yields a clear to serosanguinous or mucinous fluid; microscopic examination demonstrates amorphous debris and occasional RBCs.
- Treatment of choice is surgical excision of the affected gland (see Chapter 64).
- Advise clients that recurrence is possible.

MEGAESOPHAGUS

Megaesophagus is rare in ferrets.

Etiology

- The etiology of megaesophagus in ferrets is unknown (see list of possible causes in dogs in Chapter 65).

Clinical Signs

- Clinical signs resemble those described for the dog and include: lethargy, anorexia, dysphagia, coughing, choking, dyspnea, weight loss, and regurgitation.
- Clients may indicate that the ferret vomits up large boluses of food.

Diagnosis

- Diagnosis may be based on clinical signs and radiographic evidence of megaesophagus.
- Obtain thoracic radiographs. The esophagus is often dilated and filled with air in the cervical and thoracic regions. Food may be present within the lumen of the esophagus.
- Perform a barium contrast study to delineate the esophageal mucosa and to identify potential mural lesions, strictures, or obstructions.
- Aspiration pneumonia may be visible radiographically.

Treatment

- Follow canine treatment protocols. The prognosis is poor; response to therapy is usually not successful.
- GI promotility agents such as metoclopramide (Reglan, AH Robins Company, Inc., Richmond VA) (0.2–1mg/kg) PO tid–qid may be helpful.
- Administer H2-receptor blocking drugs such as cimetidine, ranitidine (Zantac, Glaxo Pharmaceuticals, Research Triangle Park, NE), or famotidine (Pepcid AC, Johnson and Johnson, Fort Washington, PA).
- Administer antibiotics if indicated for aspiration pneumonia.
- Supportive care includes feeding high-calorie, high-protein slurried diets 3 to 4 times per day, and elevating the ferret for 15 to 30 minutes immediately after feeding.

NAUSEA AND VOMITING

- Ferrets, like other carnivores, are able to vomit.
- Differential diagnoses to consider for vomiting include esophageal and gastroenteric disorders (see below).
- Ferrets often demonstrate symptoms associated with nausea or vomiting when gastroenteritis, GI disease, gastric ulcers, *Helicobacter mustelae* gastritis, or GI foreign bodies are present. Hypoglycemia may cause signs of nausea as well (see discussion of Insulinoma in this chapter).
- Signs of nausea include hypersalivation and pawing at the mouth.
- Ferrets may demonstrate bruxism (grinding of the teeth) when abdominal discomfort is present.

GASTROINTESTINAL PARASITES

- GI parasites are uncommon in the ferret. Coccidiosis and giardiasis are occasionally seen. Nematodiasis is rare.
- Routine fecal testing is still recommended, especially in young animals and ferrets with diarrhea or rectal prolapse.
- Young ferrets with coccidiosis may have diarrhea and may be severely dehydrated.
- Cryptosporidiosis may occur in ferrets, but typically does not result in clinical disease. The zoonotic potential is unknown; however, it may be prudent to warn immunosuppressed owners of the potential for zoonosis.

Treatment

- Treat with appropriate anthelmentics following the protocols and dosages used for cats (see Chapter 69).

GASTRITIS, AND GASTRIC AND DUODENAL ULCERS

Gastric and duodenal ulcers have been documented in laboratory ferrets and reported occasionally in pet ferrets. Clinical signs are often vague, making the diagnosis difficult.

Etiology

- The etiology is unknown but may include stress, GI foreign body, *H. mustelae* gastritis, administration of ulcerogenic drugs, GI neoplasia, and azotemia secondary to renal disease.
- *H. mustelae* is similar to *H. pylori,* the bacteria associated with gastritis and ulceration in humans. *H. mustelae* infection in the ferret can be an incidental finding, or can induce gastritis, duodenitis, and GI ulceration.

Clinical Signs

- Gastritis and ulcers may be acute or chronic.
- Clinical signs include anorexia, lethargy, hypersalivation, bruxism (tooth grinding), weight loss, vomiting, and melena.

Diagnosis

- Presumptive diagnosis may be made based on the history and clinical signs.
- Perform a CBC and serum biochemistry profile to rule out systemic and metabolic disease.
- Obtain fasting whole-body radiographs to help rule out the presence of a GI foreign body or trichobezoar.

- A barium study may be used to demonstrate GI ulceration.
- Exploratory laparotomy/gastrotomy is often required for a definitive diagnosis.
- Diagnosis of *H. mustelae* gastritis is often a diagnosis of exclusion. Definitive diagnosis requires the finding of organisms along typical histological lesions on gastric biopsy specimens.

Treatment

- Debilitated, anorexic ferrets may require hospitalization for supportive care.
- If the patient is vomiting, withhold food for 6 to 12 hours. Administer IV fluids containing dextrose, and monitor for signs of hypoglycemia. When vomiting has resolved begin to offer small, bland meals.
- Feed small meals of a bland, moist diet tid–qid (see diet recommendations in "Insulinoma" section). Avoid feeding high-fiber dry foods.
- Administer broad spectrum antibiotics if the ferret is debilitated.
- Administer a gastric protectant. Options include:
  - Bismuth subsalicylate (Pepto Bismol, Procter & Gamble) (1 ml/kg) PO tid.
  - Sucralfate (Carafate, Marion Merrell Dow, Inc., Kansas City, MO) (100 mg/kg) PO tid–qid.
  - Systemic H_2-receptor antagonists such as cimetidine and famotidine.
  - Omeprazole (Prilosec, Astra Merck, Inc., Wayne PA) (_ the contents of a 10-mg capsule mixed with soft food) PO sid-bid.
- If H. mustelae infection is suspected, administer the following three drugs concurrently for at least 2 weeks ("triple therapy"):
  - Amoxicillin (10 mg/kg) PO, SC bid.
  - Metronidazole (20 mg/kg) PO bid.
  - Bismuth subsalicylate (Pepto-Bismol, Procter & Gamble) (see dosage information above).

GASTROINTESTINAL FOREIGN BODIES

GI obstruction caused by foreign body ingestion or hairballs is one of the most common problems in pet ferrets.

Etiology

- Foreign bodies typically occur in ferrets younger than 1 year of age; trichobezoars (hairballs) are common in ferrets older than 2 years of age.

▼ ***Key Point*** Suspect the presence of a GI foreign body in any young ferret presented for anorexia, even if no vomiting is reported.

- Rubber and foam objects are the most common foreign bodies. Obstruction with a hairball (older ferrets), cloth, or plant material also may occur.

Clinical Signs

- Lethargy, partial or total anorexia, hypersalivation, bruxism, pawing at the mouth, weight loss, and diarrhea are the most common clinical signs of GI foreign body. Hindlimb weakness, dehydration, and melena may be noted as well.
- Vomiting is uncommon; however, if the ferret is vomiting, be suspicious that a GI foreign body may be present.

Diagnosis

- Diagnosis is based on the history, physical examination findings, radiographs, or exploratory laparotomy.
- History: Identify possible types or causes of foreign body ingestion. Ask the owners if hairball preventative is used routinely.
- Physical Examination: Large gastric foreign bodies are often palpable. Small foreign bodies in the small intestine may be associated with localized pain.
- Obtain fasting (4–6 hours) plain whole body radiographs. Radiographs may reveal segmental ileus, and marked gaseous distention of the stomach and/or bowel. Occasionally a foreign body or trichobezoar can be identified.
- Obtain a GI barium contrast study to identify small foreign bodies and to rule out GI ulceration.
- Perform a CBC and serum biochemical panel to rule out hepatic lipidosis and other systemic diseases.

Treatment

Surgical removal is the treatment of choice. If the ferret is debilitated, begin supportive therapy, and perform surgery as soon as possible.

- Surgery: Follow routine preoperative, operative, and postoperative procedures for gastrotomy or enterotomy (see Chapters 68 and 70). Ferret tissues are more delicate than those of a puppy or kitten of equivalent weight. Use 4-0 or 5-0 suture material to close the GI tract.
- Perform gastric biopsy to rule-out underlying *H. mustelae* infection, and other GI diseases. Perform biopsy of the liver.
- Evaluate the entire abdominal cavity prior to closure. Older ferrets often have concurrent diseases such as insulinoma or adrenal gland disease.
- The prognosis following gastrotomy is good with prompt therapy.

Prevention

▼ ***Key Point*** Instruct owners to "ferret proof" the house if ferrets are allowed to roam. In particular, restrict access to rubber toys and rubber objects.

- To prevent trichobezoars, administer a feline hairball laxative product (2–4 cm) PO 2 to 3 times per week.

EPIZOOTIC CATARRHAL ENTERITIS

Epizootic catarrhal enteritis (ECE, "green slime disease") is a highly infectious diarrheal disease that first appeared in 1993.

Etiology

The etiological agent is thought to be a coronavirus. ECE can spread rapidly through a ferret population, often affecting 100% of ferrets within 48 hours. Histological examination of intestinal biopsy samples reveals lymphocytic enteritis with villous atrophy and blunting, and degeneration of the apical epithelium.

Clinical Signs

- The history often includes recent exposure of an older ferret to a new or young ferret that appears healthy. Often within 48 hours the older ferret becomes anorexic and lethargic.
- Four clinical syndromes are typically seen:
  1. ECE may cause relatively mild diarrhea that lasts several days in young ferrets with no underlying disease.
  2. ECE may cause severe diarrhea lasting for several days that may be followed by an acute onset of severe bloody diarrhea in older ferrets or ferrets with concomitant disease. Anemia may develop as a sequelae.
  3. A wasting disease with abnormal stools that have the appearance of bird-seed or of being grainy. These stools may develop in ferrets that initially appear to have recovered from the diarrheal phase.
  4. Voluminous green, watery diarrhea and occasional vomiting followed by chronic wasting may occur in some ferrets.
- The clinical course of disease can be prolonged in some ferrets, and may last weeks to months. Affected ferrets typically appear to recover, but continue to have persistent, intermittent diarrhea.

Treatment

- No one specific treatment is consistently effective.
- Supportive care, including fluid therapy and nutritional support, is very important in the treatment of ECE.
- Treat sick ferrets with aggressive fluid therapy. Administer fluids IV, IO, PO, or SC depending on the ferret's status.
- Administer broad-spectrum parenteral antibiotics.
- Feed a bland, high-calorie diet, such as a mixture of Science Diet A/D (Hills Science Diet, Topeka, KS) mixed with Deliver 2.0 (Mead Johnson Nutritionals).
- Intestinal adsorbents or protectants (e.g., Kaopectate, UpJohn) may help in some ferrets.
- Loperamide (Imodium A-D, McNeil Consumer) (0.2 mg/kg) or (1 ml/kg) PO bid every 1 to 3 days may be helpful.
- Administration of prednisone (1mg/kg) PO bid every 14 days may alleviate the chronic, intermittent diarrhea in ferrets with long-term symptoms.
- The disease may recur in previously affected ferrets; an asymptomatic carrier state appears to be possible.
- Do not house ferrets that have had ECE with ferrets that have not had the disease.

ROTAVIRUS

- Rotavirus has been associated with several outbreaks of diarrhea and high mortality in ferret kits 2 to 6 weeks of age; it is often referred to as "ferret kit disease."
- Rotavirus also causes diarrhea in the young of several other species, including humans, cattle, swine, sheep, and rats.
- In adult ferrets, rotavirus infection is rarely fatal, but may cause bright green mucoid diarrhea that lasts for several days.
- There is no readily available antemortem test for the rotavirus infection; rotavirus particles can be identified in feces by electron microscopy.

Treatment

- Treatment consists of supportive care. Administer fluids, antibiotics, and nutritional support.

SALMONELLA

Salmonellosis is rare in the ferret, and is typically associated with exposure to contaminated raw meat and meat by-products. *Salmonella typhimurium, S. newport,* and *S. choleraesuis* may be associated with clinical disease.

- *Clinical signs* include anorexia, lethargy, fever, and diarrhea (usually bloody). Conjunctivitis and anemia have also been reported.
- *Diagnosis* is based on clinical signs and a positive fecal culture. Multiple fecal samples must be collected, and selective media is used for culture.
- *Treatment* includes aggressive supportive care and antibiotic therapy.
  - Ferrets may be presented in shock. IV fluids and administration of rapidly acting intravenous corticosteroids may be necessary for treatment of these patients.
- Other details of salmonellosis, including its public health significance, are discussed elsewhere in this text.

EOSINOPHILIC GASTROENTERITIS

Eosinophilic gastroenteritis (EGE) is an inflammatory bowel disease that occurs in ferrets and other animals.

Etiology

No specific etiological agent has been identified in the ferret, but food allergy is implicated in humans and other animals.

Clinical signs

- Chronic diarrhea with or without mucus or blood, and weight loss are the most common signs. Inappetence, intermittent vomiting, and skin lesions may be seen as well.
- On physical examination, the mesenteric lymph nodes may be enlarged and the intestines may feel thickened.
- A marked peripheral eosinophilia is often present on the CBC differential.

Diagnosis

- Presumptive diagnosis is based on history, clinical signs, physical examination findings, the presence of a peripheral eosinophilia, and/or the presence of eosinophils on fecal cytology.
- Definitive diagnosis is based on histological examination of intestinal biopsy specimens. Mild to extensive eosinophilic infiltration of the mucosa, submucosa, and muscularis of the stomach and small intestines are noted. Focal eosinophilic granulomas maybe identified in the mesenteric lymph nodes.

Treatment

- Treatment is similar to that described for treatment of dogs and cats.
- Begin corticosteroid therapy with prednisone (1.0–2.5 mg/kg) PO sid every 14 days. Perform a recheck examination and CBC 2 weeks after the last dose. If the ferret has improved clinically and the peripheral eosinophilia is resolving, decrease the prednisone dose by 50% every 14 days, and recheck again. Continue the prednisone taper at 2-week intervals until the ferret is tapered to the lowest possible dose, or withdrawn from the steroids altogether.
- Although food allergy has not been identified as a definitive etiological cause of EGE, changing the ferret to a hypoallergenic diet, such as a feline lamb and rice-based diet may be helpful in resolution of signs.
- There have been reports of ferrets with peripheral eosinophilia (up to 40%), and erythema and crusting of the feet, ears, and face. Histological lesions in biopsy specimens from affected skin were consistent with allergic dermatitis. These ferrets were treated with corticosteroids, and did respond to treatment. One also responded to diet change.

INFLAMMATORY BOWEL DISEASE

Inflammatory bowel disease (IBD) can occur in the ferret.

Etiology

The etiology is unknown; dietary factors, hypersensitivity reactions, or an immune-mediated cause have been considered.

Clinical Signs

- Clinical signs can be subtle and include diarrhea; nausea; occasional vomiting; soft, malformed stools that resemble bird seed; and weight loss. These signs often resemble ECE, EGE, and *Helicobacter* gastroenteritis.
- Affected ferrets are often young or middle-aged adults.
- Elevation of liver enzymes and serum globulins may be noted on serum biochemistry analysis.
- Lymphocytosis may be noted on the CBC.

Diagnosis

- Diagnosis is based on the history, clinical signs, and diagnostic work-up.
- Definitive diagnosis is made by histological examination of gastric and intestinal biopsy samples. Mild to severe lymphoplasmacytic gastritis and enteritis are noted on histopathology.

Treatment

- Administer corticosteroids such as prednisone (1.0–2.5 mg/kg) PO sid every 14 days initially, and taper in a manner similar to that described for EGE. Some ferrets respond poorly to steroid therapy.
- Azathioprine (Imuran, Prometheus Laboratories, San Diego, CA) (0.9 mg/kg) PO q24–72h may be used as an alternative to steroid treatment.
- Hypoallergenic diets may offer some benefit.

PROLIFERATIVE BOWEL DISEASE (PBD)

Proliferative bowel disease (PBD) in ferrets was first reported in 1982, and is similar to the PBD that occurs in swine and hamsters. PBD was a commonly encountered disease in the late 1980s and early 1990s, but is relatively uncommon now.

Etiology

PBD is caused by *Lawsonia intracellularis,* an intracellular bacteria that cannot be propagated by routine culture methods.

Clinical Signs

- This disease affects primarily young ferrets 4 to 14 months of age.
- Acute and chronic forms of the disease can occur.
- Diarrhea is present and often contains mucus and blood. Defecations are frequent and small; ferrets often cry out when they defecate. The rectum may be partially prolapsed.
- Other signs include lethargy, depression, inappetence, weight loss, dehydration, and pyrexia.
- Neurologic signs such as ataxia and muscle tremors may be present.
- The intestines may feel firm or thickened on abdominal palpation.

Diagnosis

- A tentative diagnosis of proliferative bowel disease is based on clinical signs and physical examination. Definitive diagnosis requires intestinal or colonic biopsy, but this rarely is warranted because response to therapy usually is good if initiated early.
- A polymerase chain reaction (PCR) assay specific for the swine isolate, and an indirect fluorescent antibody test (IFA) are available.
- Necropsy lesions include gross thickening and discoloration of the small intestine and/or colon. Ridges of proliferative tissue that are distinct from normal adjacent tissues are present on the mucosal surface.
- Histological examination of biopsy samples or necropsy specimens typically demonstrate epithelial proliferation, hypertrophy of the muscularis, and infiltration of the bowel wall with monocytic or granulocytic inflammatory cells. Silver-stained tissues reveal intracellular, comma-shaped organisms in crypt epithelial cells. Glandular hyperplasia consisting of irregular, branching proliferative glands that lack goblet cells, and necrotic debris may be identified in the crypts. Severe glandular hyperplasia may resemble neoplasia and can metastasize.

Treatment

- Treat mild cases on an outpatient basis.
- Hospitalization for supportive care (fluid therapy, nutritional support) may be necessary when severe disease is present.
- Administer Chloramphenicol (50 mg/kg) q12h, PO, IV, IM, or SC as the drug of choice. Treat for at least 2 weeks; longer therapy often is necessary to prevent relapse.
- Metronidazole (20 mg/kg) q12h, PO may be effective.

Prevention and Prognosis

- The prognosis is good with timely therapy.
- Some ferrets improve temporarily and then relapse at the end of the treatment period. Use a long-term course of antibiotic therapy in these animals.

RECTAL PROLAPSE

- Rectal prolapse is usually a disease of young ferrets, and is often associated with diarrhea.
- Possible causes of rectal prolapse include colitis, diarrhea, GI parasitism (e.g., coccidiosis), PBD, and other diseases that may cause straining or diarrhea.
- Other differentials include GI lymphoma, benign intestinal polyps, and postoperative complications of anal gland removal.
- Perform direct fecal and fecal flotation tests to screen for parasites.
- Medical treatment is similar to that described for other species. Administer anthelmentics and antibiotics when indicated.
- The prolapse may resolve without surgical intervention when the underlying disease process is resolved.
- Surgical correction is usually unnecessary (see below).
- If indicated, perform a biopsy of the prolapsed tissue to rule out lymphoma.

Surgical Therapy

- Flush the prolapsed tissues with sterile saline and replace them into the rectum.
- Place a purse-string suture in the anus with a small opening to allow passage of feces. Keep the purse-string suture in place for 2 to 5 days.
- In ferrets with chronic prolapse, surgery may be necessary to reduce the size of the anal opening. Excise a small triangular wedge of anal mucosa and routinely close the defect by suturing. Alternatively, consider abdominal exploratory surgery and colopexy (see Chapter 75)

ANAL SAC ABSCESS

- Clinical signs and physical examination findings in ferrets with an abscessed anal sac are the same as those described in dogs and cats.
- The recommended treatments include antibiotic therapy, lancing and drainage of the abscess, or surgical removal of both anal sacs (see Chapter 75).

Anal Sacculectomy

Anal sacculectomy is performed as a treatment for anal sac abscesses, or to decrease the musky "ferret" odor. For odor reduction, neutering should be performed simultaneously because the apocrine, perianal, sebaceous, and scent glands in the skin are under hormonal control and contribute to the overall musky odor. Some clinicians believe that neutering is sufficient to decrease odor and that routine anal sacculectomy should be discouraged.

Surgical Technique

1. Grasp the anal sac duct and hold it closed with mosquito forceps. Make a circumferential skin incision around the duct opening.
2. Apply gentle caudal traction to the anal sac, and use a scalpel blade or gauze to tease away the surrounding fascia.
3. Leave the surgical sites open, and allow to heal by second intention.

Alternative Technique

1. Make small, arc-like incisions just lateral to the duct openings.
2. Dissect the subcutaneous tissues bluntly to reveal the neck of the anal sac; grasp the opening and hold it closed with mosquito forceps.
3. Dissect the sac free of surrounding tissues, using gentle traction.
4. Do not suture the incisions.

Urogenital System

REPRODUCTIVE SYSTEM

Characteristics of the Normal Ferret Reproductive System

Ferrets reach sexual maturity during the first breeding season after birth. The breeding season runs from March to August under natural lighting conditions.

Males

- The opening of the prepuce is located just caudal to the umbilical area.
- Males (hobs) have a J-shaped os penis.
- During the breeding season (March–August), testicle size is twice that noted in the fall and winter months.
- Prostatic tissue is located at the base of the urinary bladder and surrounds the urethra. Prostatic disease associated with adrenal gland disease may occur in middle-aged and geriatric male ferrets (see "Adrenal Gland Disease" and "Prostatic Disease").

Females

- Female ferrets (jills) are seasonally polyestrous and are induced ovulators. Ovulation typically occurs 30 to 40 hours after mating.
- The vulva is located in the perineal region ventral to the anus. In non-estrous females the vulva is small, and looks like a slit; during estrus (or when adrenal gland disease is present), the vulva becomes swollen and is easily visualized.
- If mating is unsuccessful, pseudopregnancy results and lasts 41 to 43 days.
- Approximately 50% of females remain in estrus if they are not bred. The resultant prolonged elevation of serum estrogens can cause bone marrow toxicity and pancytopenia (see the discussion of anemia under "Hematopoietic System" in this chapter).
- Submit blood for a CBC and platelet count if the ferret has been in estrus for more than 28 days.
- Termination of estrus is recommended (see "Termination of Estrus in the Hematopoietic".)

Castration

- Most pet male ferrets in the United States have already been neutered prior to 8 weeks of age.
- Castrate intact male ferrets at 6 to 8 months of age in order to reduce aggressive behavior and odor.
- Castration is performed using techniques similar to those used in cats (see Chapter 87).
  - Make an incision in the scrotum over each testicle.
  - Remove the testicles using an open or closed technique.
  - Incisions may be left open to heal by second intention.

Ovariohysterectomy

- Most pet female ferrets in the United States have already been spayed prior to 8 weeks of age.
- Spaying intact female ferrets is recommended to prevent estrogen-induced bone marrow hypoplasia.
- Ovariohysterectomy is similar to the procedure performed in cats (see Chapter 91).
  - The ventral midline incision is made approximately 1 cm caudal to the umbilicus, and may be extended as necessary.
  - The uterus is bicornuate, and is located dorsal to the bladder.
  - Ovarian vasculature may be difficult to locate due to the large amount of body fat typically present in this region.

Pyometria/Metritis

- Pyometra and metritis are uncommon in pet ferrets in the United States because they are usually spayed prior to being sold as pets.

- Clinical signs may include anorexia, lethargy, pyrexia, and vulvar discharge. Polyuria and polydipsia are not usually noted.
- Persistent estrus may predispose ferrets to pyometra.
- Preoperatively perform a CBC and a serum biochemical analysis to rule out estrogen-induced bone marrow hypoplasia (see "Anemia" in "Hematopoietic System").
- Provide appropriate supportive care pre- and postoperatively.
- Perform ovariohysterectomy when the patient is stable (see Chapter 91).
- Start the ferret on broad-spectrum antibiotic therapy preoperatively, and continue postoperatively for 10 to 14 days. Use broad-spectrum antibiotics. Organisms commonly associated with pyometra include *Staphylococcus* spp, *Streptococcus* spp, *Corynebacterium* spp, and *E. coli*.

Vulvar Swelling in Spayed Females

- Vulvar swelling is an external sign of estrus in female ferrets.
- In a spayed female, a swollen vulva indicates a remnant of ovarian tissue, or another source of estrogens and estrogen precursors such as adrenal gland disease (see "Adrenal Gland Disease").
- Ovarian remnants typically induce signs of estrus in ferrets younger than 2 years of age.
- Administer HCG (100 IU) IM. Vulvar swelling should subside if an ovarian remnant is present. If no changes occur, adrenal gland disease is probably the cause of the clinical signs.
- Perform exploratory laparotomy to remove the ovarian remnant (see Chapter 91). Evaluate for uterine remnants and adrenal gland disease as well.
- Preoperatively evaluate a CBC to rule out estrogen-induced bone marrow hypoplasia.

Pregnancy Toxemia

- Pregnancy toxemia is a potentially life-threatening condition that occurs in late pregnancy. Primiparous females are most commonly affected.
- The disease results in high mortality of jills and kits.
- Toxemia can be induced if an accidental fast occurs in the last week of gestation.
- Pregnancy toxemia may also develop in primiparous jills that are carrying large litters due to nutritional compromise induced by the size of the gravid uterus and the resultant reduced capacity of the stomach.
- Advise owners that pregnant jills must have access to food and water *al lib* during pregnancy.
- Suspect pregnancy toxemia if acute lethargy develops in the last week of gestation. Other clinical sings include dehydration, melena, hypoglycemia, ketonuria, and azotemia.
- Affected ferrets usually are presented in an acute state of shock.
- *Treatment* includes aggressive supportive care including IV or IO fluids containing dextrose. Perform an immediate cesarean section (see Chapter 91).
- Postoperative care includes continued supportive care, including frequent feedings of high-calorie critical care diets.
- Jills that survive pregnancy toxemia often do not produce milk. Kits can be difficult to hand rear; if a foster jill is not available, attempts may be made to hand rear the kits using a kitten milk replacer (see below). Kits born before 40 days of gestation often do not survive.
- The prognosis is usually poor, even with aggressive treatment.

Mastitis

- Do not breed females with a history of mastitis.
- Abrasions to the mammary tissue and nipples can cause mastitis. Prevent trauma from occurring by providing a large nest box opening with smooth edges that allows the jill to pass through easily.
- Mastitis may be acute or chronic.
- *Acute mastitis* typically occurs immediately after whelping or during the third week of lactation.
  - Affected glands appear swollen, firm, red to purple in color, and are painful. Gangrene can develop within hours of clinical signs.
  - Treatment must be aggressive. Administer broad-spectrum antibiotics, and apply hot packs to the affected area 2 to 3 times per day for 2 days. Debride necrotic tissue if present. Provide supportive care and analgesic therapy.
  - Submit a sample for bacterial culture and sensitivity testing. Modify antibiotic therapy based on test results.
  - If there is no clinical response to medical therapy in 2 days, or if gangrene rapidly develops, consider surgical removal of the affected mammary tissue. Because of the potential for severe toxicity and life-threatening disease, do not delay surgery if gangrene is already present, or if there is no improvement with medical therapy.
  - If the jill continues to lactate, leave the kits with her. Supplement feed the kits with a kitten milk replacer if necessary. Do not foster the kits with another jill because this may result in mastitis in the foster jill.
  - Ingestion of infected milk may cause gastroenteritis in the kits; kits may need to be treated with antibiotics as well.
- *Chronic mastitis* is often difficult to diagnose. The affected jill often appears normal, while the kits lose weight or fail to thrive.
  - Mammary glands appear firm but are not painful or discolored; often the glands are presumed to be full of milk.

- Affected mammary glands become scarred and are no longer functional. Affected jills should be culled from the breeding program.

Foster Care of Kits

- Hand-rearing kits from birth is difficult. Prognosis is poor for survival.
- It may be necessary to provide supplemental feeding for kits if the jill's milk production is reduced, or if the litter size is large.
- Whenever possible, foster kits with another lactating jill. Most jills will accept kits of any size or age.
- Kits require a milk supplement that contains a high fat content (20%). Kitten milk replacers mixed with cream may be used.
- Feed kits as much as they will eat 4 times per day with a dropper or small pet nurser.
- Begin to mix solid food with the enriched milk replacer when kits are 4 weeks of age. This mixture may be offered in a shallow dish or bowl.
- Kits may be weaned onto a solid diet at 5 to 6 weeks of age. Feline or ferret growth diets are recommended.

URINARY SYSTEM

Characteristics of the Normal Ferret Urinary System

- The right kidney lies cranial to the left kidney. The cranial end of the right kidney often lies under the caudate lobe of the liver.
- The bladder is small, and can hold up to 10 ml of urine.
- Male ferrets have a small prostate gland that surrounds the urethra at the base of the bladder.
- Urinalysis:
  - The normal urine pH is 6.0 for ferrets on a meat-based diet.
  - Normal values for urine-specific gravity have not been reported.
  - There is evidence that proteinuria may be normal in ferrets (7–33 mg/dl in males; 0–32 mg/dl in females) and that bilirubinuria can occur in the absence of liver disease.

Renal Disease

Renal disease in not common in ferrets, but may occur.

Clinical Signs

- Clinical signs are similar to those described in other animals, and include ataxia, bruxism, halitosis, hindlimb weakness, inappetence, melena, mucus membrane ulceration, polyuria/polydipsia, vomiting, and weight loss.
- Physical examination findings may include cachexia, dehydration, irregularity in the shape and size of the kidneys, pale mucous membranes, and oral ulceration.

Diagnosis and Treatment

- Diagnosis is based on clinical signs, physical examination, and CBC, serum biochemical analysis, and urinalysis results.

▼ ***Key Point*** Hyperphosphatemia, hypocalcemia, and high BUN may be noted on serum biochemical analysis. Serum creatinine concentration is often normal or only moderately elevated.

- Treatment should address the underlying cause, if possible.
- Nonspecific treatment includes fluid therapy, nutritional supportive care, and antibiotic therapy based on culture and sensitivity when indicated.
- Prognosis is guarded, depending on laboratory findings and response to treatment.

Renal Cysts

Unilateral or bilateral renal cysts are relatively common in ferrets (see Chapter 77 for a description of this disease in dogs and cats). The condition is usually an incidental finding in middle-aged and older ferrets, although clinical signs associated with this condition can occur at any age.

Etiology

- The cause of renal cysts in the ferret is unknown.
- Heredity does not appear to be a factor. Renal cysts are not associated with hepatic or biliary cysts.
- Renal cysts typically present as one or more smooth masses on the surface of the kidney. On abdominal palpation affected kidneys feel smoothly enlarged or irregular.
- Polycystic disease is unusual in the ferret. When present, affected kidneys appear rough and irregular; multiple cysts are often distributed throughout the renal tissue. Cysts may be present in other organs as well.

Clinical Signs

- Usually there are no clinical signs associated with renal cysts.
- Rarely, there may be enough disruption of normal renal parenchyma to lead to renal failure, and subsequent clinical signs.

Diagnosis

- Palpate the kidneys for irregular shape.
- Perform a CBC, serum biochemical profile, and urinalysis.
- Abdominal radiography usually is not helpful unless the kidneys are very irregular.

- Perform an abdominal ultrasound to detect renal cysts, to evaluate renal architecture, and to rule out other conditions such as renal neoplasia.
- Intravenous pyelography or nuclear scintigraphy may be used to evaluate renal function.
- Renal cysts may be an incidental finding during abdominal surgery.

Treatment

- There is no specific treatment for renal cysts. No treatment is necessary in asymptomatic animals.
- Monitor affected ferrets by periodic abdominal palpation, serum biochemical profile, urinalysis, and ultrasound, if indicated.
- If an affected kidney becomes very large, consider unilateral nephrectomy (if the opposite kidney is functional) (see Chapter 78).
- Symptomatic ferrets may be managed using the same supportive care methods used in dogs and cats with chronic renal failure.
- The prognosis is grave for ferrets in renal failure.

Hydronephrosis

- Hydronephrosis is uncommon in ferrets. Iatrogenic hydronephrosis may occur as the result of inadvertent ligation of a ureter during ovariohysterectomy (see Chapter 77 for information about hydronephrosis in dogs and cats).

Cystitis

- Bacterial cystitis without urinary calculi is rare in pet ferrets. Follow treatment protocols for cystitis in dogs (see Chapter 79).

Urolithiasis

Urinary calculi was a common cause of stranguria in ferrets at one time; improvement in the quality of ferret diets has decreased the incidence of calculi. Calculi are usually composed of calcium oxalate or struvite (magnesium ammonium phosphate hexahydrate). Cysteine calculi also have been reported.

Etiology

- The cause of urinary calculi is unknown; however, diet is believed to be a factor.
- Diets containing plant proteins or poor quality meat-based proteins may be associated with the development of urinary calculi. Urolithiasis is uncommon in ferrets maintained on a high-quality feline or ferret diet containing high-quality animal-based proteins.
- Other factors may include urinary tract infection, metabolic, genetic, and congenital factors.

Clinical Signs

Clinical signs depend on the location of the urolith(s) and may include dysuria, stranguria, hematuria, persistent wetness in the perineal region, and frequent licking of the perineum.

- Urethral calculi may cause obstruction in both male and female ferrets.
  - Ferrets with urethral obstruction often strain and cry as they attempt to urinate.
  - If complete obstruction is present ferrets often appear lethargic and anorexic, and may not demonstrate obvious signs of dysuria.

Diagnosis

- Palpate the bladder to identify cystic calculi. The urinary bladder wall may be thickened; in ferrets with urethral obstruction, the bladder is distended and firm.
- Obtain abdominal radiographs to confirm the presence of radiopaque urinary calculi. Cysteine calculi are not radiopaque and require contrast radiography or ultrasonography for diagnosis.

▼ ***Key Point*** Small stones located at the base of the os penis can be very hard to identify.

- Renal calculi may be an incidental finding on whole body radiographs, or may be associated with renal failure.

Treatment

▼ ***Key Point*** Urethral obstruction is an emergency. Severe metabolic derangement, coma, and death may occur if urethral obstruction is not diagnosed and treated quickly.

- Stabilize non-obstructed ferrets by providing supportive care, fluids, analgesics, and antibiotics (if indicated) prior to performing cystotomy to remove the urolith(s).
- Cystic calculi may be removed surgically via cystotomy; the procedure is similar to that used in cats and dogs (see Chapter 80). Close the bladder wall with 4-0 or 5-0 absorbable sutures.
- Submit a urolith sample for analysis and bacterial culture/sensitivity testing.
- Administer antibiotics for a minimum of 10 to 14 days. Use results of follow-up urinalysis, and urine culture/sensitivity testing to determine when to discontinue antibiotic therapy.
- Begin conversion to a high-quality–animal, protein-based feline or ferret diet. Urinary acidifies are not usually necessary once the ferret is on a high-quality animal, protein-based diet, since this diet alone will cause the urine to be acidic.
- Feline calculi-dissolving diets and preventative diets may be offered to ferrets; however, many ferrets do not find these diets palatable.

- Renal calculi can often be managed medically by administering antibiotic therapy and changing the diet.

Urethral Obstruction

▼ ***Key Point*** The bladder is very fragile in ferrets. Handle ferrets with obstruction gently to avoid bladder rupture.

- Urinary obstruction in the male ferret can be difficult to manage. Catheter placement is challenging due to the small size of the urethra and the J-shaped os penis. (See Urinary Catheterization in the Techniques section of this chapter.)
- To facilitate placement of the urinary catheter, empty the bladder via cystocentesis prior to catheterization. Submit urine samples for urinalysis and bacterial culture/sensitivity testing.
- Use either a ferret urinary catheter (Slippery Sam Ferret Urinary Catheter, Cook Veterinary Products), a standard tom cat catheter, or a 3.5-Fr red rubber catheter for catheterization.
- Inhalant anesthesia with isoflurane or sevoflurane is strongly recommended to facilitate catheter placement.
- If the urinary catheter placement is not successful, consider emergency cystotomy, and attempt to perform anterograde flushing of the urethra via the cystotomy site.
- Perineal urethrostomy may be considered if cystotomy is unsuccessful (see Chapter 82).

Prevention

- Feed a high-quality, animal protein-based feline or ferret diet.

PROSTATIC DISEASE/PROSTATIC CYSTS

Prostatic disease and subsequent urethral obstruction is a potentially life-threatening condition of middle-aged and geriatric male ferrets. This condition typically occurs in association with adrenal gland disease.

Etiology

- Prostatic disease and prostatic cyst formation are presumed to be the effect of excessive androgens on the prostate. Excessive androgen production occurs with adrenal gland disease.
- Squamous metaplasia of prostatic glandular epithelium occurs and may subsequently lead to the development of cysts ranging in size from 1 to 6 cm or larger. Secondary bacterial infection and abscessation may occur.
- Prostatic abscesses associated with transitional cell tumor of the bladder, prostatic seminoma, and prostatic carcinoma have also been reported in the ferret, but are rare.

Diagnosis

History and Clinical Signs

- Clinical signs associated with prostatic disease may include symptoms associated with a urinary tract infection, urethral obstruction, or urinary incontinence.
- Signs of adrenal gland disease are often present (see "Adrenal Gland Disease").

Physical Examination

- On physical examination, a large, firm, often painful caudal abdominal mass is usually palpable. With careful palpation, this mass is found to be bilobed, representing the urinary bladder and a cystic structure. Ferrets with mild to moderate prostatic disease may appear to have a normal-sized prostate on abdominal palpation, yet are still symptomatic.

Diagnostic Tests

It is important to remember that adrenal gland disease is usually the cause of prostatic disease. Perform a complete diagnostic work-up that includes whole-body radiography, CBC, serum biochemistry analysis, and urinalysis. A plasma steroid hormone assay, and abdominal ultrasound may be indicated as well.

- Obtain abdominal radiographs; prostatic enlargement or prostatic cysts appear as mass lesions dorsal to the bladder.
- Perform abdominal exploratory surgery for a definitive diagnosis.

Treatment

- Address urethral obstruction if present (see "Urolithiasis").
- Manage medically until the ferret is stable for adrenalectomy and surgical drainage of the cysts.
- Medical management includes maintenance of urinary catheterization for several days, administration of fluids, antibiotic therapy, anti-inflammatory and analgesic therapy, and nutritional support as needed.
- Consider administration of an androgen receptor blocker (see "Adrenal Gland Disease").
- Consider administration of leuprolide acetate 30-day depot formulation (Lupron Depot, Bristol-Myers-Squibb Oncology, Princeton, NJ) (250 ug/kg) IM; prostatic tissue shrinkage may occur within 48 hours in some individuals. Some ferrets have been maintained successfully on monthly injections of this drug, although results are highly variable.
- Perform adrenalectomy and drainage of the cysts. Large cysts may require debulking.

- Perform bacterial culture and sensitivity testing of the cyst contents.

▼ ***Key Point*** Omental pull-through procedures and marsupialization have been described as means of prostatic abscess management in the ferret. These procedures should be used with some caution. Prostatic abscesses and prostatic cysts can be difficult to differentiate from paraurethral cysts. Paraurethral cysts communicate with the urethra or bladder neck. Consider performing contrast radiography to determine if there is communication between the cyst/abscess and the bladder prior to performing these procedures.

- Administer postoperative antibiotic therapy for a minimum of 10 to 14 days, along with androgen receptor blockers or leuprolide acetate.
- Base the decision to discontinue antibiotic therapy and androgen receptor blocker/leuprolide acetate therapy by monitoring changes on physical examination, follow-up radiography, and follow-up urinalysis.

Prognosis

- The long-term prognosis is good if prostatic changes regress, and if subsequent adrenal gland disease does not occur in the remaining adrenal gland.
- Some ferrets may need to be maintained on androgen receptor blockers or leuprolide acetate indefinitely.

PARAURETHRAL CYSTS

Etiology

Paraurethral cysts are thin-walled single or multiple cysts present on the dorsal aspect of the bladder and proximal urethra. These cysts appear to also be associated with adrenal gland disease and can cause urethral obstruction.

It is important to differentiate between prostatic cysts and paraurethral cysts when planning the surgical protocol.

Clinical signs

- Paraurethral cysts have been reported in male and female ferrets.
- Clinical signs are similar to those described for prostatic disease, and include symptoms associated with a urinary tract infection, urethral obstruction, urinary incontinence.
- Clinical signs of adrenal gland disease are usually present (see "Adrenal Gland Disease").

Diagnosis

Physical Examination

- A large, firm caudal abdominal mass is often palpable dorsal to the bladder, just cranial to the pelvic inlet.

Diagnostic Tests

- Perform a complete diagnostic work-up that includes whole-body radiography, CBC, serum biochemical analysis, and urinalysis.
- Because adrenal gland disease is usually the underlying etiology, consider performing a plasma steroid hormone assay.
- Radiographically, paraurethral cysts appear as mass lesions dorsal to the bladder.
- Ultrasonography may be useful in evaluation of the paraurethral cysts and adrenal glands.

Treatment

- Surgical drainage and debulking of the cysts is the treatment of choice.
- Marsupialization is an alternative, but may lead to a formation of a permanent cystotomy.
- Do not perform an omental pull-through procedure.

SUPPLEMENTAL READINGS

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Chapter

176 Rabbits

Sue Chen / Katherine E. Quesenberry

Rabbits are popular pets for both children and adults. They are easily litter trained and require minimal maintenance. This chapter stresses diagnosis and management of problems commonly encountered in pet rabbits. Refer to the supplemental readings for more comprehensive information.

BIOLOGIC CHARACTERISTICS

Rabbits, hares, and pikas are members of the order Lagomorpha. Lagomorphs have six incisors, in contrast to the closely related rodents, which have four incisors. The additional incisors (peg teeth) are small, rounded teeth located directly behind the upper incisors. Currently, there are over 100 breeds of rabbits, which vary in size, ear and body conformation, and coat type, recognized by the House Rabbit Breeders Society.

- All domestic rabbits are descendants of European wild rabbits, Oryctolagus cuniculus.
- The two main genera of rabbits are *Oryctolagus,* the European wild rabbits, and *Sylvilagus,* the cottontail rabbits. These genera differ in chromosome number and cannot interbreed.
- Rabbits can range in size weighing from 2.5 lb in the dwarf breeds up to 28 lb in the giant breeds.
- Giant breeds, which average more than 5 kg in body weight, include the American Checkered Giant, the Flemish Giant, and the Giant Chinchilla rabbits.
- Medium breeds, which average from 3.5 to 5 kg in body weight, include the Californian, the Silver Marten, and the Rex rabbits.
- Small breeds, which average less than 3.5 kg in body weight, include the Netherland Dwarf, the Jersey Wooly, and the Polish rabbits.
- Ears vary in size and shape between the different breeds, and most rabbits have upright ears. However, there are breeds that have ears in a downward carriage, which are known as "lops."
- Coats can be divided into normal, Rex, and Satin breeds. Normal fur coats have an undercoat with projecting guard hairs. Rex breeds have short guard hairs that do not project above the undercoat, thus producing a "velvety" fur coat. Satin breeds have a genetic mutation that results in a "shiny" haircoat.
- Specific information concerning breeds can be obtained from the American Rabbit Breeders Association by mail (PO Box 426; Bloomington, IL 61702) or on their Website (www.arba.net).

Anatomic and Physiologic Characteristics

- Females of several breeds of rabbits have a large pendulous dewlap under their chin. This area is a frequent site of moist dermatitis, especially in obese rabbits kept in humid, warm environments that may have difficulty grooming themselves.
- The sense organs of rabbits are well developed. Like other prey species, the eyes are laterally set. This provides a completely circular field of vision with the exception of the small area below the mouth. Thus, long sensory hairs around the snout and the sensitivity of the lips help rabbits discriminate food.
- Teeth are open rooted and grow continuously. The deciduous teeth are shed right around the time of birth and the permanent teeth complete eruption around 3 to 5 weeks of age. The dental formula is 2/1 incisors, 0/0 canines, 3/2 premolars, and 2–3/3 molars. Rabbits are distinguished from rodents by possessing an extra set of upper incisors, which are also known as "peg teeth."
- The gastrointestinal (GI) tract has a simple glandular stomach, a long intestinal tract, and a large cecum.
- The stomach serves as a reservoir for ingesta and is rarely empty. It holds approximately 15% of the GI contents. The cardia and pylorus are well developed, and, due to the anatomic arrangement of the cardia to the stomach, rabbits are unable to vomit.
- The cecum is the largest organ in the abdominal cavity and holds approximately 40% of the GI contents.
- Rabbits exhibit cecotrophy, which means they consume soft cecotrophs, also known as "night feces." Antiperistaltic contractions in the colon retrograde non-fiber particles and fluid back into the cecum for fermentation and the formation of cecotrophs, which are an important source of B-vitamins, electrolytes, and nitrogen.
- The skeletal system is light and delicate compared with most mammals. The skeleton makes up 8% of

the total body weight in rabbits, as opposed to 13% of the total body weight in cats.

▼ ***Key Point*** Red, pink, or orange discoloration of the urine occurs periodically in healthy rabbits. The color may be caused by porphyrin pigments or food-related metabolites excreted in the urine. Cytologic examination of the urine for red blood cells will help distinguish porphyrinuria from hematuria.

- Calcium and phosphorus are excreted primarily through urine in rabbits. Thus, the urine may be thick and creamy due to calcium carbonate precipitate. Calcium is excreted in the bile in most other mammals.
- In rabbits, high total leukocyte counts may not be characteristic of acute inflammation from infectious causes. Instead, the distribution of the white blood cells (WBCs) shifts from a normally high lymphocyte/low neutrophil ratio to neutrophilia and lymphopenia.

Reproductive Characteristics

- Sexual maturity varies in different breeds. As a general rule, females (does) sexually mature at approximately 4 to 8 months of age and males (bucks) sexually mature around 6 to 10 months of age.
- Females have a silent estrus and are induced ovulators.
- Breeding seasons are influenced by day length and temperature, though mating can occur year-round when environmental conditions are controlled. Gestation lasts for an average of 30 to 33 days. Pseudocyesis may last 17 days.
- Depending on the breed, litters range from 4 to 10 kits. Primaparous does usually have smaller litters. Kits are born blind and hairless and remain in the nest for approximately 3 weeks.
- Does have four and five pairs of mammary glands and nipples spread from the axilla down to the inguinal region. Does usually nurse only once daily for 3 to 5 minutes.
- Neonatal rabbits are totally dependent on milk up to day 10. Rabbit milk varies with stage of lactation but is approximately 13% protein, 9% fat, and 1% lactose. Small amounts of solid feed and hay can be digested around day 15 and cecotrophy commences on day 20.

Normal Parameters

Reference ranges for physiologic values are listed in Table 176-1. Reference ranges for hematologic values, serum biochemical values, and urinalysis are listed in Tables 176-2, 176-3, and 176-4.

Table 176-1. REFERENCE RANGES FOR PHYSIOLOGIC VALUES IN RABBITS

Temperature	38–40°C
Heart rate	130–325 beats/min
Respiratory rate	32–60/min
Life span	5–9 yrs
Blood volume	55–65 ml/kg
Food consumption	50 g/kg/day
Water consumption	
General population	50–100 ml/kg/day
Breeding does	<900 ml/kg/day

Table 176-2. REFERENCE RANGES FOR HEMATOLOGIC VALUES IN RABBITS

Erythrocytes	$5.1–7.9 \times 10^6$ m^3
Hematocrit	33%–50%
Hemoglobin	10.0–17.4 g/dl
Mean corpuscular volume	57.8–66.5 µm^3
Mean corpuscular hemoglobin	17.1–23.5 pg
Mean corpuscular hemoglobin concentration	29%–37%
Platelets	$250–650 \times 10^3$/mm^3
Leukocytes	$5.2–12.5 \times 10^3$/mm^3
Neutrophils	20%–75%
Lymphocytes	30%–85%
Monocytes	1%–4%
Eosinophils	1%–4%
Basophils	1%–7%

Table 176-3. REFERENCE RANGES FOR SERUM BIOCHEMICAL VALUES IN RABBITS

Albumin	2.4–4.6 g/dl
Alkaline phosphatase	4–16 U/L
Amylase	166.5–314.5 U/L
Bicarbonate	16–38 mEq/L
Blood urea nitrogen	13–29 mg/dl
Calcium	5.6–12.5 mg/dl
Chloride	92–112 mEq/L
Cholesterol	10–80 mg/dl
Creatinine	0.5–2.5 mg/dl
Globulin	1.5–2.8 g/dl
Glucose	75–155 g/dl
Glutamic-oxaloacetic transaminase	14–113 U/L
Glutamic pyruvate transaminase	48–80 U/L
Lactic dehydrogenase	34–129 U/L
Phosphorus	4.0–6.9 mg/dl
Potassium	3.6–6.9 mEq/L
Serum protein	5.4–8.3 g/dl
Sodium	131–155 mEq/L
Total bilirubin	0.0–0.7 mg/dl
Total lipids	243–390 mg/dl

Table 176-4. REFERENCE RANGES FOR URINALYSIS IN RABBITS

Urine volume	
Large breeds	20–350 ml/kg/day
Average breeds	130 ml/kg/day
Specific gravity	1.003–1.036
Average pH	8.2
Crystals present	Ammonium magnesium phosphate, calcium carbonate monohydrate, anhydrous calcium carbonate
Casts, epithelial cells, or bacteria present	Absent to rare
Leukocytes or erythrocytes present	Occasional
Albumin present	Occasional in young rabbits

PATIENT MANAGEMENT

Caging

- Cages or hutches can be purchased or constructed. Cages should be large enough to allow free movement. Small breeds, which weigh up to 2 kg, require a minimum of 1.5 ft^2 of floor space per animal. Large breeds, which weigh 5 kg or more, require at least 5 ft^2 of floor space per animal. Cages should be at least tall enough to allow the rabbit to stand on its hind limbs and be easy to clean.
- Cages with plastic bottoms and wire tops are easy to clean and are well ventilated. Wire mesh flooring may also be used; however, provide a solid area for the rabbit as wire flooring may predispose rabbits to sore hocks. Use 14-gauge wire with the mesh openings no greater than 1 × 2.5 cm to prevent the rabbit from getting its feet caught.
- Straw or hay bedding should be provided in one area of the cage. Soiled bedding should be cleaned out daily. Because most rabbits are fastidious and prefer to defecate and urinate in one spot, they often can be trained to use a litterbox.
- Rabbits can be housed indoors or outdoors at temperatures ranging from 40°F to 80°F. Rabbits are very susceptible to heat stroke in ambient temperatures above 85°F. If outdoor housing is used, provide ventilation or protection from direct sunlight. In temperatures below 40°F, provide heat or protection from cold.
- Rabbits should be allowed time out of the cage regularly for exercise and socialization. However, they should always be supervised, as they may chew on dangerous objects such as electrical cords and poisonous plants.

Diet

- Free-choice timothy or coastal hay should be provided to maintain the rabbit's dental and GI health. High-fiber diets are required for proper wearing of the continuously growing teeth and have a protective effect against enteritis. Inadequate fiber in the diet results in cecocolic hypomotility and ultimately changes in cecal microflora.
- A variety of vegetables and fresh, leafy greens such as dandelion greens, cilantro, parsley, and romaine lettuce should be offered as a salad one to two times daily.
- Pelleted diets are balanced and convenient; however most of these are alfalfa based and are low in fiber. Most commercial pellets are nutrient dense (high in protein and digestible carbohydrates) and can predispose rabbits to obesity. High-fiber, timothy-based pellets (Oxbow Pet Products, Murdock, NE; www.oxbowhay.com) are preferable over alfalfa-based pellets.
- The high level of calcium in alfalfa diets may result in hypercalciuria or urinary calculi.
- Rabbits like sweet foods. A limited amount (approximately 2 tablespoons per 2 pounds of body weight) of fruits such as papaya, melon, or berries can be provided as a treat or to entice an anorectic animal to eat.
- Foods high in starches or fat such as seeds, nuts, bread, and corn are not advisable as they can predispose rabbits to obesity and GI disease.
- Fresh water should always be available. Rabbits have a higher water intake than many other mammals. Their daily average water intake is approximately 50–150 ml/kg of body weight. Rabbits fed a large amount of leafy greens will have lower water intake.

CLINICAL TECHNIQUES

Restraint

▼ ***Key Point*** Restrain rabbits gently but firmly for most procedures. Inadequate restraint can result in a spinal fracture in the rabbit if it is allowed to kick with its hind legs. Support the hindquarters when carrying or lifting a rabbit to prevent spinal injuries.

- Carry the rabbit with its head tucked under one arm while supporting the body with your forearm; stabilize the back and rump with the other hand.
- Alternatively, while supporting the back of the rabbit against your body, the forelegs can be grasped between the fingers of one hand while the hind limbs are supported firmly between the fingers of your other hand. This method is effective for examining the ventrum of the patient. (Fig. 176-1)
- When examining a patient on a table, keep the rabbit close to your body and always keep a hand on it to prevent it from jumping off the table (Fig. 176-2).
- An especially nervous or aggressive rabbit may need to be wrapped securely in a towel to prevent injury to

Figure 176-1. To examine the ventrum and anal area, cradle the rabbit as shown. Be sure to provide support to the hind limbs.

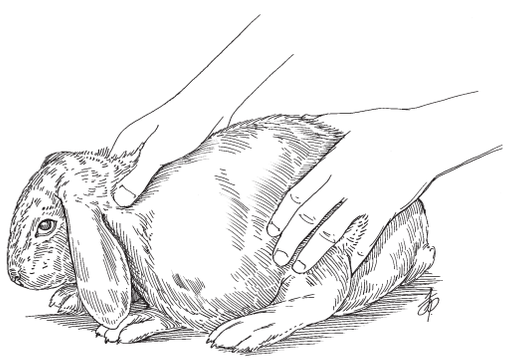

Figure 176-2. Proper method for restraining a rabbit.

itself and to the handler. Some rabbits also calm down if their eyes are covered with a hand or towel.

Diagnostic Techniques

Venipuncture

Blood can be collected from the jugular, lateral saphenous, cephalic, and lateral ear veins. Rabbit veins are thin and fragile, so small-gauge needles (i.e., 25-gauge or smaller) should be used. To prevent hematoma formation, apply direct pressure to the venipuncture site for several minutes. Pluck or wet down the fur from the site for better visibility of the vein.

- Jugular veins lie superficially in the jugular furrow. Hold the rabbit at the edge of a table with the neck held in extension. This technique can be difficult in females with large dewlaps and should not be done for patients in respiratory distress. If anesthetized, the rabbit can be placed in dorsal recumbency with the neck extended down over a table edge for better visibility of the jugular veins.
- The lateral saphenous vein is the preferred site for obtaining blood samples for routine blood tests. A fairly large volume of blood can be collected from this vein, especially in medium and large-sized rabbits. Have the handler place the rabbit in either lateral or sternal recumbency with the hind end directed towards the edge of the table. Have the handler hold off the saphenous vein by hooking one or more fingers around the back of the back leg proximal to the stifle; encircling and squeezing the proximal thigh too tightly will cause the vein to collapse. Wet down or pluck the fur from the mid-thigh region to better visualize the vein. Apply direct pressure after venipuncture to prevent hematoma formation.
- Cephalic veins can be used to collect small volumes of blood. Place the rabbit in sternal recumbency and encircle the foreleg around the elbow to extend the leg. Use either a tuberculin or insulin syringe to minimize the risk of collapsing the vein with too much negative pressure.
- Plucking the hair over the vein is easier than shaving fine fur.
- The lateral ear vein can be used for blood collection in some large rabbits. Use extreme caution however, as thrombosis of the vein can result in sloughing of the pinnae.

Radiography

- Radiographs of the head can provide important information about the sinuses and the dental roots. Sedation is usually required.
- Rabbits have very small thoracic cavities. Thoracic radiographs are useful in differentiating between pneumonia, cardiac disease, and neoplasia.
- The stomach and cecum are often full of ingesta and may obscure abdominal organs. However, moderate to severe gas distention of the stomach, cecum, or intestines suggests GI stasis.

Ultrasonography

- Ultrasound examination can provide useful information about abdominal organs such as the liver, spleen, kidneys, and reproductive tract.
- Urinary calculi and sludge can be seen on ultrasonographic examination of the bladder.
- Guided aspirates of thoracic and abdominal masses can provide representative samples for cytologic examination. However, the patient must be sedated

for the procedure, which should only be performed by experienced practitioners.

Treatment Techniques

- Subcutaneous administration of fluids is acceptable in non-critical cases and may be the only practical route of fluid administration in small rabbits. Estimate daily maintenance fluid needs at 100 to 150 ml/kg/24 hours.
- Use an indwelling catheter in critical cases.
- Small-gauge catheters (i.e., 24-gauge) can be placed in the cephalic or lateral saphenous vein in most rabbits.
- Jugular catheters can be difficult to insert and may require a cutdown procedure.
- Medications can be administered orally into the lateral cheek pouch. Use liquid or paste preparations when possible because rabbits have a long, narrow oropharynx that makes pill administration difficult.
- Anorectic animals can be syringe fed specialized hand-feeding formulas for herbivores (Critical Care for Herbivores, Oxbow Pet Products, Murdock, NE; www.oxbowhay.com). A gruel made of moistened rabbit pellets can also be used. Vegetable baby foods are low in energy content and fiber and should only be used short term.
- Nasogastric tubes can be placed in medium-to-large rabbits that require long-term nutritional support or that have had extensive oral surgery. The technique that follows is similar to that for placing a tube in a cat.
  - With manual restraint, place two to three drops of a topical anesthetic (Ophthaine, Solvay Animal Health, Inc., Princeton, NJ) in the mucosa of one nostril. Wait 5 minutes, and then repeat application.
  - Lubricate the tip of a small infant feeding tube (e.g., 5 Fr., Bard-Parker, Becton-Dickenson and Company, Rutherford, NJ) with topical lidocaine (Xylocaine) jelly. Pass the tube medially along the nasal passage to the level of the last rib. The tip of the tube is located in the distal esophagus.
  - Secure the free end of the tube to the skin above the nose and eye with a butterfly tape and suture. An Elizabethan collar may be necessary to prevent the rabbit from dislodging the tube.
- Dietary supplements containing Lactobacillus spp. may aid in the treatment of enteritis by repopulating the GI tract with healthy bacterial flora, decreasing intestinal or cecal pH, and competing with bacterial pathogens for mucosal attachment sites. Commercial products in paste form are available (e.g., Bene-Bac, Pet-Ag, Inc, Hampshire, IL).
- Commonly used antibiotics are listed in Table 176-5.

Tranquilization and Anesthesia

- Injectable tranquilizers are suitable for short diagnostic or surgical procedures. Ketamine (5–10 mg/kg) and medetomidine (Domitor, Pfizer Animal Health, Exton, PA) (0.15–0.18 mg/kg) in combination given IM or IV provides adequate relaxation and sedation.
- Use inhalant anesthesia for long or painful surgical procedures. Clinically, isoflurane and sevoflurane are commonly used. Anesthetic induction and recovery are usually faster with sevoflurane. Gas anesthesia in rabbits can be induced by face mask or in an induction chamber. Premedicate with a combination of ketamine with medetomidine, diazepam, or midazolam as needed, especially if using isoflurane. Buprenorphine and glycopyrrolate can also be given as needed. Gradually increase the concentration of isoflurane over several minutes until a surgical plane of anesthesia is reached. Anesthesia usually is maintained at 0.25% to 2% isoflurane in oxygen. With sevoflurane, use an induction level of 5% to 8%, reducing to 0.5% to 3% for maintenance.

▼ ***Key Point*** Intubation can be difficult because of the long, narrow oropharynx, large incisors, and large fleshy tongue that can obstruct the view of the pharyngeal cavity. Intubation is most successful in large rabbits; consider intubating medium-sized rabbits for long surgical procedures. However, repeated attempts to intubate can damage the larynx, causing soft tissue trauma or laryngospasm that can be fatal after the rabbit is extubated. If laryngeal trauma occurs during intubation attempts, abandon the procedure and use a face mask, or postpone the procedure to another day. Corticosteroids may or may not be helpful in decreasing inflammation of the larynx and tracheal mucosa.

- The following technique can be used to intubate medium to large rabbits.
  - Administer ketamine (5–10 mg/kg IM) and medetomidine (0.15–0.35 mg/kg IM) in combination. Supplemental isoflurane may be necessary to further relax the rabbit for intubation.
  - Place the rabbit in sternal recumbency. Extend the neck straight up and forward.
  - Place the tip of the short, flat-blade laryngoscope blade (i.e., Miller blade), at the base of the tongue. Hook the base of the blade against the top front incisors, and use the blade as a lever to see the glottis. Pass a small endotracheal tube along the blade into the opening of the glottis. Depending on their size, most rabbits require a 2.5- to 5.0-mm

Table 176-5. DRUGS COMMONLY USED IN RABBITS

Drug	Dose	Comments
Antimicrobials/Antifungals		
Benzathine, penicillin G	42,000–84,000 IU/kg q7d × 3 treatments SC	For treatment of *Treponema cuniculi*
Chloramphenicol	30–50 mg/kg q12h PO	
Ciprofloxacin	10–20 mg/kg q12–24h PO	Have a suspension made by a compounding pharmacist for easy administration
Enrofloxacin	5–15 mg/kg q12h PO, SC, IM	Limit subcutaneous and intramuscular administration due to potential tissue necrosis at injection sites
Gentamicin	4 mg/kg q24h IM, IV, SC	Use with caution or avoid use
Griseofulvin	12.5 mg/kg q12h PO	
Penicillin	40,000–60,000 IU/kg q48 hr SC	Use with caution
Tetracycline	50 mg/kg q8–12h PO	
Trimethoprim/sulfa	30 mg/kg q12h PO, IM, SC	
Antiparasitics/Insecticides		
Fenbendazole	10–20 mg/kg PO, repeat in 14d	
Lime sulfur solution	2.5% dip q7d for 4 weeks	Used in young animals for treatment of mites, fleas, fungal dermatitis
Ivermectin	0.2–0.4 mg/kg q10–14d SC for 2–3 treatments	Effective against ear and fur mites
Piperazine citrate	200 mg/kg; repeat in 2 weeks	
Pyrantel pamoate	5–10 mg/kg; repeat in 2 weeks	
Pyrethrin products	Topically as directed q7d	
Selamectin	6 mg/kg topically	
Sulfadimethoxine	50 mg/kg PO first dose, then 25 mg/kg q24h PO for 10–20 days	For treatment of coccidiosis
Tranquilizers/Premedications		
Acepromazine	0.5–1.0 mg/kg IM/SC	
Atipamazole	Give same volume SC as medetomidine	Reversal for medetomidine
Diazepam	1–3 mg/kg IV, IM	Used in combination with ketamine
Glycopyrrolate	0.01–0.02 SC	
Ketamine	20–50 mg/kg IM	
Ketamine/acepromazine	40 mg/kg (K)/ 0.5–1.0 mg/kg (A) IM	
Ketamine/diazepam	10–15 mg/kg (K)/ 0.3–0.5 mg/kg (D) IM, IV	
Ketamine/medetomidine	0.15–0.35 mg/kg (M) IM/ 5–20 mg/kg (K) IV later	
Ketamine/midazolam	25 mg/kg (K)/ ≤ 2 mg/kg (M) IM	
Medetomidine	0.25 mg/kg IM	
Midazolam	1–2 mg/kg IM or slow IV	
Propofol	2–15 mg/kg IV	
Xylazine	1–5 mg/kg SC, IM	
Analgesics		
Aspirin	10–100 mg/kg q8–24h PO	
Buprenorphine	0.01–0.05 mg/kg q6–12h SC, IM, IV	
Butorphanol	0.1–1.0 mg/kg q4–6h SC, IM, IV	
Carprofen	1.0–2.2 mg/kg q12h PO, SC, IM	
Flunixin meglumine	1.1 mg/kg q12–24h SC, IM	
Ibuprofen	2.0–7.5 mg/kg; PO q12–24h	
Ketoprofen	1 mg/kg q12–24h IM	
Morphine	2–5 mg/kg q2–4h SC, IM	
Oxymorphone	0.05–0.20 mg/kg q8–12h SC, IM	

endotracheal tube. The glottis cannot be seen while trying to pass the tube.

- Alternatively, the glottis can be visualized with an otoendoscope or endoscopic telescope in a sedated rabbit. The endotracheal tube is passed along the endoscope and inserted as above.
- Use a face mask to maintain anesthesia during short procedures or if intubation attempts are unsuccessful.
- Monitor all rabbits closely during any anesthetic episode. A Doppler, EKG monitor, and pulse oximeter can be used to monitor heart rate and oxygen saturation.

DERMATOLOGIC PROBLEMS

Dermatitis/Alopecia

Etiology

- Mange, fur, and ear mites cause localized or diffuse dermatitis, alopecia, or both. The area involved

depends on the type of mite (see "Ear Mites"; "Fur and Mange Mites").
- Dermatophytosis is associated with alopecia and a scaly dermatitis, particularly around the head and ears (see "Superficial Mycosis").
- Fur-barbering is common in rabbits on diets deficient in roughage. A high incidence of barbering in does is seen during breeding season; this is probably related to hormonal influences.
- Ptyalism, alopecia, and dermatitis around the mouth are associated with malocclusion.
- Moist dermatitis of the dewlap is common in does during breeding season, especially in warm or humid environments.
- Moist dermatitis with erythema and ulceration of the ventral abdomen and perineal area results from urine scald. Urine scald is associated with urinary incontinence, cystitis, excessive calcium in the urine, uterine adenocarcinoma, or poor management and unclean caging.
- Treponematosis (rabbit syphilis), caused by Treponema paraluiscuniculi causes a scaly dermatitis in the genital area. The nose, lips, and periorbital area are less commonly involved.

Clinical Signs

- Mite infestations produce clinical signs characteristic of the mite involved (see "Ear Mites"; "Fur and Mange Mites"). Pruritis is common with sarcoptic mite infestations.
- Dermatophytes cause a partial alopecia with slight scaliness and erythema. Rabbits are usually pruritic.
- Fur-barbering is characterized by alopecia of the dewlap, back of the neck, and paws. The underlying skin is normal.
- Moist dermatitis of the dewlap or ventral abdomen is typically erythematous with scaling and ulceration. The fur around the alopecic areas is moist. Rabbits sometimes self-mutilate this area; use a collar to prevent further trauma.

Diagnosis

Determine the primary cause of the alopecia to make a diagnosis.

- Examine skin scrapings of scaly areas for evidence of adult mites or eggs.
- Obtain samples of fur and keratin debris for fungal culture.
- Submit a skin biopsy specimen for histologic examination if the causative agent cannot be determined by other diagnostic tests.
- Examine the teeth in rabbits with excessive ptyalism and alopecia around the mouth (see "Malocclusion").
- Obtain abdominal radiographs of rabbits with urine scald for evidence of cystic calculi. Submit a urine sample for urinalysis and bacterial culture and sensitivity testing.
- Submit a blood sample for serum biochemical analysis to check for high concentrations of calcium, blood urea nitrogen, and creatinine.

Treatment

Treatment is directed toward the primary cause (see "Ear Mites"; "Fur and Mange Mites"; "Hairballs"; "Malocclusion"; "Treponematosis"; "Cystitis"; "Superficial Mycosis").

- Correct the diet to include adequate roughage if fur-barbering is suspected. Perform ovariohysterectomy in females with a suspected hormonal basis for fur-barbering.
- Treat adult rabbits with suspected mite infestations with ivermectin (see Table 176-5).
- Treat treponematosis with penicillin (see "Treponematosis").
- Treat dermatophytosis with antifungal agents, administered topically or orally depending on the extent of lesions.

Ear Mites (Psoroptes cuniculi)

Etiology

- Ear mites are common ectoparasites.
- Psoroptes cuniculi is a large, non-burrowing mite that spends its 3-week life cycle on the host rabbit.
- Mites have biting mouthparts and cause inflammation by biting and chewing the epithelial surface of the skin.

Clinical Signs

- Infestation with psoroptic mites usually is confined to the inner epithelial surface of the ear. Lesions begin in the concha and eventually extend to the inner surface of the pinna. Other areas, such as the dewlap and feet, sometimes are involved.
- Lesions consist of thick, dry, flaky, gray-to-tan crusts on the inner surface of the ear pinna. The underlying epithelial surface is raw, inflamed, and hemorrhagic.
- Psoroptic mites cause intense pruritus. Affected rabbits shake their heads or scratch their ears with the rear feet.

Diagnosis

- Psoroptic mites are large and sometimes visible with the unaided eye.
- Use an otoscope to detect movement of the mites within the ear canal.
- Microscopic examination of crusts and exudate usually reveals mites and eggs.
- Check rabbits with mild cases of otitis for the presence of mites.

Treatment

- Ivermectin is effective against ear mites (see Table 176-5). Repeat treatment in 3 weeks. A combination therapy of ivermectin and topical acaricides can be used for severe infestations.
- Because the lesions are usually very painful, and the aural crusts resolve after ivermectin treatment, avoid pulling off the crusts to clean the ears. Ears can be cleaned 1 to 2 weeks after pain subsides and lesions heal.
- Apply an antibiotic cream topically if a secondary bacterial infection is present. Topical application of anti-inflammatory agents may be beneficial once bacterial infection is under control.

Prevention

- Psoroptic mites are transmitted easily between rabbits. Isolate affected rabbits from healthy rabbits.
- Keep cages and bedding clean to minimize spread through contaminated fomites. The environment should be treated with flea products safe for cats to prevent re-infection.

Fur and Mange Mites

Etiology

- Cheyletiella parasitivorax is the common fur mite of rabbits. Because of its large, white, flake-like appearance, it is often called "walking dandruff." Infestations with other species of Cheyletiella occasionally occur. Listrophorus gibbus is a less common fur mite and is considered nonpathogenic.
- Cheyletid mites are non-burrowing, obligate parasites with an approximate 35-day life cycle.
- Cheyletid mites may cause a self-limiting, transitory dermatitis in humans.
- The cheyletid mite is a known vector of rabbit myxomatosis in Australia.
- Mange mites (e.g., Sarcoptes scabiei, Notedres cati) occur infrequently in rabbits.

Clinical Signs

- Lesions produced by cheyletid mites consist of a scaly dermatitis with a flaky, grayish-white exudate. Mites primarily inhabit the dorsal trunk and scapular region. The underlying skin may appear erythematous and inflamed. Pruritus is not a major clinical sign.
- Other areas of the body can be involved in severe infestations. Rabbits may act as if they are depressed and in pain.
- Mange mites produce a crusty dermatitis with alopecia.
- Intense pruritus results from mites burrowing in the epidermis.

Diagnosis

- Cheyletid mites are easily identified through microscopic examination of cellophane tape preparations of affected skin. Press a strip of cellophane tape to the skin lesions to obtain a sample.
- Deep skin scrapings are necessary to find mange mites. Results are sometimes falsely negative. Differential diagnosis then is based on the typical clinical signs of each type of mite.

Treatment

- Ivermectin (0.4 mg/kg SC q10–14d for three treatments) is effective against most mites that infest rabbits. The treatment period should extend through the life cycle of the mite.
- Topical acaricides, including pyrethrins, carbamates, and lime sulfur solution dips (see Table 176-5), are also effective against fur and mange mites. However, these products should be used cautiously as they have been associated with toxicity in rabbits.
- Cheyletid mites can exist off the host for short periods. Treat the home environment with parasiticides and eliminate potential fomites.
- The mite is highly contagious and all rabbits in contact with the affected rabbit should also be examined and treated. Other pets in the household kept in contact with infested rabbits should be examined.

Myiasis

Etiology

- Myiasis (fly larval infestation) occurs in rabbits kept outdoors in warm weather. Rabbits can become infested with cuterbrid larvae or maggots of the flesh fly. Maggot infestation is also known as "fly strike."
- Obesity, perineal dermatitis, and urine scald predispose rabbits to maggot infestation.

Clinical Signs

- Although some rabbits can be asymptomatic, rabbits may appear to be in pain, reluctant to move, or lame.
- Cuterebrid larvae burrow into subcutaneous tissue and cause one or more firm, fistulated, subcutaneous swellings surrounded by necrotic tissue. Areas commonly involved include the ventral cervical, inguinal, hindquarter, dorsum, and axillary regions.
- Aberrant migrations to the nasal passages, eyes, sinuses, and ear canals have also been described. An infection of the eye is known as ophthalmomyiasis.
- Maggots usually burrow through large, moist necrotic areas at the base of tail and dorsum, as these are difficult areas to groom for overweight rabbits.
- Secondary bacterial infections of the lesion are common.

Diagnosis

Diagnosis is based on a history of outdoor housing, clinical signs, and presence of larvae in wounds.

Treatment

- Sedation and pain medication are usually indicated before clipping soiled fur and removing larvae from the wounds.
- Remove cuterebrid larvae intact with hemostats if possible. Avoid rupture of the larvae.
- Remove maggots from the necrotic wounds.
- Thoroughly debride wounds of necrotic tissue. Perform complete surgical excision of any abscessed skin. Clean the surgical site daily and allow the wound to heal by second intention.
- Ivermectin (0.4 mg/kg SC q14d for two treatments) can be administered to kill larvae, but the larvae still need to be removed from the sites.
- Observe affected rabbits carefully for several weeks for additional lesions.
- Antibiotics with good skin activity such as trimethoprim-sulfa (30 mg/kg PO bid) are recommended for treating secondary bacterial infections.

Prevention

- Keep outdoor rabbits in screened hutches, especially during summer and fall.

Superficial Mycosis

Etiology

- Trichophyton mentagrophytes is the most common dermatophyte that affects rabbits and is usually self-limiting. Infections with Microsporum spp. and other dermatophytes occur much less frequently.
- Infection occurs by direct contact with infected animals, contaminated fomites, or asymptomatic carriers.

Clinical Signs

- Lesions usually appear on the head and ears and can extend to the neck, legs, feet, and nail beds.
- Lesions consist of areas of alopecia with erythema and scaly dermatitis. Rabbits are usually pruritic. Alopecic areas may be circular with slightly raised edges.

Diagnosis

Dermatitis resulting from dermatophytosis must be differentiated from other possible causes, including mites, fur-barbering, and bacterial dermatitis.

- Submit samples of fur from the edge of the lesion for culture on dermatophyte-culture medium.
- T. mentagrophytes does not fluoresce with ultraviolet light.
- The organisms can be demonstrated with either periodic acid schiff (PAS) or silver stains in histologic sections of skin biopsy specimens.

Treatment

Treatment of dermatophytosis is directed toward elimination of the organism while preventing spread of disease. Other animals and humans, especially children, are susceptible to infection.

- Clip affected areas and apply topical antifungal agents daily for 3 to 4 weeks.
- For extensive lesions, lime sulfur solution dips (2%–3%) given every 5 to 7 days are often effective for treating fungal dermatosis. Continue treatment for 4 weeks.
- Griseofulvin is effective if given daily for 4 weeks or until the infection clears (see Table 176-5). Give griseofulvin with fats to enhance absorption. Gris-PEG (Allergen, Inc.), an ultramicronized formulation for improved absorption, is given at one-half the normal dose. Griseofulvin should be administered cautiously, because it can cause bone marrow suppression and panleukopenia at high doses. Do not give it to breeding does, as it may be teratogenic.
- Instruct owners to wear gloves when handling or treating affected animals because of the zoonotic disease potential.
- Check other animals in the household for evidence of dermatophytosis.

Prevention

- Prevent contact with infected animals.
- Disinfection of the environment is important. Vacuum the contaminated area and wipe down all surfaces with a 1:10 dilution of bleach and water. Foggers containing enilconazole or formaldehyde can be used for carpeted areas.

Ulcerative Pododermatitis (Sore Hocks)

Etiology

- Ulcerative pododermatitis (sore hocks) usually develops as a result of management-related problems. Soiled or wet bedding, abrasions from flooring, sedentary behavior caused by obesity, small cages that restrict movement, and abrasions from thumping are predisposing factors.
- Ulcerative granulomatous lesions involve the plantar surface of the hocks and may be unilateral or bilateral. Forepaws are less commonly affected.
- Secondary bacterial infections, usually S. aureus, are common with severely ulcerated lesions.
- Chronic infections can develop into abscesses or may spread to underlying bone, resulting in osteomyelitis.

Clinical Signs

- Early or mild lesions are areas of erythema and thinning fur on the plantar surface of the hock.
- Lesions may progress to raw, ulcerative sores with scabs. Mucoid, purulent, or thick caseous exudate is present with secondary bacterial infections.
- Severe lesions cause lameness and reluctance to move. Rabbits may be anorectic and depressed.

Diagnosis

- Diagnosis is based on clinical signs. If wounds appear infected, submit samples for bacterial culture and sensitivity testing.
- Radiographs of the hocks may be indicated in severe cases to evaluate underlying bone involvement.

Treatment

- Correct the predisposing management and environmental factors.
- Thoroughly clean and debride necrotic wounds. An antibiotic cream such as silver sulfadiazine can be applied topically.
- Topical astringents such as Domeboro solution (Bayer, Inc., West Haven, CT) are beneficial in treating moist wounds. Apply the solution daily until the wound appears dry.
- Protect wounds with sterile, soft, padded bandages.
- Healing is often prolonged. Clean the wound with an antibacterial soak, topical antibiotics, and bandaging, daily or every other day.
- Systemic antibiotics are necessary if infection is present.

Prevention

- Wire flooring should be smooth, nonabrasive, and of sufficient width to prevent abrasions. Place soft, dry bedding, such as hay or several thicknesses of newspaper, in one area of the cage.
- Cages should be clean and of sufficient size to allow free movement.
- Check the feet and hocks periodically for signs of inflammation.
- Overweight rabbits should undergo weight reduction to decrease the risk of developing sore hocks.

RESPIRATORY DISEASE

Respiratory disease is common in pet rabbits and can result from many interrelated factors. Historically, *Pasteurella multocida* has been implicated as the major cause of respiratory disease, though it is probably now less common than in the past. Other bacteria, viruses, and non-infectious causes such as allergens, thoracic/nasal neoplasia, cardiovascular disease, nasal obstruction due to dental disease, and exposure to respiratory irritants should also be considered when working up a patient with respiratory disease.

- Respiratory irritants such as excessive ammonia in dirty, poorly-ventilated cages, aromatic wood shavings (cedar), and cigarette smoke may predispose some rabbits to respiratory infections.

Upper Respiratory Tract Infection (Snuffles)

Etiology

- Bacterial agents that haven been implicated in sinusitis and rhinitis in rabbits include: Pasteurella multocida (see Pasteurellosis), Bordetella bronchiseptica, and Staphylococcus and Pseudomonas species.
- Infections can be transmitted from the doe to offspring or by direct contact with infected rabbits. Infection also may be spread by aerosol (sneezing) or fomites.
- Chronic disease may be subclinical and precipitated by stress.

Clinical Signs

- Intermittent episodes of sneezing and rhinitis with serous or mucopurulent nasal discharge are common findings.
- Exudate can block the nasolacrimal duct resulting in conjunctivitis, serous-to-mucopurulent ocular discharge, and periorbital matting or alopecia. One or both eyes may be affected.
- Auscultation of the nares and trachea often reveal rattles and rales.
- Many rabbits have no other clinical signs. Rabbits with severe disease may be anorexic and lethargic.

Diagnosis

Diagnosis of rhinitis is based on clinical signs and isolation of the causative agent through bacterial culture and sensitivity testing.

- Submit a swab of nasal or conjunctival exudate for bacterial culture and sensitivity testing. Small-tipped culturette swabs are convenient for sample collection (e.g., BBL CultureSwab, Becton, Dickinson & Co., Franklin Lakes, NJ).
- Skull radiographs provide useful information about the nasal passage and sinuses. Increased opacity may indicate accumulation of exudate. Decreased opacity may indicate lysis from advanced infections or neoplasia. Elongated roots of cheek teeth obstructing the nasal passage may be visible. Thoracic radiographs help differentiate upper airway disease from pneumonia, cardiovascular disease, and thoracic neoplasia.
- If available, computed tomography (CT) of the skull will provide detailed information about the nasal passages and sinuses.

Treatment

- Give antibiotics at the first signs of respiratory disease (see Table 176-5). Chloramphenicol, enrofloxacin (Baytril, Bayer Animal Health, Shawnee Mission, KS), trimethoprim-sulfa, or parental penicillin G can be administered until culture results are known. The antibiotic choice may change based on results of bacterial culture and sensitivity testing.
- If conjunctivitis is present, cannulate and flush the nasolacrimal duct of the affected eye or eyes with sterile water or saline. A topical ophthalmic anesthetic is necessary for this procedure. Repeated flushes of the nasolacrimal duct daily for 2 to 3 days or every 3 days for four or five treatments is most effective. Apply an ophthalmic antibiotic solution such as ciprofloxacin (Ciloxan, Alcon Laboratories, Fort Worth, TX) gentocin, or chloramphenicol four to six times daily for 14 to 21 days.
- Long-term therapy may be necessary with chronic disease.

Prevention

General preventive measures are described in the following section on Pasteurellosis.

Pneumonia

Pneumonia can be acute or chronic and may occur alone or accompany upper respiratory disease.

Etiology

- Pasteurellosis is the most common cause of pneumonia in rabbits, though other bacteria such as *B. bronchiseptica* and *S. aureus* may also be involved. The infection spreads to the lungs from the upper respiratory tract through the trachea or, less frequently, through the bloodstream.
- Stress is an important factor in disease. Sudden temperature changes, poor sanitation, or poor ventilation in high-ammonia areas contribute to the development of disease.

Clinical Signs

- Chronic pneumonia is characterized by labored breathing, weight loss, cachexia, and anorexia.
- Clinical signs are often inapparent until disease is advanced.
- Acute death is common in young rabbits.

Diagnosis

Diagnosis of pneumonia is based on clinical signs and supportive diagnostic tests.

- Auscultate the thorax for crackles, expiratory wheezes, or decreased lung sounds over areas of consolidation or abscess.
- Thoracic radiographs help determine the extent of disease and may reveal lung lobe consolidation, air bronchograms, or well-delineated soft-tissue opacities if pulmonary abscesses are present.
- Results of a complete blood count (CBC) may reveal a relative increase in heterophil numbers or a reversal of the lymphocyte/heterophil ratio, indicating an inflammatory response.
- Tracheal washes are very difficult in rabbits because of the anatomy of the oropharynx and are not recommended.
- Postmortem lesions may include acute fibrinopurulent pneumonia, pleuritis, and septicemia.

Treatment

- Parenteral antibiotic therapy is preferred in rabbits with severe pneumonia.
- Supportive therapy includes supplemental fluids, vitamins, and force-feeding of anorectic animals.
- If an indwelling catheter can be placed, give fluids intravenously. Administer subcutaneous fluids if catheter placement is too stressful.
- Force-feed anorectic animals. Hold recumbent animals sternal while feeding and give food slowly to minimize stress and to prevent aspiration.
- Place severely dyspneic rabbits in an oxygen cage.
- Euthanasia often is elected for severely debilitated rabbits with advanced disease.

Pasteurellosis

Etiology

- Pasteurellosis is an endemic bacterial disease of rabbits. It is caused by *Pasteurella multocida,* a small, gram-negative, bipolar coccobacillus.
- Infection is spread by direct contact with infected rabbits or contaminated fomites, aerosolization, or from does to offspring during birth and nursing.
- Bacteria colonize the soft palate and nasal turbinates and may produce a lifelong infection. Infection may be subclinical with intermittent episodes of mucopurulent nasal discharge, which often is precipitated by stress.
- Spread from the nasal cavity can occur by several routes:
  - The eustachian tube to the middle or inner ear, meninges, and brain
  - The nasolacrimal duct to the conjunctiva
  - The trachea to the lungs
  - Hematogenously to the peripheral lymph nodes, reproductive tract, lungs, or other organs.
- Pasteurella infections can also result in abscesses in the subcutaneous tissues, retrobulbar space, and internal organs. Culture of the abscess capsule wall is recommended however, since other bacterial organisms have also been implicated.

Clinical Signs

Clinical signs of disease depend on the site and chronicity of infection.

- Respiratory signs associated with pasteurellosis include rhinitis, conjunctivitis, and pneumonia.
- Neurologic signs, including head tilt, torticollis, nystagmus, and facial nerve deficits, can be seen with infections of the middle or inner ear, meninges, or brain.
- Abscesses can occur in the joints, tooth roots, various organs, and in subcutaneous tissue. Exudate is typically white, thick, and caseous.
- Abscesses in the retrobulbar space often result in exopthalmus and subsequent ocular infections and corneal ulcers.
- Generalized illness, fever, and peracute death may occur from septicemia or pleuropneumonia of more pathogenic strains of *P. multocida*.

Diagnosis

- Submit samples from exudate, blood, or tissue for bacterial culture and sensitivity testing.
- Isolation of *P. multocida* is sometimes difficult. To maximize culture results, the swab should be inoculated onto a blood agar plate or Cary-Blair transport medium. Additionally, when collecting samples from an abscess, the swab should be directed toward the inner wall of the capsule as the necrotic centers are often sterile.
- Enzyme-linked immunosorbent assays (ELISAs) have been developed to detect antibodies to *P. multocida* and may be helpful in detecting subclinical carriers. The test requires whole blood or serum and is reported as high positive, low positive, or negative. Results must be interpreted with discretion, as low positives can occur with antibodies of closely related, but normal bacteria or from maternally acquired antibodies. False negatives may occur early in an infection or in immunocompromised individuals.
- Radiographs of affected areas can help delineate the extent and severity of the disease.

Treatment

▼ ***Key Point*** Successful treatment of pasteurellosis can be difficult, especially in rabbits with advanced disease.

- Antibiotic therapy should be based on culture and sensitivity testing. Enrofloxacin (5–10 mg/kg PO q12h) and chloramphenicol (50 mg/kg PO q12h) administered for several months have been used successfully in the treatment of rabbits with chronic pasteurellosis.
- Injections of penicillin G benzathine/penicillin G procaine (40,000 IU/kg SC q24h for 2 weeks, then q48h for 2 or more weeks) have also had reported success in the treatment of pasteurellosis.
- Perform complete surgical excision of subcutaneous abscesses; the thick-capsule wall and caseous nature of the exudate preclude simple lancing and draining.
- Mandibular or joint abcesses require extensive debridement and wound care (see Mandibular and Joint Abscesses).
- Daily management includes thorough cleaning and flushing until healing is well advanced.
- Debilitated rabbits require supplemental fluids, force-feeding, and general nursing care.

Prevention

- Pasteurellosis is an endemic disease in rabbits, and control is difficult. Colonies are kept Pasteurella-free through serologic testing and strict isolation and sanitation procedures.
- Prevention involves isolation of healthy animals from rabbits with clinical signs of disease. Eliminate rabbits with evidence of disease from breeding colonies.
- Closely examine pet rabbits for signs of respiratory disease before purchase. New rabbits should be quarantined from other rabbits in the household until their disease status is known.
- Minimizing stress, feeding the rabbit a proper diet, and using good husbandry practices are important in preventing the spread of pasteurellosis.

GASTROINTESTINAL DISEASES

Rabbits often are anorectic when a primary GI disease is involved. Anorexia is also common with metabolic abnormalities such as kidney disease and lead toxicoses and with any severe systemic infection. A change in food intake can alter the flora of the GI tract, resulting in the excessive production of volatile fatty acids and subsequent change in cecal pH. This can lead to the overpopulation of pathogenic bacteria resulting in either diarrhea or GI stasis.

Diarrhea/Enteritis/Enterotoxemia

Etiology

▼ ***Key Point*** Lack of roughage in the diet, stress, and antibiotic therapy are all factors that contribute to disruptions in cecal microflora and pH, which can result in diarrhea.

- Diets high in digestible carbohydrates contribute to overgrowth of pathogenic bacteria by supplying a ready source of fermentable products. Toxins produced by these bacteria are primary factors in enterotoxemia.

Bacterial Pathogens

- Clostridium spiroforme, a gram-positive, anaerobic, spore-forming rod, is one of the primary pathogens in bacterial enteritis in rabbits. Although this organism can be present as normal GI flora, with a ready supply of fermentation products (digestible carbohydrates) it produces iota toxin, which causes severe enterotoxemia.
- Escherichia coli causes diarrhea in young rabbits and has a variable morbidity and mortality rate depending on the pathogenicity of the serotype involved. *E. coli* is not part of the normal gut flora but often is found in large numbers in the cecum of rabbits with diarrhea. The bacteria attach to the mucosal epithelium, causing necrosis and disruption of normal intestinal and cecal function. Enterohemorrhagic *E. coli* have also been isolated from rabbits and may pose a zoonotic risk.
- Clostridium piliforme (formerly Bacillus piliformis), which causes Tyzzer's disease, is associated with acute diarrhea and death, primarily in young weanling rabbits. *C. piliforme* may be a subclinical inhabitant of the gut. With stress, the bacteria proliferate and cause severe epithelial necrosis of the cecum, colon, and distal ileum.
- Lawsonia intracellularis, an intracellular, gram-negative, curved to spiral-shaped bacteria has been associated with proliferative enterocecocolitis in weanling rabbits.

Viruses

- A coronavirus has been described as a cause of diarrhea and subsequent death in 3- to 10-week-old rabbits. The virus denudes the intestinal villi; diagnosis is made by identifying the virus in feces or cecal contents.
- Rotavirus may be present as normal flora, but may act as a mild pathogen by destroying cells that produce disaccharidases and by contributing to carbohydrate overload. Severity of the diarrhea is variable and is affected by other contributing microorganisms.

Parasites

- Intestinal coccidiosis is primarily a disease of young rabbits. Twelve species of intestinal Eimeria infect rabbits. Diarrhea secondary to intestinal coccidiosis is usually mild; however, coccidia may predispose rabbits to bacterial enteritis (see "Coccidiosis"). The highly pathogenic Eimeria stieda infects the liver.
- Cryptosporidia parvum may cause a transient diarrhea in young rabbits for 3 to 5 days. No known treatments are available.

Management Related Factors

- Antibiotic therapy can cause suppression of normal gut flora and overgrowth of pathogenic bacteria. Diarrhea is associated with antibiotics that are active against gram-positive aerobes and selective gram-negative anaerobes. Antibiotic-induced diarrhea has been associated with the oral administration of lincomycin, clindamycin, erythromycin, ampicillin, amoxicillin, cephalosporins, and penicillin.
- Stress is a major factor in diarrhea. Stress-related epinephrine release may have a direct effect on intestinal motility and digestion, allowing overgrowth of pathogenic organisms.

Clinical Signs

- Diarrhea may vary from soft, pasty stool to a profuse, malodorous liquid. Mucus and blood may also be present. The perineal region and hindlimbs are often stained with feces.
- Rabbits with mild diarrhea may be otherwise normal. Severe diarrhea may be accompanied by lethargy, weight loss, anorexia, and dehydration.
- Intestinal gas often is detected on abdominal palpation.
- Sudden death may be the only clinical sign in peracute disease. In chronic cases, the rabbit has intermittent bouts of diarrhea and anorexia and may have progressive weight loss.

Diagnosis

Diagnosis of the primary cause is based on clinical signs, history, and specific tests.

- Dietary history is very important. Determine the fiber content of the normal feed and the amount of supplemental roughage.
- Identify bacterial pathogens by submitting fecal samples for aerobic and anaerobic bacterial culture and sensitivity testing.
- Do a direct fecal smear or fecal flotation to check for spore-forming gram-positive bacteria and coccidia.
- Results of serum biochemical analysis often reveal electrolyte and metabolic abnormalities in animals with moderate-to-severe diarrhea.

Treatment

- Correct the diet in animals on marginal or deficient dietary fiber levels.
- Dietary Lactobacillus supplements such as Bene-bac may help repopulate the GI tract with normal flora.
- Metronidazole (20 mg/kg PO, IV q12h) has been effective in treating rabbits with enterotoxemia caused by C. spiroforme.
- Enrofloxacin (10 mg/kg PO q12h) or trimethoprim/sulfa (30 mg/kg PO q12h) is indicated if E. coli bacterial enteritis is suspected.
- Chloramphenicol (30–50 mg/kg PO q12h) can be used to treat proliferative enteritis caused by L. intracellularis.

- Oral administration of antibiotics is effective in rabbits with mild-to-moderate diarrhea. Give antibiotics parenterally in rabbits with severe clinical signs. Avoid antibiotics that may induce enteritis.
- Intravenous fluid therapy is indicated for rabbits with moderate-to-severe diarrhea. Subcutaneous fluids are usually adequate for cases with mild diarrhea.
- Anorectic animals should be force fed replacement diets such as Critical Care for Herbivores (Oxbow Pet Products, Murdock, NE; www.oxbowhay.com).
- If young rabbits test positive for coccidiosis, administer appropriate therapy (see Coccidiosis).

Prevention

- Instruct owners to feed their rabbits proper diets with an adequate content of indigestible fiber, such as timothy hay.
- Minimize stress in young or weanling rabbits. Sudden temperature changes, changes in food, overcrowding, or poor sanitation contribute to disease.
- Isolate diseased animals from healthy rabbits.
- Screen young rabbits for coccidiosis or give prophylactic therapy.

Coccidiosis

Etiology

- Coccidia are host-specific protozoan parasites.
- Twelve different species of intestinal Eimeria infect rabbits, with *E. perforans* being the most common. Pathogenicity varies according to species. *E. magna* is the most pathogenic species affecting the small intestine.
- Hepatic coccidiosis results from infection with the highly pathogenic Eimeria stieda.
- Infection results from the ingestion of sporulated oocysts.
- Coccidiosis is primarily a disease of young and weanling rabbits. Natural immunity develops against each Eimeria species after exposure. No cross protection in immunity exists between different Eimeria species. Adult animals can become ill if exposed to a species against which they have no immunity.
- The severity of disease is determined by the age at time of exposure, the species of Eimeria involved, the number of oocysts ingested, and environmental stress factors.

Clinical Signs

- Intestinal coccidiosis is often subclinical or causes only intermittent mild-to-moderate diarrhea and associated dehydration. However, coccidia may predispose the rabbit to bacterial enteritis (see "Diarrhea/Enteritis"). Clinical signs are usually most apparent in young rabbits.
- Severe diarrhea, intussusception, and death may occur with heavy infections. Blood and mucous may also be associated with the diarrhea.
- Hepatic coccidiosis is associated with anorexia, weight loss, abdominal enlargement, diarrhea, icterus, and acute death.

Diagnosis

- Presumptive diagnosis is based on identifying Eimeria oocysts in a fecal sample or intestinal scrapings. The presence of organisms on histologic examination is required for definitive diagnosis.

Treatment and Prevention

- The age of the host and the severity of clinical signs are factors to consider in treatment. Animals with light parasite burdens usually develop immunity to the organism and recover without therapy.
- Therapy with coccidiostats is more prophylactic than therapeutic. Coccidia are susceptible to treatment only during a specific period in the protozoan life cycle. Clinical signs are usually inapparent during this period.
- Coccidiostats may slow multiplication until host immunity develops.
- Trimethoprim/sulfamethoxazole (30 mg/kg PO q12h for 10 days) has proved effective for the prevention and treatment of coccidiosis.
- Sanitation is of utmost importance for effective therapy and prevention. Routinely disinfect cages, food bowls, and water bottles.
- Screen rabbits for shedding of coccidial oocysts. Separate or cull carriers from colonies.
- Check all young rabbits for coccidia.

Gastrointestinal Stasis

Etiology

- Dietary factors

▼ ***Key Point*** Lack of roughage in the diet is a major predisposing factor in GI stasis.

- Stress is a major factor in GI stasis. Stress-related hormonal release may have a direct effect on intestinal motility and digestion, allowing overgrowth of pathogenic organisms.
- Hairballs slow GI motility, prolonging retention of fermentable food.

Clinical Signs

- No fecal pellet production in over 24 hours. Patients are also often anorectic.
- Some rabbits have painful abdomens and may stay in a hunched position. The stomach or cecum may be

distended with intestinal gas that may be detected on abdominal palpation.

Diagnosis

- Dietary history is very important. Determine the fiber content of the normal feed and the amount of supplemental roughage.
- Results of serum biochemical analysis often reveal electrolyte and metabolic abnormalities.

Treatment

- Fluid therapy is critical in the treatment of rabbits with GI stasis. Stable patients can be administered fluids subcutaneously once to twice a day. Critical patients require IV catheterization.
- Correct the diet in animals on marginal or deficient dietary fiber levels.
- Broad-spectrum antibiotics, such as the fluorinated quinolones, trimethoprim/sulfa, or chloramphenicol are indicated if bacterial enteritis is suspected. Oral administration is effective in animals with mild-to-moderate diarrhea. Give antibiotics parenterally in rabbits with severe clinical signs. Avoid antibiotics that may induce enteritis.
- Force-feed anorectic animals with Critical Care for Herbivores (Oxbow Pet Products) or softened rabbit pellets mixed with vegetable baby food or canned pumpkin.

Prevention

- Instruct owners to feed their rabbits proper diets with an adequate content of indigestible fiber.
- Minimize stress in young or weanling rabbits. Sudden temperature changes, changes in food, overcrowding, or poor sanitation contribute to disease.

Malocclusion

Etiology

▼ ***Key Point*** Malocclusion is one of the most common causes of anorexia in rabbits.

Clinical Signs

- Rabbits with malocclusion often have no other clinical signs. Owners may report that the rabbit shows interest in food, but stops eating after a few bites. Most remain alert and active.
- Excessive salivation is common in rabbits with malocclusion.

Diagnosis

- Perform a thorough oral examination in all anorectic rabbits. Examine the back molars with an otoscope or nasal/vaginal speculum. Sedation may be necessary in some especially nervous or active rabbits.

Treatment

- Incisors can be cut with a diagonal cutter or, preferably, a dental drill. Both pairs of upper incisors should be clipped.

▼ ***Key Point*** Do not use Resco-type nail clippers to cut incisors because excessive trauma can result in split incisors and loosened tooth roots.

- Molar malocclusion requires dentistry with sedation. The procedure is usually short and can be done with an injectable tranquilizer. A combination of medetomidine (0.15–0.35 mg/kg SC, IM) and ketamine (5–10 mg/kg SC, IM) works well and can be reversed when the procedure is finished. Gas anesthesia can be used by holding the anesthetic mask over the rabbit's nostrils, leaving the oral cavity free for working in the mouth.

Technique—Teeth Triming

1. Place the rabbit in sternal recumbency with an assistant extending the neck and head forward.
2. The mouth can be held open by looping strips of gauze around both upper and lower incisors. The assistant holds the gauze around the lower molars in one hand, while the second hand is placed on top of the rabbit's head and holds the gauze looped around the top incisors, forcing the head and neck into extension. Make sure the nostrils are not occluded and the neck is extended or the rabbit will have difficulty breathing. Alternatively, a metal speculum made for rabbit dentistry can be used to hold the mouth open; however, this tool can damage the oral mucosa if used inappropriately.
3. Use a short vaginal or nasal speculum with an attached light source to examine the oral cavity. Check both lateral and medial edges of upper and lower molars.
4. A dental drill rounds and smoothes sharp edges but must be used with care. Use a tongue depressor or the speculum to isolate the arcade and prevent damage to the tongue or buccal mucosa. Burr guards can also be purchased. Long-shank burrs made specifically for use in the long, narrow oral cavity of rabbits are available.
5. A small bone rongeur can be used to clip the sharp edges of the cheek teeth. Use a tongue depressor or speculum to push the tongue to one side while clipping the medial edges of the lower cheek teeth. This method is quick and easy but leaves rough edges and may cause fractures of the teeth.

- Root elongation of the premolars and molars can develop in rabbits with chronic malocclusion. Elongated roots of the mandibular teeth can be palpated as firm bony nodules on the ventral mandible. Roots of the maxillary teeth can invade the nasal passages, sometimes causing obstruction and resulting in inspi-

ratory stridor. The roots often become infected, resulting in mandibular, maxillary, or retrobulbar abscesses (see "Mandibular and Joint Abscesses").

Prevention

- Most rabbits with incisor malocclusion need their incisors clipped every 4 to 8 weeks.
- Check rabbits with molar malocclusion every 2 to 3 months. Dentistry may be needed as often as every month or only once yearly.
- Rabbits with malocclusion should not be bred.
- Instruct owners to feed a high-roughage diet to encourage normal wear of the teeth.

Hairballs (Trichobezoars)

Etiology

▼ ***Key Point*** Inadequate dietary roughage is associated with gastric hairballs in rabbits.

- Other factors may contribute to formation of hairballs. Long-haired breeds may consume large amounts of hair while grooming during shedding. Hormonal influences in breeding season may contribute to aggression and fur-barbering. Mineral deficiencies may cause pica of hair. Boredom also may be a factor in fur-barbering.
- Rabbits are unable to vomit, contributing to accumulation of hair in the stomach.

Clinical Signs

- Anorexia is the primary clinical sign associated with trichobezoars. Often rabbits remain alert and active, with no other signs.
- Weight loss, depression, and palpable intestinal gas may be present in some rabbits. Fecal pellets may appear small, the amount of pellets passed may be less than normal, and hair may be visible in the pellets, causing them to "string" together.
- Diarrhea may develop in some animals because of changes in the cecal microflora from decreased gastric motility (see "Diarrhea/Enteritis").
- Acute pyloric obstruction causes severe depression, lethargy, bloating, dehydration, hypothermia, and shock.

Diagnosis

▼ ***Key Point*** Suspect a trichobezoar in an anorectic but otherwise alert rabbit with a history of inadequate dietary fiber and excessive shedding.

- A soft mass palpable in the stomach area of an anorectic rabbit is evidence of a hairball. The stomach of a healthy rabbit is normally full. However, a rabbit that has been anorectic for several days should have an empty stomach.
- Radiographs are used to confirm a diagnosis. An enlarged stomach may be visible on plain radiographs. Contrast radiography of the upper GI tract may outline the hairball. Give barium at a standard small-animal dose of 10 to 14 ml/kg orally into the cheek pouch.
- Ultrasound examination can be used to detect a mass in the stomach area.
- A CBC and serum biochemical analysis are indicated in dehydrated, severely ill, or debilitated animals.

Treatment

▼ ***Key Point*** Providing adequate dietary roughage and making sure that the rabbit is hydrated are extremely important for successful treatment of rabbits with trichobezoars.

- Medical management is successful in most rabbits. Although a few clinicians advocate routine surgical removal of hairballs, the risk of surgical or anesthetic complications is high considering the debilitated condition of most of these rabbits.
- Give supplemental fluids (approximately 100–150 ml/kg/day) subcutaneously or, preferably, by intravenous catheter in debilitated animals.
- Stimulate GI motility by encouraging the animal to move around. Allow the rabbit out of the cage as much as possible to exercise. Administer GI motility stimulants if no intestinal blockage is suspected and gut motility is poor.
- Give the rabbit petrolatum-based oral lubricants such as Laxatone at 1 to 2 ml/day for 3 to 5 days to aid in fur passage.
- Offer free-choice hay and fresh vegetables at all times. Force-feed anorexic patients with products such as Critical Care for Herbivores (Oxbow Pet Products) several times a day.
- Pain medication such as buprenorphine (0.01–0.05 mg/kg SC, IM q6–12h) or flunixin meglumine (1.1 mg/kg SC, IM q12h for no more than 3 days) may be indicated in patients with abdominal pain and distention.
- Although rare, rabbits with acute pyloric obstruction must be treated surgically. Even with surgery, the mortality rate in rabbits with pyloric obstruction is high.

Prevention

▼ ***Key Point*** Correct the diet to include adequate dietary fiber (see Diet). Provide free-choice timothy hay and fibrous vegetables. Feed rabbit pellets that have a high-fiber content (>20%).

- Routinely brush long-haired rabbits or heavy shedders.
- Some owners administer a petrolatum-based cat laxative to their rabbits every 1 to 2 months.

- Encourage rabbits to exercise. Prevent obesity by restricting the amount of pellets fed and not feeding sweet "treats".

UROGENITAL/REPRODUCTIVE DISEASES

Uterine Adenocarcinoma/Hyperplasia

Etiology

▼ ***Key Point*** Uterine adenocarcinoma is the most common tumor in domestic rabbits.

- Adenocarcinoma rarely occurs in does younger than 4 years of age. The incidence in rabbits older than 4 years of age ranges from 50% to 80% in certain breeds such as the Dutch, French Silver, and Havana, suggesting a genetic component to the disease. Occurrence is independent of breeding status.
- Endometrial changes such as atrophy of the glandular epithelial cells and increased collagen content are associated with development of uterine neoplasia.
- Endometrial changes that may precede neoplastic changes include endometriosis, endometritis, and papillary, cystic, or adenomatous hyperplasia.
- Local metastasis can extend through the uterine myometrium and invade adjacent structures in the peritoneum such as lymph nodes. Hematogenous spread to the liver, lungs, and brain occurs late in the clinical course, after 10 to 12 months.

Clinical Signs

Uterine adenocarcinoma is a slow-growing tumor that can be multicentric and involve both horns of the uterus.

- Clinical signs are usually inapparent during the early hyperplastic stages.
- Hematuria or a serosanguineous vaginal discharge is often the first clinical sign noted.
- Decreased reproductive performance such as small litter size, stillbirths, dystocia, litter desertion, and infertility are seen in breeding does.
- Cystic mastitis is associated with uterine changes in many does.
- Depression, anorexia, dyspnea, and ascites are often noted in late-stage cases, especially if metastasis to the lungs has occurred.

Diagnosis

- An enlarged, thickened uterus or multiple rounded caudal abdominal masses may be palpable on physical examination. A mass may be difficult to differentiate from abdominal fat in small does.
- An enlarged uterus may be visible on abdominal radiographs. Thoracic radiographs should be taken to screen for pulmonary metastasis.
- Abdominal ultrasonography also can be used to identify an enlarged uterus or uterine masses and to detect liver or lymph node metastases.

Treatment

- Ovariohysterectomy is successful if done before metastasis has occurred.
- Surgical resection of early focal abdominal metastasis is the treatment of choice but carries a guarded prognosis because of metastasis that may not be visible at the time of surgery.
- Prognosis is poor after pulmonary metastasis has occurred. Euthanasia is recommended.

Prevention

- Routine ovariohysterectomy of does before 2 years of age is recommended.
- Educate owners with intact does about the early clinical signs of uterine adenocarcinoma and recommend yearly to semi-annual check-ups once the patient is 3 years of age.
- Consider ovariohysterectomy in does older than 3 years of age with evidence of cystic mastitis or increased aggressive behavior.

Mastitis

Etiology

Mastitis in rabbits can be either septic or nonseptic.

- Septic mastitis is most common in lactating does. Trauma from abrasive bedding or caging, heavy lactation, and poor sanitation predispose the mammary gland to infection.
- Staphylococcus aureus and Pasteurella and Streptococcus spp. are the most commonly isolated bacteria. E. coli and Pseudomonas, Pasteurella, and Klebsiella spp. also may cause mastitis.
- Nonseptic, cystic mastitis is seen in both breeding and non-breeding females older than 4 years of age. It may be associated with high estrogen levels, uterine hyperplasia, and uterine adenocarcinoma. In some cases, malignant cellular changes may occur and develop into mammary adenocarcinoma.

Clinical Signs

- With septic mastitis, the affected gland is swollen, firm, erythematous to blue-tinged, and warm to the touch. Infection spreads until all glands are affected.
- Abcesses of the mammary gland can develop independent of lactation status.
- Systemic signs of septic mastitis include pyrexia, depression, anorexia, death of neonates, or death of the doe.
- With cystic mastitis, glands became swollen, firm, and blue-tinged with a clear-to-dark serosanguineous discharge from the teats. Rabbits are not systemically ill.

Diagnosis

- Diagnosis of septic mastitis is based on clinical signs, history of lactation or pseudocyesis, and isolation of bacteria on culture of gland tissue or exudate.
- Cystic mastitis must be differentiated from septic mastitis and mammary neoplasia. Culture and sensitivity testing of the discharge is negative for bacterial growth. Fine-needle aspiration and cytology is indicated to identify any neoplastic tissue.

Treatment

- Administer antibiotics for septic mastitis. Base therapy on results of culture and sensitivity testing.
- Pain medication such as buprenorphine is indicated if the rabbit appears to be in pain. Warm compresses 2 to 3 times daily may be helpful. Consider surgical drainage or excision of mammary abscesses.
- Suckling kits need to be removed from the doe as they may become infected with the bacteria and die from septicemia.
- Cystic mastitis usually resolves within 3 to 4 weeks after ovariohysterectomy. Severely affected glands may require surgical excision.

Prevention

- Keep lactating does in a clean environment. Make sure no sharp surfaces or wire edges are present that can traumatize the teats.
- Routinely examine lactating does for evidence of inflammation or teat injuries.
- Cystic mastitis can be prevented by routine ovariohysterectomy of young, healthy does.

Dysuria/Hematuria

Etiology

- Red, pink, or orange discoloration of the urine occurs periodically in healthy rabbits. The color may be the result of porphyrin pigments or food-related metabolites excreted in the urine.
- Thick, creamy to sandy, white urine indicates the presence of excess calcium in the urine. Unlike most mammals, intestinal absorption of calcium does not depend on vitamin D. Increases in dietary calcium intake results in large amounts of calcium being excreted in the urine.
- Hematuria occurs commonly with cystitis. Frank blood independent of or at the end of urination may indicate uterine adenocarcinoma.
- Cystic calculi occur in both male and female rabbits. Calculi usually are composed of calcium carbonate or calcium oxalate and may be associated with high dietary calcium intake.

Clinical Signs

- Rabbits with urinary pigment changes or excessive calcium in the urine usually have no other clinical signs.
- Dysuria, stranguria, urine scald, lethargy, anorexia, and depression may be seen in rabbits with cystitis or cystic calculi. Rabbits may also exhibit teeth grinding or stay in a hunched position in response to abdominal pain.

Diagnosis

- Differentiate hematuria from pigment changes in the urine by simple dipstick analysis for blood. If urine discoloration is intermittent, dispense dipsticks for owners to check the urine at home.
- Submit a urine sample for urinalysis in rabbits with clinical signs of cystitis, cystic calculi, or hematuria. Calcium oxalate crystals are commonly present, though ammonium phosphate, calcium carbonate, and monohydrate crystals are also often seen. If bacteria are identified, a urine sample collected by cytocentesis should be submitted for culture and sensitivity testing.
- A serum biochemical analysis and a CBC are necessary to assess renal function.
- Distinguish between hematuria and hemorrhagic vaginal discharge occurring secondary to uterine adenocarcinoma by physical examination, history, urinalysis, abdominal radiographs, and abdominal ultrasonography. Uterine adenocarcinoma is likely in a doe older than 3 years of age with a thickened uterus or multiple abdominal masses.
- Obtain abdominal radiographs if cystic calculi are suspected. Calculi are usually radiopaque and therefore visible in the bladder or urethra. Calculi may also be visible in the ureters or kidneys. Large amounts of calcium sediment may be visible in the bladder in rabbits excreting large amounts of calcium.

Treatment

Treatment is not necessary in rabbits with pigment-based changes in urine color.

- Instruct owners to decrease the dietary calcium levels in rabbits with hypercalciuria. Grass hay (e.g., timothy) has a lower calcium content than legume hay (e.g., alfalfa). Feed grass hay, green leafy vegetables, and timothy-based pellets.
- Treat rabbits with simple bacterial cystitis with antibiotics. A 3-week course of chloramphenicol or trimethoprim/sulfa is usually effective. Submit a second urine sample for bacterial culture and sensitivity testing after 4 to 6 weeks.

- Cystic calculi must be removed surgically. Submit calculi for stone analysis. Decrease dietary calcium after surgery to help prevent recurrence.

Prevention

- For prevention, decrease dietary calcium levels, especially in mature or aged rabbits.
- Many pelleted diets are derived from alfalfa and exceed dietary calcium requirements. Change to timothy-based pellets and substitute grass or timothy hay for alfalfa hay in the diet. Discontinue any supplemental vitamins.
- Overweight rabbits are predisposed to hypercalciuria and urolithiasis. Decrease or eliminate pellets from the diet and encourage rabbits to exercise to prevent obesity.

Treponematosis

Etiology

- Treponema paraluiscuniculi is the causative agent of rabbit syphilis.
- T. paraluiscuniculi is a spiral-shaped bacterium transmitted by direct and venereal contact between breeding rabbits or from doe to offspring. It is not a zoonotic disease.

Clinical Signs

- Most lesions develop on the external genitalia and perineum. Infection of the nose, eyelids, lips, and chin may result from autoinfection. Lesions initially consist of erythematous vesicles that progress to papules, ulcerations, scaliness, and dry crusty lesions.
- Nasal lesions in pet rabbits are commonly mistaken for dermatophyte lesions.
- Rabbits remain alert, responsive, and active.
- The incidence of abortions, metritis, and infertility may increase in breeding females.

Diagnosis

- Diagnosis is based on history, clinical signs, distribution of lesions, and response to therapy.
- Submit fur samples for fungal culture and do skin scrapings to rule out dermatophytes and ectoparasites.
- Treponema organisms can be identified by darkfield microscopic examination of skin scrapings. The organisms also can be demonstrated histologically with silver stains of skin biopsy sections.
- Serologic tests such as the rapid serum regain (RPR) are available commercially to determine the presence of antibodies against T. cuniculi. A fluorescent antibody test against treponemal antigen also is used, and an ELISA is available to screen for antibodies. These tests are used for screening in rabbit-breeding colonies.

Treatment

- T. paraluiscuniculi is susceptible to penicillin. Give injections of benzathine penicillin G (a long-acting penicillin) at 42,000 to 84,000 IU/kg IM at weekly intervals for 2 to 3 weeks. Response is rapid; lesions dramatically regress, usually after one injection.
- Tetracyclines and chloramphencol have also been effective against T. cuniculi.

Prevention

- Screen rabbits in breeding colonies for treponematosis.
- The incidence of disease in pet rabbits is low. Preventive serologic screening is not necessary.

NEUROMUSCULAR/SKELETAL DISEASES

Mandibular and Joint Abscesses

Etiology

- Abscesses of the mandible and joints occur frequently in pet rabbits. Bacteria such as Pasteurella multocida, Staphyloccoccus aureus, Pseudomonas aeruginosa, Fusobacterium nucleatum, Peptostreptococcus micros, Strepcococcus milleri group, Actinomyces israelii, Arcanobacterium haemolyticum, Prevotella spp., Proteus spp., and Bacteroides spp. have been isolated. Bacteria can also spread hematogenously from the initial infection.
- Malocclusion and root elongation of the cheek teeth sometimes accompany mandibular abscesses. Infection may spread from the oral cavity along the tooth root.
- Soft-tissue abscesses can also occur in the oral cavity or joints secondary to a penetrating wound from a foreign body.

Clinical Signs

- Joint abscesses are most frequent in the distal limb joints. The swellings are large, firm, and warm to the touch. Rabbits may be lame, depending on which joints are involved.
- Mandibular abscesses occur as firm swellings in the ventral facial area. Abscesses are sometimes quite large before they are apparent to the owner. Excessive ptyalism may be an early symptom.
- Affected rabbits may refuse to eat if mandibular abscesses are accompanied by dental disease.
- Many rabbits remain active and alert with no other clinical signs.

Diagnosis

- Thick, white purulent exudate is present on fine-needle aspirate of the swelling. Cytologic examination of the exudate shows neutrophils and

proteinaceous debris; bacteria may or may not be visible.
- Obtain radiographs to check for and evaluate the extent of any bone involvement.
- Submit tissue samples for bacterial culture and sensitivity testing. Because the necrotic centers are often sterile, collect samples from the inside of the abscess capsule wall.

Treatment

▼ ***Key Point*** Simple lancing of mandibular and joint abscesses is ineffective because of the thick, caseous nature of the exudate.

- Complete enbloc surgical excision of the abscess is the preferred treatment. However, depending on the extent of involvement, this may not be possible and aggressive surgical debridement is the next best option. Remove any molars or premolars that are loose or that have radiographic evidence of extensive infection of the roots. Flush the soft tissue with copious amounts of sterile saline.
- Abscesses often re-occur and multiple surgeries concomitant with antibiotic therapy may be required for resolution.
- Antibiotic-impregnated polymethylmethacrylate (AIP-MMA) beads can improve the success rate of surgical treatment of mandibular abscesses if abscessed tissue cannot by completely excised.
- Amputating the affected limb may be the most effective therapy for abscesses involving the joint and surrounding bone. Rabbits adapt well to amputation of either a fore or rear limb.
- Disease may recur in other joints, even if amputation of the affected limb has been performed. Hematogenous spread of the bacterial infection to other joints may occur at any time during the clinical course.
- Long-term antibiotic therapy is necessary. Some rabbits respond to oral fluoroquinolone or injectable penicillin therapy in combination with surgical debridement or amputation.
- Owners must be able to do extensive nursing care at home. Have the owners flush open wounds with sterile saline once or twice daily.
- The prognosis for successful therapy is guarded. With bony involvement, the prognosis is poor.

Torticollis/Head Tilt/Ataxia

Etiology

- Bacterial infection of the inner ear, middle ear, or meninges is the most common cause of torticollis in pet rabbits. Pasteurella multocida is often implicated as a primary cause, though other bacteria may also be involved.
- Encephalitozoon cuniculi is another common cause of torticollis and incoordination in rabbits.
- Vascular lesions, infection with herpesvirus, cerebral nematodiasis, hypovitaminosis A, and toxicoses (e.g., lead poisoning) are less common causes of head tilt and uncoordination.

Clinical Signs

- Onset may be acute or slowly progressive. The head tilt may be mild or accompanied by torticollis, incoordination, and the inability to stand.
- Some rabbits have no other clinical signs. Other rabbits become depressed, anorexic, and lethargic.
- Rabbits with severe depression, positional nystagmus, and facial nerve deficits may have brain or meningeal lesions.

Diagnosis

Diagnosis is based on clinical signs. Establishing the exact cause may be difficult.

- Carefully examine both ear canals for evidence of infection.
- Rabbits with severe otitis media may have swellings at the base of the ear. White, creamy, caseous debris can often be massaged out of the ear canal. Cultures and sensitivity testing can be helpful in identifying organisms and in directing antibiotic therapy.
- Results of a CBC may reveal an inflammatory response.
- Skull radiographs may aid in diagnosis. Anesthesia is usually necessary for proper positioning. Bony changes in the bulla may indicate osteomyelitis.
- Serologic tests can be used to detect antibodies against E. cuniculi or P. multocida. A positive result is not diagnostic of the specific agent but is helpful in ruling out some possible causes.
- Often, the cause cannot be established, and a tentative diagnosis is based on response to therapy. Rabbits with pasteurellosis often improve with long-term antibiotic therapy and supportive care. Rabbits with parasitic migration may remain unchanged or improve gradually. Rabbits with clinical signs secondary to encephalitozoonosis are usually unresponsive to treatment or they deteriorate clinically.
- The cause sometimes is determined only on postmortem examination.

Treatment

- Give antibiotics long-term, usually a minimum of 4 to 6 weeks. Choose an antibiotic that penetrates the blood-brain barrier and is effective against pasteurellosis (e.g., chloramphenicol and enrofloxacin).
- If exudate is visible in the ear canal, clean and flush the ear thoroughly. Tranquilization or anesthesia may be necessary. Administer a topical antibiotic in the ear canal 3 to 4 times daily. Administer systemic antibiotics based on culture and sensitivity testing.

- Administer an oral Lactobacillus supplement during long-term antibiotic therapy.
- Supportive care is necessary in rabbits that are laterally recumbent or that have severe torticollis. Recumbent rabbits should be turned every 6 to 8 hours or propped up sternally to prevent hypostatic congestion of the lungs. Apply eye lubricants several times daily if the blink reflex is diminished. Hand-feeding may be required. Keep rabbits on clean, dry bedding to prevent urine scalding and contact dermatitis.
- Inform owners about the amount of supportive care needed in recumbent rabbits. Many owners elect euthanasia when faced with the difficulties and the time required for long-term nursing care.
- Euthanasia often is selected in debilitated rabbits if no clinical improvement is seen after several days of therapy.

Encephalitozoonosis *(Encephalitozoan cunuculi)*

Etiology

- *E. cuniculi* is an obligate, intracellular, microsporidian parasite prevalent in domestic and wild rabbits. The organism infects mice, rats, hamsters, and guinea pigs less commonly.
- The major route of transmission is by ingestion of spore-contaminated urine. Inhalation and vertical transmission can also occur. *E. cuniculi* spores are environmentally resistant and can survive for 4 weeks in mild environmental conditions.
- The organism can infect lungs, kidneys, liver, heart, brain, and eye. Many infected rabbits are asymptomatic, or may develop clinical signs after a stressful event or other immunosuppressive conditions.

Clinical Signs

- Depending on the site of infection, clinical signs can vary and include: torticollis, ataxia, nystagmus, rolling, seizures, paresis, and death. Clinical signs of encephalitozoonosis are similar to those of the neurologic form of pasteurellosis.

Diagnosis

- Presumptive diagnosis is based on clinical signs and results of diagnostic testing of rabbits exhibiting neurologic signs.
- Serologic tests are available to detect the presence of antibodies against *E. cuniculi*. These include ELISAs and indirect fluorescent antibody assays.
- Definitive diagnosis requires histopathologic examination of affected tissues. Spores can be seen in the tissue and lesions in the brain usually consist of multifocal areas of necrosis and granulomas with perivascular lymphoplasmacytic cuffing.

Treatment

- Several treatment protocols have been reported; however, results have been variable. Administer fenbendazole (20 mg/kg q24h for 28 days), oxibendazole (30 mg/kg PO q24h for 7–14 days, then reduced to 15 mg/kg q24h for 30–60 days), or albendazole (30 mg/kg PO q24h for 30 days, then 15 mg/kg PO q24h for 30 days or 10–15 mg/kg PO q24h for 3 months).
- Clinical signs may recur in some rabbits when drugs are stopped. These rabbits may require medications indefinitely to control clinical signs.
- For rabbits with suspected concurrent bacterial infection, antibiotic therapy with chloramphenicol (30–50 mg/kg PO q12h for 7 days) can be administered while awaiting the results of serologic testing.
- Patients with severe neurologic signs are often anorectic and will require supportive care such as fluids and force feeding until clinical signs abate.

Prevention

- Identify carriers in rabbit colonies and breeding facilities through serologic testing. Cull animals that test positive.
- Eliminate urine contamination between cages through proper sanitation procedures. Most disinfectants, such as quaternary ammonium compounds, iodophors, phenolic derivatives, alcohols, and hydrogen peroxide, are effective in inactivating spores.
- Prevent possible contact between pet rabbits housed outdoors and wild rabbits or rodents by elevating cages off the ground or housing pets in a rodent-proof enclosure.

Vertebral Fractures/Luxation

Etiology

- The rear leg muscles of rabbits are well developed for strong kicking and thumping.

▼ ***Key Point*** If rabbits are restrained poorly with inadequate control of the rear legs, animals may kick suddenly, resulting in fracture of their spinal vertebrae.

- The lumbosacral region (L7) is the most common site for fracture or luxation.

Clinical Signs

- Clinical signs of a fractured back depend on the degree of spinal cord damage and can include partial or complete paralysis of the rear legs and loss of normal bladder and bowel function.
- Signs are acute in onset and directly related to a traumatic incident.

- Other disease problems may cause clinical signs similar to a vertebral fracture. Multifocal infection of the spinal cord secondary to pasteurellosis, parasite migration, or vascular thrombosis within the cord can cause neurologic deficits. The clinical onset is usually more chronic and slowly progressive than that of a fracture.

Diagnosis

- Diagnosis is based on history and clinical signs.
- Obtain radiographs of the vertebral column to confirm a fracture or luxation.

Treatment

- If a diagnosis is made within 6 to 12 hours of the time of the fracture, administer methylprednisolone sodium succinate, prednisolone sodium succinate, or dexamethasone at shock dosages.
- Conservative medical management such as cage rest and nonsteroidal anti-inflammatory agents can be used to manage mild cases. Anti-inflammatory and pain medication such as Carprofen (Rimadyl, Pfizer Animal Health, Exton, PA) or Meloxican (Metacam, Boehringer, Ingelheim Vetmedica, St. Joseph, MO) are often effective in making the patient more comfortable. Attempts to stabilize the fracture surgically are usually not practical because of the poor prognosis and degree of nursing care necessary.
- Some owners try long-term supportive care to see whether neurologic function returns. They must be instructed on manual expression of the bladder and general nursing care. The rabbit's bedding should be changed multiple times a day to prevent urine scald. The patient will also need to be placed on alternating sides frequently prevent formation of pressure sores.
- Prognosis for recovery is guarded to poor. Euthanasia usually is recommended in rabbits with complete transaction of the cord resulting in complete rear limb paralysis and urinary and fecal incontinence.

Prevention

- See Figs. 176-1, and 176-2 for proper restraint of rabbits.

Bone Fractures/Joint Luxations

Etiology

- The skeleton of the rabbit is light and fragile. The tibia, radius, and ulna fracture easily with traumatic events such as getting a limb caught in wire caging or accidentally being dropped or stepped on.
- Traumatic joint luxations of the elbow or stifle joint occasionally occur.

Clinical Signs

- Rabbits with bone fractures or luxations are acutely lame.
- Rabbits have minimal soft tissue to protect the long bones below the elbow and stifle from penetrating the skin, thus open fractures are common at these sites.
- Fractures are usually palpable on physical examination. Joint luxations are palpable as firm swellings.

Diagnosis

- Diagnosis is based on history, clinical signs, and physical examination.
- Obtain radiographs to evaluate fractures for surgical repair or to confirm joint luxations.

Treatment

- *Splints* used in combination with padded bandages are usually adequate to stabilize metatarsal, metacarpal, and phalangeal fractures. Bandage the foot in a functional position. Contour a moldable splint or casting material such as Orthoplast (Johnson & Johnson, New Brunswick, NJ) or Vet-lite (Runlite SA, Micheroux, Belgium; see www.runlite.com for distributors) along the plantar surface.
- External coaptation can also be effective for closed, simple, long-bone fractures. Maintain the limb in a normal position and incorporate both the joints above and below the fracture into the splint. Ideally, there should be at least 50% cortical contact between the fragment ends.
- *Intramedullary pins* can be used for better axial alignment of long bone fractures and to minimize bending and rotational forces. The pins should occupy at least 60% to 70% of the medullary cavity. Cross-pins can be used for supracondylar humeral or femoral fractures. Bone plates are not usually recommended other than in large rabbits because the thin cortices of rabbit bones makes screw placement difficult.
- *External skeletal fixation* provides rigid stability with minimal soft tissue disruption. Because fixator pin diameter should not exceed 20% of the bone diameter, Kirschner wires are often used in smaller patients. Most metal bars and clamps are too large or heavy for rabbits; therefore, bone cement or acrylics injected into appropriately sized rubber tubing are effective as fixator bars. (see Chapter 111 for examples of external skeletal fixators)
- Severely comminuted or open fractures may be best managed with limb amputation. Rabbits usually adapt well to amputation and can ambulate easily on three limbs. Forelimb amputation is best performed by removing the scapula. Mid-femoral amputation

of the hind limb is preferred over coxofemoral disarticulation.
- With a joint luxation, anesthesia is needed to manipulate the joint into normal position. With the joint reduced and the limb in extension, apply a splint to allow the surrounding soft tissue to develop fibrosis and keep the luxation reduced. Some luxations may additionally require a transarticular pin to stabilize the joint.

See Section 8 for treatment of orthopedic disorders in dogs and cats.

Postoperative Care

- Obtain a radiograph of the leg after repair to assess bone alignment and placement of pins (if used).
- Postoperative management vital for successful healing includes strict cage rest, a clean environment, a good diet, and frequent monitoring any bandages or fixators.
- Antibiotics are indicated in all open and contaminated fractures to prevent subsequent osteomyelitis and abscess formation.

SUPPLEMENTAL READING

Harcourt-Brown F: Textbook of Rabbit Medicine. Oxford, Butterworth-Heinemann, 2002.

Quesenberry KE, Carpenter JW (eds): Ferrets, Rabbits, and Rodents: Clinical Medicine and Surgery. 2nd edition. W.B. Saunders, St. Louis, 2004.

Chapter

177 Pet Rodents

Nancy L. Anderson

Many small rodents are commonly kept for companionship and enjoyment. This chapter provides information needed to diagnose and treat the most frequently encountered problems of mice, rats, gerbils, hamsters, guinea pigs, and chinchillas.

HUSBANDRY

Caging and Sanitation

- Cages should be made of stainless steel, hard plastic, or glass. These materials are cleaned and sanitized easily and are resistant to gnawing or corrosion from urine and fecal matter. Minimum floor space and height requirements are listed for each species in Table 177-1. With the exception of guinea pigs, all cages need secure lids.
- Guinea pigs can be housed in open-topped enclosures with walls higher than 10 inches. Ensure that dogs, cats, wild animals, and small children do not have unsupervised access to these cages.
- Clean cages as needed, usually 1 to 3 times per week for most rodents. A scrub brush, dish soap, and water work well. If cages are not kept clean, ammonia, other irritants, moisture, and bacteria concentrations rise to harmful levels, predisposing animals to disease.
- Disinfect the cage twice a month with 1 part sodium hypochlorite (household bleach) mixed in 30 parts water. Let the bleach solution stand for at least 15 minutes. Rinse the cage well afterward.
- All solid-floored cages need to be covered in bedding. Shredded paper, non-resinous wood shavings, wood wool, and corn cobs are all acceptable. Provide at least 2 inches of bedding. Most rodents enjoy burrowing in deeper bedding when it is provided in one corner of a cage. Do not, however, fill the entire cage with deeper bedding. This usually leads to poor sanitation as a result of owners' failure to recognize buildup of hidden wastes such as moisture from leaking water bottles, cached foods, urine, and feces.
- Wire mesh floors can be used successfully only if the dimension of the mesh is correct. Size the openings to be just large enough for an adult to retract a tarsal joint back through the mesh. Larger holes make it difficult for the animals to walk and cause pressure sores. Smaller openings may cause injuries such as tibial fractures and self-mutilation while struggling to free trapped appendages. Bedding above the wire keeps waste from dropping through the wire and therefore is not recommended. Wire bottom cages do not work well for breeding animals because neonatal rodents must be surrounded by nesting material to maintain moisture in the nest and prevent dehydration. Young rodents often cannot walk correctly on mesh sized for adult feet.
- All pet rodents require visual security. Tubes, jars, or cans made of nontoxic, nonabrasive substances work well for this purpose. Also provide objects for gnawing. Rodents possess open-rooted teeth, and constant wear is necessary to maintain normal dentition. Mice, rats, gerbils, and hamsters enjoy and benefit from exercise wheels.
- A good room temperature range for most pocket pets is 70°F to 75°F. Keep rodents with disease at 85°F to 90°F unless hyperthermia is of concern (some chinchillas).
- Provide 10 to 12 hours of darkness to 12 to 14 hours of light. This light cycle is essential if breeding is desired.
- Hamsters, guinea pigs, and chinchillas that are exposed to temperatures below 65°F may hibernate for a few days or until the ambient temperature rises. Heart rates may be less than 5 bpm during hibernation.

Nutrition

▼ ***Key Point*** Feed pet rodents laboratory animal chow appropriate for their species (Table 177-2). Seed diets are deficient in protein and contain excessive fat.

- Seeds, as well as vegetables and other foods, may be fed as treats but not to provide more than 15% of calories. Intermittent exposure to vegetables and seeds causes mild, transient diarrhea.
- Supplementation of vitamin C is recommended for all guinea pigs.

Table 177-1. CAGING AND ENVIRONMENTAL REQUIREMENTS FOR POCKET PETS

Requirement	Rat	Mouse	Guinea Pig	Chinchilla	Hamster	Gerbil
Air changes/hour	10–15	10–15	10–15	>6	>6	>6
Minimum cage floor space/animal (square inches)	35	15	101	288	20	36
Minimum cage height (inches)	>6	>5	>10	>12	>6	>6
Recommended room temperature (°C)	21.1–26.6	21.1–29.4	18.3–23.8	15.5–21.1	18.3–23.8	21.1
Maximum-minimum room temperature (°C)	18.3–29.4	18.3–31	12.7–32.2	10–23.8	12.7–23.8	18.3–29.4
Room humidity (%)	50–70	30–70	40–70	40–60	30–70	30–50
Cage-cleaning frequency (days)	2–7	2–7	3–4	7	3–7	14
Light cycle-hours light: hours dark	12–14:10–12	12:12	12:12	>12.5:11.5	12:12	12:12

Table 177-2. DIETARY INFORMATION FOR POCKET PETS

	Rat	Mouse	Guinea Pig	Chinchilla	Hamster	Gerbil
Recommended diet	Laboratory rodent chow	Laboratory rodent chow	Guinea pig chow	Chinchilla chow	Hamster chow	Laboratory rodent chow
Supplements	<15% of calories, avoid seeds	<15% of calories, avoid seeds	Vitamin C 200 mg/L, drinking water cabbage/kale	Ad lib grass, hay	<15% of calories, avoid fats and seeds	<15% of calories, avoid fats and seeds
Food consumption (g food/100 g body weight/day)	5–10	15	3–6	3–6	10–12	5–8
Water consumption (ml water/100 g body weight/day)	10–12	15	10–40		8–30	4–7
Recommended protein (%)	12–27	16–20	18–30		15–25	16–22
Recommended fat (%)	5–25	5–25			3–5	2–4
Recommended carbohydrate (%)		45–55	16		8	
Recommended minimum fiber (%)			16–18			

- Adult chinchillas that are not obese should be fed high quality, fresh grass hay ad libitum. Obese animals may need to have the hay rationed. Chinchillas require $^1/_8$ to $^1/_4$-cup of fresh pellets per animal each day. Feeding pellets free choice leads to obesity, and the high protein and calcium levels in these diets may predispose animals to urinary tract disease. Most pellets also do not provide sufficient fiber to maintain normal gastrointestinal (GI) motility.
- Store food in tightly sealed containers at less than 60°F; keep food refrigerated if possible.
- Feed all diets within 90 days of milling to ensure the highest nutritional value. Encourage owners to check dates on packages and ask pet store managers about providing dates on bulk items.
- If possible, feed pet rodents except guinea pigs from overhead racks. These devices reduce wastage and eliminate fecal contamination of food. Covered hoppers, heavy crocks, or stainless steel bowls that are attached to the side of the cage to eliminate spillage are acceptable and recommended for guinea pigs.
- Feed breeding females and their litters from the floor of their cages until the young are large enough to reach overhead feeders or crawl in and out of crocks.
- Cannibalism of neonates commonly occurs as the result of stress associated with cage cleaning. To minimize cannibalism, clean the cage and provide a 10- to 13-day food supply 1 to 2 days before parturition.

Water

▼ ***Key Point*** Provide fresh water in clean containers daily.

- Do not provide water in open crocks. These are contaminated or spilled easily and are a common cause of dehydration and poor sanitation.

Table 177-3. NORMAL PHYSIOLOGIC DATA FOR POCKET PETS

	Rat	Mouse	Guinea Pig	Chinchilla	Hamster	Gerbil
Life span (yrs)	2–4	1–3.5	3–6	8–10	1.5–2.5	3–5
Heart rate (bpm)	250–600	325–780	150–400	40–100	250–600	360
Respiratory rate (breaths/min)	33–127	60–230	42–130	40–80	33–155	70–120
Body weight (g)						
Male	300–520	38–42	900–1200	450–600	85–110	60–110
Female	250–300	30–35	700–900	550–800	95–120	50–80
Birth weight (g)	5–6	0.5–1.5	60–115	30–50	2–3	2.5–3
Body temperature (°C) 35.9–38.2	35.5–38	37.2–40	36.1–37.8	36.2–37.5	38.1–38.4	
Gender determination in neonates	At 7 days, the anogenital distance of males is 5 mm; of females, 2.5 mm. Females show nipples at 8–15 days	Identify testicles through skin in neonates	Anogenital distance in males is 10 mm; in females, 5 mm			

- Sipper tubes and water bottles work well. Clean with dish soap and water daily and disinfect them weekly. Guinea pigs expel food from their mouths into their sipper tubes, so more frequent cleaning is needed.
- Some water bottles have special valves to minimize backflow. Supplement guinea pigs' water daily with 200 mg vitamin C/L. If the water is not dechlorinated, it will inactivate the vitamin C.

Quarantine

Quarantine all newly acquired animals in a different room from current pets for a minimum of 30 days. Feed and handle quarantined animals last. Recommend that caretakers wash their hands and change clothes before handling current pets. Avoid the introduction of adult animals because this frequently results in fighting. Instead, place animals together while young and allow them to mature together. Avoid keeping more than one male per cage because this also usually leads to fighting.

HISTORY AND PHYSICAL EXAMINATION

A systematic history and physical examination are mandatory. Many disease syndromes are caused by poor husbandry. Pets that have been kept isolated from other rodents or acquired from a private breeder are less likely to harbor infectious disease than animals obtained from a pet store, laboratory, or wholesaler. See Table 177-3 for normal physiologic data.

Obtain the following information:

- Species, age, sex (species and sex may not be obvious or the owner may not know this information)
- Origin (e.g., private individual, breeder, pet shop, research laboratory, supply house)
- Length of ownership, owner's previous experience
- Environment, caging (ask owner not to clean cage before coming to hospital), cleaning, temperature, humidity, photoperiod, person responsible for care
- Diet: brand, dating on packages, storage, supplements, type of feeder and waterer and method and frequency of cleaning, feeding schedule, person responsible for feeding
- Cagemates, other pets, quarantine history, presence of aggressive behavior
- Dates of unusual activity: breeding, parturition (Table 177-4), cannibalism, abnormal urination or defecation
- Medical history, previous weights
- Purpose for ownership: pet, breeder, display, education
- Purpose for visit: purchase examination, checkup, problem

Examination of Patient and Environment

- Become familiar with normal behavior, locomotion, haircoat, and stools of each of the pet rodent species.
- Observe the pet in its cage for mentation, activity, locomotion, dyspnea, head posture, haircoat, and any grossly observable abnormalities.
- Note respiratory and heart rates before restraint when possible. Observe the condition of cagemates.

▼ ***Key Point*** If dyspnea or severe depression is detected, warn the owner that the animal is critically ill and could die of stress brought on by an examination.

- Handle such animals as little as possible. Initially, treat severely ill animals symptomatically, then

Table 177-4. REPRODUCTIVE DATA FOR POCKET PETS

	Rat	Mouse	Guinea Pig	Chinchilla	Hamster	Gerbil
Age at puberty						
Males	42–110	35–50	60–120	240–540*	45–98	70–85
Females	42–110	50–60	60–90	240–540*	30–84	65–85
Length of estrous cycle (days)	4–5	4–5	15–17	41	4	4–6
Gestation (days)	21–23	19–21	63–68	105–115	15–18	24–26
Average litter size	6–14	10–12	3–4	2–3	6–8	4–6
Age at weaning (days)	21	18–28	14–28	36–48	20–25	20–30
Litter development	Eyes open 12–17 days	Eyes open 10–14 days	Precocious; eats solid food by 5 days	Precocious	Ears open 4–5 days; eyes open 14–16 days	Eyes open 16–20 days;

*Fall babies breed 1 year later. Normal breeding season is November through May.

perform a complete physical examination after the pet's condition has stabilized.

Evaluate the Cage

- Note the type of diet and bedding as well as the level of sanitation and compare these with what was described in the history.
- Observe quantity and quality of feces and urine. Diarrhea, soft stools, absence of stools, copious urine, and discolored urine all can be signs of illness.
- Coprophagy is a normal behavior in rodents.
- Check the diet and water supply for freshness, quantity, source, and accessibility.
- Evaluate the presence and suitability of cage furniture. Adequate visual security and the ability to exercise and gnaw are extremely important.

Examine the Animal

- An accurate weight in grams is extremely important for evaluating an animal's body condition, calculating drug dosages, and monitoring treatment. The easiest method of weighing a pet rodent is to place it in a box and then subtract the weight of the container.

Restraint

- Restraint of pet rodents is easy with experience. Pets that have been handled frequently and gently by the owners require only minimal restraint. Gentle pressure directs the animal as needed. Grasp less cooperative patients (except chinchillas and guinea pigs) by the scruff over the back of the neck with thumb and forefinger (Fig. 177-1). Take care to pinch enough skin to prevent the animal from turning around, yet leave enough slack for respiration. On smaller specimens, hold the base of the tail, if present, between the fourth and fifth fingers to provide additional restraint.

Figure 177-1. "Scruffing" a mouse.

- Hold docile guinea pigs with the palm of one hand supporting the chest while the other hand supports the hind quarters (Fig. 177-2). Place the thumb and forefinger of the first hand in the axillas for additional control.
- Take care to minimize damage to the fur when handling chinchillas because they lose hair easily. Grasp the animal by the tail and scoop it up into the palm of the same hand (Fig. 177-3). If necessary, grasp the thorax just behind the axillas.
- Calm uncooperative rodents by placing an appropriately sized towel over the head. Complete the physical examination by wrapping the patient in a towel and exposing only needed areas. Even oral, ophthalmic, and aural examinations can be performed with minimal effort if the animal is given the chance to relax in the towel "burrow."
- Remove particularly aggressive patients from their cages by scooping them up in a can or bucket; then slide them out onto a slick surface and pick them up or transfer them to a holding area or scale.

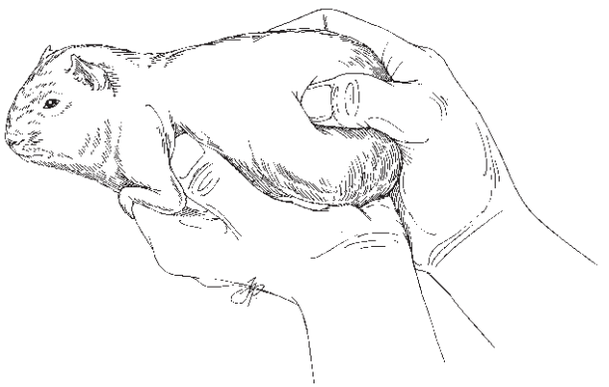

Figure 177-2. Proper method for restraint of guinea pig.

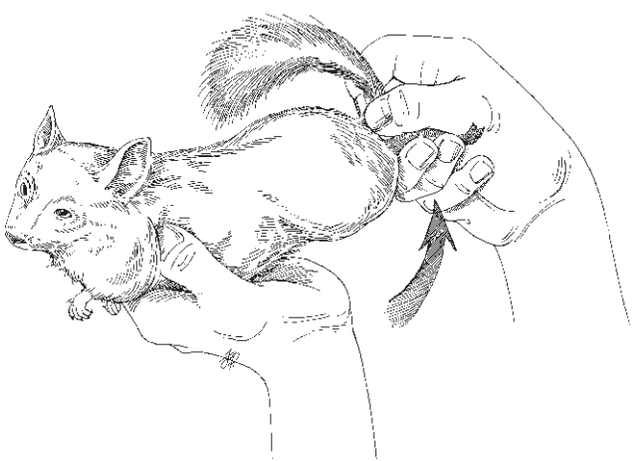

Figure 177-3. Proper method for restraint of chinchilla.

▼ ***Key Point*** Lift the hind quarters of mice and rats by the base of their tails to facilitate scruffing. Never use the tip of the tail for restraint, or the skin of the tail may slough.

Physical Examination

Once the animal is restrained properly, examine the head. Assess the cranial nerves. Check the nose for presence and character of discharge. Examine the mouth for ptyalism, swelling, overgrown incisors, or discharges. To inspect the oral cavity, place an avian speculum across the mouth just caudal to the incisors. Use a light source and a pair of hemostats as retractors to improve access. Alternatively, use an otoscope with a pediatric head to examine the premolars and molars of guinea pigs and chinchillas for overgrowth. Examine the cheek pouches of hamsters for swelling, impaction, or discharge. An ophthalmic examination, including a fundic examination, is important.

- Use a slit lamp to identify superficial pathology, especially corneal ulcers or foreign bodies.
- If indicated, perform fluorescein stain and conjunctival scrapings or cultures.
- Note the presence of conditions such as discharge, asymmetry, and exophthalmos.

▼ ***Key Point*** Gerbils, rats, and mice produce red tears (chromodacryorrhea) with stress or disease. Do not confuse them with hemorrhage.

- Guinea pigs suffering from hypovitaminosis C often produce dry, white tears.
- Check ears for discharge, foreign bodies, and mites. Bluish discoloration of the ears is a sign of cyanosis. Bright red injected coloration is associated with septicemia. Sores behind the ears and on the neck are often a sequela of aural disease.
- Evaluate submandibular, axillary, inguinal, and popliteal lymph nodes for size and consistency. Enlargements usually indicate infectious or neoplastic disease.
- Reevaluate respirations and heart rate after the stress of handling and compare them with the resting rate noted when the animal was in the cage. Note dyspnea or respiratory sounds. Auscultate animals weighing more than 200 g. Counting every third or fourth beat and multiplying by the appropriate factor allows recording of heart rates up to 500 bpm.
- Palpate the abdomen. Pay special attention to differentiating pregnancy from the bladder, kidneys, abdominal masses, enlarged cecum, and fecal balls in the colon. While palpating the abdomen, examine the mammary chain of all female rodents for signs of mastitis, lactation, or neoplasia. Also check male mice and rats for mammary neoplasia. Mammary tissue extends from the base of the neck to the base of the tail. Gerbils typically have an elliptical sebaceous gland on their ventral midline. Do not confuse this with neoplasia or infection. Check the rectum and perineal area for signs of diarrhea, prolapse, irritation, parasites, and bite wounds. Note that coprophagy is normal in rodents.
- Evaluate the urogenital tract for signs of inflammation, foreign bodies, urine scalding, and vaginal discharge. Locate and palpate the testicles in males. The easiest method of determining sex in pet rodents is to compare the anogenital distance, which is twice as long in males as in females. Other characteristics that allow the determination of sex are as follows:
  - Visualization or palpation of testicles or extrusion of the penis from the prepuce indicates a male.
  - The presence of two external openings (i.e., anus and urethra) indicates a male.
  - The presence of three openings (i.e., anus, vagina, and urethra) indicates a female.
- Examine the skin and fur for conditions such as crusts, alopecia, masses, herniations, and wounds.

- Check tail and feet for swellings, coloration, sores, length of toenails, and condition of footpads.
- Evaluate the extremities for trauma or other abnormalities.

DIAGNOSTIC TESTS

Skin and Ear

Apply cellophane tape to crusted areas of the skin and view under a microscope as an aid in diagnosing ectoparasites such as lice, mites, and fleas. Skin scrapings are beneficial in detecting mites and dermatophytes. Dermatophytes are diagnosed best through culture of broken hairs or crust on dermatophyte test medium.

Use small, cotton-tipped swabs to obtain ear swabs from animals weighing more than 25 g. Mix debris with mineral oil and view under low magnification to test for ear mites, or roll onto a glass slide and Gram stain to look for bacterial or yeast infections.

Urine and Fecal Collection

Collect urine by placing the rodent in a clean mesh-bottomed cage with a plastic liner. After enough urine has been produced, collect it off the bottom of the cage with hematocrit tubes or a syringe and a 25-gauge needle. Perform cystocentesis on non-pregnant animals weighing more than 100 g with a 25- to 27-gauge needle.

Collect feces over several hours to provide a volume sufficient for fecal flotation. Flotation allows the detection of nematodes and some trematodes and cestodes. Cellophane tape applied to the perineal area and then viewed under a microscope often reveals oxyurid eggs. Use a fresh saline smear or fecal sedimentation to diagnose protozoal parasites. Fecal cultures are useful in diagnosing bacterial diarrhea.

Radiology

Radiology is an extremely useful tool. Machines capable of exposures as low as 40 kvp and 3 to 10 MAS effectively image mice. Most radiograph machines are capable of generating diagnostic radiographs of guinea pigs, chinchillas, and mature rats at settings used for kittens. Positioning is accomplished with masking tape or Velcro straps. Sedate unruly animals. Techniques used in cats for contrast studies of both urinary and GI systems are modified easily for use in pocket pets.

Blood Samples

- Use lateral or medial saphenous veins to obtain samples in animals heavier than 100 g. Liberally clip the area to allow exposure of the vessel before attempting venipuncture. Place a 25- to 27-gauge needle in the vein and collect blood into microtainers or hematocrit tubes as it drips from the hub of the needle (Fig. 177-4). Take extreme care not to collapse and lacerate the vein with overzealous aspiration if a syringe is attached to the needle.
- It is also possible to use the cephalic vein in guinea pigs.
- Jugular veins are good alternatives in thin individuals under sedation.
- An alternative technique that is useful in smaller animals is to coat the skin over the vein with a thin layer of petroleum jelly and then to puncture the vessel. Blood is collected with a hematocrit tube as it exits the wound. Samples up to 1% of the animal's weight are considered safe, even in stressed animals.

Figure 177-4. Medial saphenous venipuncture; *inset*, lateral tarsal venipuncture.

▼ ***Key Point*** Attempt tail bleeding only as a last resort in mice, rats, gerbils, and hamsters. These techniques often are not acceptable to owners.

To bleed the tail, warm the tail with water or compresses to dilate the tail vessels. In large rats, perform venipuncture with a needle and obtain blood in the usual fashion. In smaller animals, lacerate the tip of the tail. Blood from the wound is collected as described previously. See Tables 177-5 and 177-6 for hematology and chemistry values.

ROUTINE PROCEDURES

Oral Medications: Nutritional Support

Incorporate oral medications into a treat, or administer them in liquid form. If the medication is palatable,

Table 177-5. NORMAL HEMATOLOGIC VALUES FOR POCKET PETS

Indices	Rat	Mouse	Guinea Pig	Chinchilla	Hamster	Gerbil
Erythrocytes ($\times 10^6/mm^3$)	7–10	7–12.5	4.5–7	5.2–10.7	4.0–10	7.0–10
Packed cell volume (%)	35–49.3	35–49	37–55	27–54	31–57	41–52
Hemoglobin (mg/dl)	11–18	10–20	11–16.5	8–15.4	10–19	12.1–16.9
Leukocytes ($\times 10^3/mm^3$)	5–17.2	4–12	7–19	4–11.5	3–11	4.3–12
Neutrophils (%)	9–50	5–40	15–60	9–45	10–42	3–41
Lymphocytes (%)	50–85	30–90	30–72	19–98	50–95	32–97
Monocytes (%)	0–5.0	0–10	3–12	0–6	0–3	0–9
Eosinophils (%)	0–6.0	0–8.0	1–5.0	0–9.0	0–4.5	0–4.0
Basophils (%)	0–1.5	0–1.5	0–3.0	0–1.0	0–1.1	0–2.0
Total protein (g/dl)	5.6–7.6	3.5–7.2	4.4–6.2	5.0–6.0	4.5–7.5	4.3–12.5
Platelets ($\times 10^3/mm^3$)	500–1300	100–1000	250–850	254–740	200–670	400–638

Table 177-6. NORMAL SERUM CHEMISTRIES FOR POCKET PETS

Indices	Rat	Mouse	Guinea Pig	Chinchilla	Hamster	Gerbil
Sodium (mEq/L)	135–155	112–193	132–156	130–155	128–144	144–158
Potassium (mEq/L)	4–8	5.1–10.4	4.5–8.9	5–6.5	3.9–5.5	3.8–5.2
Chloride (mEq/L)		82–114	98–115	105–115		
Calcium (mg/dl)	5.3–13	3.2–8.5	3–12	5.6–12.1	5–13.2	3.7–6.2
Phosphorus (mg/dl)	5.3–8.3	2.3–10.4	3–12	4–8	3–9.9	3.7–7.0
Albumin (g/dl)	3.4–4.8	2.5–4.8	2.1–3.9	2.5–4.2	2.6–4.9	1.8–5.5
Globulin (g/dl)	1.3–3.0	0.6	1.7–2.6		2.7–4.2	1.2–60
Glucose (mg/dl)	50–217	60–250	60–125	60–120	40–200	50–135
Blood urea nitrogen (mg/dl)	6–23.9	17–28	9–31.5	10–25	12–25	17–27
Creatine (mg/dl)	0.2–0.8	0.3–1.0	0.5–2.2		0.1–1.0	0.6–1.4
Alanine aminotransferase (IU/I)	16–89	26–77	10–25	10–35	22–128	
Aspartate aminotransferase (IU/I)		54–269		96	28–122	
Alkaline phosphatase (IU/I)	16–125	45–222	18–28	3–47	45–187	
Total bilirubin (mg/dl)	0.2–0.6	0.1–0.9	0.3–0.9	0.4	0.1–0.9	0.2–0.6
Cholesterol (mg/dl)	40–130	25–82	20–66	40–100	25–180	90–150

administer it by placing the tip of a dosing syringe into the diastema.

▼ ***Key Point*** Take care not to place the tip into the contralateral cheek pouch, or the patient may store the medication and expel it later.

Administer medication in small amounts. Ensure that the animal swallows the medication in its mouth before more is administered. This technique is useful for force-feeding pellet gruels to anorexic pets if the caregiver is patient. Medication or food that is administered too quickly will be spit out or aspirated.

For rodents that are intractable or for administration of unpalatable substances, pass a stomach tube per os.

- Metal feeding needles, red rubber urinary catheters, or infant feeding tubes work well. Selection is based on the size of the animal and individual preference. Metal feeding needles with ball tips frequently are used in patients weighing less than 100 g (Fig. 177-5). The metal provides the necessary stiffness to pass a tube of small diameter. The ball at the end of the needle makes it difficult (but not impossible) to pass the tube into the trachea. These tubes have the potential to create esophageal tears with improper restraint or when excessive force is applied.
- Measure the length from the tip of the nose to the last rib. Ventroflex the head slightly, and place the tip of the tube through the diastema and over the

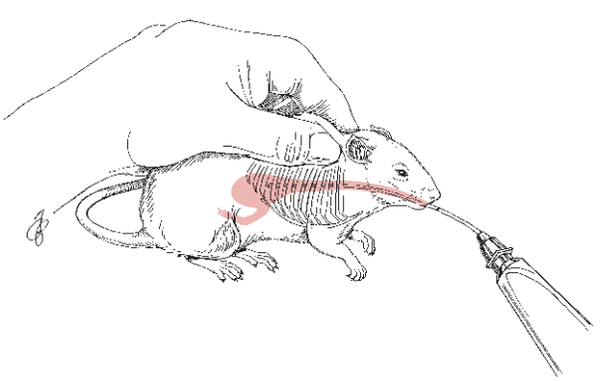

Figure 177-5. Proper placement of a metal feeding tube.

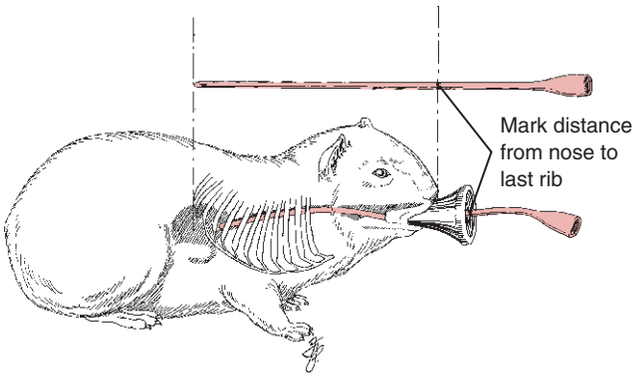

Figure 177-6. Measurement and use of a flexible catheter as a feeding tube.

tongue. If the tube does not pass easily down the esophagus to the premeasured distance, check the tube size and/or reposition the tube before attempting further advancement. The needle is easily palpable percutaneously if it is placed correctly. It is usually safe to administer up to 3 ml/100 g body weight.

- A flexible catheter is ideal for use as a stomach tube in larger rodents (Fig. 177-6). Use a speculum to prevent chewing on the tube. An otoscope head, avian speculum, or piece of wood or plastic with a hole drilled in the center works well. Measure and mark the tube for the distance from the tip of the nose to the last rib. Place the speculum in the mouth and over the tongue. Pass the tube while holding the speculum in place and slightly ventroflexing the head. Resistance is encountered if the tube is malpositioned or is an inappropriate size. The tube must pass over the tongue before it can be advanced down the esophagus. This is difficult in some animals. Palpate the throat to confirm the presence of the feeding tube in the esophagus.

▼ ***Key Point*** Because the placement of a stomach tube is a blind procedure, administer a small volume of sterile saline into the tube before administering the medication to ensure that the tube is not in the trachea. Misplaced medications are fatal.

- This method is also useful for administration of nutrition to anorexic patients. Place a pharyngostomy tube if repeated dosing is necessary, using the technique for cats. Flush pharyngostomy tubes with water at least every 4 to 6 hours. Nasogastric tubes are not recommended because they are difficult to place and maintain patency because of their small size. Securely suture all tubes to the skin. Place a tube collar made of radiographic film or use rear leg hobbles to prevent removal of tubes.
- Nutritional support is critical in rodents because of their high metabolic rate. Provide supplements in animals that are anorexic for longer than 12 hours. If the GI tract is capable of digestion, use a slurry of pellets mixed with a high-calorie supplement. If the tube diameter is too small for this mixture, use avian hand-feeding formula or a mixture of vegetable and cereal baby foods in place of the pellets. If the ability of the GI tract to tolerate enteral feeding is questionable, first try isotonic electrolyte or dextrose solutions. Parenteral nutrition is used successfully in research animals and may be feasible in select pet cases.

Subcutaneous Injections

Administer SC injectable medications or fluids over the shoulder blades or in folds of skin on the flank.

- Avoid irritating substances in rats and mice because their mammary tissue extends into these areas. The resulting inflammatory response is thought to increase the occurrence of mammary neoplasia.

▼ ***Key Point*** In general, avoid streptomycin and the carrier procaine in all pet rodents because of a high incidence of toxicity and hypersensitivity reaction.

Intramuscular Injections

Give IM injections in the semimembranous and semitendinous muscles. Inject only small volumes of nonirritating substances, or tissue damage with resulting self-mutilation may occur. Use the epaxial or triceps muscles if repeated injections are necessary.

Intraperitoneal Injections

▼ ***Key Point*** Use intraperitoneal (IP) injections only as a last resort for large volumes of fluids or for irritating injections that cannot be administered via an IV or IO route.

Express the bladder and aseptically prepare the abdomen.

Restrain the rodent with its head down to move the abdominal organs cranially. Give the injection 0.5 to 2 cm lateral to the midline in the caudal abdomen. Aspirate before injecting to ensure that the injection is not being given into the bladder or bowel. Never use this technique in pregnant animals.

Intravenous Injections

Give IV injections into any of the veins as previously described. In addition, the penile vein may be used in hamsters and guinea pigs. Placement of IV catheters is possible in animals heavier than 100 g.

For small rodents, give a bolus of fluids every 2–4 hours, followed by a diluted heparin flush. A pediatric IV pump is used for continuous infusion of fluids to

larger animals. Maintenance of catheters in active animals is extremely difficult.

Intraosseous Injections

For IO injections, place a spinal needle into the proximal tibia or femur following the technique used for placing an intramedullary pin. Once the needle is seated, remove the stylet. Aspirate and check the hub of the needle for bone marrow. The tip of the needle should be in the bone marrow cavity that directly drains into the central venous system in normal bones (i.e., the cortex must be intact). Administer drugs, blood, or fluids at a rate similar to that used for IV catheters.

ANESTHESIA

Premedication and Patient Preparation

- In chinchillas and guinea pigs, withhold food for 6 hours before anesthesia. Withhold food from smaller, mature rodents for 2 hours. Withhold food from immature animals for up to ½ hour depending on age and condition.
- Use heat lamps and heating pads to prevent hypothermia. Have a prewarmed incubator available for recovery. Preoperative or intra-operative warmed SC or IV fluids are strongly recommended. Place IV or IO catheters whenever possible.
- Administer atropine preoperatively to reduce airway secretions. Acepromazine, diazepam, or midazolam work well as premedications for other anesthetics. Avoid acepromazine in gerbils because it potentiates seizures. See Table 177-7 for anesthetic drugs and dosages.

Monitoring

Surgical anesthesia is reached when toe, tail, and ear pinch fail to generate a withdrawal reaction.

Depth of anesthesia is best monitored by pulse and respiratory rate and character. Pulses drop to within normal ranges after induction. Further reduction, especially to less than 80% of the original stabilized value, is an indication to lighten the plane of anesthesia. Monitor the electrocardiogram (ECG) of small patients by clamping the alligator clips onto the hubs of all-metal 27-gauge needles or steel sutures placed through the skin at the usual sites. Tape cables to the table to maintain placement. Doppler units taped over the chest also provide accurate heart rates. Pulse oximeters are easier to use, more sensitive, and more expensive than the instruments mentioned previously. These instruments are easily taped to the patient's ear, foot, or tail and provide heart rates as well as information regarding oxygenation.

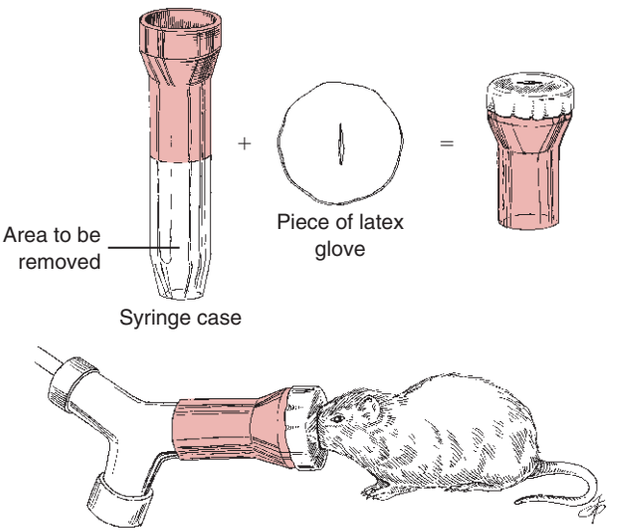

Figure 177-7. A nose cone for anesthesia delivery can be made from a cut-down plastic syringe case and material from a latex glove. Syringe cases from 12 to 60 cc can be used, depending on the size of the patient.

Respirations are often shallow and rapid during induction. They become deep and regular as a surgical plane of anesthesia is reached.

The corneal reflex varies markedly between individuals and anesthetic agents. If the animal has a corneal reflex after induction and then loses it, reduce the anesthetic.

Inhalation Anesthesia

Induction

Induce gas anesthesia using small face masks purchased from laboratory supply houses or make them from syringe cases and latex gloves (Fig. 177-7). Induction in an anesthetic chamber is also possible.

All rodents induced and maintained on gas anesthesia require some form of non-rebreathing system. Usual induction is achieved between 2% and 3% for isoflurane and 2% and 4% for halothane. Maintenance for isoflurane and halothane varies from 0.25% to 2%. There is marked individual variation in the amount of anesthetic required for induction and maintenance. Use of 50% nitrous oxide in oxygen reduces anesthetic concentration requirements for other gases.

▼ ***Key Point*** Some chinchillas and guinea pigs hold their breath while being induced with gas anesthetics and then take deep rapid breaths. If the concentration of anesthetic gases is high enough, this behavior results in death.

The risk of this behavior is reduced by premedication with tranquilizers, initial induction with nitrous oxide with later addition of primary anesthetic gas after

Table 177-7. ANESTHETIC AND ANALGESIC DRUG DOSAGES FOR POCKET PETS

Agent (Effect)	Rat	Mouse	Guinea Pig	Chinchilla	Hamster	Gerbil
Atropine sulfate (parasympatholytic)	0.04 mg/kg, IM, SC	0.04–0.1 mg/kg, IM	0.1–0.2 mg/kg, IM, SC	0.2 mg/kg, IM, SC	0.04 mg/kg, IM, SC	0.04 mg/kg, IM, SC
Acepromazine (sedation)	1–2 mg/kg, IM	—	—	—	0.5–1.0 mg/kg IM	*Do not use*
Buprenorphine (analgesia)	0.02–0.5 mg/kg SC/IM/IP	0.05–2.5 mg/kg SC/IM/IP	0.05mg/kg SC	0.05 mg/kg IM	0.1–0.5 mg/kg SC	—
Butorphanol (analgesia)	1–2 mg/kg SC, IP, IM	1–5mg/kg SC, IP, IM	0.4–2.0 mg/kg SC	0.2–2.0 mg/kg IM	1–5 mg/kg SC	—
Carprofen (analgesia)	5–10 mg/kg PO	—	1–2 mg/kg PO	4 mg/kg PO	—	—
Diazepam (sedation)	3–5 mg/kg, IM	3–5 mg/kg, IM	0.5–3 mg/kg, IM	—	3–5 mg/kg, IM	3–5 mg/kg, IM
Ketamine hydrochloride (light sedation)	22 mg/kg, IM	22 mg/kg, IM	22–64 mg/kg, IM	40 mg/kg, IM	40 mg/kg, IM	40–60 mg/kg, IM
Ketamine hydrochloride (heavy sedation)	25–40 mg/kg, IM	44 mg/kg, IM	44–256 mg/kg, IM*	—	40–150 mg/kg, IM*	70–200 mg/kg, IM*
Ketamine hydrochloride/ xylazine (anesthesia)	60–80 mg/kg/ 7–12 mg/kg, IP, IM	80 mg/kg/16 mg/ kg, IP, IM	35–40 mg/kg/4–8 mg/ kg, IP, IM	35–40 mg/kg/ 4–8 mg/kg, IM	50–100 mg/kg/ 10 mg/kg, IP	50 mg/kg/2 mg/kg, IP
Ketamine hydrochloride/ acepromazine/xylazine (anesthesia)	22 mg/kg/0.75 mg/ kg/2–5 mg/kg, IM	44 mg/kg/0.75 mg/ kg/2–5 mg/kg, IM	22–64 mg/kg/ 0.75 mg/kg/2–5 mg/kg, IM	40 mg/kg/0.5 mg/ kg/0 mg kg, IM	*Do not use*	—
Ketamine hydrochloride/ diazepam (anesthesia)	—	—	35–40 mg/kg/5–10 mg/ kg, IM	—	—	—
Ketoprofen (analgesia)	—	—	1 mg/kg SC, IM	1 mg/kg SC, IM	—	—
Meloxicam (analgesia)	0.1–0.5 mg/kg PO	—	0.1–0.3 mg/kg PO	0.1–0.5 mg/kg PO	—	—
Midazolam (sedation)	1–2 mg/kg IM	1–2 mg/kg IM	1–2 mg/kg IM	1–2 mg/kg IM	—	—
Nalorphine (reverses fentanyl)	2–5 mg/kg, IV	—	—	—	—	—
Pentobarbital sodium (aneshesia)†	25–40 mg/kg, IP, IV	40–80 mg/kg, IP, IV	30–40 mg/kg, IP, IV	30 mg/kg, IV 35–40 mg/kg, IP	50–90 mg/kg, IP	30 mg/kg, IV 40–60 mg/kg, IP
Thiopental sodium (anesthesia)†	25–50 mg/kg, IP	25 mg/kg, IV 50 mg/kg, IP	20 mg/kg, IP	—	20–40 mg/kg, IV	—

*Wide dosage ranges are due to marked individual variation. Use lower dosages first.
†Dilute concentration to 10 mg/ml before injection.

relaxation, and low induction settings. Changes in respirations, especially erratic or apneustic patterns and decreased respiratory rates, indicate deepening anesthesia.

Endotracheal Intubation

Most pet rodents are not intubated for anesthesia because of their small size. When necessary, as in prolonged oral and other procedures, endotracheal intubation is accomplished with the animal in dorsal or ventral recumbency, depending on the clinician's preference. Small non-cuffed or Cole endotracheal tubes work well. A stylet usually is required to provide enough stiffness for the tube to pass the larynx. Extend the animal's head and neck. Grasp the tongue with forceps and use gentle traction. The tip of the tube then is advanced above the tongue and just past its base. The hard palate is used to deflect the tip of the tube ventrally into the glottis. This is a blind procedure that is difficult to master. Use of a laryngoscope is helpful in larger rodents.

Another technique is to place an over-the-needle catheter in the trachea and move it up retrograde through the larynx to act as a guide. The catheter is removed after the endotracheal tube is in place.

▼ ***Key Point*** If endotracheal intubation is performed, it is extremely important that the tube be checked for patency. Rodents produce copious respiratory secretions, which frequently clog endotracheal tubes.

The small diameter allows these tubes to collapse or kink, resulting in asphyxiation of the patient. Check patency at least every 2 minutes by applying positive pressure ventilation at 10 to 15 cm water and watching for excursion of the chest wall. If extending the head and neck does not result in air flow, suction the tube. If this is either not successful or impossible, remove the tube and continue anesthesia with a mask or reintubate the animal with a new tube. Because of the small diameter of the trachea, endotracheal tube-induced tracheitis and subsequent swelling of the trachea may become a life-threatening situation.

Injectable Anesthesia

Doses and routes for injectable anesthetics are listed in Table 177-7. Needed doses for injectable anesthetics are tremendously variable among species and individuals. Most injectable anesthetics provide safe sedation for minor procedures, but very few induce a safe surgical plane of anesthesia on a consistent basis.

- Ketamine in combination with diazepam is easily obtainable, is given intramuscularly, and has a wide margin of safety, but it does not provide good analgesia.
- Intraperitoneal injections of barbiturates provide surgical anesthesia but have a low margin of safety and a significant mortality rate. Barbiturate anesthesia can result in fatal ileus.

EUTHANASIA

Euthanasia is performed easily by induction of inhalant anesthetic through a mask or chamber followed by an overdose of barbiturates given intraperitoneally, IV, or intracranially. Euthanasia by IP injection of barbiturates alone causes pain in some animals.

SURGERY

Hemostasis

- Surgical techniques for pet rodents are similar to those used in cats and birds.
- Hemostasis is critical because of small blood volumes.
- Electrosurgery for incisions and cautery is highly recommended.
- If necessary, give fresh blood transfusions drawn from a donor of the same species and mixed with sodium heparin (1000 IU/ml) at a rate of 0.005 ml/1 ml of blood directly into an IV or IO line.
- The lack of a filter creates a potential for thrombosis.
- Transfusion reactions are possible.

Pain Management

Administer postoperative analgesics to all rodents undergoing surgical or dental procedures. Common analgesics include buprenorphine, butorphanol, ketoprofen, carprofen and meloxicam. See Table 177-7 for dosages.

Common Procedures

The most common surgeries are laceration repair and removal of dermal or SC masses.

- Most rodents will not gnaw on skin sutures.
- If this occurs, use steel sutures, subcuticular sutures, or tissue glue.
- If an animal still chews at its suture line, physical restraint, such as a tube or an Elizabethan collar, is required.

Castration

Castration is a common procedure in guinea pigs. This usually is performed when owners want to house more than one male together or do not wish to breed their female any longer.

Technique

1. Make a skin incision over each testicle or one incision on the midline just cranial to the prepuce.
2. Remove the testicles via a closed technique (i.e., do not open the vaginal tunics). All rodents possess open inguinal rings and can eviscerate if a closed technique is not used. Ligate the testicular vessels and vas deferens with absorbable suture
3. Close the skin incision with a subcuticular pattern using 4-0 synthetic absorbable suture.

Some surgeons partially suture the inguinal rings for extra security. This technique is also applicable to other rodent species.

Abdominal Surgery

Common abdominal surgeries include cystotomy for urolith removal in guinea pigs and rats, and cesarean section (C-section) in guinea pigs and chinchillas because of dystocia.

Use a technique similar to those described for dogs and cats. Preplaced stay sutures are recommended to define incision edges for closure. Use 4-0 polyglactin 910 or polydioxanone (PDS) on a taper needle and suture in a simple continuous pattern to close the body wall. Close the skin with a subcuticular suture (absorbable) or interrupted skin monofilament, nonabsorbable suture.

Fracture Fixation

Fracture fixation is accomplished best with intramedullary pinning or Kirschner apparatus. Rodents gnaw on bandages until they remove them. If they are unable to remove a splint, self-mutilation often results in self-amputation. If a cast or splint is necessary, physical restraint often is required. Healing usually takes 3 to 6 weeks.

Dental Procedures

Incisors can be trimmed with nail trimmers, but this technique often fractures the tooth, causing abscesses of the root. Instead, use a high-speed dental burr or a flat cutting disk on a Dremel hand tool. Trim molars with a high-speed drill or pediatric rongeurs. A mouth speculum that deflects the tongue and other soft tissues is essential to prevent lacerations and provide working space (Fig. 177-8). Intubate the trachea to prevent aspiration pneumonia when working on molars.

If a tooth is abscessed, extract both it and the occlusal tooth.

- If necessary, approach cheek teeth via an incision through the cheek.
- Use a fine dental elevator to loosen the teeth.
- Patience and firm but gentle pressure are needed, or the root or surrounding bone may fracture.

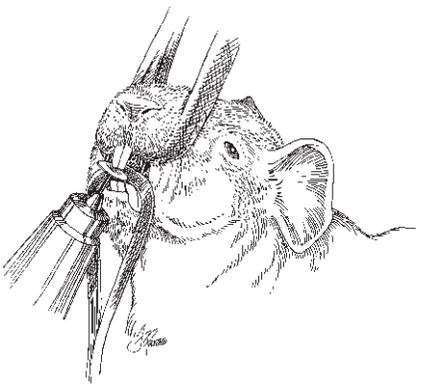

Figure 177-8. Proper technique for dental trimming.

- The roots of the maxillary incisors curve dramatically back into the head. Take care to follow the curve of the tooth.
- Packing an infected tooth socket with a calcium hydroxide paste may decrease the occurrence of persistent infection. Remove the paste in 3 to 4 days.
- Administer meloxicam, carprofen or ketoprofen postoperatively to control pain. See Table 177-7 for dosages.

In chinchillas with dental malocclusion, the roots of the molars can become impacted, causing swelling of the mandible or exophthalmos and epiphora. These teeth are extremely difficult to extract without causing extensive bony and soft-tissue damage. Discourage breeding of animals with malocclusion, unless it was acquired as a result of trauma or infection, because this trait is hereditary.

MOUSE

Most pet and laboratory mice are derived from *Mus musculus*, which is the common house mouse. Mice sold in the pet trade are randomly bred and less likely to suffer from the genetic problems associated with inbred laboratory rodents. Mice possess brown fat tissues between their scapulae that also are known as hibernating glands; these are thought to provide an energy store. The spleen in male mice is 50% larger than that of females.

Dermatology

Ectoparasites

Ectoparasites usually are found in new acquisitions.

- Alopecia and pruritus, especially on the back of the head and dorsal midline, usually are associated with lice (Polyplax serrata), mites, or fleas.

Table 177-8. PARASITICIDE DOSAGES FOR PET RODENTS

Agent	Rat	Mouse	Guinea Pig	Chinchilla	Hamster	Gerbil
Fenbenda zole	20 mg/kg q24h for 5 days	see rat	see rat	see rat	see rat	see rat
Flea powders	3–5% Malathion or 0.5% Pyrethrin powder 3 times per wk for 3 wks	see rat	5% carbaryl powder or 0.1% pyrethrin powder 1 time per wk for 3 wks	see guinea pig	see rat	see rat
Ivermectin	200–400 µg/kg, q7d for 3 wks SQ, PO	see rat	see rat	see rat	200–500 µg/kg q14d for 3 treatments, SC, PO	see rat
Lime-sulfur dip	Dilute 1 : 40. Dip q7d for 6 wks	see rat	see rat	see rat	see rat	see rat
Malathion	0.5% spray or 2% dip q7d for 3 wks	see rat	see rat	see rat	see rat	see rat
Mebendazole	40 mg/kg q7d PO for 3 wks	see rat				
Methyridine	100 mg/kg, SC					
Niclosamide	100 mg/kg repeat in 2 wks, PO	see rat	see rat	200 mg/kg, repeat in 2 wks, PO	see rat	see rat
Piperazine adipate	200 mg/kg, q24h for 7 days,	wait 7 days and repeat, PO, or 0.5 g/L drinking water for 3 wks			200–600 mg/kg, q24h for 7 days, wait 7 days and repeat, PO	
Piperazine citrate	2–5 mg/ml drinking water for 7 days, wait 7 days and repeat	see rat	see rat	see rat	see rat	see rat
Praziquantel	30 mg/kg q14d for 6 wks, PO	see rat	6–10 mg/kg q7d for 3 wks, PO	see guinea pig	see guinea pig	see rat
Quinacrine HCl	75 mg/kg, q8h					
Thiabendazole	200 mg/kg, q24h for 5 days, PO treatments,	100 mg/kg q7d for 4 PO	100 mg/kg q24h for 5 days, PO	100 mg/kg q24h for 5 days, PO	100 mg/kg q24h for 5 days, PO	100 mg/kg q24h for 5 days, PO

PO, by mouth (per os); SC, subcutaneous.

- Mite infestation (e.g., *Mycoptes musculinus, Myobia musculini, Radfordia affinis*) often causes a greasy haircoat and folliculitis.

Transmission of lice and mites occurs via direct contact. Fleas are transmitted by other household pets, such as cats and dogs.

- *Diagnosis* is based on clinical signs, history, visualization of parasite, skin scrape, and cellophane tape test.
- *Treatment* of fleas and lice is with Pyrethrin powder. Ivermectin is recommended for treatment of mites (see Table 177-8).
  - Change the bedding and thoroughly clean the cage between treatments to prevent reinfestation. Occasionally, the surrounding environment needs to be treated with a premises spray used for killing fleas.

Dermatophytosis

- Alopecia also may be the result of dermatophytes (see Chapter 42). Lesions are often hyperkeratotic.
- *Diagnosis* is made by skin scrape or isolation on culture. Most dermatophytes found in pet rodents do not fluoresce under a Wood's lamp.
- *Treatment* is with lime-sulfur dip or griseofulvin (Table 177-9).

Bacterial Disease

- Ulcerative dermatitis is a common syndrome caused by *Staphylococcus aureus* characterized by pododermatitis, mastitis, and abscesses in other areas.
- Administer antibiotics based on culture and sensitivity tests. Chloramphenicol is recommended pending culture results (see Table 177-9). The application of hot packs, local drainage, and topical medications are also beneficial in selected cases.
- Mastitis also may be caused by *Escheria* coli or *Pasteurella,* Klebsiella, Pseudomonas, or *Streptococcus* species. Mastitis usually is caused by poor sanitation, abrasive bedding, or overly aggressive young.
- Preputial gland abscesses are fairly common in males and are usually caused by *E. coli* or *S. aureus.*

Local flushing and topical treatment are usually adequate.
- SC abscesses can be the result of the aforementioned bacteria or *Actinobacillus* spp. or *Corynebacterium kutscheri*. *Corynebacteria* is associated with widespread abscesses, septic arthritis, gangrene, and ulcerated draining tracts. Diagnosis is based on finding gram-positive pleomorphic rods on Gram stain and isolation on culture.
- The bacteria are usually sensitive to ampicillin, chloramphenicol, and tetracycline (see Table 177-9).

Neoplasia

- Lymphoma and mammary neoplasia are common causes of SC masses. Mammary neoplasia is usually malignant in mice, and metastasis to the lungs is common. (Mice have five pairs of mammary glands—three thoracic and two abdominal.)
- Obtain thoracic radiographs before surgery.
- Give a guarded prognosis for long-term survival.
- Other possibilities for SC masses are fungal granulomas, nodules from the *Psorergates* simplex mite, hematoma, hernia, non-neoplastic lymphadenopathy, or emphysema.

Otitis

- Otitis externa usually is caused by ear mites, although bacteria or fungi also may cause primary or secondary otitis.
  - Clinical signs include erythema, pruritus, waxy debris, and excoriations behind the ears.
  - Mites may be diagnosed by identification on otoscopic examination or microscopic examination of ear swabs (see "Techniques").
  - *Treatment* requires cleaning debris from ears with a commercial ear cleanser followed by administration of three doses of ivermectin at 2-week intervals or topical acaricides used daily for 3 to 4 weeks (see Table 177-9).
- Bacterial and fungal otitis is diagnosed by identification of organisms or Gram-stained specimens and isolation on culture.
  - *Treatment* is similar to that used in cats.
- Otitis media/interna usually are caused by hematogenous spread or local invasion of bacteria from a primary abscess.
  - Clinical signs include head tilt, circling, facial nerve paralysis, and otitis externa.
  - Rule out mouse hepatitis virus as the cause of the head tilt (see "Gastroenterology").
  - If treatment of the primary disease is successful, the otitis media usually resolves, although a residual head tilt may persist.
  - If a cluster of *Pseudomonas* infections occurs in a population, evaluate the water source and produce for contamination. Use sodium hypochlorite in the drinking water at 10 ppm to control an outbreak while water quality is being restored.
- Damage to the pinnae can be associated with trauma, dermatitis, pox virus, hypersensitivity reactions, and vasculitis. Dry gangrene is a common sequela and is usually self-limiting.

Miscellaneous

I have observed a steroid-responsive pruritus in pet mice. The pruritus is severe enough to result in significant self-mutilation. This condition has been nonresponsive to treatment with ivermectin, lime-sulfur dips, griseofulvin, multiple antibiotics, oral prednisolone, and antihistamines. Attempts at bacterial and fungal culture have failed to identify a pathogen. An inflammatory response is observed on histologic examination. Mice with this condition respond to repository methylprednisolone injections every 2 to 4 weeks (1.0 mg/kg IM). Most owners have not elected to continue injections for longer than a few months. Once the injections are stopped, the pruritus returns, often requiring euthanasia of the affected mouse.

- Bilateral alopecia found around the muzzle associated with no other abnormalities usually is caused by friction from overhead feeders.
- Alopecia occurring in smaller, weaker individuals is often the result of barbering. Removal of the mice in best condition from the cage results in normal appearance of barbered mice in 2 to 3 weeks.
- Tailhead alopecia and scabbing are usually the result of aggression. Separate affected animals, or additional trauma may occur.
- Other rare causes of alopecia are endocrinopathies, leprosy, and hereditary alopecia in nude mice.

Ophthalmology

Epiphora

- Epiphora is a common condition of pet mice. The most common causes in pets owned for longer than 2 months are ammonia fumes and overgrown incisors.
- Ammonia causing contact irritation is diagnosed by examining an uncleaned cage and checking for odor.
  - *Treatment* is improved sanitation.
- Overgrown incisors are diagnosed easily by oral examination. Treat by trimming the affected teeth and providing opportunities for gnawing.
- Foreign bodies and the resultant corneal ulcers can cause epiphora. An eye examination, including fluorescein stain, is indicated. Treat by removing the foreign body and administering an ophthalmic antibiotic (gentamicin, tetracycline, or chloramphenicol in affected eye, q8h–q6h).
- In newly acquired pets, epiphora is often the first clinical sign of an upper respiratory infection. *Pasteurella*

Table 177-9. ANTIBIOTIC, ANTIFUNGAL, AND ANTIPROTOZOAL DOSAGES FOR PET RODENTS

Agent	Rat	Mouse	Guinea Pig	Chinchilla	Hamster	Gerbil
Amikacin	2–5 mg/kg q8–12h, SC, IM, IV, IO	2–5 mg/kg q8–12h, SC, IM, IV, IO	2–5 mg/kg q8–12h, SC, IM, IV, IO	2–5 mg/kg q8–12h, SC, IM, IV, IO	2–5 mg/kg q8–12h, SC, IM, IV, IO	2–5 mg/kg q8–12h, SC, IM, IV, IO
Ampicillin	20–100 mg/kg, BID, IM, SC, PO	20–100 mg/kg, BID, IM, SC, PO	DO NOT USE	NO NOT USE	NO NOT USE	6–30 mg/kg, TID, PO
Carbenicillin	100 mg/kg, BID, PO	100 mg/kg, BID, PO				
Cephaloridine	10–25 mg/kg, SID, IM, SC	10–25 mg/kg, SID, IM, SC	10–25 mg/kg, SID-TID, IM		10–25 mg/kg, SID, IM	
Chloramphenicol palmitate	50 mg/kg, TID, PO	50 mg/kg, TID, PO	50 mg/kg, TID, PO	50 mg/kg, TID, PO	50 mg/kg, TID, PO	50 mg/kg, TID, PO
Chloramphenicol succinate	30 mg/kg, TID, IV, IM	30 mg/kg, TID, IV, IM	30 mg/kg, TID, IV, IM	30 mg/kg, TID, IV, IM	30 mg/kg, TID, IV, IM	30 mg/kg, TID, IV, IM
Enrofloxacin	2.5–5.0 mg/kg q12h SC, IM, PO	2.5–5.0 mg/kg q12h SC, IM, PO	2.5–5.0 mg/kg q12h SC, IM, PO	2.5–5.0 mg/kg q12h SC, IM, PO	2.5–5.0 mg/kg q12h SC, IM, PO	2.5–5.0 mg/kg q12h SC, IM, PO
Gentamicin	5 mg/kg, SID, IM, SQ	5 mg/kg, SID, IM, SQ	5 mg/kg, SID, IM, SQ	5 mg/kg, SID, IM, SQ	5 mg/kg, SID, IM, SQ	5 mg/kg, SID, IM, SQ
Griseofulvin	25–50 mg/kg q12h, PO	25–50 mg/kg q12h, PO	25–50 mg/kg q12h, PO	25–50 mg/kg q12h, PO	25–50 mg/kg q12h, PO	25–50 mg/kg q12h, PO
Metronidazole	40 mg/kg q24h, PO	40 mg/kg q24h, PO	10–40 mg/kg q24h, PO	50–60 mg/kg q24h, PO	70 mg/kg, q24h, PO	40 mg/kg q24h, PO
Neomycin	2.6 mg/ml drinking water = 10 g/gallon = 2650 mg/L	2.6 mg/ml drinking water = 10 g/gallon = 2650 mg/L	12–16 mg/kg, BID, PO	15 mg/kg q24h, PO	100 mg/kg, PO, SID or 0.5 mg/ml drinking water = 500 mg/L = 1.9 g/gallon	2.6 mg/ml drinking water = 10 g/gallon gallon = 2650 mg/L
Oxytetracycline	3–5 mg/ml drinking water	3–5 mg/ml drinking water	Do not use oral 5 mg/kg, BID, IM	1 mg/ml drinking water	3–5 mg/ml of drinking water	10 mg/kg q8h, PO
Sulfamethazine or sulfamerazine	1 mg/ml drinking water	1 mg/ml drinking water	1 mg/ml drinking water	1 mg/ml drinking water	1 mg/ml drinking water	0.8 mg/ml drinking water
Sulfadiazine and trimethoprim	30 mg/kg, SID-BID, PO, SC	30 mg/kg, SID-BID, PO, SC	30 mg/kg, SID, SC	30 mg/kg, SID, SC	30 mg/kg, SID, SC	30 mg/kg, SID, SC
Sulfamethazole and trimethoprim PO			15 mg/kg, BID, PO	15 mg/kg, BID, PO	15 mg/kg, BID, PO	15 mg/kg, BID, PO
Tetracycline	20 mg/kg, BID, PO	20 mg/kg, BID, PO	20 mg/kg, BID 0.2–0.35 mg/ml drinking water	20 mg/kg, BID, PO	55–65 mg/kg, TID, PO 0.4 mg/ml drinking water	15–20 mg/kg, TID, PO 20 mg/kg, SID, IM
Tylosin	10–20 mg/kg, SID, IM 10 mg/kg, PO, SID-BID	10–20 mg/kg, SID, IM 10 mg/kg, SID-BID, PO	DO NOT USE	10 mg/kg q24h, PO SC, IM	DO NOT USE	10 mg/kg q24h, PO, SC, IM

BID, twice a day; IM, intramuscular; IO, intraosseus; IV, intravenous; PO, by mouth (per os); SC, subcutaneous; SID, once a day; TID, three times a day.

pneumotropica is the most common pathogen, although *Salmonella* spp., mycoplasma, Sendai virus, lymphocytic choriomeningitis, and mouse pox also may cause epiphoria. The ocular discharge later appears mucopurulent (see "Respiratory").

Retinal Degeneration

Retinal degeneration can be either hereditary or (in albino mice) may be caused by exposure to high-intensity lighting. The resulting blindness often goes undetected because patients adapt well and behave normally in their cages.

Miscellaneous

- Cataracts are usually hereditary or post-inflammatory.
- Other hereditary conditions are posterior lens capsule rupture, eyelid malformation, optic nerve hypoplasia, microphthalmos, and retinal dysplasia.

Respiratory

Pneumonia

- *Murine respiratory mycoplasmosis* (MRM) is one of the most common respiratory diseases in pet mice. It is caused by *Mycoplasma pulmonis*. The infection remains dormant for long periods of time and is activated by stress. There are many asymptomatic carriers, and transmission is by aerosol and direct contact. Spread of infection can be hematogenous, causing abscess of the middle ear, uterus, or joints.
- *Clinical signs* include dyspnea (often described as chattering), mucopurulent oculonasal discharge, hunched posture, and anorexia. Animals with a chronic history of this disease are often cachexic.
- Radiology aids in determination of the extent and severity of the pneumonia and the absence or presence of distant foci of infection.
- *Treatment* with tylosin is successful in controlling the disease if it is not too advanced. Tetracycline, enrofloxacin, and chloramphenicol also have been used (see Table 177-8).
- Many patients need nutritional support.
- Mice with pyometra or other abscesses require surgical debridement.
- Recovered animals are carriers and stress elicits clinical signs. Strictly quarantine these animals.

Sendai Virus

A common cause of pneumonia in newly acquired mice is Sendai virus. Acute fatalities are seen in suckling or weanling mice.

- Transmission is by aerosol or direct contact.
- *Clinical signs* in adults are caused by secondary bacterial infections and are similar to those in MRM.
- *Diagnosis* is based on clinical signs and serologic testing.
- *Treat* with antibiotics to control the secondary bacterial infection and provide supportive care as needed.
- Prohibit breeding for 4 to 6 weeks.
- A killed vaccine is available.
- Recovered animals are resistant to new infection.

Bacterial Pneumonia

Common primary or secondary pathogens causing respiratory signs in mice are Streptococcus pneumoniae, Corynebacterium kutscheri, Pasteurella pneumontropica, Pseudomonas aeruginosa, and Klebsiella pneumoniae. Treatment is empiric or based on culture and sensitivity of a tracheal swab sample.

Neoplasia

Dyspnea often is caused by metastasis to the lungs from mammary adenocarcinomas. Primary lung tumors, especially pulmonary adenomas, also occur frequently.

Other

Although not frequently diagnosed, cardiac disease can result in signs of respiratory disease. Diagnosis is based on radiographic evidence of cardiomegaly and pulmonary edema.

Gastroenterology

Parasites

- Tapeworms usually do not cause clinical signs. Occasionally, heavy burdens may cause diarrhea or weight loss. The chief concern is the zoonotic potential of one species, *Hymenolepis nana,* which is directly transmissible to humans.
  - *Diagnosis* is made from visualization of eggs in the feces. Treat with praziquantel or niclosamide (see Table 177-8). Improve sanitation, and remove indirect hosts (e.g., fleas, beetles, roaches).
- Pinworms *(Syphacia obvelata, Aspiculuris tetraptera)* may cause anal pruritus and, in severe cases, rectal prolapse.
  - *Diagnosis* is based on clinical signs and observation of eggs on cellophane tape after application to the perineal region. Treat with piperazine or mebendazole every 7 to 10 days for three treatments or with fenbendazole once daily for 5 days (see Table 177-8) and provide improved sanitation.
- The protozoal parasite *Spironucleus muris* causes diarrhea and slow growth associated with a pot-bellied appearance in young mice.
  - *Diagnosis* is by fecal wet mount, although false-negative findings are common.
  - *Treat* with oxytetracycline (see Table 177-9). Supportive care to combat dehydration and hypothermia is extremely important.
  - Control is achieved with improved sanitation.
- *Giardia* spp. and, rarely, *Eimeria falciformis* show signs similar to *Spironucleus*. Giardiasis is zoonotic. Treat

with metronidazole. Treat *Eimeria* with sulfadiazine/trimethoprim (see Table 177-9). Most other protozoa are considered nonpathogenic.

- *Cysticercus fasciolarus* causes nonpathologic cysts of the liver. These cysts are the infective form of *Taenia taeniaformis* in carnivores.

Diarrhea

Viral Diseases

- Diarrhea in mice 10–20 days old usually is caused by lethal intestinal virus of infant mice (LIVM).
  - This virus may be a variant of mouse hepatitis virus. The mortality rate can reach 80%.
  - *Clinical signs* are yellow diarrhea that mats on the perineal region, causing obstipation and perineal necrosis, anorexia, and stunted growth.
  - Transmission is aerosol or feco-oral from the mother.
  - *Treat* supportively, and quarantine survivors.
- Epizootic diarrhea of infant mice (EDIM) is clinically similar to LIVM. This disease usually affects mice younger than 2 weeks of age but can occur in mice up to 21 days of age.
  - There is low mortality, and nursing continues through the infection.
  - Transmission is feco-oral.
  - *Diagnosis* is based on clinical presentation.
  - *Treat* supportively. Survivors usually are growth-stunted. Quarantine them from other mice.
- Mouse hepatitis virus is a corona virus. Most infections are latent. Outbreaks of yellow diarrhea and encephalitis secondary to viral hepatitis occur in mice 7 to 13 days of age. Older animals show clinical signs of infertility, jaundice, and hemoglobinuria as a result of a slowly progressive hepatitis.
  - *Diagnosis* is based on clinical presentation, serology, and presence of syncytial giant cells in the epithelium of the small intestine.
  - *Treat* supportively, and quarantine affected individuals. The prognosis is grave.
- Although less commonly seen in pet mice, reovirus occurs in older suckling mice. It is characterized by an oily diarrhea, which results in a greasy haircoat. Other signs are conjunctivitis, stunted growth, and tremors. Transmission is by ingestion.
  - *Diagnosis* is based on clinical signs, histology, and serology.
  - *Treat* supportively. The long-term prognosis is grave. Initial survivors are weak and jaundiced, suffer from alopecia, and eventually die.

Bacterial Diseases

- Transmissible murine colonic hyperplasia (MCH) caused by *Citrobacter freundii* is characterized by diarrhea followed by rectal prolapse and stunted growth. Transmission is feco-oral.
  - *Diagnosis* is made by clinical signs and fecal culture.
  - *Treat* with neomycin, tetracycline, or sulfamethazine until sensitivity results are available (see Table 177-9). Severe thickening of the distal half of the colon is observed at necropsy.
- Salmonellosis, also known as mouse typhoid, is transmitted by latent carriers or contaminated feed or bedding. Incubation lasts for 3 to 6 days.
  - *Clinical signs* are lethargy, anorexia, purulent conjunctivitis, arthritis, and diarrhea.
  - *Diagnosis* is based on clinical signs and fecal culture. Treat supportively. Use of antibiotics is controversial.
  - Quarantine survivors.
  - Sanitation is extremely important because *Salmonella* spp. are zoonotic. On gross postmortem examination, erythema of distal ileum and congestion of the spleen and liver are seen. With more chronic infections, necrotic foci are seen in the liver, spleen, and lymph nodes. Prevent infection by feeding a fresh laboratory chow from a reputable source. Thoroughly wash all produce and then dip it in a diluted bleach solution. Rinse completely before feeding.
- Tyzzer disease is caused by *Bacillus piliformis*. Transmission is feco-oral.
  - *Clinical signs* are precipitated by stress and consist of anorexia, diarrhea, and high mortality in weanlings.
  - *Diagnosis* is made by clinical signs or isolation on culture. Enteritis and multiple gray-yellow necrotic foci in the liver are seen on gross postmortem examination.
  - Administer tetracycline for 4 to 5 days (see Table 177-9) and reduce stress to control the disease.

Theriogenology

Breeding systems vary; from one to six females may be placed with one male. All animals are housed together, and the young are removed after weaning. Females in proestrus have swollen vulvas. Vaginal plugs are present post-copulation.

Female mice that have been bred within 4 days abort if a new male is placed in the cage. Inappropriate light cycle, inappropriate age, crowding, and poor nutrition are the most common causes of infertility in pet mice. Pyometra due to *Pasteurella pneumontropica, Mycoplasma* spp., or other bacteria is also common.

Desertion of litters is usually a result of stress, lack of nesting materials, agalactia, or mastitis.

Urology

- Urethral obstruction from proteinaceous plugs of inspissated ejaculum may develop in aged male mice. *Pseudomonas, E. coli,* or *Proteus* are the most frequently cultured pathogens. Before complete obstruction, chronic hematuria may be noticed by the owner.

- Antibiotics, which are chosen based on the results of urine culture, are often curative with early presentation. Complete obstruction requires surgical removal.
- Glomerulonephritis is very common in geriatric mice. It frequently is secondary to chronic viral infection. Clinical signs are anorexia, lethargy, dehydration, and cachexia. Urinalysis demonstrates proteinuria. As the disease progresses, the urine becomes isosthenuric, the blood urea nitrogen (BUN) and creatinine levels rise, and other electrolyte abnormalities typical of chronic renal failure occur. Treat supportively. Prognosis for long-term survival is grave.
- Coccidia (e.g., *Klosseilla muris*) occasionally is found in the urine. The clinical significance of its presence is unknown.
- Mice can be asymptomatic carriers of leptospirosis; however, this is rarely seen in pet mice.
  - *Diagnosis* is based on darkfield microscopy of urine, serology, or histopathology. Euthanasia of carriers is recommended.

Musculoskeletal

- Infectious polyarthritis or mouse rheumatism is caused by *Streptobacillus moniliformis*. In humans, it is known as rat bite or Havernill fever. Transmission is by direct contact. Clinical signs are cachexia, keratitis, edema and ulceration of the appendages, and ankylosing arthritis.
  - *Diagnosis* is based on the bacterial culture findings or the presence of caseous pericarditis and arthritis on necropsy.
  - *Treat* with antibiotics chosen through the results of culture and sensitivity tests. Use penicillin while awaiting results. Supportive care is important. Animals that recover remain arthritic. Control is achieved through quarantine and sanitation.

Neurology

- The most frequently diagnosed neurologic disease in pet mice is head tilt resulting from bacterial otitis media (see "Otitis"). The second most common cause of neurologic signs is trauma.
  - *Diagnosis* is based on history and clinical signs. Consider neoplasia in aged mice with slowly progressive signs.
- Lymphocytic choriomeningitis is a zoonotic arenavirus. Transmission is airborne, transplacental, or by direct contact, fomites, or insect vectors. Acute signs usually occur in mice that are 3 to 6 weeks old. Approximately 20% of infected individuals show acute clinical signs, which include lethargy and photophobia followed by convulsions and paralysis. In animals that are latently infected, glomerulonephritis develops later. Mice infected after weaning and before 1 year in age lose weight, appear arthritic, and show signs of conjunctivitis and photophobia. The virus runs its course in several weeks. Animals that recover show no residual signs.
  - *Diagnosis* is based on clinical signs and the presence of immunofluorescent antibody (IFA). Pleural effusion, splenomegaly, and hepatic lipidosis are found on necropsy. Treat supportively. House survivors separately.
  - Prevent the disease by improving sanitation, providing pest control, and cleaning produce. Consider euthanasia because of the zoonotic potential of the virus.
- Mouse poliomyelitis/encephalomyelitis, also known as Theiler disease, causes clinical signs in 1 in 10,000 infected mice. Two-thirds of healthy mice are carriers. Transmission is by oral or respiratory routes. Mice younger than 4 weeks of age show signs of encephalitis. Animals that are 6 to 10 weeks old are weak in the rear legs and progress to paralysis. The tail may remain mobile. Affected mice continue to eat and be alert. Albino mice are predisposed to show clinical signs.
  - *Diagnosis* is based on clinical signs, serology, or histopathology that shows necrosis of the ganglionic cells of the anterior horn of the spinal cord.
  - *Treat* supportively. Consider euthanasia because of poor prognosis.
- Seizures in mice commonly result from otitis media, trauma, liver or kidney failure, toxin, bacterial meningitis, neoplasia, or viral encephalitis.

Hematology

- Leukemia in mice is usually viral in origin. Transmission is trans-mammary or trans-placental.
  - *Clinical signs* are anemia, dyspnea (with thymic involvement), and those signs that are compatible with chronic disease.
  - *Diagnosis* is based on complete blood count (CBC), bone marrow aspirate, or histopathology. Prognosis is grave.
- *Eperythrozoon coccoides* is a rickettsial red blood cell (RBC) parasite of mice. Affected mice are usually asymptomatic. Occasionally, fever, anemia, and splenomegaly develop in infected animals. Transmission is through the louse *Polyplax serrata*. Control is by extermination of the louse.
  - *Treat* with tetracyclines.

RAT

Pet rats are derived from the Norwegian or brown rat *(Rattus norvegicus),* which did not originate from Norway, but from Asia. Breeds of rats are called strains when they are inbred extensively and stocks when strains are hybridized. Rats have brown fat, as discussed in the section on mice. They do not possess a gallbladder. Their mandibular symphysis is articulated normally.

Rats are neophobic; therefore, make gradual changes in food or environment when possible.

Dermatology

- Fleas, mites (e.g., *Radfordia ensifera, Ornithonyssus bacoti*), lice (i.e., *Polyplax spinulosa*), ear mites (i.e., *Notoedres muris*), and dermatophytes cause similar signs in both mice and rats. Treatment also is similar (see "Mouse").
- SC masses in rats are similar to mice. *Pasteurella pneumotropica* is a very common pathogen in mastitis and SC abscesses.
  - *Treat* with chloramphenicol until culture results are available (see Table 177-9).
- Mammary cancer develops in 50% to 90% of adult female rats and in approximately 15% of male rats. Always submit biopsy specimens for histologic examination. Most, but not all, of these tumors are fibroadenomas, which are benign. Prognosis for long-term survival after surgical removal is good. Other common neoplasms include interstitial cell tumors of the testes, which cause SC swellings in the inguinal region, and squamous cell carcinomas of the Zymbals gland of the external ear canal.
- Ulcerative dermatitis occurs in rats as well as mice. *Staphylococcus aureus* is the causative agent. *C. kutscheri* follows a similar course in rats and mice (see "Mouse").
- Ringtail is the formation of constrictive bands of fibrous tissue around the tail in nestling rats. These bands result in gangrene of the distal tail. This disease occurs when environmental humidity is less than 40%.
  - *Treat* by making a longitudinal incision of the ring to release the stricture and apply topical dimethyl sulfoxide (DMSO), steroid, and antibiotic solution (10 ml DMSO, 6 ml 50 mg/ml amikacin, 4 ml 2 mg/ml dexamethasone) four times daily.
  - To prevent ringtail, keep humidity above 50%, use solid-bottom cages and provide ample nesting material. Prognosis for life is excellent. Prognosis for retention of the distal tail is guarded.

Ophthalmology

- Epiphora and blepharospasm are caused mostly by ammonia fumes, overgrown incisors, or foreign bodies (see "Mouse").
- Sialodacryoadenitis virus is a coronavirus that is endemic in many rat populations.
  - *Clinical signs* vary from mild keratoconjunctivitis to blepharospasm, chromodacryorrhea, severe uveitis, hyphema, buphthalmos, periorbital swelling, and pneumonia. The clinical course of the disease lasts 10 to 14 days. Rats maintain normal activity levels and appetite.
- *Treatment* is not necessary for mild infections. Place rats showing marked ocular disease or discomfort on the appropriate ophthalmic ointments (e.g., atropine, antibiotic, steroid) based on presentation. Administer parenteral antibiotics to animals that show signs of respiratory problems. Recovery is usually complete unless the eye ruptures or self-mutilation occurs.
  - Control is achieved by not introducing new animals for 4 weeks.
- In contrast to mice, Sendai virus rarely causes clinical signs in rats.
- Mucopurulent ocular discharge also may be caused by infection with mycoplasmosis, *Streptococcus pneumoniae, Pseudomonas* spp., and other less common bacterial or viral agents that cause pneumonia.
- Cataracts are primary hereditary defects or occur secondary to severe uveitis or diabetes mellitus. Retinal dystrophy and colobomas are also inheritable traits in rats. Retinal degeneration occurs in rats housed under intense lighting.

Respiratory

- MRM is extremely common in pet rats. Its presentation is similar to the disease in mice (see "Mouse").
- *Streptococcus pneumoniae* is normal flora for rats. However, during stressful situations, bacteremia may occur, resulting in pneumonia. Clinical signs are similar to MRM. Differentiation is based on culture and the presence of extensive fibrinopurulent pleural effusion on necropsy.
  - Ampicillin controls clinical signs if treated early in the course of disease (see Table 177-9). Prevent the condition by minimizing stress.
- *Corynebacterium kutscheri* and *Pasteurella pneumotropica* cause signs similar to MRM (see "Mouse"). There is a serologic test for *C. kutscheri*. See the Mouse section for a discussion of *Pseudomonas aeruginosa*.
- *Pneumocystosis carinii* is an uncommon protozoa that infects the lung. Cysts and trophozoites live in the alveoli. Clinical signs occur only in immunocompromised or geriatric individuals. Signs are cachexia, cyanosis, and dyspnea.
  - *Diagnosis* is based on clinical signs, tracheal wash, response to therapy, or histologic examination.
  - *Treat* with sulfadiazine/pyrinrethamine (see Table 177-9).

Cardiovascular System

- Myocardial degeneration and subsequent congestive heart failure are fairly common in geriatric rats. Diagnosis is based on radiographs of the thorax and clinical signs. Treat supportively, and use furosemide and digitalis at cat dosages to alleviate pulmonary edema.
- Polyarteritis nodosa is an idiopathic condition of geriatric rats that results in thickening and tortuosity of arteries, especially in the mesentery, pancreas, and testicles. Affected areas are predisposed to clot formation and aneurysms.

Gastroenterology

Parasites

- Nematode *(Syphacia muris),* cestode, and intestinal protozoal parasite infestations are similar to those in mice.
- *Capillaria hepatica* has no clinical significance. Yellow streaks on the liver are an incidental finding at necropsy.

Dental

The causes and treatment of malocclusion are similar to those for mice.

Diarrhea

- Epizootic diarrhea of suckling rats is a viral disorder found in rats 7 to 14 days old. The infection causes a mild diarrhea. Most animals recover. Occasionally, stunting occurs. Treat supportively.
- Salmonellosis in rats is similar to that in mice.

Theriogenology

- If breeding is desired, take females showing signs of estrus (e.g., lordosis, hyperactivity, quivering ears, and swollen vulva) to a male rat's cage for 24 hours, or keep one male in a cage with up to six females. Check females for a post-copulatory plug to confirm breeding. Remove females just before parturition, and house females individually while raising the young. A vaginal discharge is seen 1.5 to 4 hours before labor. Parturition is accompanied by stretching and extension of the rear legs. All neonates usually are delivered within 1 to 2 hours.
- Infertility is usually the result of age, malnutrition (e.g., protein, vitamin E), uterine infection, or improper light cycle, temperature, or humidity.
- Litter desertion is usually the result of stress. Inadequate nesting material or agalactia are other significant causes of abandonment and death.

▼ ***Key Point*** To prevent cannibalism, remove male rats from the cage before parturition and do not return them until after weaning is complete.

- Rat virus infection is a parvovirus that is usually inapparent unless individuals are infected in utero. Small litters or jaundiced, stunted neonates are often the only clinical signs. Transmission is both vertical and horizontal.
  - *Diagnosis* is by serologic testing and characteristic histologic findings. Permanently quarantine all in-contact animals.

Urology

- Urolithiasis commonly occurs in older rats. Uroliths usually are composed of ammonium magnesium phosphate or calcium carbonate.
  - *Clinical signs* include anorexia, stranguria, hematuria, and abdominal distention. Urinary obstruction can occur.
  - *Diagnosis* is based on clinical signs, urinalysis, and radiographs.
  - *Treat* by surgically removing uroliths and providing antibiotics based on culture and susceptibility testing.
- Two extremely common conditions in geriatric rats are nephrocalcinosis and chronic progressive nephropathy. Clinical signs are compatible with those of chronic renal failure. Enlarged or small irregular kidneys may be found on physical or radiographic examination. Isosthenuria and marked proteinuria are found in urinalysis.
  - Definitive *diagnosis* is based on renal biopsy.
  - *Treat* supportively. Prognosis for long-term survival is grave.
- *Trichasomoides crassicauda* is an uncommon parasite of the urogenital tract. The adult worms usually reside in the kidney, but they occasionally may wander into the genital tract. The ova are passed in the urine.
  - *Clinical signs* are hematuria and stranguria. Proliferative mucosa of the bladder occasionally may be palpated as an abdominal mass.
  - *Treatment* is somewhat successful with methyridene (see Table 177-8). Sanitation is critical in control of this disease.
- *Klossiella muris* is an incidental coccidia of the urinary tract.

Neurology

- Many geriatric pet rats have chronic progressive radiculoneuropathy.
  - *Clinical signs* are compatible with cauda equina syndrome, including posterior paresis progressing to paralysis, urine retention, and incontinence. Prognosis is grave.
  - *Treat* supportively or euthanize.
- *Streptobacillus moniliformis,* a normal bacteria found in the oral, nasal, and pharyngeal cavities of rodents, is isolated from 43% of middle ear infections and 35% of chronic pneumonias in rats. The bacteria is nonpathogenic for gerbils and guinea pigs.
  - *Clinical signs* vary with the site of infection. Head tilt and circling, septic arthritis, and respiratory disease commonly are seen.
  - *Diagnosis* is based on isolation on culture. The clinical signs mimic many other diseases, especially MRM and *Pseudomonas* infection (see "Mouse").
- Head tilt in rats also may be the result of trauma or neoplasia, especially pituitary adenomas.

Hematology

- *Hemobartonella muris* is an RBC parasite of rats that is nonpathogenic unless the rat is immunocompromised or splenectomized. Transmission is through the louse *Polyplax spinulosa.*

- *Clinical signs* result from hemolytic anemia and hemoglobinuria.
- *Treat* with tetracyclines (see Table 177-9).

HAMSTER

Mesocricetus auratus, better known as the golden or Syrian hamster, is a primarily nocturnal rodent that originated in the Middle East. Almost all hamsters in the United States are the offspring of three siblings imported in the 1930s. Many color variations are available. Long-haired hamsters are called "teddy bear" hamsters. The stomach has two compartments, a non-glandular forestomach, which functions like a rumen, and a glandular stomach. Hamsters are very territorial. They possess flank glands, which are larger in males, that are rubbed against objects to mark their territory. Females are larger than males. Except during estrus, they use this size advantage to attack males. Do not allow groups to estivate together or recently awakened animals may cannibalize sleeping hamsters.

▼ ***Key Point*** Hamsters are extremely sensitive to antibiotics.

Penicillins, clindamycin, lincomycin, streptomycin, tylosin, erythromycin, and cephalosporins eliminate the normal intestinal flora, allowing overgrowth of pathogenic bacteria, particularly *Clostridium difficile*. Diarrhea, which is almost always fatal within 3 to 7 days, subsequently occurs. Even antibiotics considered to be safe can have this effect. Treat by discontinuing antibiotics, providing a *Lactobacillus* supplement, and giving supportive therapy.

Dermatology

- Hamsters are susceptible to *Demodex criceti* and *D. aurati* mites. *D. criceti* is limited to skin folds. *D. aurati* causes hyperpigmentation, alopecia, and seborrhea sicca affecting the dorsal midline. *Demodex* is carried by many normal-appearing hamsters.
  - *Clinical signs* occur in immunosuppressed animals, as would occur with stress, chronic infection, pregnancy, or malnutrition.
  - *Diagnosis* is based on clinical signs and deep-skin scrapings.
  - *Treat* with amitraz every 2 weeks for two treatments past two consecutive negative skin scrapings. Use the manufacturer's recommended dilution for dogs.
- *Sarcoptes* mites infrequently cause facial alopecia. Diagnosis is based on skin scraping. Treat with ivermectin (see Table 177-8). Do not confuse this condition with alopecia caused by contact with feeders or barbering.
- *Notoedres* mites affect only the external ear canal in female hamsters but may affect the ears, feet, genitalia, and tail in males. Diagnosis is made by observation of mites on samples from ear swabs, skin scrapings, or both. Treat with ivermectin (see Table 177-8).
- Other less common causes of alopecia in hamsters are dermatophytosis, endocrinopathies, and genetic defects.
- Dermal SC masses are usually abscesses caused by *Pasteurella pneumotropica, S. aureus,* or *Streptococcus* spp. Treatment is based on results of culture and susceptibility testing. Use chloramphenicol until culture results are available. Other frequent causes of SC swellings are distended cheek pouches and testicles, mastitis, hernias, neoplasia, and lymphadenopathy.

Ophthalmology

- Epiphora and conjunctivitis are caused most frequently by increased environmental ammonia concentrations, incisor overgrowth, foreign body, or lymphocytic choriomeningitis (see "Rat"; "Mouse").
- Mucopurulent discharge is caused by secondary infection by *Pasteurella* or *Streptococcus* spp.
- Hamsters are predisposed to rupture of the eye following trauma or infection. Surgical enucleation is advised. Electrosurgery is extremely helpful in controlling bleeding but do not apply heat to the stump of the optic nerve or vessels, or thermal injury to the brain may result. Place gelfoam in the socket to enhance clot formation.

Respiratory

- Hamsters are susceptible to viral respiratory infections of humans.
  - *Clinical signs* include nasal discharge, sneezing, otitis media, fever, and pneumonia. Uncomplicated cases last 5 to 7 days. Complications are usually the result of secondary bacterial infections.
  - *Treat* supportively. Use of antibiotics is indicated if copious nasal discharge, dyspnea, anorexia, or marked lethargy is observed. Overuse of antibiotics may cause diarrhea-related death in hamsters that might have recovered uneventfully if left untreated.
- Most dyspnea in hamsters is caused by blunt thoracic trauma. Hamsters often bite when startled. Reflex actions on the part of humans, especially children, cause hamsters to be flung against hard objects.
  - *Diagnosis* is by history and presence of fresh epistaxis.
  - *Treat* supportively. Emergency shock therapy, consisting of supplemental heat, oxygen administration, parenteral fluids, and glucocorticoids, frequently is required.
- Sendai virus can cause death in suckling hamsters housed with mice. Adults show no clinical signs (see "Mouse").
- Primary bacterial pneumonia most frequently is caused by *Yersinia pseudotuberculosis, Pasteurella pneumotropica,* or *Streptococcus.* Clinical signs are compati-

ble with those of pneumonia seen in other species, as well as weight loss and conjunctivitis. All three agents have a tendency to form distant abscesses, especially in the uterus.
- *Diagnosis* is based on clinical signs and isolation on culture.
- *Treat* with chloramphenicol until antibiotic susceptibility results are available. Abscesses require surgical debridement; however, anesthesia in affected animals is very risky. Recovered hamsters are carriers and must be quarantined from other rodents. Prognosis is guarded.

Cardiology

- Cardiac thrombosis is seen in 73% of geriatric hamsters. Most thromboses occur in the left atrium and are secondary to degenerative cardiomyopathy, cardiac amyloidosis, sepsis, or calcification of the great vessels. Congenital myocardial necrosis also occurs.
- *Clinical signs* include cyanosis, dyspnea, and acute death. Enlargement of the cardiac silhouette and pulmonary edema sometimes can be seen on thoracic radiographs.
- Furosemide and digitalis (using standard cat doses) may temporarily alleviate clinical signs.

Gastroenterology

Parasites

- Hamsters can carry the zoonotic tapeworm *H. nana* (see "Mouse").
  - *Treat* with niclosamide or praziquantel (see Table 177-8) and provide improved sanitation.
- Pinworms (Aspicularis tetraptera, Syphacia muris, S. obvelata) occur in hamsters as well as in mice.
  - *Treat* with fenbendazole (see Table 177-8).

Dental/Oral

- Hamsters are predisposed to dental caries. A large percentage of affected teeth become abscessed, causing facial swelling, ptyalism, and anorexia.
  - *Diagnosis* is based on clinical signs, oral examination, skull radiographs, and isolation on culture.
  - Extract the tooth and administer antibiotic therapy based on results of susceptibility testing. Prognosis is variable depending on the condition of the animal, tooth affected, and extent of the abscess (see "Mouse").
- Overgrown incisors also occur, as in mice.
- The cheek pouches are very distensible. Impaction of the pouches occurs on occasion.
  - *Clinical signs* vary from ptyalism to swelling from abscess. In simple cases, removal of the material from the pouch with fine forceps is sufficient. Sedation usually is not required.
  - If a fungal or bacterial infection of the pouch is present, remove the exudate, submit samples for Gram staining and bacterial or fungal culture, and flush the pouch with diluted iodine solution. If cellulitis is present, administer systemic antibiotics as well. Fistulas often heal spontaneously.

Diarrhea

- Proliferative ileitis (i.e., wet-tail disease) is thought to be caused by a *Campylobacter*-like organism with or without concurrent bacterial or viral infections. More than 90% of animals with clinical signs die. The highest morbidity and mortality rates occur in hamsters 3 to 8 weeks of age. Teddy bear hamsters may be more susceptible to infection than shorter-haired varieties. Transmission is feco-oral.
- *Clinical signs* include diarrhea, which mats on the ventrum and perineum, and results in anorexia, dehydration, and a hunched posture. The abdomen frequently seems painful on palpation. Bowel loops often are distended on palpation because of ileal obstruction or intussusception. Rectal prolapse usually occurs.
- Administer neomycin, gentamicin, metronidazole, or tetracycline (see Table 177-9). Supportive care is critical. Prognosis is grave, even with treatment. Gross postmortem findings include gas and yellow diarrhea in the distal intestinal tract, mucosal thickening in the ileum and distal jejunum, peritonitis, and liver abscesses.
- Other common causes of bacterial diarrhea include *E. coli,* Tyzzer disease, or *Salmonella* spp. (see "Mouse").

Liver

In hamsters older than 1 year of age, liver cysts that are derived from the biliary duct often develop. Less frequently, similar cysts arise from the pancreas, epididymis, and seminal vesicles. This syndrome is called *polycystic disease.* No clinical signs are associated with cysts in these structures, which are an incidental finding on abdominal palpation. No treatment is recommended.

Theriogenology

- Timing is critical to prevent injury to the male when breeding hamsters. Transfer the female to the male's cage in the early evening 3 days after a creamy, viscous vaginal discharge is noticed. Monitor the pair carefully. Remove the male immediately if the female is aggressive. Remove the male after mating or after 1 to 2 hours even if mating has not occurred. Two days after successful copulation, a gray malodorous vaginal discharge is observed. Pregnancy is highly likely if there is no translucent vaginal discharge 5 to 9 days post-breeding. Pseudopregnancies last 8 to 12 days. Normal gestation is 15 to 16 days. Before par-

turition, a hemorrhagic vaginal discharge appears, and the female may pant. Hamsters rarely suffer from pregnancy toxemia (see "Guinea Pig").
- Infertility may be caused by pyometra (see *P. pneumotropica* and lymphocytic choriomeningitis).
- Cannibalism is most frequently a result of stress or mastitis.

Urology

- In almost 90% of geriatric hamsters, renal amyloidosis develops. The disease tends to develop more rapidly in females.
- *Clinical signs* include edema and ascites due to protein loss in the urine, as well as the typical signs of chronic renal failure.
- *Treat* supportively. Prognosis for long-term survival is grave.

Neurology

- Head tilt is usually secondary to otitis media. Also consider lymphocytic choriomeningitis or neoplasia as differential diagnosis (see "Rat").
- In hamsters fed all-seed diets and deprived of exercise, cage paralysis syndrome often develops. Usually pets are presented for acute posterior paresis which, in reality, was slowly progressive. The distinction is important in ruling out trauma. In mild cases, the hamster is able to move its hind limbs but unable to support weight. Vitamin D and E supplementation, along with nutritional improvement and providing exercise, is curative in 1 to 2 weeks. In severe cases, recovery is negligible or incomplete.

Hematology/Oncology

Lymphoma and lymphosarcoma may be viral in origin. Diagnosis is made by biopsy or fine-needle aspiration of affected lymph nodes. Rule out lymphadenopathy caused by lymphadenitis from infection with *Streptobacillus moniliformis* (see "Rat"). Although many hamsters initially respond well to chemotherapy protocols established for cats and dogs, prognosis for long-term survival is grave.

GERBIL

The Mongolian gerbil *(Meriones unguiculatus)* originates from the deserts of Mongolia and northern China. Gerbils alternate between periods of activity and rest throughout the day. Peak periods of activity are in the late evening. Seed storage and burrowing are important natural behaviors. Most gerbils are brown with cream-colored abdomens (i.e., agouti). Several color variations are available (black, black and white). Gerbils drum their hind legs when alarmed. In general, gerbils are non-aggressive. However, introduction of unfamiliar adults results in fighting.

Dermatology

- Rarely, *Demodex* spp. mites cause alopecia in gerbils.
  - *Diagnosis* is based on skin scraping.
  - *Treat* with rotenone ointment or amitraz dips every 2 weeks for three to six treatments. Use manufacturer's recommended dilution for dogs.
- Acute moist dermatitis usually is caused by *S. aureus* infection. Infection on the face often begins with the harderian glands. The gland secretion is viscous and causes matting, with secondary *staphylococcal* infection occurring under the mats. Attempts at grooming spread the infection to the feet and abdomen.
  - *Diagnosis* is based on clinical signs and isolation on culture.
  - Administer enrofloxacin, tetracycline, or chloramphenicol and apply warm, moist compresses to remove dried debris. Remove possible irritants from cage (e.g., pine or cedar shavings, ammonia). Occasionally, surgical removal of a chronically infected or inflamed gland is needed.
- Alopecia of the facial area, especially when it is symmetric, is usually the result of self-trauma from feeders, cage bars, or overzealous burrowing.
  - *Treat* by changing cage construction or providing better visual security.
- Gerbils that catch their tails in crevices or are restrained inappropriately by their tails often are presented for avulsion of the skin from their tails.
  - *Treat* initially by controlling hemorrhage and hypovolemic shock.
  - Amputate the tail after patient stabilization to prevent ascending infection. In some animals, the infection is localized to the distal tail, which is sloughed in approximately 3 to 4 weeks.
- Generalized alopecia is normal in some weanling gerbils. The hair grows in as the animals mature.
- Melanomas are found most frequently on the ears, feet, or base of the tail.
  - *Diagnosis* is based on biopsy.
  - *Treat* by surgical removal.
- Sebaceous gland disease is usually the result of bacterial infections or neoplasia.
  - *Diagnosis* is based on cytologic examination, culture, histologic examination, and response to antibiotic therapy.
  - *Treat* bacterial infections with parenteral or topical antibiotics based on the severity of signs.
- Sebaceous gland adenomas, basal cell tumors, and squamous cell carcinomas are the most frequently encountered neoplasms.
  - Take a radiograph of the thorax to diagnose metastases. Prognosis for long-term survival is based on tumor type, stage, and character.
  - *Treat* by surgical excision.

Ophthalmology

Chromodacryorrhea and epiphora occur as in mice.

Gastroenterology

Parasites

Tapeworms (i.e., H. nana and H. diminuta) and pinworms (i.e., Syphacia obvelata, Dentostomella translucida, and Aspicularis tetraptera) occur as in mice.

Dental

Incisor overgrowth occurs as in mice.

Diarrhea

- *Salmonella* spp. cause transient diarrheas in gerbils. The source of infection is usually unwashed greens, contaminated feed, or carrier rodents of another species. Most recover. Animals that die have a fibrinosuppurative peritonitis.
  - *Treat* supportively. Use antibiotics in severe cases based on results of culture and susceptibility testing.
- Tyzzer disease, caused by *Bacillus piliformis*, is seen most often in weanlings at 3 to 7 weeks of age and in post-partum females.
  - *Clinical signs* include anorexia, lethargy, rough haircoat, and sometimes diarrhea. Gross postmortem findings include yellow-gray nodules in the liver and hemorrhage at the ileocecal junction.
  - *Diagnosis* is based on postmortem examination or response to therapy.
  - *Treat* with oxytetracycline (see Table 177-9) and supportive care.

Liver

Hepatic lipidosis and gallstones are frequent sequela to lipemia in gerbils fed diets with excessive fat.

Theriogenology

- Breeding is most successful if animals are paired at weaning and kept in these pairs. Male gerbils aid in raising the young. Pairing older animals causes fighting. An average of 20% of neonates fail to survive to weaning. This is usually the result of agalactia and crushing.
- Chronic hemorrhagic discharge from the vulva is usually the result of cystic ovaries or ovarian tumors. Most tumors occur in animals older than 2 years of age and consist of granulosa cell tumors or theca cell tumors. Leiomyomas of the uterus also cause similar clinical signs.
- Rule out urinary tract disease by performing a urinalysis via cystocentesis. Large masses may be visualized on abdominal ultrasound. Definitive diagnosis is based on vaginal cytology followed by exploratory laparotomy.
- Ovariohysterectomy is curative for cystic ovaries and tumors if they have not metastasized.

Urology

- Chronic renal failure develops in most gerbils older than 2.5 years of age.
- *Clinical signs* are polyuria, polydipsia, weight loss, and anorexia. Urinalysis demonstrates proteinuria, hematuria, casts, and an increase in white and red blood cells.
- *Treat* supportively. Prognosis for long-term survival is grave.

Neurology

- Up to 50% of gerbils in certain family lines suffer spontaneous epileptiform seizures. The seizures are induced by stress and are self-limiting. Seizures usually start as the gerbil reaches 2 months of age.
- Treatment is unnecessary.

CHINCHILLA

Chinchilla laniger and *C. brevicaudata* are nocturnal rodents from the Andes mountains in South America. Most animals kept in the United States are the descendants of 11 animals. Aside from pets, chinchillas are raised commercially for their pelts. The most common coat color is gray; the most valuable coat color is black.

▼ ***Key Point*** Chinchillas are sensitive to antibiotics (see "Hamster"); therefore, avoid use of penicillins, lincomycin, erythromycin, and cephalosporins.

House chinchillas in a cool environment because they are prone to overheating. If heat stroke occurs, treat with tepid water baths and supportive therapy.

Dermatology

- Chinchillas require dust baths to keep their skin in condition. Use commercially available chinchilla dust only. Sand substitutions do not condition the coat and occasionally cause conjunctivitis. Offer dust at least once a week.
- Dermatophytosis occurs as in guinea pigs.
- Fur chewing is a serious problem in chinchillas that are farmed for pelts and often is seen in pet chinchillas that are recent culls from a ranch. The etiology of fur chewing is unknown. Some cases seem to be related to chronic disease, malnutrition, poor caging, or stress. Theories for undiagnosed cases include genetic abnormality; undiagnosed dermatophytosis; or adrenal, pituitary, or thyroid gland abnormalities.
- Diagnostics such as skin scraping, fungal culture, fecal, CBC, history profile, and biopsy are recommended. In general, if changes in diet and husbandry do not elicit a response or an underlying treatable disease condition is not discovered, prognosis for cure is grave.

- One source advocates plucking all remaining underfur in chewed areas in an attempt to stimulate new hair growth. Place collars after this procedure until the fur has grown in completely.
- Cystic SC masses may be caused by the intermediate stage of *Multiceps serialis*. Transmission is by ingestion of feed contaminated with canine feces.
- *Diagnosis* is made by histopathologic or cytologic examination of tissue samples. Treat by surgical removal of the masses.
- Otitis caused by *Pseudomonas* spp. occurs as in rats.

Ophthalmology

- Conjunctivitis occurs as in mice.
- Cataracts are congenital or developmental.
- Asteroid hyalosis occurs as a degenerative change.

Respiratory

Pneumonia occurs as in guinea pigs.

Gastroenterology

Parasites

Tapeworms (i.e., *H. nana*) occur as in mice.

Dental

Malocclusion of incisors and cheek teeth occurs as in guinea pigs.

Diarrhea

- Diarrhea is caused most often by *Coccidia* or *Giardia* spp. or a bacterium.
  - *Clinical signs* range from soft stools and weight loss to fluid diarrhea, dehydration, bloating, septicemia, and sudden death.
  - The protozoal parasites are best diagnosed on fresh saline smear or necropsy.
- Bacterial diarrhea is most often caused by contaminated feed and is diagnosed by isolation on culture. *Clostridium* spp., *Pseudomonas aeruginosa, E. coli, Salmonella enteritidis,* and *Pasteurella* spp. are the most common isolates.
  - *Treat* supportively and use appropriate antiprotozoal or antibiotic drugs.
- *Pasteurella pseudotuberculosis* causes acute death from septicemia or a chronic weight loss with intermittent diarrhea. Enlarged mesenteric lymph nodes are a hallmark of this disease.
  - *Diagnosis* is based on clinical signs, histopathologic examination of tissue samples, and isolation on culture.
  - *Treat* with sulfa drugs until sensitivity results are available. Prognosis for recovery is poor. Gross postmortem examination reveals yellow to white necrotic foci in the liver.

Theriogenology

- Check male chinchillas four times per year for penile hair rings. Roll back the prepuce and expose the penis. Roll hair rings off the penis after application of a water-soluble lubricant. Treat ulcerations topically or systemically as needed.
- Dystocia is fairly common in chinchillas (see "Guinea Pig").
- Metritis is suspected when post-partum vaginal discharge, failure to return to a normal estrus cycle, anorexia, weight loss, polydipsia, polyuria, and chewing at flank and abdomen are present.
  - *Diagnosis* is based on history, physical examination, abdominal radiographs, culture, ultrasound, and CBC. It usually is caused by bacteria introduced by the male or spread from an internal abscess. Retained placentas, macerated fetuses, and dystocia are predisposing factors toward metritis.
  - *Treat* with ovariohysterectomy after stabilization. Females used only for breeding purposes may be treated with antibiotics alone, but the prognosis is poor.
- Female chinchillas are aggressive toward male chinchillas when not in estrus. Breeding operations usually have separate cages for females and an interconnecting run for the male. Females are kept out of the male's run by their larger size or collars. The young are precocious and do not need a nest. Chinchillas only produce two litters per year.

Mastitis

- *Clinical signs* include hot, swollen mammary glands. Suspect mastitis if previously healthy neonates become restless, then lethargic.
- Perform bacterial cultures on milk samples, and treat with antibiotics based on susceptibility testing. Administer sulfa drugs until susceptibility results are available. Local hot packing is also beneficial. Occasionally, surgical drainage is required. Foster neonates to another female if possible, or use puppy or kitten milk replacers to hand-raise babies.

Neurology

- Chinchillas seem to be particularly sensitive to *Listeria monocytogenes*. Clinical signs can mimic *P. pseudotuberculosis* and include anorexia, lethargy, abortion, generalized central nervous system (CNS) signs, hepatitis, mild enteritis, and mild emphysematous pneumonia. Necropsy shows yellow foci in the liver.
  - *Diagnosis* is based on isolation on culture.
  - *Treat* with sulfa drugs (see Table 177-9) until sensitivity results are available. The prognosis is poor.
- Other less common causes of neurologic disease in chinchillas include lymphocytic choriomeningitis, *Streptococcus* spp., *Balisascaris procyonis* (i.e., aberrant migration of raccoon roundworm), lead poisoning, and thiamine deficiency.

GUINEA PIG

Guinea pigs *(Caviae porcellus)* are nocturnal rodents that originated in the Andes mountains. They are known for their dietary need for vitamin C. They are used as a food source in their native lands. There are three basic types: English, which have short hair; Abyssinian, which have short, cowlicked hair; and Peruvian, which have long hair. Male guinea pigs are known as boars and the females as sows.

Guinea pigs become neophobic as they mature. Offer a variety of foods early in life and make changes in diet or environment gradually. Guinea pigs stampede when excited. Square cages and strategically placed barriers on external walls prevent the trampling of small or weak animals.

The smooth muscle of the bronchial tree is quite developed in guinea pigs. This places them at high risk for asthmatic-type anaphylactic reactions.

Both male and female guinea pigs have one pair of inguinal mammary glands; however, only the female's are well developed.

▼ ***Key Point*** Antibiotic toxicity (see "Hamster"): guinea pigs also may be sensitive to tetracyclines.

Dermatology

- *Fleas* occur as in mice.
- *Lice* (i.e., *Gliricola porcelli, Gynopus ovalis*) usually cause no clinical signs except occasional alopecia, seborrhea, and trauma secondary to pruritus.
  - *Diagnosis* is made by observation of lice on skin scraping.
  - *Treat* with ivermectin, 5% malathion dust, or pyrethrin shampoo (see Table 177-8).
- The mite *Trixacarus caviae* causes severe pruritus and is zoonotic. It mainly affects the dorsal midline and is difficult to find on skin scraping. It occurs most frequently in recently post-partum females, in which alopecia is the predominant clinical sign. Treat with excellent sanitation and ivermectin (see Table 177-8).
- *Chirodiscoides caviae* lives on the hair shaft of the perineal regions. It does not cause clinical signs.
  - *Treat* with 5% carbaryl or lime-sulfur dip (1:40) (see Table 177-8). Sanitation is critical in preventing reinfestation.
- About 6% to 13% of guinea pigs are carriers of *Trichophyton mentagrophytes.*
  - *Clinical signs* are alopecia and seborrhea sicca, usually starting on the face and spreading along the dorsum.
  - *Treat* with lime-sulfur dips or griseofulvin (see Table 177-9) combined with topical povidone iodine or chlorhexadine shampoos.
- Other causes for alopecia are barbering, alopecia of the flanks in late-gestation females, and generalized alopecia of young at weaning. Subclinical hypovitaminosis C causes a poor hair coat and seborrhea sicca, as well as anorexia and large, malodorous stools.
- "Lumps" is the lay terminology for *cervical lymphadenitis,* which is characterized by lymphadenopathy in the ventral neck region. *Streptococcus zooepidemicus* and *Streptobacillus moniliformis* are the two most frequently cultured pathogens. Transmission is through abrasions of the oral mucosa. The enlarged lymph nodes are filled with purulent exudate.
  - *Treat* with chloramphenicol or sulfa drugs until culture results are available. If surgery is required, attempt to remove encapsulated abscesses intact. If this is not possible, excellent drainage is required. The infection may spread, causing otitis, arthritis, or upper respiratory tract infection. Recovered individuals are carriers. Quarantine both sick and recovered animals.
- *Mammary tumors* occur in the inguinal areas. About 30% are adenocarcinomas; the rest are usually benign fibroadenomas. Other possible causes of masses under the skin include hernias, neoplasias, granulomas, hematomas, or other abscesses.
  - *Diagnosis* is based on cytologic or histopathologic examination of tissue samples. Use thoracic radiographs to determine the presence of metastases.
- *Pododermatitis and sore hocks* are very common in guinea pigs. Predisposing factors are untrimmed toe nails, poor sanitation, and wire flooring. *S. aureus* is the most commonly cultured pathogen.
  - *Clinical signs* range from small ulcers on the soles of the feet to abscesses and gangrene. Radiography is essential in determining whether bony involvement is present. Untreated pododermatitis usually develops into osteomyelitis, which is very difficult to cure.
  - *Treat* mild cases by improving sanitation and grooming. Place affected individuals in solid-floored cages with paper bedding. Use sulfa drugs (see Table 177-9) until results of susceptibility testing are available. Surgically remove or curette abscesses, and apply topical therapy and hot packing. Amputation may be necessary when severe osteomyelitis exists.

Ophthalmology

- Conjunctivitis and epiphora occur as in mice.
  - Inclusion body conjunctivitis is caused by *Chlamydia psittaci* and is self-limiting in 3 to 4 weeks.
  - Perform a conjunctival scraping to differentiate inflammatory conjunctivitis secondary to infection from allergy. I have observed an idiopathic, topical steroid-responsive lymphoplasmacytic conjunctivitis in guinea pigs.
- White, dry ocular discharge is an early sign of hypovitaminosis C.

- "Pea-eyes" is the lay terminology for subscleral fatty deposits or protrusion of the lacrimal gland through the lower conjunctiva. The condition is thought to be hereditary. Treatment is not required.
- Cataracts occur and are either congenital or developmental.
  - Diabetes mellitus in guinea pigs also may cause cataracts. Usually, no other clinical signs are present and urine glucose is greater than 100 mg/dl whereas blood glucose remains within normal limits.
- Corneal or scleral calcification is usually an incidental finding. A thorough workup, including serum chemistry profile and radiographs, is recommended to ensure that generalized metastatic calcification is not present.

Respiratory

- Pneumonia in guinea pigs usually is caused by infection with S. pneumoniae, S. zooepidemicus, or Bordetella bronchiseptica. S. aureus, P. aeruginosa, Klebsiella pneumoniae, and Pasteurella multocida also are cultured frequently. Transmission is by direct contact, fomites, or aerosol. Hypovitaminosis C and stress often predisposes guinea pigs to bacterial respiratory infections. Weanlings are particularly susceptible. Clinical signs and diagnosis are similar to other small mammals (see "Mouse").
  - Take radiographs to rule out abscesses, pleural effusion, or pericardial effusion in refractory cases.
  - *Treat* with chloramphenicol, sulfa drugs, or enrofloxacin (see Table 177-9) and vitamin C (Table 177-10) until results of culture and susceptibility testing are available. Cats, dogs, rabbits, and rats are reservoirs for *Bordetella* spp. As in other rodents, respiratory infections may lead to otitis interna/media. *Bordetella* spp. also cause pyometra and abortions.

Table 177-10. MISCELLANEOUS INJECTABLE MEDICATIONS FOR USE IN PET RODENTS

Rights were not granted to include this table in electronic media. Please refer to the printed publication.

- Nasal discharge is most frequently a sign of upper respiratory tract infection but also may be associated with allergies or volatile irritants.
  - The diagnosis of allergic rhinitis is made by exclusion and through response to antihistamines or environmental changes.
- Bronchogenic papillary adenoma develops in approximately 30% of guinea pigs older than 3 years of age.
  - *Diagnosis* is often an incidental finding when thoracic radiography is performed for another problem.
  - Occasionally, clinical signs are seen as a result of pressure on the heart or great vessels.
- Dyspnea most frequently is caused by heat stress or trauma. Other causes are pregnancy toxemia, gastric bloat, volatile irritants, pleural effusion, pneumonia, or pulmonary edema.

Cardiology

Rhabdomyomatosis is a common necropsy finding. Gross lesions appear as pale foci located on the endomyocardium and valves. Histologic examination reveals myocardial cells that have stored excessive glycogen. Do not confuse these areas with thrombi, abscesses, or neoplasia. Their clinical significance is unknown.

Gastroenterology

Parasites

- *Paraspidodera ucinata* is the cecal pinworm of guinea pigs. They are generally asymptomatic, but heavy infestations can cause diarrhea and weight loss.
  - *Diagnosis* is based on fecal examination or cellophane tape test.
  - *Treat* with piperazine or fenbendazole (see Table 177-8).
- Coccidiosis caused by *Eimeria caviae* is a fairly common cause of diarrhea in guinea pigs recently purchased from pet stores.
  - *Clinical signs* are tenesmus, diarrhea, dehydration, and death.
  - *Diagnosis* is based on fecal examination. On gross postmortem examination, petechiation and thickening of the colon are seen.
  - *Treat* supportively and administer sulfa drugs (see Table 177-9).
- *Cryptosporidium wrairi* and *Giardia* spp. are found rarely. They cause a chronic enteritis. *Balantidium* spp. are thought to be nonpathogenic.

Dental

- Malocclusion in guinea pigs is diagnosed on oral examination.
  - *Clinical signs* are ptyalism and anorexia. The premolars are the most commonly affected teeth.

- Gingivitis secondary to hypovitaminosis C causes similar clinical signs, but the teeth appear normal.
- Long-standing hypovitaminosis C predisposes guinea pigs to malocclusion.
  - *Treat* malocclusion as in other rodents (see "Dental Procedures").

Diarrhea

- Hypovitaminosis C (i.e., scurvy) is associated with soft, malodorous feces. Degeneration of the epithelium of the intestinal tract adversely affects digestion and absorption and allows secondary bacterial infections.
  - *Diagnosis* of scurvy is based on clinical signs, the exclusion of other causes of diarrhea, and response to vitamin C therapy (see Table 177-10).
- Salmonellosis usually is contracted through contaminated feed.
  - *Clinical signs* range from sudden death to diarrhea and anorexia. The diarrhea is frequently light colored. Sepsis is common and may cause conjunctivitis, shock, pneumonia, abortion, and neurologic symptoms.
  - *Diagnosis* is based on isolation on culture of feces or other appropriate tissue samples.
  - *Treatment* is controversial because recovered individuals remain carriers. Use sulfa antibiotics or enrofloxacin (see Table 177-9) until sensitivity testing results are available. Supportive care is essential.
- *E. coli, Arizona,* and *Clostridium* are other commonly cultured diarrhea-causing organisms. *Clostridium* are diagnosed most easily by finding large numbers of spores on a Gram stain fecal specimen. Treat with metronidazole (see Table 177-9).
- *Yersinia pseudotuberculosis* either causes an acutely fatal diarrhea or localizes into regional lymph nodes.
  - *Diagnosis* is based on culture.
  - *Treat* by surgical removal or drainage of abscessed lymph nodes. Mesenteric lymph node involvement necessitates abdominal surgery. Treat with sulfa drugs or enrofloxacin until susceptibility testing results are available (see Table 177-9).

Theriogenology

- One male usually is housed with four to six females for breeding purposes. Signs of estrus are vulvar swelling, lordosis, and opening of the vaginal closure membrane. Fetuses are palpable at 4 to 5 weeks of gestation. Parturition occurs within 48 hours after the pubic symphysis has reached 15 mm. Neonates weighing less than 60 g have a grave prognosis for survival even with intensive care. Neonates normally do not nurse for the first 12 to 24 hours. Litters with five or more fetuses usually result in abortion.
- Dystocia commonly occurs in females bred after the age of 6 to 9 months. After this age, the symphysis fuses and is unable to open the 2 to 3 cm required to allow passage of a fetus. Dystocia in younger guinea pigs may be caused by obesity, large fetal size, fetal malpresentation, subclinical ketosis, or uterine inertia. On presentation, check the pelvic symphysis. If active contractions are present and the symphyseal gap is less than 2 cm, perform a C-section. Normal parturition is very rapid, with a rest of only 3 to 7 minutes between fetuses.
- Perform a C-section if active straining does not produce a fetus within 15 to 20 minutes. Radiograph sows with a history of weak contractions to determine the stage of pregnancy and evaluate the size of the fetuses. If well-developed skeletons of appropriate size are seen and the pubis has not yet fused, give oxytocin and calcium (see Table 177-10). If no fetuses are produced within 15 to 20 minutes, perform a C-section.
  - If poorly developed fetuses are seen radiographically, consider fetal death, ketosis, or a nonreproductive disorder as possible causes of dystocia.

▼ ***Key Point*** Pregnancy toxemia usually is seen in obese sows with large litters in late pregnancy. Other risk factors include systemic disease or diet change causing anorexia, genetics, stress, and first litter.

  - *Clinical signs* are tachypnea, depression, malodorous breath, seizures, and icterus. A urine pH of less than 6 with marked proteinuria is compatible with pregnancy toxemia. A marked hyperkalemia and elevation of liver enzymes often occurs. Thrombocytopenia may be present.
  - *Treat* with IV or IO saline, dextrose, glucocorticoids, and calcium. Surgical abortion of the fetuses may be attempted, but the anesthesia risk is quite high. Prognosis for survival is grave. Do not rebreed affected females. Do not breed sows heavier than 900 g.
- Large litters can cause a hemorrhagic syndrome. Compression of the portal vein and liver causes hepatic dysfunction, which results in vitamin K and clotting factor deficiency.
  - *Treat* with vitamin K supplementation (see Table 177-10). Response is poor in severely compromised patients. Affected individuals are at risk of ketosis developing. Prognosis is guarded.
- Vaginitis in guinea pigs frequently is caused by foreign bodies, usually bedding.
  - *Diagnosis* is made on vaginal examination.
  - *Treat* by flushing the vagina to remove the foreign material.
- Vaginal discharge also can be caused by pyometra, uterine torsion, urinary tract infection, or urogenital neoplasia.
  - *Diagnosis* is based on findings on abdominal palpation, vaginal cytology and culture, urinalysis,

abdominal radiographs, ultrasound, and exploratory.
  - *Treatment* varies with the condition and is similar to that used in cats.
- Ovarian teratomas and uterine tumors occasionally are diagnosed and usually resolve with ovariohysterectomy.
- A symmetric alopecia with concurrent abdominal enlargement may be seen in female guinea pigs with cystic ovaries.
  - *Diagnosis* is based on abdominal palpation, cytology, and ultrasound.
  - *Treat* by performing an ovariohysterectomy. If the guinea pig is not a good candidate for surgery, human chorionic gonadotropin (hCG, 1000 USP units IM, repeat in 1 week) may temporarily resolve clinical signs.
- Male guinea pigs are prone to preputial foreign bodies. A preputial discharge is the usual presenting complaint.
  - *Diagnosis* is based on physical examination.
  - *Treat* by removing foreign bodies and performing local flushing. Chronic problems require a change in bedding.
- Male guinea pigs produce sebaceous secretions in the folds around their perineal area. Clean these areas with soap and water semiannually to prevent localized pyoderma.
  - If pyoderma occurs, treat with topical therapy and oral antibiotics.

Urology

Bacterial cystitis and urolithiasis are relatively common in guinea pigs. Diagnosis is based on a history of stranguria, hematuria, painful abdomen, and anorexia, in addition to abdominal palpation, urinalysis, urine culture, abdominal radiographs, and ultrasonography.

Treatment consists of antibiotics based on results of culture and susceptibility testing and surgical removal of calculi, if present. Prevention of recurrence is difficult if the calculi are not caused by a bacterial infection. Addition of vitamin C to the drinking water as well as changing the brand of diet are sometimes helpful in preventing recurrence of metabolic stones.

Klossiella cobayae is a coccidia that lives in the renal tubules. It has no clinical significance.

Musculoskeletal

The most common orthopedic problem seen in guinea pigs is overgrown toenails. This leads to pododermatitis and sore hocks as well as to degenerative joint disease and a predisposition to tibial fractures.

Tibial fractures are the most common fracture seen in guinea pigs. They most frequently occur after foot entanglement. Internal fixation with an IM pin or application of a Kirschner apparatus is the repair of choice.

▼ ***Key Point*** Signs of hypovitaminosis C or scurvy start to develop in guinea pigs as early as 10–15 days if they are placed on diets 100% deficient in vitamin C.

Early signs are soft, malodorous stools, weight loss, poor hair coat, and anorexia. Later, petechia, gingivitis, cutaneous and oral sores, swollen costochondral junctions, joint pain and hemorrhage resulting in lameness, and conjunctivitis become apparent. Treat supportively and administer parenteral vitamin C (25 mg/day).

Neurology

- Lymphocytic choriomeningitis occurs as in mice.
- Guinea pig paralysis syndrome starts with mild pyrexia and urinary incontinence, followed by weight loss and posterior paresis that progresses to paralysis. Currently, the etiology is unknown, but it does not appear to be contagious.
- *Treat* with supportive care. Prognosis for long-term survival is grave.
- Head tilt is usually the result of otitis or trauma (see "Mouse").

Hematology

Cavian leukemia has a viral etiology. The liver, spleen, and lymph nodes are the primary organs involved. There is no current treatment. Quarantine exposed individuals. Death usually occurs within 5 days after discovery of lymphoblasts in the peripheral blood.

Neutrophils normally have red granules. Kurloff bodies are normally occurring eosinophilic intracytoplasmic inclusion bodies that are found in mononuclear cells. They are seen most frequently in females and appear to correspond positively with estrogen levels.

Metastatic calcification occurs in most guinea pigs older than 1 year of age. It is more severe in females than in males. The stomach is one of the first organs affected. Dysfunction in motility causes obstruction. The tendency appears to be exacerbated by high calcium and low phosphorus diets.

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Chapter

178 Basic Husbandry and Medicine of Pet Reptiles

Nancy L. Anderson / Raymund F. Wack

Boas, pythons, king snakes, rat snakes, and milk snakes are the most common snakes kept as pets. Iguanas, geckoes, monitors, and bearded dragons are frequently encountered pet lizards. Amphisbaenians are small, worm-like reptiles not commonly found in the pet trade. Snakes, lizards, and amphisbaenians are all in the order Squamata. The order Chelonia has approximately 235 species and consists of turtles, tortoises, and terrapins. Of the chelonians, box turtles, red-eared sliders, and a variety of tortoises are kept most commonly as pets. The order Crocodilia has only 21 species, including alligators, crocodiles, caimans, and gharials.

PET INDUSTRY

Determine whether an animal is captive bred or wild caught. Captive-born animals have been somewhat genetically selected to tolerate manufactured environments and accept domestic sources of food. In general, they are less likely to be harboring overwhelming numbers of infectious agents (especially parasites) than their wild-caught counterparts. Many wild-caught animals have been collected overseas, then housed in inadequate, overcrowded facilities, and finally shipped to suppliers without having eaten. The ones that survive often are dehydrated, immunosuppressed, and have been exposed to a wide variety of pathogens. Some imported reptiles are injected prophylactically with antibiotics, which, in combination with dehydration, predisposes them to renal failure. Because of the slow metabolic rate of reptiles, many animals survive this abuse for many months before demonstrating obvious clinical signs.

▼ ***Key Point*** Encourage novice potential reptile owners to buy their pets only from reputable breeders.

COMPARATIVE ANATOMY AND PHYSIOLOGY

Body Temperature

Most reptiles need to maintain their core body temperature well above ambient temperatures for at least part of the day and generally achieve this by absorbing radiant heat. Reptiles can minimize body temperature fluctuations by modifying behavior. Reptiles that become too cool seek elevated areas to bask, lay perpendicular to the sun's rays, maximize their surface area by expanding their rib cage, and darken the pigment of their skin to increase heat absorption. If no sunlight is available, some reptiles burrow into warm soil or lay on objects previously warmed by the sun.

- Overheated reptiles place themselves parallel to the sun's rays, seek shade, pant, lighten skin color, and burrow into cool soil to decrease body temperature.
- Overall, reptiles have a limited ability to control their core body temperature. If they are unable to cool themselves, death due to thyroid dysfunction and/or hyperthermia may occur.
- When the body temperature falls below a critical point, enzymes are unable to function. Digestion then ceases or becomes incomplete, immunity is impaired, and reproductive function declines.
- Chilled animals are at high risk of disease, and if they become chilled for a long period, they fall into torpor. Under natural conditions, some reptiles hibernate, but in captivity, reptiles are unable to prepare for hibernation on their own.
- Hibernation is a period of dormancy marked by a decrease in metabolic rate. Before hibernation in the wild, most reptiles have completed metabolically taxing activities (such as reproduction) and have accumulated energy reserves. A period of reduced food sources then begins. The resulting fast empties the gastrointestinal (GI) tract just before hibernation.
- In captivity, this energy loading to provide fat stores and the subsequent fast must be duplicated, in order to prevent putrefaction of undigested food. The most common mistake made by pet owners attempting to hibernate their reptile is to cool the animal into torpor (i.e., it cannot eat) but not enough to truly slow metabolism. In this state, the reptile often slowly starves. Systemic infections are also common while in torpor. Metabolic processes are too slow to allow proper immune function, yet microorganisms still proliferate. Females cannot successfully hibernate if they are in the process of producing eggs or offspring.

Table 178-1. PREFERRED OPTIMUM TEMPERATURE BASED ON HABITAT

Habitat	Temperature Range (°F)
Tropical	85–100
Desert	80–102
Lowland temperate	70–90
Mountain temperate	70–85

Table 178-2. PREFERRED OPTIMUM TEMPERATURE FOR COMMON REPTILES

Common Species	Temperature Range (°F)
Boas and pythons	75–95
Rat/milk/king/garter snakes	68–95
Desert tortoises	65–105
Painted turtles	55–95
Box turtles	65–90
Anoles	70–90
Chameleons	55–75
Green iguanas	75–105

- The ideal temperature range for a reptile is referred to as its *preferred optimum temperature (POT) range*. This range includes all the temperatures that a reptile needs to maintain optimal body function. The cage should contain areas with both the high and low ends of the animal's POT range so that it has an opportunity to self-regulate, much as it would in the wild. Suggested guidelines for temperature ranges based on natural habitats and common pet species are listed in Tables 178-1 and 178-2.

Circadian and Annual Rhythms

Tropical animals in the wild are exposed to very little variation in environmental temperature and therefore are not tolerant of large fluctuations. This is in contrast to desert animals that endure and require high daytime temperatures with an evening cooldown period. Reptiles from temperate climates can be very tolerant of temperature extremes (within reason) if they are free of disease. These species experience seasons in the wild and require seasonal changes in light cycle, temperature, and water or food availability to stimulate behaviors such as hibernation and breeding.

Skin and Sense Organs

Turtle Shells

The upper half of the shell is referred to as the carapace. The bottom half is the plastron. The shell is composed of bone and incorporates the sternum, vertebrae, ribs, and pelvis. Bone is covered by epidermal scales or skin. The shell is metabolically active.

Speculum

The speculum or spectacle is a clear epithelial covering that lies over the cornea of snakes and some lizards, such as Tokay geckoes. Speculums should be shed with the skin at ecdysis. Abnormal retention of these structures is a common problem in snakes. Topical ophthalmic preparations do not penetrate through the speculum.

Oral/Nasal Salt Glands

Salt glands are located in the nares or on the tongue. The glands excrete excess salt and allow conservation of water. Salt is excreted by burrowing or sneezing. Pet green iguanas often are presented for sneezing small amounts of clear fluid that dries to crystals on the walls of the cage. Do not confuse this normal salt elimination with a respiratory infection.

In snakes, the vomeronasal organ is a highly innervated area used in the sense of smell. It is located on the roof of the mouth within the vomer groove and is an extremely sensitive organ.

Parietal Eye

The "third" or parietal eye appears as a grey or clear dot on the forehead of green iguanas. The organ is an evagination of the thalamus and is connected to the pineal gland via the parietal nerve. It aids in regulation of circadian and annual rhythms.

Gastrointestinal Tract

The hyoid apparatus is very well developed in most reptiles. In snakes, it usually extends to the tenth cervical vertebra, allowing the tongue to be extremely mobile. This enables the snake to breathe directly through its glottis even while swallowing prey. In chameleons, the hyoid apparatus extends the full length of the abdomen to the cloaca. This structure allows their long, well-developed tongues the motility and strength necessary to catch flying insects.

▼ ***Key Point*** In reptiles, restrain the head only by its dorsolateral surfaces to avoid damage to the hyoid apparatus and subsequent loss of tongue function. Avoid restraint that places pressure on the ventral cervical region.

Snakes possess an open mandibular symphysis and flexible rami that allow them to swallow large, intact prey. These features also make iatrogenic injury to the mandibles common, especially while performing an oral examination.

▼ ***Key Point*** *Never* force open a reptile's mouth. To open the mouth of a snake or lizard, place a plastic credit card or hard rubber spatula at the corner or front of the mouth and use gentle, prolonged pres-

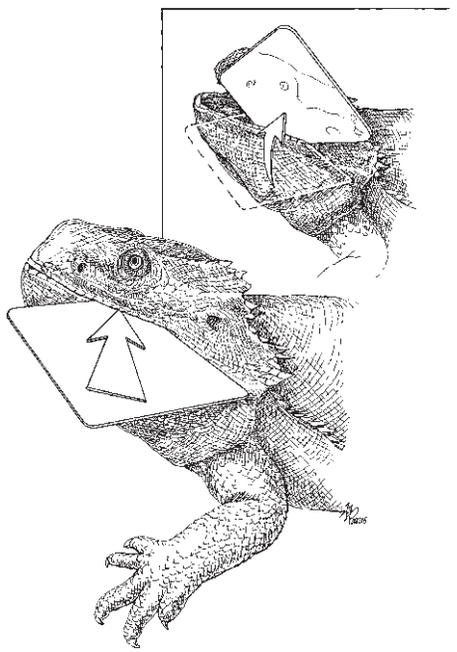

Figure 178-1. To open the mouth, place a plastic credit card or hard rubber spatula at the corner or front of the mouth and use gentle, prolonged pressure combined with a slight wiggling motion.

sure combined with a slight wiggling motion. Once the mouth is opened, slide the card or spatula across the jaws (Fig. 178-1). The beak of larger chelonians can bite through many plastics, so a thin, but sturdy metal spatula may be required to open the mouth. Be careful not to crack the beak. Anesthesia may be required to open the mouths of very large reptiles.

Snakes typically have four rows of teeth in their upper jaw. The teeth of snakes and lizards are fragile and curved caudally to aid in pulling food into the mouth. Be careful not to catch materials on teeth. If items such as swabs or gauze become caught, push caudally to disentangle the fibers before pulling out, or the teeth may break. Broken teeth cause oral pain and anorexia until a new tooth emerges.

Chelonians do not have teeth but rather a horny beak made of keratin similar to that of birds. Treatment of beak problems is similar to beak repair in birds.

The esophagus is lined liberally with mucous glands. Although the musculature surrounding the esophagus is extremely strong in snakes to move whole prey caudally, the esophagus itself is thin and tears easily.

▼ ***Key Point*** When performing stomach intubation in snakes, the esophagus "grabs" the tube. Use liberal amounts of water-soluble lubricating jelly and gentle, constant pressure to pass the tube smoothly. If firm resistance is felt, redirect the tube. Never force a stomach tube because perforation may occur.

In many species of turtles, the esophagus makes a 90 degree turn before entering the stomach. Place medications administered by stomach tube in the distal esophagus. Use small volumes to prevent regurgitation. Also, in chelonians, the pancreatic and bile ducts enter the pylorus instead of the duodenum.

When present, the gallbladder usually is found near the liver in lizards and chelonians but is located caudal to the stomach in snakes. This is an important difference to recognize when performing surgery or diagnostics in this region.

The reptilian pancreas, although sometimes structurally different than in the mammal, is functionally similar. The pancreas usually is located between the ascending and descending portion of the duodenum in chelonians and lizards. In snakes, the pancreas is located caudal to the pylorus in the region of the gallbladder and spleen. In some snakes, the pancreas and spleen are fused.

The cecum is rudimentary in carnivorous reptiles such as snakes, crocodilians, and monitors. The cecum is present in chelonians and herbivorous lizards and functions in post-gastric fermentation in these species.

The cloaca is a common collecting chamber for wastes from the colon and ureters and for the reproductive tract. The cloaca also receives urine from the bladder in species that possess a bladder. It is important to note that unlike mammals, in reptiles, the ureters empty into the cloaca and not the bladder. In males, the hemipenes or phallus everts from the caudal aspect of the cloaca. In some aquatic species, oxygen can be exchanged across the cloaca. Obstruction of the cloaca affects *all* of the aforementioned systems and is therefore much more detrimental than mere constipation affecting the GI system in mammals.

Respiratory System

All reptiles possess a cleft palate (choana) that is necessary for nasal breathing. In contrast to birds, which have a single central cleft, reptiles have paired paramedian clefts. These clefts allow passage of air from the nares into the oral cavity and trachea.

Most reptiles lack a diaphragm, and breathing is accomplished by expansion of the chest wall by intercostal muscles (except turtles), pectoral limb movement (except snakes), and smooth muscle contraction in the lung. Crocodilians also use movement of the liver to create negative pressure. Chelonians use movement of front limbs and visceral organs instead of excursion of the chest wall, which is impossible because of their rigid shell. A minimal amount of oxygen can be extracted from water through the skin in certain species of all reptilian orders. Some aquatic turtles can exchange dissolved oxygen across their pharynx and cloaca while

submerged, although these sources only provide maintenance levels of oxygen.

- In crocodilians, the pharynx has a membrane that can be constricted to allow breathing while the mouth is full of water or food. This membrane must be pushed dorsally to place an endotracheal or stomach tube.
- The glottis in most species is located at the base of the tongue. This makes endotracheal intubation extremely easy. The glottis is very mobile in snakes to allow for respirations while swallowing whole prey.
- The tracheal rings are covered dorsally by smooth muscle in squamates. The rings are complete in chelonians and crocodilians. Therefore, use non-cuffed endotracheal tubes in reptiles. The trachea is lined with many goblet cells that produce thick secretions, which may clog endotracheal tubes. Atropine administration appears to make secretions even more viscous. In some crocodiles, the trachea is bent on itself, making intubation difficult and bronchoscopy impossible. The trachea bifurcates more cranially in chelonians than in other orders, and a short endotracheal tube is needed to ensure aeration of both lung fields.
- The reptilian lung is composed of open-ended sacs lined with alveoli, structurally supported by smooth muscle. Each sac connects directly to a bronchus or to secondary bronchi in more developed species. In many species, the lungs end in thin-walled air sacs. Air sacs aid in respiration and can be inflated for use as a defense mechanism or buoyancy control device. Vipers possess a tracheal lung, which is a collection of alveolar tissue on the dorsal portion of the trachea. This allows for gas exchange even when large swallowed prey compresses the lungs. In most species of snakes, the right lung is larger than the left.

Cardiovascular

Reptiles (except for crocodilians) have a three-chambered heart with two atria and one common ventricle. Deoxygenated blood from the body empties into the right atrium via the sinus venosus. The left atrium receives oxygenated blood from the lungs. In non-crocodilians, both atria open on the left side of the ventricle. Blood from the right atrium tends to stay on the right side of the ventricle and enter the pulmonary artery. Reptiles have two aortic outflow tracts, the right and the left aortas, which combine caudal to the heart into a common aorta. The left aortic arch comes from the right side of the ventricle, carrying less-oxygenated blood. The right aortic arch comes from the left side of the ventricle, which has richly oxygenated blood. The right aortic arch supplies oxygenated blood to the head region before it combines with the left aortic arch.

- Diving causes increased pulmonary resistance, which causes more deoxygenated blood to be shunted into the left aortic arch. This results in increased mixing of oxygenated and deoxygenated blood.
- To shed the skin around the head region, squamates use a vascular phenomenon called the "swell mechanism." Blood pools in the vessels around the head, resulting in swelling of the head area to split the skin.
- The central ventral vein is a large vessel that runs down the ventral midline of lizards and snakes. Avoid this vein during laparotomy. Do not use this vein for venipuncture because life-threatening hematoma formation can occur.
- Paramedian vessels run as pairs parallel to the ventral midline under the shell in chelonians. During celiotomy, after shell removal, use a midline approach to the peritoneum to avoid these vessels. These vessels may be ligated if needed.

Renal System

Most aquatic reptiles excrete ammonia, urea, and uric acid as nitrogenous waste products. Urea and ammonia require more water for their excretion compared with uric acid excretion. Terrestrial animals excrete mostly uric acid. However, sea turtles excrete almost exclusively ammonia or urea; semi-aquatic turtles excrete 0% ammonia, 40%–50% urea, and 50%–60% uric acid; and desert tortoises excrete more than 90% uric acid.

Reptiles can only produce isosthenuric urine. The reptilian nephron contains no loop of Henle and therefore lacks the ability to concentrate urine. Water can be resorbed from the bladder or cloacal wall. If renal blood flow is diminished below a critical level (as in dehydration), urates precipitate in the nephron, causing irreversible obstruction.

Reptiles possess a renal portal system that allows blood from tissues caudal to the kidneys to be shunted directly to kidneys. A valve exists at the junction of the abdominal and femoral veins. When the valve is closed, blood is shunted through the iliac vein into the kidney. When the valve is open, blood enters the systemic circulation through the abdominal vein. Blood entering the kidney through the renal portal system is supplied to the tubules and does not enter the glomerulus. Therefore, drugs such as penicillins, which are cleared via tubular secretion, can be removed by the renal portal system, but drugs cleared by the glomerulus (e.g., gentamicin) are not affected.

▼ ***Key Point*** Do not administer drugs that are cleared by tubular secretion in the caudal half of the body. These drugs may be cleared before achieving therapeutic levels or, if the drug is nephrotoxic, may reach the kidneys in concentrations high enough to cause toxicity.

Not all reptiles have a urinary bladder. The bladder is most highly developed in terrestrial chelonians and some lizards. The bladder acts as a reservoir to store

urine and conserve water. Isosthenuric urine from the kidneys is diverted from the cloaca to the bladder, where water is reabsorbed. The concentrated urine then is routed back to the cloaca for excretion. In reptiles without a bladder, diluted urine is moved from the cloaca into the large colon for water absorption. Salts also may be reabsorbed.

Reproductive System

Male Reproductive System

All reproductive organs, including the phallus in most species, are paired. Chelonians and crocodilians are the exception and have a single phallus. The phallus of adult crocodilians is fibrocartilaginous and is therefore palpable in the cloaca. This is a common sex determination technique used in this order. The male copulatory organs of squamates are paired and are composed of highly vascular fibrocartilaginous and elastic connective tissue called *hemipenes*. Erection occurs secondary to engorgement with blood and contraction of the propulsor muscle, causing eversion of the organ. Hemipenes may be ossified in some monitors and geckoes; sex determination of these individuals can be performed radiographically. Hemipenes frequently have keratin spicules to aid in maintenance of copulation. Only one hemipene is used at a time and it may prolapse if traumatized or following prolonged use.

Seasonal variation in testicular size exists in most species. This is caused by an increase in the number of interstitial androgen-producing Leydig cells during breeding season. Spermatozoa move through the seminiferous tubules and are stored in the epididymis. During breeding, spermatozoa leave via the vas deferens, cloaca, and then hemipene or phallus. The male copulatory organs of reptiles do not contain a urethra and is not involved in the elimination of nitrogenous wastes. Therefore, amputation does not affect urination but does affect breeding ability in animals with nonpaired organs.

Female Reproductive System

The right ovary is located cranial to the left in snakes. Fertilization occurs in the upper portion of the oviduct. Crypt-like pits in the oviduct can store sperm for up to 6 years in some species. Reproduction may be oviparous (egg-layers), ovoviviparous (hold eggs in oviducts until they hatch), or viviparous (live-bearers), depending on the species. The oviduct produces albumin, shell membranes, and the shell. In viviparous species, a placenta-like structure is formed.

Environment for Egg Laying

Many reptiles indefinitely delay oviposition until the right conditions for egg laying occur. These conditions vary with the species. In aquatic turtles, this may be as simple as providing a moist sand pit of sufficient depth for the turtle to dig a nest. In other cases, a female in a multiple-specimen cage may not lay her eggs unless she is housed singly. Certain environmental clues may be required to trigger hormonal cycles necessary to stimulate egg laying. The absence of the proper environmental triggers often leads to dystocia.

Sex Determination in Common Pet Reptiles

Snakes

Females have short, abruptly tapering tails; males have longer, thicker tails necessary to accommodate the hemipenes. In very young snakes, a finger can be rolled from the mid-tail region toward the cloaca in an attempt to evert the hemipenes. This technique is only moderately reliable, and there is a risk of injuring a hemipene.

- Another technique for sexing snakes is commonly referred to as "probing." Commercially available metal probes or small red rubber feeding catheters are used to explore the caudal lateral aspect of the cloaca. In females, the probe falls into a scent gland and advances caudally two to four scales past the vent. In males, the probe enters the inverted hemipene and usually advances at least seven to eight scales caudal to the vent. There have been occasional reports of damage to the hemipene using this technique.
- In boas and pythons, male snakes have more developed paracloacal spurs than females.

Tortoises

In general, female tortoises and box turtles have a flat plastron with a notched caudal region to allow for the passage of eggs. Most females have short, poorly developed tails. The males have a concave plastron to allow for balancing on the female. Males also have long, well-developed tails to allow for copulation and storage of the phallus. Female box turtles have brown to orange irises, whereas male box turtles have bright red irises.

Water Turtles

It is more difficult to differentiate gender in water turtles than in their land counterparts. The females usually have shorter tails than the males. Because the water in the environment bears the male's weight, male water turtles usually do *not* have concave plastrons. In the *Emydoidea* genus, males have very long front claws that they wave in front of females during courtship.

Lizards

In general, males become more brightly colored during the courtship season. Males have more highly developed dorsal spines, dewlaps, and horns. Male iguanas produce keratinaceous plugs along the insides of their thighs from glands called femoral pores. Their function is unknown, but they are thought to be used for

marking territories and to stimulate females by rubbing (scratching) the femoral pores over the female's hind quarters. Females have smaller versions of these pores. Only males of some gecko species have preanal pores that appear as little black pores located near the vent.

Immune System

- Reptiles do not have well-defined lymph nodes but do possess lymphoid aggregates. Lymphatic vessels exist and are well developed. Lymphocytes congregate in a bursa of the cloacal wall, thymus, and spleen. The thymus in chelonians is a distinct lobulated organ in the cervical area adjacent to the parathyroid glands. The spleen may be contiguous with the pancreas in chelonians and snakes.

Endocrine System

- Most reptiles have one to two pairs of parathyroid glands containing a cell type similar to mammalian chief cells. The glands are located at the base of the heart or along the carotid or jugular vessels. They are imbedded in the thymus in chelonians.
- The thyroid, when visible, is found at the base of the heart. The thyroid gland controls both metabolism and ecdysis.

The adrenal glands usually are located just cranial to the kidneys. In the green iguana, the left adrenal gland lies in the mesovarium and must be avoided during ovariectomy. The cortex contains chromaffin cells that produce neuroactive substances. The more centrally located population of cells produce adrenocorticosteroids. The structural architecture of these glands varies tremendously from species to species.

Special Sense Organs

Reptilian ears have no incus, malleus, or cochlea. In snakes and some lizards, the cavity of the middle ear and the tympanic membrane are vestigial. There is no external auditory opening in snakes. In these species, the stapes articulates directly with the quadrate bone. This mechanism picks up low-frequency sound and vibrations. Some snakes can "hear" vibrations transmitted from the body wall overlying the lungs. Crocodilians have a movable ear flap that is located just behind the eye. They are able to open and close this flap to keep water out of their ears.

The eyes of most reptiles (except snakes) are similar to those of mammals with a few exceptions. Bony scleral ossicles support the globe. The iris and ciliary body are composed of striated muscle and do not respond well to mydriatics. The retina contains a darkly pigmented projection called the conus papillarus, similar to the pecten in birds.

- Color vision is present in varying degrees in chelonians and lizards.
- In lidless lizards, a spectacle is present. Lidless lizards have long tongues, which are used to clean their eyes.

Snake eyes are unique among the animal kingdom and are thought to be the result of redevelopment of once rudimentary eyes. The lens accommodates by moving forward and backward. The eyes are covered by a spectacle that is impervious to topical ophthalmic preparations. The retina does not have a conus papillarus but is covered by a thin mat of vessels called the membrana vasculosa.

▼ ***Key Point*** The nasolacrimal ducts drain tears from the subspectacular space of the eye into the oral cavity. Infections in the oral cavity often ascend this duct. Always examine the mouth whenever a snake is presented for ocular disease.

Miscellaneous

Depot fat is stored in fat bodies within the abdominal cavity. These can be quite large and may be detected during abdominal palpation. A lack of fat bodies at surgery or necropsy is a strong indication of starvation.

HUSBANDRY

▼ ***Key Point*** The principal cause of disease and death in reptiles is poor husbandry.

Caging

Terrestrial Animals

Cages should be non-abrasive, escape proof, well insulated, easy to disinfect, and roomy. Aquariums, plastic sweater boxes, and polyurethane-sealed wood and glass cages work well.

Size

Cramped quarters induce stress. Snakes need room to stretch out to at least two-thirds of their length. For lizards, provide a minimum of 6 square inches of cage per inch of body size. Tortoises require a minimum of three times their body area. These are minimum areas for solitary animals. To reduce the chance of cagemate aggression, increase the cage size for more than one animal and for breeding. Clients should be counseled about the size their pet will reach as an adult.

Interior

Cage wall surfaces should be smooth to prevent abrasions, particularly to the nose. A rough branch or stone can be placed in the cage to aid in shedding. Provide cage "furniture," such as plastic containers, clay pots, and plastic plants, to provide visual security. Access to these hiding places allows reptiles to relax and prevents cage pacing. Provide additional furniture that provides a varied terrain, without hazards, to stimulate activity.

Substrates

The ideal cage liner is paper, such as newspaper. It is non-toxic, inexpensive, and disposable. Change cage papers at least once daily or after feeding or defecation for animals that are fed infrequently. Artificial turf is a good alternative to newspaper. Change the turf as soon as it is soiled. It requires 48 hours to completely clean and dry turf, so make plenty of replacement pieces available. Remove loose strings to prevent foreign bodies. Rabbit or guinea pig pellets or recycled paper bedding may be used as cage substrates for herbivorous reptiles if they are replaced at least two times per week, or more often if moist, to prevent fungal and bacterial growth. Large stone gravel and bark chips also can be used but are less desirable because they can be ingested and harbor bacteria, parasites, and moisture. Thoroughly clean and sanitize or replace substrates at least once a month (can be expensive).

▼ ***Key Point*** Do *not* use kitty litter, small gravel, or corncobs as cage liners. These materials often are ingested and cause GI impactions or can be associated with skin infections.

Sand is recommended for desert species only. Other species contaminate sand quickly and are prone to GI sand impactions. Even products commercially marketed as "reptile-safe" such as Calcisand may be ingested and can cause intestinal impactions. Some colors may be more attractive to reptiles to ingest than other colors. Dry sand potentiates low environmental humidity, which is ideal for desert species but causes dehydration in non-desert species. If sand is used for burrowing desert species, it must be changed frequently to prevent buildup of wastes.

Humidity

The environmental humidity should be kept low for most species, because high humidity predisposes animals to disease. Excellent sanitation prevents buildup of wastes, and adequate ventilation allows evaporation of residual moisture, thus keeping the humidity low. Ventilation holes or screening on the top of cages is usually adequate. However, screen lids do not work well for animals that pace in their cage. These animals often rub their noses along the lid, resulting in severe nasal abrasions. Cages used to house animals that produce copious stools, require moisture-laden food, or have high water consumption may need shielded fans to aid in evaporation. On the other hand, some tropical species may require specially designed humidifiers to maintain a supply of fresh, humid air.

Temperature Regulation

Maintain the ambient cage temperature as a gradient incorporating as much of the POT range as possible. One of the easiest methods of accomplishing this is to place a heat source at one end of the enclosure. The heat source should be able to heat the closer end of the cage to the high end of POT and the far end of the cage to the low end of POT. Thermal burns are a common problem. To decrease the possibility of thermal burns if heater malfunctions occur, be certain that the surface temperature at the hottest spot is no hotter than the top range of POT and never higher than 115°F. Heating pads or heating tape *designed for use with reptiles* are the safest to use. It is safest not to place heating elements within a cage. Instead, place the cage on small blocks to create an airspace ($\frac{1}{4}$ inch to $\frac{1}{2}$ inch) between the outside of the cage floor and heat sources. The air space will even out potential hot spots.

Heat lamps also can be used successfully if care is taken to prevent thermal burns. Radiant heat actually is required by many large herbivorous lizards, such as adult green iguanas. To prevent burns, check the temperature by placing a hand directly under the heat lamp (at the site that the reptile would be basking) for 15 minutes after the lamp has been on for 2 to 3 hours. If it is uncomfortable to leave your hand in one spot, the lamp light is too intense. Also, place a thermometer on the surface to ensure that the POT has not been exceeded. Hot rocks are unreliable and only provide enough heat for small species. Any heat sources placed within the cage need to be shielded to prevent animals from coming in direct contact with them.

▼ ***Key Point*** *Any* heating elements that have the potential to attain temperatures greater than 105°F must be shielded. *Routinely* test the thermostats on heating devices. Malfunctioning thermostats cause animal deaths and fires.

Annual and daily temperature fluctuations may be required by some species to maintain health and stimulate breeding.

Arboreal Animals

For arboreal animals, caging is similar to that for terrestrial animals but incorporates more vertical space and objects for climbing. Do not place climbing structures over water or food containers to prevent fecal contamination. Willow, bamboo, oak, birch, beech, and most fruit trees provide safe branches.

Aquatic

▼ ***Key Point*** Strict attention to water quality is essential. A filter system or *frequent* water changing is absolutely necessary.

Never use an under-gravel filter because these may cause anaerobic toxins to accumulate in the gravel. Disturbance of the gravel or an overturn of tank water

allows release of these toxins and may kill tank inhabitants. An out-of-tank biologic filter works best. Flush the sand, gravel, or fibers in these systems frequently to remove gross debris. Even these systems often cannot handle both fecal and discarded food loads. Therefore, offer food for limited periods in a separate tank, then return the reptile to its usual enclosure. The feeding tank does not need a filter because the water is changed completely before and after each feeding session and/or group of animals. Disinfect the tank and allow it to dry after feeding to prevent waste buildup and transmission of disease.

Overpopulation exacerbates water quality problems. A rule of thumb is 1 gallon of water per square inch of turtle carapace.

All aquatic reptiles except sea snakes and sea turtles need adequate basking space. Most "water" turtles drown because of exhaustion if not allowed to rest out of the water. In group tanks, this is often the cause of unexplained deaths of smaller animals. These losses can be eliminated by adding several basking areas, which allows the smaller reptiles to rest even when dominant individuals are defending their territories. Basking also is needed to allow drying of the skin and shell. An increased incidence of skin disease also is seen in reptiles not allowed to bask under ultraviolet (UV) light.

Maintaining appropriate water temperature is very important. A *reliable* waterproof heater is essential. Electric shock from non-waterproof heaters kills not only animals in the tank but also human caretakers. In addition, malfunctions resulting in overheating or failure to heat a tank may kill aquatic animals. In small tanks, an aquarium heater with an *in-water* thermostat works well. Heaters with thermostats above the surface may under- or overheat the water because the thermostat measures the air temperature and not the water temperature.

Take care to ensure tank inhabitants will not burn themselves if they decide to wrap around the heater. This is accomplished most easily by screening the heater. Water temperature in larger enclosures can be maintained by keeping the room temperature at the lower end of the POT range and using infrared lights or heaters at one end to maintain a gradient. Temperature gradients over the basking areas are controlled as in terrestrial cages.

Ultraviolet Light

Many herbivorous and insectivorous reptiles require UV light (280–315 nm) to synthesize vitamin D_3. This spectrum of light is best provided by *unfiltered* sunlight (i.e., *not* passing through glass or plastic). Most plant lights do *not* provide adequate light in the appropriate spectrum. Vita-lite (Durotest, Fairfield, NJ), ReptiSun (Zoomed, San Luis Obispo, CA) are two products that produce the appropriate wavelengths. The intensity of all these lights is much less than that produced by natural sunlight. These lights produce UV radiation in the appropriate spectrum for only 2 to 4 months. Black lights also may be used, but the potential for damage to human as well as reptile vision has not been evaluated. Provide UV light at a rate of 20 watts/3 to 6 cubic feet. Place a basking area 18 to 24 inches from the source. Shield the light from direct animal contact. Provide UV light 8 to 10 hours a day. Constant UV light overstimulates the pineal gland and destroys normal circadian rhythms, which can lead to anorexia and disease.

Light Cycle

Provide 10–14 hours of light *and* dark daily. Base the proportion of light to dark on seasonal variations in the animal's natural habitat. Room light or light from an incandescent bulb used for heating left on at night does not provide adequate darkness. Only use infrared or ceramic bulbs if heating lamps must be used for 24 hours. If room lights must be on into the dark part of the cycle, cover the cage.

Sanitation

Reptiles rarely come in contact with their excrement in the wild. In captivity, the goal is to minimize this contact and the chance of spreading disease when contact occurs. The most important part of sanitation is mechanical removal of fecal material, urates, and leftover food. This can be as simple as removing a soiled sheet of paper, or as time consuming as scrubbing stones. Only after gross debris is removed can disinfectants destroy microbes that cannot be killed by cleaning alone. Disinfection is not a substitute for cleaning.

▼ ***Key Point*** Phenolic cleaners such as Lysol and Pine-Sol can be toxic to reptiles. Bleach (sodium hypochlorite) diluted 1:30 with water is an excellent, safe, and inexpensive disinfectant. It is inactivated by organic matter. Chlorhexidine and Roccal also can be used safely.

Non-sealed and porous surfaces cannot be disinfected thoroughly. Therefore, discard items such as wood, pottery, artificial turf, porous rocks, and bedding if they become too soiled. Do not transfer these items from one group of animals to another. Use great caution in cleaning reptile cages in kitchen sinks or bathtubs as these are likely situations in which salmonella may be transmitted to people.

Cage Density

Plenty of space and visual security is essential when housing more than one animal in an enclosure. Signs of inadequate space are cagemate aggression, disease, high parasite loads, starvation, and cannibalism. Some animals naturally prey on cagemates. These animals should be housed alone or at least with non-prey species.

Mixed-Species Enclosures

Do not mix species. Mixing genuses is often disastrous because organisms that are symbiotic or cause only mild diseases in one species may be fatal to another. An example is amebiasis, which causes a mild disease in turtles but may be fatal in snakes and tortoises.

Quarantine

New animals should be quarantined in a separate building for at least 90 days. Many sources recommend 180 days. If the ideal situation is not possible, quarantine animals in separate rooms. Service new animals last and make sure that clothes are not contaminated. Dispose of wastes and wash hands thoroughly. Clean and disinfect food and water dishes at a separate location from the food preparation area. Animals should be tested for parasites and infectious disease before entering the main collection.

Nutrition

Clean Water

Change water at least every 24 hours. Clean water containers with soap and water daily and disinfect weekly. Large, shallow water dishes that allow reptiles to soak and defecate are preferred. Some lizards (e.g., chameleons, anoles) will not drink from bowls and require a drip watering system or mist sprayed on plants or the side of the cage.

Carnivore

Providing a complete and balanced diet is accomplished more readily in carnivorous reptiles compared with herbivorous or omnivorous ones. Most wild carnivorous reptiles eat whole animals (usually rodents or small birds), which are easily supplied in captivity. When they are fed whole prey, few nutritional deficiencies or excesses occur in this group of reptiles. Severe nutritional disease is seen in animals mistakenly fed only animal parts (e.g., all muscle, liver, etc.).

- Feed carnivores frozen and thawed (to 100°F) or freshly killed prey animals. Live prey may attack and seriously injure reptiles. Domestic animals fed as prey should simulate prey eaten in the wild as much as possible.
- Food animals should be raised on excellent diets because they are the only source of nutrients for the reptile. Do not offer obese prey animals because the excess fat may cause steatitis. Supplements for reptiles eating warm-blooded prey usually are not recommended.

▼ ***Key Point*** Some carnivores such as king snakes only eat other snakes. Be sure that "feeder" snakes used as prey are free from disease and parasites. If the snake eats thawed, frozen prey, it is recommended to freeze all food snakes for at least 30 days before feeding to prevent transmission of parasites. Good-quality feeder snakes can be difficult to obtain. Some snake eaters accept mice stuffed into a shed snake skin.

Some carnivores eat only amphibians or small reptiles of various genera. Freezing to prevent disease transmission is extremely important in these species as well. Some amphibian eaters can be trained to eat mice by placing a mouse inside a fresh frog skin or smearing a mouse with frog slime. Be careful not to attempt to feed amphibians, which produce toxic skin secretions.

Some snakes and monitors eat mostly eggs. Ideally, these eggs should be fertilized and contain embryos at different stages of development. Reptiles fed only unfertilized hen eggs suffer many nutritional deficiencies.

Some reptiles only eat crustaceans, gastropods, worms, or other specialized diets. Special attention needs to be paid to the natural history of reptiles needing specialized diets. If the suitable prey items cannot be obtained year-round, do not keep the animal in captivity.

Crocodilian

Nutritional diseases such as secondary hyperparathyroidism commonly occur when owners feed their crocodiles hamburger or table scraps. Feed only whole-animal diets (e.g., whole fish, rats, chickens, rabbits) to prevent nutritional diseases. Feed crocodilians individually whenever possible to prevent feeding frenzies and subsequent cagemate trauma.

Insectivore

Crickets, mealworms, and inch worms commonly fed to reptiles in captivity are deficient in nutrients. Provide an excellent diet for these insects to replace missing nutrients. To maximize their nutritional worth and provide extra nutrients from the intestinal contents of the insect, raise these insects on a high-calcium medium such as chicken layer mash or commercial cricket diet from a reputable company. Use of dark, leafy greens or orange vegetables as a water source for insects further increases their nutritional value. Before feeding the reptile, dust crickets and mealworms with a vitamin and calcium supplement (daily for reproductively active females and juveniles, 1–3 times per week for others). Large insectivores may accept young, hairless mice (commonly called "pinkies") or captive reared earthworms as an additional source of nutrients. Feed small, chiten-free insects, such as juvenile crickets, mealworms, or wingless fruit flies to small or neonatal insectivores. Some insectivores require highly specialized diets. Do not feed fireflies to reptiles because they are often toxic.

Herbivore/Omnivore

Adult herbivores, such as green iguanas, should receive 90% to 98% of their calories from plants. Ninety percent of the plant diet should consist of a mixture of dark leafy greens, with 10% mixed vegetables and fruits. Many adult herbivorous tortoises require high-fiber diets, such as high-quality grass hay or fresh grass. Omnivores or young herbivores should receive 70% to 95% of their calories from plants. Most herbivores and all omnivores require the addition of some protein to their diets. Good sources of protein are crushed hard-boiled egg (with shell), prepared reptile diets from reputable companies, trout chow, pinkie mice, alfalfa pellets, or tofu. Dog food or monkey chow should not be fed. These foods contain excessive amounts of vitamin D and may cause metastatic calcification of soft tissues and renal failure when fed extensively. Although some experts believe that feeding *any* animal protein to herbivores may cause renal disease, we have found that renal disease is related to the *quantity* rather than the source of protein. To avoid over feeding, be aware that the concentration of nutrients and calories in animal-based food is usually at least an order of magnitude greater than in the same volume of vegetable matter.

- Vitamin and calcium supplements may be used in moderation, but avoid calcium supplements that contain phosphorus and extra vitamin D. These supplements often contribute to metastatic calcification because most reptile diets are already too high in phosphorus from meat and fruit. We recommend Calcium glubionate syrup (Calcionate, Rugby, Norcross, Georgia; 1 tsp = 115 mg Ca glubionate). This syrup is free of phosphorous, is highly palatable, and is readily accepted from a syringe or dropper, allowing individual dosing. Alternatively, crushed *boiled* egg shells, calcium carbonate, or oyster shells are other excellent sources of phosphorus-free calcium. Healthy, adult herbivorous reptiles on excellent diets and provided adequate UV light usually only require vitamin and mineral supplements four to six times per month.

RESTRAINT

Lizards and Crocodilians

Restrain small lizards and crocodilians by using the thumb and forefinger to grasp the caudal mandibular area. Cradle the dorsal body in the palm of the same hand. Control the abdomen, chest, and pelvis with the remaining fingers, thus allowing for respiration (Fig. 178-2).

Grasp medium-sized lizards and crocodilians over the dorsal surface of the head and neck with one hand, and grab the base of the tail and pelvis with the other hand (Fig. 178-3). Wrap the reptile securely in a towel to prevent the back legs from scratching. If necessary, restrain the back legs by taping them to the tail. To capture mildly aggressive animals, use a towel as a blind to hide the restrainer's hand from view. If an aggressive animal is brought in a sack, use the sack as a blind and grasp the head through the sack. Peel the sack away from the body without losing control of the head. A snare or snake hook can be used to pin the head if the animal is extremely aggressive. Care must be taken to use just enough pressure to prevent escape but not enough to cause trauma. Large lizards and crocodilians can inflict serious bites and often use their powerful tails as whips. Tape the snout of aggressive crocodilians shut with duct tape. The masseter muscles are extremely strong; the digastricus muscle, which opens the jaw, is very weak.

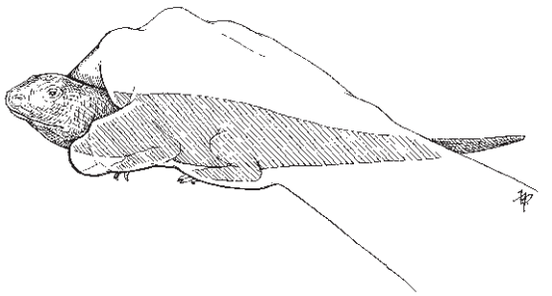

Figure 178-2. One-handed technique for proper restraint of a small lizard.

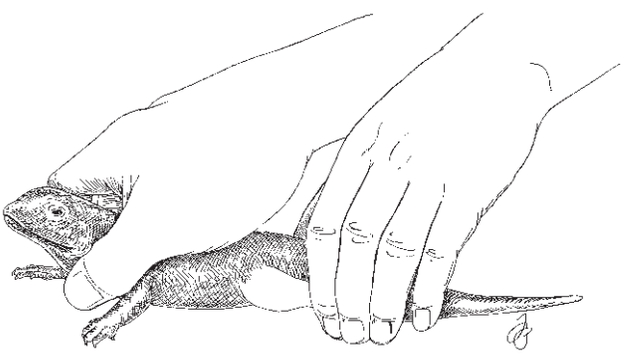

Figure 178-3. Proper restraint of a medium lizard.

Stroking the ventral midline or pushing on the eyes of some lizards induces vasovagal response and a short trance-like state.

▼ ***Key Point*** Large reptiles can inflict serious damage, even death, to the handler. Attempt to handle these animals only if you are experienced and have adequate assistance.

Snakes

Most non-aggressive snakes may be picked up mid-body and allowed to glide from hand to hand. Some snakes

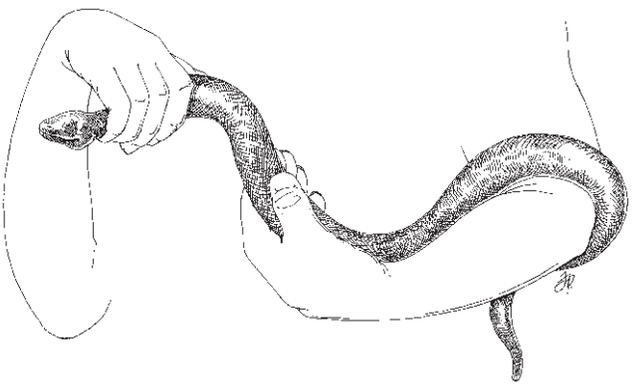

Figure 178-4. Proper restraint of a non-aggressive, non-venomous snake.

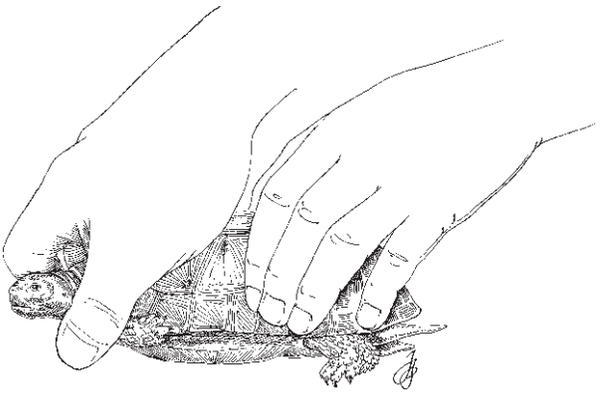

Figure 178-5. Proper restraint of a turtle.

are more secure if allowed to coil around an arm (Fig. 178-4). Most snakes struggle less when handled with minimal restraint. Never let any snake near your face or around your neck!

▼ ***Key Point*** Never pick a snake up only by its head only because serious damage to the spine may occur. Reptiles only have one occipital condyle, making it relatively easy to luxate the spine from the head. Always support the body.

If an aggressive, non-venomous snake arrives in a bag, grasp the head through the bag. If necessary, gently pin the head of free individuals with a snake hook or snare. Be careful not to injure the snake. Alternatively, grab the snake using a towel as a blind.

Large snakes can be very dangerous and may require up to six experienced people to restrain. Squeeze cages and sedation may be required to safely handle extremely large or aggressive individuals.

▼ ***Key Point*** Never handle venomous reptiles without expert assistance and the appropriate antivenin. Any mistake made by the veterinarian, a technician, or the owner may result in human death.

Chelonians

Hold chelonians by the dorsal caudal portion of the shell (Fig. 178-5). This placement makes it difficult for the animal to reach around and bite, or to scratch with its rear feet. Be sure to have a firm grip, especially if the turtle is wet. Always hold a chelonian over a table. Dropping a turtle may cause severe life-threatening shell fractures. Handle soft-shelled turtles with rinsed examination gloves, thus preventing damage to the delicate shell. Snapping turtles and some other long-necked turtles can reach the rear of their shells with their beaks. Grasp these turtles by the base of the tail. Hold them with tail in one hand and the front of the carapace just over the head in the other hand. Large snapping turtles are very dangerous to handle and should be left to experts.

Transportation

Transport non-venomous reptiles of moderate size in a tied cloth sack placed in a styrofoam or dedicated camping cooler containing air holes. Chelonians do not need to be placed in a sack. Coolers can be fitted with space for hot or cold water bottles or chemical packs if extreme temperatures are anticipated. These methods are to be used for transporting animals a short distance only.

History

▼ ***Key Point*** For most reptiles, improper husbandry is the primary predisposing factor for many diseases. Unless the diet and environment are improved, the best treatment plan will fail.

Ask the owner about the following:

- Species, age, sex
- Origin: initially, wild caught or captive bred; recently, pet shop or supply house
- Length of ownership, previous experience
- Environment, caging, cleaning, temperature, humidity, photoperiod, UV light source
- Diet: supplements, appetite, last meal, last stool
- Dates of unusual activity, breeding, egg laying, shedding
- Cagemates, quarantine history, aggressive behavior
- Medical history, previous weights
- Purpose of ownership: pet, breeder, display, education

Physical Examination

Observe the animal's behavior in the cage before handling. If necessary, observe healthy animals to become

familiar with normal behavior, locomotion, weight, skin tone, and color. All terrestrial lizards (legged) and chelonians normally can lift their bodies off the ground when they walk. Fork-tongued reptiles frequently should flick their tongues to sample the air. Prolonged head tilts are abnormal. Legs and/or epaxial muscles should be full and have good tone. The skin should have a healthy color and texture, without moist, discolored, or ulcerated areas. Dyspnea is abnormal, but do not mistake hissing for dyspnea. Examine the stools for abnormal color, consistency, urates, grossly visible parasites, and polyuria.

Develop a routine, systematic technique when performing the physical examination, such as working from head to tail. Check the nose for abrasions or discharge. Perform a thorough oral examination. Look for cyanosis, hyperemia, ulcers, discharge, abscesses, broken teeth, or parasites. Take samples of the choana or tracheal swabs for Gram staining or culture. Clear, viscous saliva is normal. Examine the mandibles for evidence of fibrous osteodystrophy or trauma. Examine the underside of the jaw and the periocular area for parasites. Look for retained spectacles when appropriate, and use a slit lamp and ophthalmoscope to examine the interior of the eyes. Examine the tympanic membrane, when present, which should be pliable with no exudate.

The heart of most herbivorous and insectivorous lizards is located under the pectoral girdle. To auscult the chest, place a moistened gauze sponge between the bell of the stethoscope and the skin, thus minimizing sounds from scales rubbing. The technique can be applied to turtles and crocodiles, but the shell of chelonians and the thick skin of crocodilians make interpretation more difficult. The heart beat of all but the largest snakes can be palpated through the ventral scutes. The heart is located in the first 15% to 25% of the body. Doppler units are helpful for determining heart rates.

Palpate the abdomen to detect masses, eggs, bladder, and feces. In snakes, start cranially and move caudally, letting abdominal organs slip through your hands. A mass is less likely to be overlooked when this method is used.

Check the vent for normal tone. This is an excellent time to obtain cloacal samples for Gram staining or culture and to examine the cloaca for parasites (especially ticks and mites). It is normal for stressed turtles to urinate, providing an opportunity to collect a urine sample. If a turtle does not urinate, this may be a sign of dehydration.

Palpate all extremities and check the skin for lesions. Especially examine the leg cavities in chelonians for external parasites and the ventral surface of all reptiles for signs of cutaneous lesions.

TECHNIQUES

Oral Examination

Snakes and Lizards

Use caution when opening the mouth. The teeth are sensitive and fragile, and broken teeth can cause prolonged anorexia. A snake's mandibles are very flexible and have an open symphysis. The jaws therefore are fractured easily if too much pressure is applied. Support the cranial cervical region to immobilize the head, and use the maxilla as a leverage point. Support the neck to minimize trauma to the cervical spinal cord. Use a thin plastic card or hard rubber spatula as a wedge in the corner of the mouth to gently pry open the mouth. Place pressure only on the gum line and never on the teeth. Once the mouth opens a little, slip the card across the mouth (see Fig. 178-1). A wedge or speculum may be necessary to hold the mouth open if the animal is large. Dewlaps, if present, may be used to provide downward traction.

Chelonians

To capture the head, wait until the turtle extends its head beyond the edge of its shell and quickly grasp the base of the head from over the top of the shell, using the shell as a blind. If a land turtle refuses to open its shell, it can be submerged in water to cover the opening to their shell. The head then can be grasped as it is extended to breathe. Remember this is stressful to the tortoise. Once the turtle is caught, extend the neck and restrain the head from the sides just behind the mandibles. Do not grasp the dorsal or ventral surfaces of the neck because the trachea or hyoid apparatus may be crushed. Gently and with persistent pressure pry the beak open with a thin metal spatula. An avian mouth speculum or hard rubber spatula then may be placed across the mouth. Always use a hard speculum if soft materials such as rubber catheters are going to be placed into the mouth. Use caution when opening the beak of an ill or malnourished turtle because beaks are often friable and easily damaged. Gauze strips may be useful in keeping the beak open and will not damage the beak. Some chelonians, especially tortoises, seal up in their shells, thus requiring sedation to extract their heads.

Venipuncture

Lizards and Snakes

Use the tail vein to draw blood from lizards, large snakes, and chelonians (Fig. 178-6). In snakes and lizards, the vein usually runs just ventral to the spine. In

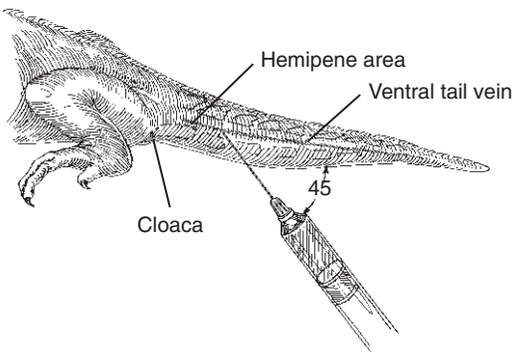

Figure 178-6. Venipuncture of ventral tail vein of a lizard.

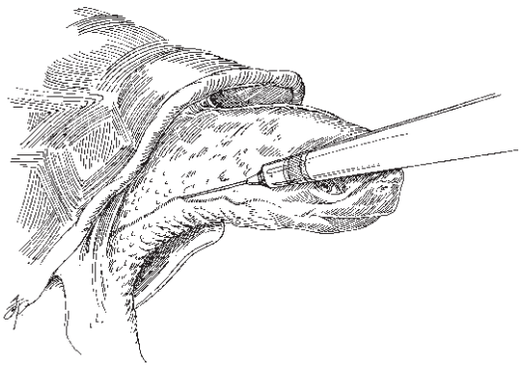

Figure 178-8. Jugular venipuncture site in a turtle.

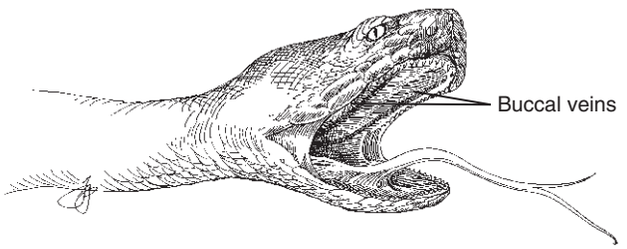

Figure 178-7. Venipuncture sites for the dorsal buccal veins of a snake.

males, be sure to insert the needle caudal to the hemipenes. Insert the needle in a cranial direction at a 45 to 60 degree angle. After the needle contacts the vertebral body, withdraw it 1 to 2 mm while aspirating until blood is seen in the hub of the needle. Aspirate gently to prevent collapse or laceration of the vein. A 1- or 3-ml syringe with a 25- or 27-guage needle works well. In all species, lymphatic vessels run parallel to the tail veins. Mixing of lymph and blood significantly alters hematology and some chemistry results.

Alternatively, open the mouths of boas and pythons with a soft spatula or tongue depressor to collect blood from the buccal veins on the inside of the mouth (Fig. 178-7). We have drawn intracardiac blood samples in hundreds of snakes with no pain response or subsequent ill effects observed.

Chelonians

Collect blood from the jugular vein whenever possible (Fig. 178-8). The vein is very mobile, so position the neck in a straight line. Hold off the vein at the base of the neck and locate the jugular vein visually or by palpation. Holding the turtle in a head-down position helps with filling of the vein. These vessels have a tendency to spasm; use atraumatic technique. Occlude the vessel for at least 2 minutes after venipuncture to prevent hematoma formation. Alternatively, blood may be collected from the tail vein, which is located on the dorsal surface of the spine at the base of the tail. The subcarapacial site is useful as it can be used to draw blood with the chelonian's head withdrawn or extended. A 1- to 1.5-inch needle may be advanced through the skin where it meets the carapace on the dorsal midline. Applying gentle suction, the needle is directed to the base of the eighth cervical vertebrae and into the anastomosis of the common intercostal veins until blood is seen in the hub of the needle. Brachial and femoral veins can also be used in chelonia.

Stomach Intubation

Non-Chelonians

- Warm fluids or formulas to 80°F to 90°F.
- To minimize regurgitation, administer no more than 1 to 6 ml/100g body weight per feeding.
- Measure the distance from the tip of the nose to the last rib in lizards and crocodilians, or from the tip of the nose to the first 10% of the body length past the heart in snakes.
- Open the mouth as described previously.
- Visualize the glottis at the base of the tongue. Avoiding the glottis, pass a flexible tube to the premeasured distance. Be certain the tube is not in the trachea and identify the glottis before administering any medication. If the glottis is not visible, palpate the neck for both the trachea and feeding tube, and administer sterile saline first.
- In animals with jaws strong enough to sever a stomach tube, use an avian speculum, a block speculum with a hole drilled in the center, or a sized-down Frick tube to protect the feeding tube.

▼ ***Key Point*** Medications given inadvertently in the trachea are usually fatal.

Chelonians

- Turtles are more difficult to intubate because their glottis frequently is hidden by the tongue. Some species possess a 90 degree turn in the esophagus just cranial to the stomach.

- Measure the distance from the nose to halfway down the plastron.
- After placing a speculum, aim the tip of the tube toward the dorsocaudal pharynx. Let the tube follow the dorsal wall down into the esophagus. Try to identify the glottis by gently pushing up on the hyoid apparatus. This pushes the tongue forward. If the glottis still is not visible, palpate the neck for both the trachea and feeding tube. Check tube placement with sterile saline before administering medications.

▼ ***Key Point*** Never force a stomach tube because this may create an esophageal tear.

- If regurgitation occurs, cover the end of the tube to prevent dribbling and withdraw the tube. Turn the animal's head down and wipe out the mouth with paper. (Cotton or cloth will entangle on squamate teeth.) Wait until the animal is recovered and less stressed before making a second attempt, and decrease the volume to administer by one half. If no regurgitation occurs, slowly increase the volume over several feedings to the desired amount.

Perform a *stomach wash* on all vomiting reptiles. Intubate the stomach as aforementioned with a red rubber feeding tube, and give warmed 0.9% NaCl (3–6 ml/100 g body weight). Gently massage the stomach and aspirate the fluid. Use the fluid for bacterial or fungal cultures, cytologic examination, Gram staining, immunofluorescent antibody (IFA) tests for *Cryptosporidia*, or direct saline smear for evidence of parasites.

Enema

Administer a mixture of 50% K-Y jelly and 50% 80°F water into the cloaca/colon at a rate of 1 to 3 ml/100 g body weight. Excellent restraint is essential. Select a red rubber urinary catheter that is approximately 0.25 times the size of the vent opening. In very small animals, tomcat catheters may be used to provide rigidity. The catheter is lubricated with a water-soluble lubricating jelly. Start the catheter at a 90-degree angle to the body. After the tip of the catheter passes the opening of the vent, aim it cranially, parallel to the colon, and advance. Never force the catheter or fluid into the cloaca, or cloacal perforations may occur. Never use high pressure to inject fluid into the cloaca. This may cause feces to be forced into the ureters or oviducts, resulting in life-threatening infection.

Injections

Always administer injections cranial to the kidneys to avoid the renal portal system (Fig. 178-9).

Subcutaneous

In non-chelonians, administer fluids or other therapeutic agents over the axillary region as in mammals. In turtles, use the skin folds located around the front and rear legs. If using the inguinal region, be sure not to puncture through the body wall. Fluids should be warmed to 80°F to 95°F.

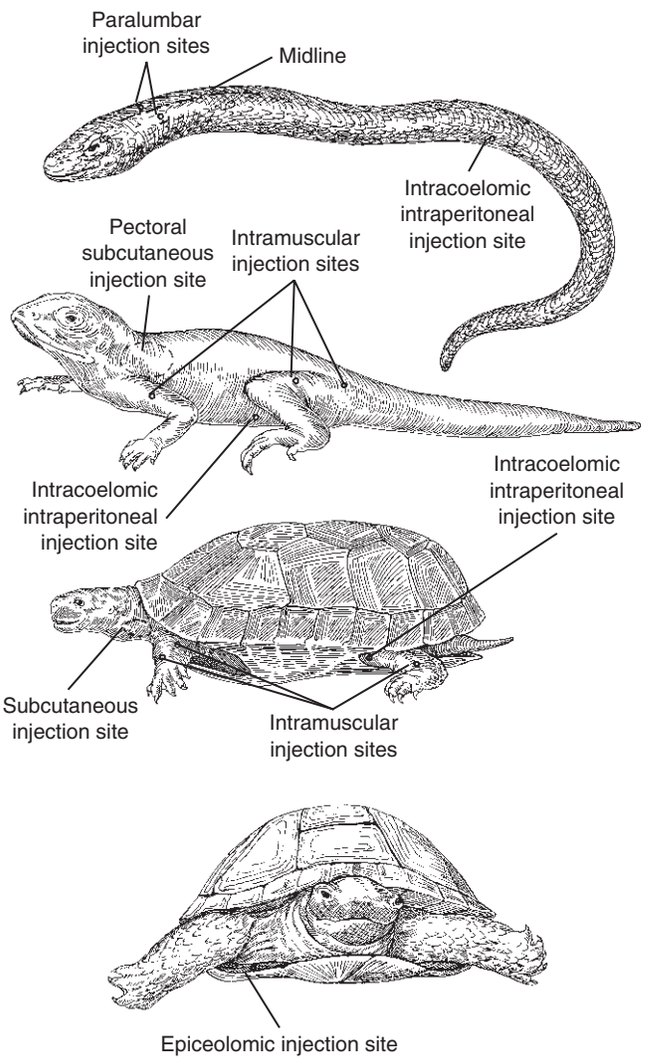

Figure 178-9. Common injection sites in a snake *(top)*, lizard *(center)*, and turtle *(bottom)*.

Epicoelomic

This region is medioventral to the front legs and is used to administer fluids to chelonians. Absorption is excellent in animals with adequate perfusion (see Fig. 178-9).

Intramuscular

In snakes and legless lizards, administer IM injections into the epaxial muscles. In all other reptiles, use the muscles of the front legs. The rear legs and the epaxial muscles of the tail may be used for injection of non-nephrotoxic drugs. Insert the needle between scales to

minimize damage to the skin. With the bevel of the needle pointing up, aim proximally using a 45-degree angle. Always aspirate before injecting.

Intraosseous

Because most reptilian veins are not easily accessible, it may be necessary to use an IO route to administer medications and fluids. In lizards, try the distal femur, proximal tibia, proximal humerus, or distal radius.

- Surgically prepare the entry site.
- Choose a spinal needle that is 33% to 66% the diameter and length of the chosen bone.
- Identify the tibial crest or the dorsal midline of the distal femur just proximal to the condyles. Advance the tip of the needle through the skin at a 45- to 90-degree angle until the tip of the needle is through the cortex of the bone.

▼ ***Key Point*** It is extremely important to keep the needle straight while boring through the cortex to avoid extravasation of fluids.

- A sudden lack of resistance is felt once the tip of the needle enters the marrow cavity. At this point, angle the needle down the length of the bone and advance it until the hub is seated against the skin. The needle should advance easily.
- Once the needle is seated, remove the stylet. Attach a syringe and aspirate. In most cases bone marrow can be seen in the hub of the needle. If no marrow is identified on cytology, obtain radiographs to ensure appropriate placement of the catheter. Flush the intraosseous catheter with heparinized saline. Secure it to the skin with sutures.
- Although it is wise to avoid caustic substances, treat the catheter as if it were an intravenous catheter. Catheters can be maintained for 72 hours.
- In turtles, administer intraosseous fluids into a thickened area of bone (bridge) that underlies the shell where the plastron and carapace meet (Fig. 178-10). Use a spinal needle.

Intracoelomic

▼ ***Key Point*** Intraperitoneal injections have the potential for causing peritonitis or respiratory compromise. Always prepare the area with a surgical scrub.

Use this technique for administration of fluids when other routes are not possible. Warm fluids to 80°F–85°F. Avoid caustic substances because they can cause chemical peritonitis. In chelonians, give injections just cranial to the rear legs. Extend the rear legs and administer the injection with the animal in held in a head-down position. In snakes and lizards, inject fluids slightly off the ventral midline in the caudal third of the abdomen. Hold the head in a downward position while injecting (see Fig. 178-9). Always aspirate to ensure that the injection is not being given into the bladder, oviduct, or bowel.

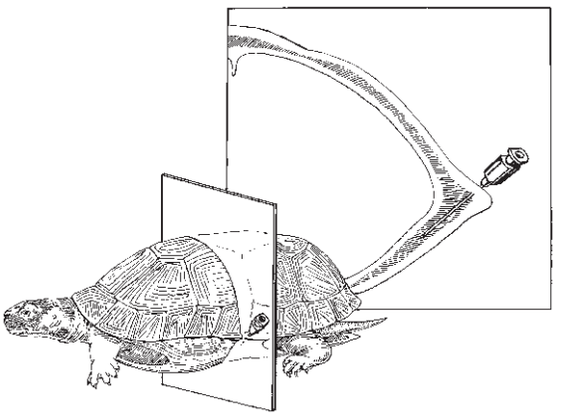

Figure 178-10. Intraosseous injection site of the turtle.

- **Do not use this technique in gravid females. Exceeding 2% to 3% of the body weight in fluids may result in respiratory compromise.**

Radiography

Diagnostic radiographs require a machine capability of at least 100 ma and exposure times of less than 1⁄60 second. Use rare earth screens when possible. Diagnostic radiographs require two views. Dorsal ventral views and standing lateral views are easier to obtain and interpret than ventral dorsal or lateral recumbent films.

To evaluate the lungs of turtles with suspected pneumonia, obtain an anterior/posterior horizontal beam view in addition to those aforementioned.

Contrast Radiography

GI transit times in reptiles are normally prolonged compared with those of mammals. Therefore, contrast studies have limited use. When 20–50 ml/kg of barium is administered to carnivorous lizards, it may take 3–6 days to reach the cloaca. When this dosage is administered to snakes, crocodilians, and herbivorous lizards, it may take up to 30 days. At a dosage of 20 ml/kg, barium requires 40 days to reach the cloaca in tortoises. Always ensure that the animal is well hydrated before the administration of barium, or it may become desiccated in the bowel, often requiring surgical removal. We have had excellent results using a 1:3 dilution of iohexol:saline as a contrast agent.

For evaluation of the coelomic cavity, ultrasound is an extremely useful diagnostic technique. A 5.0, 7.5, or 10 mHz transducer is necessary.

ANESTHESIA

Isoflurane is the anesthetic agent of choice for reptilian patients. Although the recovery period is prolonged, halothane also has been used successfully for anesthe-

sia in reptiles. Methoxyflurane also has been used successfully, but deaths in snakes have been reported. Sevoflurane can be used, but the increased cost compared to isoflurane may not be justified.

A single intravenous or intraosseous bolus of propofol is an excellent induction agent and is also useful for short procedures. Anesthesia from a single injection usually lasts 10 to 15 minutes and reptiles are usually fully recovered in less than 40 minutes. A short-term, self-limiting apnea is common. It is prudent to provide positive pressure ventilation if the apnea persists longer than 2 minutes. All anesthetized reptiles should receive supplemental oxygen.

▼ ***Key Point*** Creating a hypothermic state is never an acceptable method of anesthetizing reptiles. Hypothermia does not provide analgesia, slows healing, and depresses the immune system.

Anesthesia in reptiles is highly temperature dependent. External heat sources are necessary during anesthesia and recovery. Heating pads and forced air warmers work well intra-operatively. Always place the animal in a preheated incubator during recovery. Cold reptiles are immunocompromised, heal slowly, and may take days longer to recover from anesthesia.

Induction

Use mask induction with 2% to 4% isoflurane with the animal restrained in a towel or use propofol. An induction chamber is useful for aggressive animals. The first sign of anesthetic induction is excitement, then voluntary motor control is lost. Loss of the righting reflex is followed by muscle relaxation, indicating a surgical plane of anesthesia. Reptiles with third eyelids retain a slowed third eyelid reflex even when no pain response is elicited. In these animals, a loss of the blink reflex indicates a need to lighten the depth of anesthesia.

Chelonians, aquatic squamates, and crocodilians can hold their breath for long periods of time, so induction with injectable anesthetics is often necessary (see below).

▼ ***Key Point*** Once relaxation occurs, intubate the animal and begin positive pressure ventilation.

If placing an endotracheal tube is difficult in a chelonian, move the front limbs in and out to maintain air flow until a tube is placed.

Intubation

Inflatable cuffs are not recommended for small animals. Inflating the cuff may cause tracheal inflammation severe enough to occlude the trachea. Endotracheal tubes for small individuals can be fashioned from catheters and infant feeding tubes. Because most reptiles become apneic during anesthesia, always have the animal intubated to provide positive pressure ventilation. Ventilate animals at a rate of 3–6 breaths per minute.

Maintenance

Maintain anesthesia at 1% to 2% isoflurane at 1 L of oxygen per 0.3 to 1 kg of body weight. Larger reptiles usually require 1 L per 5 to 10 kg of body weight. Be sure to monitor heart and respiratory rates. A marked reduction in either of these two values is an indication to lighten anesthesia.

Recovery

When isoflurane is used, animals may recover within 20 minutes. Many other anesthetics (and occasionally isoflurane) may cause prolonged recovery periods, lasting hours to days. Assisted ventilation is required until spontaneous respirations occur. Be prepared to offer ventilatory assistance as long as necessary, even if the reptile takes hours to breathe on its own. To speed recovery times, place the animal in a warm environment and continue fluid therapy during recovery. Ventilating with room air or providing small levels of carbon dioxide (such as exhaled air) instead of 100% oxygen will sometimes stimulate the respiratory centers.

Injectable Anesthetics

Isoflurane or propofol should be used for anesthesia whenever possible because recovery times are prolonged and dosage titration can be difficult when using other injectable anesthetics.

Ketamine Hydrochloride

Most reptiles require 20 to 60 mg/kg IM or 5 to 15 mg/kg IV. Crocodilians often require the higher end of the dose range. Ketamine provides marginal relaxation and analgesia. It may be used for as sedation for non-painful procedures or as a preanesthetic for reptiles that cannot be induced with a gas anesthetic.

Tiletamine Hydrochloride

The dose for tiletamine is 10 to 40 mg/kg IM in squamates, 15 mg/kg IM in crocodilians, and 5 to 15 mg/kg IM in chelonians. Induction usually requires less than 30 minutes. At safe levels of anesthesia, the righting reflex is slowed but not eliminated. Expect bouts of paddling and head pressing and expect the palpebral reflex to be unaffected. The recovery period lasts an average of 3 hours. This drug is not recommended for surgical procedures.

Medetomidine

Combinations of medetomidine and ketamine have been used successfully in reptiles. Dose and effect are species dependent. Alligators have been anesthetized with 100 mcg/kg medetomidine and 7 mg/kg ketamine

IM with atipamazole given at 500mcg/kg to reverse the anesthesia. Tortoises typically require less medetomidine with dose ranges of 20 to 60 mcg/kg with 2.5 to 10 mg/kg of ketamine. Consult the literature for specific doses for the species in question.

Propofol

In reptiles with adequate venous access, propofol provides a safe, rapid induction of anesthesia sufficient for short procedures or to facilitate intubation and maintenance with gas anesthetics. Doses range from 2.5 to 15 mg/Kg IV or IO. Supplemental oxygen should always be used, because propofol can cause hypoventilation including apnea.

Analgesia

Reptiles have neurological components similar to those found in birds and mammals and have been shown to experience pain. With careful observation, reptiles can be seen displaying appropriate behavioral responses to nociception stimulation. All procedures that would be considered painful in other classes of animals should include analgesics to alleviate pain. Hypothermia is not considered a effective or humane analgesic. Preemptive analgesia helps to decrease postoperative pain including both neuropathic and inflammatory pain. Butorphanol has been used an analgesic as well as an anesthetic premedication. Meloxicam has been used as a nonsteroidal analgesic for many years in reptiles in Europe prior to its release in the United States. To prevent renal side effects, reptiles should be well hydrated when receiving nonsteroidal anti-inflammatory medications.

SURGERY

Suture Materials and Suture Placement

- Reptiles do not possess the enzymes needed to absorb gut sutures. Polydioxanone is the absorbable suture of choice. Polyglactin 910 or similar materials also may be used. In sea turtles poliglecaprone 25 and polyglyconate caused less tissue reaction than chromic gut or polyglactin 910.
- When closing the coelomic cavity, the peritoneum and muscle layers should be closed, but the skin is the holding layer.
- The skin must be closed in an everting pattern to allow dermis-to-dermis contact. Non-absorbable sutures, such as nylon, should be removed after one to two sheds have occurred.

Approach to the Coelomic Cavity

A perimedian approach is necessary in non-chelonian species to avoid the central ventral vein. In snakes, the location for the approach is usually one to two scale rows dorsal to the belly scute. This site avoids the central ventral vein and the ribs and prevents placement on a surface in constant contact with the ground. Seek assistance before performing a plastronotomy on a chelonian for the first time.

DRUG THERAPY

The use of various drugs in reptiles is similar to that in other genera with application of the following guidelines:

- Maintain reptiles at the high end of POT to enhance normal metabolism of drugs.
- Pay attention to species differences. A snake is less related to a turtle than a cat is to a cow. Drug clearances and toxicities are often species related.
- When available, use published dosages based on pharmacokinetic studies. Be aware that metabolic scaling is not always accurate.
- Weigh all animals before dosing drugs. Accurate dosages based on body mass are extremely important in avoiding side effects.
- When in doubt about renal clearance or hydration status, institute fluid therapy.
- Use bactericidal versus bacteriostatic antibiotics whenever possible.

In general avoid use of injectable gentomycin. Amikacin is much safer. The authors recommend that use of gentomycin be limited to topical preparations.

In general reptiles are exquisitely sensitive to glucocorticoids. Only use when indicated. Use the lowest effective dose for the shortest length of time. Be aware that immunosuppression may persist for months.

▼ ***Key Point*** Never use ivermectin in chelonians. It is toxic and is associated with neurologic dysfunction and possible death.

- See Table 178-3 for dosages of common chemotherapeutic agents used in reptiles.

COMMON DISEASES OF REPTILES

Failure to adapt to captivity is the principal cause of death in captive reptiles. The captive environment is so alien to a wild-caught reptile that stress induces immunosuppression and anorexia. Secondary infections and starvation cause death of the animal.

▼ ***Key Point*** Most diseases of reptiles are secondary to poor husbandry and nutrition.

Bacterial Infections

Both enteric commensal bacteria and pathogenic bacteria are usually gram negative. Large numbers of

Table 178-3. REPTILE CHEMOTHERAPEUTICS

Drug	Species	Dosage	Route	Frequency	Notes
Acyclovir	Tortoises	30–80 mg/kg	PO	sid or tid 10 days	Herpes virus
Allopurinol	Most species	10–20 mg/kg	PO	sid	
	Chelonians	50 mg/kg	PO	sid × 30d, then q72h	
Amikacin sulfate	Sea Turtle	2.5–3.0 mg/kg	IM, SC	q72h × 5 treatments	Loading dose 5 mg/kg, keep hydrated
	Lizards	5 mg/kg	IM, SC	sid	
	Various snakes	2.5–5 mg/kg	IM, SC	q72h	
Aminophylline	Most species	2–4 mg/kg	IM		
Amoxicillin	Most species	10–22 mg/kg	IM	sid, bid	Anaerobic spectrum
Ampicillin	Most species	8–10 mg/kg	IM	bid	Anaerobic spectrum
	Most species	20 mg/kg	IM	sid	
Atropine	Most species	0.01–0.04 mg/kg	IV, IM	q8–24h	
Azithromycin	Ball Python	10 mg/kg	PO	q48–72h	
Barium	Most species	5–20 ml/kg	PO		Contrast studies
Buprenorphine	Most species	0.005–0.02 mg/kg	IM	sid to qid	Analgesic
Butorphanol	Green Iguana	2 mg/kg	IM		Premedicate before administering isoflurane, high dose in literature
Butorphanol	Most species	0.05–1 mg/kg	IM, IV, PO	bid	Analgesic
Calcium glubionate	Most species	1 ml/kg	PO	sid	Rugby Laboratories, Inc., Norcross GA; oral calcium supplement
Calcium glubionate	Most species	10 mg/kg	PO	sid, bid	Hypocalcemia
Calcium gluconate	Most species	10–100 mg/kg	SC, IM, IP	sid	
Calcium lactate/glycerophosphate		5–25 mg/kg	SC, IM	sid	
Carbenicillin	Most species	200–400 mg/kg	IM	sid q48h	Often combine with aminoglycoside
Carprofen	Most species	1–2 mg/kg	IM, SC, PO	q24–72h	Loading dose 2–4 mg/kg, hydration important
Ceftaxidime (Fortaz)	Various turtles	20 mg/kg	IM	q72h	Shell infections
Ceftiofur	Most species	2–4 mg/kg	IM	sid	
Cephalexin	Green Iguana	40 mg/kg	PO	bid	Prophylactic antibiotics during surgery
Clindamycin	Most species	2.5–5.0 mg/kg	PO	sid	Anaerobic spectrum
Colchicine		Dose not established			Treatment of gout
Dexamethasone SP	Most species	0.125–0.75 mg/kg	IM, IV	Once	Use sparingly—prolonged depression of immune system
Diazepam	Most species	2.5 mg/kg	IV, IO		Treatment of seizures
Doxapram	Most species	5 mg/kg	IM, IV		Respiratory stimulant
Enrofloxacin	Leopard Gecko	10 mg/kg	PO	q48h	
Enrofloxacin	Most species	5–10 mg/kg	IM, SC, PO	sid	Irritating IM or SC
Epinephrine 1 : 1000	Most species	0.5–1.0 ml/kg	IV	Once	Cardiac arrest
Fenbendazole	Most species	50–100 mg/kg	PO	Single dose	Repeat in 2 wks
Fluconazole	Sea Turtle	10 mg/kg	PO	q5d	Loading dose, 21 mg/kg
Fluids	Most species	20–25 ml/kg/24hr	IV, PO, IO	Daily	Maintenance dose, shock dose 1–3% BW
Gentocin			TO		Use topically only—renotoxic
Halofusinon		Dose not established			Used in treating cryptosporidium
Iohexol 240mg/ml	Most species	5–20 ml/kg	PO		Contrast studies
Iron Dextran	Crocodilians	12 mg/kg	IM	q2 wks	Anemia
Itraconazole	Sea Turtle	5 mg/kg	PO	sid	
Ivermectin	Most species	0.2 mg/kg	PO, SC		*Never in turtles*
Ketoconazole	Most species	15–25 mg/kg	PO	sid	Antifungal
Ketoprofen	Most species	2 mg/kg	SC, IM	q24–48h	Hydration is important
Levamisole	Various turtles	5 mg/kg	IM	Once	Antiparasitic treatment, can be hepatotoxic

Table continued on following page

Table 178-3. REPTILE CHEMOTHERAPEUTICS—cont'd

Drug	Species	Dosage	Route	Frequency	Notes
Meloxicam	Most species	0.1–0.2 mg/kg	PO	sid	Analgesic
Metoclopromide	Most species	0.06 mg/kg	PO	sid	
Metoclopromide	Tortoises	1–10 mg/kg	PO	sid	
Metronidazole	Corn snake	50 mg/kg	PO	q48h	
Nystatin	Most species	100,000 IU/kg	PO	sid	Antifungal
Oxyglobin	Most species	10 ml/kg	IV		Blood loss, shock, give over 10–15 min, follow with crystalloid fluids
Oxytocin	Turtles	1–10 IU/kg	IM	sid	Induction of oviposition, risk of oviduct rupture
Paromomycin	Green Iguana	100 mg/kg	PO	sid 14 days	Treatment for cryptosporidium—variable results
Pipercillin	Green Iguana	100 mg/kg	IM	q48h	
Praziquantel	Loggerhead Sea Turtles	25 mg/kg	PO	3 doses 3 hours apart	Treatment for spirorchiids, based on plasma levels
Praziquantel	Most species	5–8 mg/kg	IM, PO	Single dose	Repeat in 2 wks
Probenecid		Dose not established			Treatment of gout
Propofol	Marine Iguana	12–15 mg/kg	IV		Anesthesia induction
Propofol	Snakes	2.5–10 mg/kg	IV, IC		Anesthesia induction
Propofol	Various turtles	10 mg/kg	IV		Anesthesia induction
Provent-a-mite	African Spurred Tortoise	Spray on tortoise	TO	q5d	For 6 treatments
Provent-a-mite	Green Iguana, Rosy Boa	Spray in cage	TO	q5d	For 6 treatments
Pyrantel pamoate	Most species	5 mg/kg	PO	Single dose	Repeat in 2 weeks
Sodium bicarbonate 8.5%	Most species	0.5–1.0 mEq/kg	IV		
Spiramycin		Dose not established			Used in treating cryptosporidium
Sulfadimethoxine	Most species	45 mg/kg	PO	sid 5 days	Loading dose 90 mg/kg, maintain hydration
Sulfinpyrazone		Dose not established			Treatment of gout
Toltrazuril		Dose not established			Toxic in lizards
Trimethoprim sulfadiazine	Most species	15–25 mg/kg	IM	sid	Broad spectrum
Tylosin	Most species	5 mg/kg	IM	sid	10–80 days mycoplasma
Vasotocin	Turtles	0.01–1.0 µg/kg	IV, IM	Once	Use with calcium for ovipositioning
Vitamin A	Turtles	1000–2000 IU/kg	PO +/− IM	Weekly	Treatment hypovitaminosis A, watch toxicity
Vitamin B complex	Most species	5–10 mg/kg	SC, IM		
Vitamin B_1 (thiamine)	Most species	25 mg/kg	PO	sid	
Vitamin B_1 (thiamine)	Most species	3 mg/kg (fish)			Fish supplement
Vitamin B_6 (biotin)	Most species	Use vitamin B complex			
Vitamin C	Most species	10–20 mg/kg	IM	Single dose	
Vitamin D_3	Most species	200 IU/kg	PO, IM	Weekly	
Vitamin E	Most species	1 IU/kg	IM		
Vitamin K_1	Most species	0.25–0.5 mg/kg	IM		

monomorphic gram-negative bacteria or identification of intracellular bacteria on Gram-stained specimens are suggestive of bacterial disease. Perform bacterial cultures on samples collected from suspected infection sites. Anaerobic bacteria are common pathogens found in reptiles with lower respiratory infections.

▼ ***Key Point*** Reptiles are known carriers of leptospirosis and *Salmonella* spp. Inform clients of potential zoonoses. *Salmonella* spp. live in the intestines and are transmitted to people when fecal material is handled.

Many species of reptiles have adapted to some strains of *Salmonella* spp. These bacteria do not cause disease and may be necessary components of the normal intestinal flora. *Salmonella* spp. in this category may or may not cause disease in humans or other species of reptiles. However, certain serotypes of *Salmonella* are highly pathogenic and may cause diarrhea, pneumonia, or septicemia. Fecal cultures do not distinguish pathogenic from nonpathogenic *Salmonella* serotype. Consider *Salmonella* spp. to be a significant pathogen when isolated directly from a grossly visible lesion, the respiratory tract, or intestinal tract of animals demonstrating clinical signs of enteric disease. Prophylactic treatment with antibiotics does not eliminate carrier stages.

It is almost impossible to eradicate *Salmonella* from pet reptiles. The following recommendations are aimed at controlling the spread of *Salmonella* and its ability to cause disease.

1. Minimize stress. Keep reptiles in the best husbandry situation possible. Avoid mixing species.
2. Proper hygiene is essential. Disinfect and clean cages regularly, but do not clean cages in food preparation areas (kitchens) or bathrooms. Wash hands/equipment between animals, after handling, and before eating or smoking.
3. Perform a necropsy on all dead animals.
4. Reptiles are not recommended pets for immunocompromised people, such as infants, toddlers, elderly people, chemotherapy recipients, and people with acquired immunodeficiency syndrome (AIDS).

COMMON DISORDERS IN BOAS, PYTHONS, AND LIZARDS

Anorexia in Boas and Pythons

Etiology

Anorexia may occur with or without obvious weight loss. Obtain a thorough history. Often there are no other signs of disease. Inadequate husbandry, particularly in the areas of temperature gradient, seclusion, selection of prey item (e.g., color, size, temperature if thawed, species, ability to attack), light cycle, crowding, and adequate hydration or access to water, are the most common causes of anorexia.

Diagnosis

If husbandry problems are found and the animal appears otherwise healthy, perform a fecal float and fecal direct smear to rule out intestinal parasitic infections.

If the animal has not eaten for more than 2 months and has lost significant body condition, consider further diagnostics such as hematology, serum chemistry, cultures and radiographs.

Treatment

Treatment is based on improving husbandry and removing any parasites. Common helpful recommendations include:

- Use a thermometer to accurately measure the temperature gradient in the cage.
- Provide a hide box and feed stunned prey in the hide box.
- Monitor the light cycle. Ensure a 12-hour-to-12-hour light-dark cycle.
- Try another species, color, or different size prey. Warm dead prey to 100°F in a plastic bag and ensure that the prey item is not wet when offered to the snake.
- Feed when quiet or dark. Do not handle snakes for 1 week after feeding.
- Provide a water dish large enough for the snake to sit in.
- Feed stunned prey if dead prey are not accepted.

If the reptile appears ill, assume that it also is dehydrated. Rehydrate with intraosseous (non-snakes), subcutaneous, or oral fluids depending on the state of hydration. Pass a stomach tube and administer warmed isotonic fluids to prepare the gut to receive solid food. Later, add glucose or electrolyte powders to increase the osmolality. Once this solution is tolerated, the formula may be changed to an iso-osmolar enteral feeding product such as (Ensure or Critical care). If this is tolerated, add meat baby food to the mixture to begin to introduce solid foods to carnivores. When ready to feed prey to carnivores, offer pinkies or small rodents first, and slowly increase the size of the prey.

In severely ill lizards and chelonians, placement of a pharyngostomy tube will greatly facilitate administration of supplemental nutrition. After herbivores or omnivores accept iso-osmolar diets, use a mixture of vegetable baby food mixed with alfalfa pellets or commercial diet formulated for rabbits mixed with water to increase the fiber load. First feed softer plants and/or insects to herbivores and insectivores to prepare the gut for a regular diet. As these are accepted and digested normally, slowly add in the normal diet.

Respiratory Disorders

Pneumonia

Etiology

Pneumonia is usually secondary to poor husbandry, bacterial septicemia, oral infections (stomatitis) or lung parasites.

Clinical Signs

The clinical signs of pneumonia include nasal discharge, gurgling, bubbling, open-mouthed breathing, and anorexia. Concurrent eye and mouth infections are common.

Diagnosis

Diagnosis usually is based on tracheal cytology and cultures. Other useful diagnostic tests include fecal flotation, hematology, bronchoscopy, and radiography.

Treatment

Administer antibiotics based on culture and sensitivity testing, or anthelmintic or antifungal drugs if indicated. Increase the environmental temperature to the high end of the POT. Parenteral vitamin C, fluid therapy, and nebulization therapy may be necessary.

Nebulize warmed saline to loosen debris in the bronchi. Antibacterial or antifungal medications may be added. A crude but apparently effective form of "nebulization" can be accomplished by the owner at home by using a hot shower to fill a bathroom with steam for 1 hour daily. Severely dyspneic individuals may require oxygen therapy. The long-term prognosis for these animals is grave. Arranging cage furniture to allow postural drainage is particularly helpful in some snakes.

Pentastomids

Etiology

Pentastomids are degenerate arthropod parasites of reptiles that resemble segmented worms. Infection occurs through an indirect life cycle involving insects and mammals. The parasites may live anywhere in the body but prefer the lungs and subcutaneous space.

Clinical Signs

Clinical signs in severely affected animals include dyspnea, hemoptysis, and cachexia. Occasionally a pentastomid may penetrate the body wall. Pentastomids can be acutely fatal in hatchling crocodilians.

Diagnosis

Diagnosis is based on fecal examination, tracheal cytology, or bronchoscopy.

Treatment

There is no routinely effective treatment for pentastomiasis. Ivermectin will kill adults, but debris from dead parasites often still causes clinical signs. A group of Boelen's pythons were successfully treated with a combination of fenbendazole 50 to 100 mg/kg and ivermectin 0.2 mg/kg PO SID for three treatments. Because this parasite may be zoonotic and is not readily treatable, consider euthanizing infected animals. Infection can be avoided in captive-reared animals by feeding only domestically reared prey items.

Infectious Stomatitis (Mouth Rot, Ulcerative Stomatitis)

Etiology

Mouth rot is usually secondary to poor husbandry, trauma from cage rubbing, or trauma from a rodent bite. The most common bacterial agents are *Aeromonas* and *Pseudomonas,* although other bacteria and fungi also are involved frequently. Neoplasia, mycotic infections, parasitic granuloma, or mandibular fractures also may cause stomatitis. Herpes virus in tortoises and vitamin A deficiency in turtles are also often associated with oral ulcers and caseous plaques (See "Chelonians").

Clinical Signs

Early signs of mouth rot include oral petechia, ptyalism, and anorexia. As the infection progresses, caseous exudate, tooth loss, and osteomyelitis may be present. Mouth infections are frequently the nidus for concurrent eye infections and pneumonia.

Diagnosis

Perform a thorough oral examination and collect samples for cytologic examination. Obtain samples for bacterial culture and sensitivity testing, especially if caseous debris is found. The most accurate culture samples are obtained by making a small slit in an affected area of the gum and swabbing the underlying tissues. In advanced cases, perform skull radiographs to determine the extent of osteomyelitis. If animals are anorexic, collect blood samples for hematology and blood chemistries.

Treatment

In mild cases in which petechia and ptyalism are present without anorexia, apply topical iodine, chlorhexidine solution, or hydrogen peroxide twice daily and instruct owners to improve husbandry. Reptiles with stomatitis should be housed at the high end of the POT. In more advanced cases, surgical debridement of the caseous debris, nutritional support, fluid therapy, and systemic antimicrobials may be required. Administer a combination of enrofloxacin and amoxicillin until culture results are available (see Table 178-1).

Prognosis

In mild cases, the prognosis is excellent if husbandry improves. The prognosis is guarded for cases with significant caseous debris and grave for reptiles with significant osteomyelitis.

Gastrointestinal Disorders

Regurgitation in Boas and Pythons

Vomitus often looks like a stool containing no urates. Use pH papers to identify vomitus if necessary. Fresh vomitus has an acid pH, whereas feces are basic. Old vomitus becomes alkaline with bacterial decomposition. The regurgitation of only mucus is a grave sign.

Poor Husbandry

Excessive handling of snakes within 48 hours of ingesting a meal may result in regurgitation. In these animals, regurgitation occurs shortly after handling. Base the diagnosis on history, lack of other clinical signs, and radiographic evidence of calcified remains of a meal in the stomach for more than 50 hours post-prandially.

Diagnosis

A low body temperature inhibits the action of digestive enzymes, resulting in putrefaction of the ingested meal. In these snakes, regurgitation usually occurs 3 to 5 days post-prandially. The diagnosis is based on history and a lack of other clinical signs.

Treatment

Treat by providing an adequate, safe heat source 24 hours a day.

Obstruction

Foreign bodies usually are ingested with prey items and include cage substrates, cage furniture, and foreign bodies inside of prey items. Clinical signs include regurgitation, absence of fecal material, abdominal swelling, and anorexia. Diagnosis is similar to that for mammals and includes plain radiography or endoscopy. Perform hematology and blood chemistries on systemically ill animals.

Treatment

Treatment is similar to mammals. In mild cases in which the obstruction consists of small pieces of granular material, administer saline or mineral oil via stomach intubation. Parenteral fluids are also helpful. If a large foreign body is located in the stomach, endoscopic retrieval is often possible. Gastrotomy or enterotomy may be required to remove large objects or objects distal to the stomach.

Similar clinical signs may be seen in animals with intraluminal or extraluminal GI masses. Causes include neoplasia, abscess, or granuloma of the GI tract or other nearby organs, parasitic blockage, or organomegaly. Diagnosis is based on radiographs, ultrasound, fine-needle aspirate for cytologic examination and culture, or laparotomy and biopsy. Hematology or blood chemistries usually are indicated.

Diarrhea

Etiology

Gastroenteritis may be caused by enteric parasitic infections, gram-negative bacterial or clostridial infection, viral infections, or enteric fungi.

Diagnosis

- To rule out parasitic infections, perform fecal flotation, a fecal wet mount, and stomach wash, especially if diarrhea is accompanied by vomiting. Fecal sedimentation may be required if trematodes are suspected. Most cysts, eggs, and larvae can be identified to taxonomic family to direct anthelmintic treatment.
- Clinical bacterial or mycotic enteritis is often secondary to significant parasite infestations. Perform a fecal Gram stain to diagnose clostridial overgrowth or enteric yeasts. High numbers of monomorphic gram-negative rods are supportive of a diagnosis of bacterial enteritis (see "Bacterial Infections"). Routine culture techniques are not reliable in detecting *Salmonella*.
- Other diagnostic tests that may be useful include hematology, serum biochemistry, peritoneal lavage, and endoscopy.
- Other causes of diarrhea include foreign body, ruptured coelomic abscess, septicemia, and liver or pancreatic disease.

Treatment

- Administer fenbendazole for the prophylactic treatment of intestinal parasites.
- Administer praziquantel if cestodes or trematodes are suspected or found on fecal examination.
- Levamisole or ivermectin may be effective against acanthocephalans. Ivermectin is toxic to chelonians.
- Pending bacterial culture results, administer fluid therapy and parenteral antibiotics. In mild cases of dehydration, subcutaneous lactated Ringer's solution is an excellent choice. Fluid volumes should be calculated as for mammals, incorporating fluid losses from vomiting and diarrhea as well as maintenance needs. In severely dehydrated reptiles, use intraosseous fluids when possible. Administer half-strength lactated Ringer's solution or saline with 2.5% dextrose for the first 4 hours, followed by lactated Ringer's or other balanced electrolyte solution alone. Monitor serum or plasma potassium levels and add potassium to the fluids as needed.
- Parenteral administration of antibiotics is necessary in reptiles with GI disease. A combination of enrofloxacin with amoxicillin or ampicillin is usually effective in the treatment of most gram-negative,

gram-positive, and anaerobic bacterial pathogens. This combination does not appear to have detrimental effects on GI flora when administered parenterally and has low potential for nephrotoxicity in dehydrated reptiles.

Cryptosporidium

Etiology

- *Cryptosporidium serpentis* is a protozoal parasite of snakes and some lizards and tortoises. The parasite infects the stomach and large and small intestines, causing atrophy of intestinal villi and hypertrophy of the stomach wall.

Clinical Signs

- The classic clinical signs include diarrhea, regurgitation 2 to 3 days post-prandially, and marked gastric distention causing a visible fusiform swelling in the stomach region. It has also been associated with biliary disease in corn snakes, otitis in iguanas, and general enteritis in many lizard and snake species. Renal cryptosporidium has been seen in iguanas and chameleons. Chronic disease causes anorexia and weight loss. A subclinical carrier state exists. Cryptosporidium tends to be a gastric disease in snakes and an intestinal disease in lizards.

Diagnosis

- Diagnosis is confirmed by identification of cysts on cytologic examination of fluid obtained from a stomach wash or stomach biopsies. Cysts occasionally are seen in feces. Cysts are 2.6 to 6.0 µm in diameter and stain blue on Giemsa stain. Yeasts can look very similar. If in doubt, stain the slide with iodine. Yeast turns brown and cysts remain colorless. Alternatively, *Cryptosporidium cysts* stain positive with acid fast stains, whereas yeasts do not. Immunofluorescent antibody (IFA, Merifleur) testing is available and is 16 times more sensitive than acid fast stains especially when performed on stomach biopsies. A serological enzyme-linked immunosorbent assay (ELISA) test is available for use in snakes.

Treatment

- There is no effective treatment for cryptosporidiosis. Paromycin, halofuginone, spiramycin reduce shedding of oocysts, but do not eliminate infection. Toltrazuril has been used to relieve clinical signs in one group of tortoises, but is toxic in snakes. Bovine hyperimmune colostrums to *Cryptosporidium parvum* administered via gavage at 1% of body weight once a week for 6 weeks reduced clinical signs and oocyst shedding in several snakes and geckoes, but did not clear the infection. Recommend permanent isolation from uninfected reptiles or euthanasia because animals remain carriers and *Cryptosporidium* oocytes are extremely resistant to environmental degradation.

Amebiasis

Etiology

Amebiasis caused by *Entamoeba invadens* is diagnosed commonly in recently acquired snakes and lizards. The likelihood of infection increases if the animals previously were exposed to chelonians. Amoebiasis can also affect normally resistant groups of reptiles (water turtles, crocodilians, and reptile-eating snakes and lizards). The parasite causes a hemorrhagic gastroenteritis and liver necrosis.

Clinical Signs

Clinical signs include anorexia in early infestations, followed by regurgitation and hematochezia.

Diagnosis

Diagnosis is based on identification of cysts or trophozoites on cytologic examination of fluid obtained from a stomach wash or fecal smear.

Treatment

Administer metronidazole and initiate supportive therapy as needed. Prognosis for early infections is excellent, but for severe infestations is grave.

Constipation

Etiology

Many underlying causes for constipation exist, including exposure to cool temperatures, ingestion of foreign material (especially bedding), and an abrupt dietary change to more fibrous food. There is often a history of recent escape. Constipation also can occur secondary to compression of the colon by extraluminal masses such as eggs, organomegaly, granulomas, or uroliths. In chronic cases, renal failure may occur secondary to compression of the ureters by clocaliths (inspissated feces and urates in the cloaca). Constipation may also occur secondary to spinal osteopathy which impinges on spinal nerves.

Clinical Signs

Clinical signs of constipation vary from decreased stool production alone to signs of GI obstruction such as anorexia and vomiting. The animal may be cachetic if anorexic for long periods of time. Most affected animals are chilled and dehydrated.

Diagnosis

In early cases, abdominal palpation reveals a firm-to-doughy mass in the cloacal region. In chronic cases, the mass is hard and firm, and the animal may be bloated from retained ingesta. Radiographs and, if necessary, ultrasound may delineate the obstruction.

Treatment

If signs of systemic illness are not present, treat simple constipation at home with 1-hour warm water (85°F) body soaks administered two to three times over a 24-hour period. If defecation is not induced, administer an enema consisting of warm water/water soluble lubricating jelly enemas (see "Techniques"). If treatment is effective, some stool should be passed after one to three enemas. If the impaction has been long-standing and large amounts of ingesta are present, consider giving an enema every 2 to 3 days until all the material is expelled. In chronic cases in which stool will not pass and in cases in which the obstruction is secondary to a foreign body or extramural compression of the colon, perform a laparotomy. Because these patients usually are debilitated, surgery is risky. Strict attention to aseptic technique is essential to avoid peritonitis or abdominal abscesses. The surgical approach to the colon is similar to that in mammals.

Cloacal Prolapse

Etiology

- Cloacal prolapse usually is the result of straining due to enteritis, cloacitis, or dystocia.
- Pinworms are the most common cause of cloacal prolapse in lizards.

Diagnosis

Hyperemic, inflamed tissue is observed protruding from the vent on physical examination. Active straining may be present. The prolapse of other organs, such as the hemipene or oviduct, or cloacal neoplasia may appear similar. Use digital manipulation to determine the source of the prolapsed tissue. If in doubt, perform contrast radiography using iohexol (diluted 1:3 with warm water) administered as an enema to delineate the source of the tissue. Determine the primary cause of the straining. Fecal flotation, direct fecal wet mounts, and fecal Gram stains are the minimum diagnostic tests necessary to rule out parasites or clostridial or gram-negative bacterial enteritis.

▼ ***Key Point*** Diagnose and treat the underlying cause of cloacal prolapse to prevent recurrence.

Treatment

Clean the cloaca with warmed sterile saline. Avoid abrading the tissue. Use light sedation with isoflurane, propofol, or ketamine if the animal appears in pain or is difficult to restrain. Once the debris is cleaned from the tissue, determine whether the tissue is in fact the cloaca, and if it is intact. Ensure that the proximal colon is not involved in the prolapse. Until the primary cause for the prolapsed cloaca can be controlled, keep the cloaca in correct anatomic position.

If only the cloaca is involved, lubricate the tissue with water-soluble jelly and replace the cloaca with digital pressure. The application of topical hemorrhoidal medications or 50% dextrose may help reduce edema. If the cloaca is too small for digital pressure, use a well-lubricated cotton swab. Be sure to invert the cloaca entirely into its original position. Place a large horizontal mattress suture at the opening of the cloaca. Pass the needle perpendicular to the cloaca. Leave the ends of the suture long to adjust tension. In general, for reptiles less than 100 g, the opening should allow the passage of one lubricated cotton swab. Reptiles larger than 500 g usually require an opening large enough to accommodate four to six swabs. Adjust the tension so that the animal can defecate through the reduced opening, but the cloaca remains in normal position.

Instruct owners to watch for normal volumes of feces. Sutures are usually left in place 7 to 14 days. Feed a low-residue diet for 2 weeks. If necessary, mix mineral oil with baby food and administer orally to soften the feces.

If the proximal colon is involved in the prolapse, perform surgical correction and cloacopexy. The technique is similar to that used in mammals. If the cloaca is damaged severely, partial amputation can be attempted as long as the ureters and a connection to the GI tract are left intact.

Prognosis

The prognosis for cloacal prolapse detected early with treatable predisposing diseases is good. The prognosis for a long-standing cloacal prolapse or prolapse involving more than the cloaca is guarded. For severely traumatized prolapses in compromised animals, euthanasia may be the most humane alternative.

Reproductive Disorders

Dystocia

Dystocia is the inability to expel term eggs (oviposition) or fetuses. This is in contrast to retained ovarian follicles (see "Green Iguanas").

Etiology

Dystocia usually results from inadequate husbandry, such as inadequate nutrition (especially calcium), temperature, lighting, seclusion, physical activity, or substrate on which to lay. Dystocia also can result from infections of the oviduct or other abdominal disease.

Clinical Signs

Clinical signs include anorexia, partial lay, or straining to lay with no result. The history may suggest that the reptile is overdue for oviposition based on previous laying dates. Some species of reptiles normally harbor eggs internally; therefore determine that dystocia is actually present.

Diagnosis

Diagnosis is based on abdominal palpation and history. Radiographs and/or ultrasound may demonstrate

mature eggs or fetuses in oviducts. Large or misshapen eggs are strong evidence of dystocia. In most gravid reptiles, serum calcium, phosphorus, cholesterol, and total protein levels are higher than concentrations seen in mammals or non-gravid, healthy reptiles. Differential diagnosis for the abdominal masses and clinical signs include granuloma, neoplasia, intestinal obstruction, metastatic calcification, or gout.

Treatment

▼ ***Key Point*** Always determine whether dystocia is present. If the animal is not showing signs of being obstructed or critically ill, try modifying the environment. Provide a warmer temperature, a hide box, and an adequate moistened laying substrate, such as sand or soil.

If eggs are not produced within 2 to 3 days, administer parenteral calcium and either vasotocin or oxytocin. Drugs may be administered every 3 to 4 days as long as a few eggs are passed until all eggs are expelled. Do not give oxytocin or vasotocin daily or if eggs are not produced consistently, or oviductal rupture may occur. If these steps are unsuccessful, gentle manual expression of eggs can be attempted, but oviductal rupture is a common sequela if the veterinarian is not experienced. This technique is usually only effective if only a few (1–3) eggs are left and positioned close to the vent. Use copious lubrication. If a large or misshapen egg is palpated, the contents of the egg may be aspirated percutaneously via an 18-gauge needle and syringe. The resulting reduction in size sometimes allows these eggs to pass on its own. Do not try to manually express over large or misshapen eggs.

- Oviductectomy or oviductotomy frequently is required. If performed before severe systemic illness, the prognosis for life is excellent and for fertility (with oviductotomy) is good. If the animal is systemically ill, stabilize the patient with intraosseous or intravenous fluids and antibiotics before surgery. Correct electrolyte imbalances and perform surgery as quickly as possible.
- If the oviducts have ruptured and yolk is in the abdomen, the prognosis for long-term recovery is grave. Egg-yolk peritonitis not only affects the GI tract but also often induces liver failure. Egg yolk frequently embolizes and can cause infarcts in any tissue including the brain. If infection is present in the oviducts, submit the contents for bacteria culture and remove the oviducts and ovaries.

Prolapsed Hemipenes or Paraphimosis

Etiology

Prolapsed hemipenes usually occur after prolonged breeding. In chelonians, phallus prolapse occurs secondary to trauma by cagemates.

Clinical Signs

A prolapsed male copulatory organ is observed protruding from the cloaca. Bristles may be observed on the surface of the hemipenis in most species of snakes. In all reptilian species, the unique appearance of the hemipenes is sufficient to be differentiated from a prolapsed cloaca, bladder, or oviduct.

Treatment

Clean the exposed tissue with saline and lubricate with water-soluble jelly. If the tissue is swollen, ointments used for the treatment of human hemorrhoids can be used to reduce swelling. Replace the hemipene using gentle digital pressure, inserting the organ through the cloaca in a caudal direction. Place a horizontal mattress suture around the vent to keep the organ in place. In case of recurrent prolapse, a hemipene or phallus can be amputated without affecting urination because the hemipene does not contain a urethra and is only used to transport sperm. Amputation is accomplished under anesthesia by ligating the proximal portion of the organ with horizontal mattress sutures and using sharp dissection to remove the distal portion.

Dermatologic Disorders

Mites

- *Ophionyssus natricus,* or the snake mite, can be seen macroscopically as 0.5-mm black dots on the animal or on paper bedding. Look closely at the spectacle, in the gular fold, and around the vent. Mites can cause anemia and debilitation. They are also vectors for bacteria such as *Aeromonas* as well as viruses and blood parasites.
- Green iguanas have their own species of mite, which is red or gray in color. This mite causes spreading black patches of hyperkeratosis and can be diagnosed with skin scrapings.

Treatment

Treatment with ivermectin is usually effective. Never give ivermectin to turtles. The author has also successfully used products used to remove lice from children to treat many reptile species for mites. The skin of the reptile is rubbed with the product, the animal is restrained for 15 minutes and the product washed off with water.

- Be sure to clean and disinfect the cage. In severe infestations, treat the entire room with a pyrethrin flea product. Treat all animals and the environment every 2 weeks for three treatments. Discard any porous substances such as wood, paper, plants, or non-glazed pottery.

Ticks

Ticks are large enough to be observed macroscopically, with their heads buried under scales. They can be well

camouflaged and tend to congregate under the jaw and around the vent in snakes and in the axilla or groin in tortoises and lizards. As with mites, ticks can carry blood parasites, viruses, and bacteria.

Treatment

Spray a permethrin or pyrethrin flea spray that is labeled safe for use in kittens on a cotton swab and apply it directly to the head region of the tick. Once the tick is stunned, remove it using forceps. Be careful to remove the tick's head to avoid abscessation.

▼ ***Key Point*** Many ticks are imported with the reptile from regions of the world that have serious zoonotic diseases that can be transmitted by ticks. Always use gloves or forceps when removing ticks. Dispose of the remains as biohazardous waste.

Blister Disease

Etiology

Blister disease is a lay term for vesicular dermatitis. It is most frequently caused by a bacterial infection resulting from unsanitary and high-humidity conditions. Occasionally, vasculitis from a viral, fungal or bacterial septicemia causes similar clinical signs.

Clinical Signs

Fluid-filled vesicles or brown desiccated areas may be found on the ventral surface of the abdomen. These lesions may progress to ulcerations.

Diagnosis

Obtain a sample of the fluid within a vesicle for cytologic examination, bacterial and fungal culture.

If the reptile is systemically ill, further diagnostics such as hematology and blood chemistries are recommended.

Treatment

Improve sanitation. Apply topical diluted iodine, and administer parenteral antibiotics. Administer parenteral amoxicillin and enrofloxacin until culture results are available. Nutritional and fluid support is essential in severe cases because these animals may lose large amounts of serum through the vesicles.

Thermal Burns

Etiology

Burns are usually the result of contact with a heat lamp or a "hot rock."

Treatment

Administer parenteral antibiotics to prevent secondary bacterial infections. Apply topical diluted iodine and topical silver sulfadiazine cream daily. Monitor for secondary fungal infections. If large, full-thickness burns are present, fluid and protein losses can be excessive. If the patient becomes dehydrated, administer appropriate fluid therapy. It may be necessary to supplement protein with parenteral amino acids or plasma transfusion. If large areas of skin slough, apply a self-adhesive burn dressing such as Tegaderm (3-M Corporation Minneapolis, MN). This dressing provides the equivalent of a second skin and encourages healing while decreasing pain and fluid losses.

▼ ***Key Point*** Treat thermal burns as soon as possible to decrease the risk of bacterial septicemia and excessive fluid or protein losses. Instruct owners to bring the animal in for treatment as soon as the burn is discovered. The extent of the burn may take several days to become apparent.

Abscesses

Etiology

Abscesses may be secondary to either external trauma or bacterial septicemic emboli. If the abscess is secondary to septicemia, the primary infection must be identified and treated.

Diagnosis

Examine the skin for evidence of a firm swelling in the dermis. Palpate the abdomen to detect firm masses. Aspirate the swelling for cytologic examination and culture to confirm the diagnosis. Cultures taken from the edge of an abscess are the most useful. Blood cultures may be helpful in identifying the causative organism. Most abscesses consist of gram-negative or anaerobic bacteria intermixed with copious fibrous tissue. Other differentials include neoplasia, fungal granuloma, foreign body, parasites, or cyst.

Treatment

Reptilian abscesses contain caseous exudate, which does not drain well. Surgically excise the abscess along with the intact capsule whenever possible. If the entire abscess is not resectable, curette the remaining lesion until only healthy tissue remains. Use local or general anesthetic for this procedure. After surgery, leave the abscesses open to heal by second intention. Flush the lesion with dilute iodine every 6 to 8 hours until completely healed. Enzymatic ointments may be helpful in breaking down caseous debris. In addition to topical treatment, use parenteral amoxicillin and enrofloxacin or amikacin pending culture results.

Nasal Trauma

Reptiles that are kept under inadequate husbandry conditions often pace their cages, resulting in injury to the rostral jaws. Excitable reptiles also may run into walls, which results in trauma to the same area.

Infectious stomatitis is a frequent secondary problem. Treatment is similar to that for abscesses and infectious stomatitis.

▼ ***Key Point*** Providing adequate husbandry is critical. Provide visual security and a smooth cage interior. Padding the cage interior may be necessary.

Gangrene or Abscesses of Extremities

Avascular Necrosis

Etiology

The most common cause of toe loss in lizards is avascular necrosis. Necrosis results from the formation of constricting bands when shedding of the skin on the toes or tail is incomplete. These bands usually form under conditions of low humidity and poor nutrition. Thromboembolism secondary to bacteremia is an additional cause of avascular necrosis.

Diagnosis

Diagnosis is based on clinical signs.

Treatment

Amputation of the affected extremity usually is required. To prevent future lesions, educate the owner about proper husbandry. Recommend warm water soaks to soften and remove dry skin on the extremities. Aggressively treat septicemic reptiles with parental antibiotics.

Trauma Etiology

A second common cause of avascular necrosis is trauma due to tail thrashing or entrapment of a toe in caging. Open or closed contusions, lacerations, or fractures are apparent on physical examination. If the wounds are old, they may be infected or gangrenous.

Treatment

Treat with topical or parenteral antimicrobials. Cultures are indicated if the wound is old. Amputation usually is required. Modify the environment to minimize the chances of trauma's recurring.

Vasculitis

Etiology

Occasionally, gangrene of extremities is seen in reptiles with no known history of trauma. Often, these patients are systemically ill. The lesions are usually caused by vasculitis secondary to septicemia, mycobacteriosis, viral or fungal infection, gout, or ingestion of mycotoxin. In some cases, bites from mites may induce vasculitis resulting in skin necrosis. Diagnosis is based on cytology, including special stains for mycobacteria and fungi, culture and sensitivity, hematology, blood chemistry, histopathology, or feed analysis for mycotoxins.

Treatment

Treat supportively and with appropriate antimicrobials. Surgical amputation of affected extremities almost always is required. Because the disease is usually systemic, prognosis is guarded to grave. Treatment for mycobacteria is difficult, and the zoonotic potential must be considered.

Neoplasia

Most neoplasia in reptiles are either sarcomas or lymphoproliferative disorders and are often associated with retroviruses. In general reptiles are tolerant of most chemotherapy and especially radiation therapy schedules used in mammals. Lympohoblastic leukemia has been successfully treated with radiation therapy. Due to the frequent association with retroviruses the prognosis for remission is guarded. Local tumors can be successfully cured by complete excision. Ovarian teratomas have been found in a significant number of green iguanas. Diagnosis is made by ultrasound examination and biopsy. Early surgical excision may be curative but metastasis is common.

Ocular Disorders

Retained Spectacles

Etiology

Retained spectacles are associated with dysecdysis (abnormal shedding). Poor husbandry, especially low humidity and low temperature, usually is the cause. This condition commonly occurs in pet snakes.

Clinical Signs

Clinical signs include cloudy eyes after a recent shed or a silvery, wrinkled appearance to the eye. If more than a few spectacles are retained, the snake experiences blindness and stops eating. A subspectacular or eye infection may occur below the spectacle.

Treatment

Soak the animal in a warm water bath for 1 to 3 hours. Once softened, the eye cap can be removed by rubbing with a wet cotton ball or with fine forceps. If the spectacle cannot be removed after soaking for a few hours, soak the animal right before next full shed. If the spectacle persists, refer the animal to a hospital equipped to perform microsurgical removal.

▼ ***Key Point*** If the spectacle does not lift easily do *not* force removal, or the primary spectacle may be avulsed, leaving the cornea unprotected. Loss of the eye may ensue.

Subspectacular Infection

Etiology

This is the most common ophthalmic infection in snakes. These infections almost always are associated with stomatitis. The bacteria ascend the nasolacrimal duct, which empties into the space between the spectacle and the cornea.

Clinical Signs

The eye appears to be cloudy. Further inspection reveals that the fluid is under the speculum and there is distention of the subspectacular space. A 27- to 25-gauge needle may be used to aspirate fluid from the space for cytologic examination and culture. In severe cases bulphophthalmia may be present.

Treatment

Treatment with parenteral antibiotics is usually curative. Do not use topical medications because these cannot penetrate the spectacle. In severe cases in which the cornea is in danger of perforation, remove a wedge from the ventral spectacle to allow drainage, flushing, and administration of topical medications. Flush the subspectacular space with saline until all debris is removed, then apply an appropriate topical ophthalmic drop through the wedge. Once this surgery is performed, the cornea is exposed for approximately 2 weeks or until the snake next sheds. Therefore, apply ophthalmic lubricants until the new spectacle forms.

Neuromuscular Disorders

Inclusion Body Disease Virus

Etiology

This disease is believed to be caused by a retrovirus. Transmission may be vertical, by direct contact, from fomites, and through mites. Burmese pythons and boa constrictors seem to be particularly susceptible.

Clinical Signs

Python and boid snakes, especially Burmese pythons, demonstrate neurologic signs such as head tilt, ataxia, opisthotonos, anisocoria, and muscle tremors. Often, the front half of the snake coils in loops. Some snakes, especially boa constrictors, present for chronic regurgitation (not Burmese pythons) with no neurologic component. Burmese pythons often present with neurologic signs only. Stomatitis, lymphoproliferative disorders, and cutaneous sarcomas have been associated with the virus. In general, the virus is slowly progressive.

Diagnosis

Diagnosis currently requires histopathologic observation of inclusion bodies. Submit esophageal lymphoid aggregates, kidney, pancreas, liver, and stomach samples. Snakes with neurologic signs may have lesions limited to the central nervous system, which makes antemortem diagnosis difficult. The main differential diagnosis includes bacterial meningoencephalitis and paramyxovirus. The total white blood cell count in affected snakes is often high (>30,000/uL). In rare cases, occlusion bodies are observed in lymphocytes on blood smears.

Treatment

Although the disease is progressive in most individuals, we have provided supportive care to several boa constrictors that seemed to return to normal after 2 to 3 months of therapy. All affected snakes should be considered carriers that should be kept in strict isolation from unaffected snakes or euthanized. A *minimum* of a 90- to 180-day quarantine is recommended for all snakes entering a new collection. Treatment with nucleoside reverse transcriptase inhibitors (NRTIs; human HIV drug combos) has been attempted but safety and efficacy have not been adequately reported.

Adenovirus of Bearded Dragons

Etiology

Adenovirus in bearded dragons causes acute hepatic coagulation necrosis. Horizontal and vertical transmission is suspected. A case of transmission from juvenile to adult lizards has been documented.

Clinical Signs

Clinical signs occur in neonates and young adults and include seizures, muscle tremors, opisthotonos, lethargy, and icterus. Bearded dragons normally have yellow oral mucous membranes. Lizards with icterus have a deep golden brown colored oral mucous membranes and yellow sclera.

Diagnosis

Diagnosis is based on clinical signs and inclusion bodies in the liver and GI tract. Viral inclusion can sometimes be found in liver biopsies, intestinal biopsies or electron microscopy (EM) of fecal material. The main differential diagnosis for seizures in bearded dragons is hypocalcemia, a common problem in animals fed an all-cricket diet.

Treatment

There is no effective treatment. The morbidity rate appears to be 50%–60%. With supportive care, 30% of animals showing clinical signs survive. Many have residual neurologic deficits. Quarantine survivors and siblings permanently. Do not use these animals for breeding.

Adenovirus in Snakes and Lizards

Adenoviruses have been associated with hepatitis and enteritis in many reptiles. Recently an adenovirus was

recovered from a king snake that had suffered from intermittent head and body tremors for 4 years. Histopathological pathology was limited to the nervous system.

Spondylitis in Snakes

Etiology

Spondylitis is caused most commonly by infection with *Salmonella* spp., although other bacteria have been described. Snakes with spondylitis appear to be stiff or fall off a snake hook.

Diagnosis

Physical examination reveals segmental fused vertebrae and crepitus of the spinal column. In chronic cases, intestinal impaction due to loss of intestinal innervation is palpable. Take a radiograph of the spine to look for lesions suggestive of discospondylitis. Neoplasia should be considered as a differential diagnosis.

Treatment

The prognosis for cure is grave. Progression can be arrested temporarily with parenteral antibiotics based on culture and sensitivity. Surgery can be used to decompress spinal nerves but is not strongly recommended, as lesions are often extensive by the time that clinical signs are noted.

Paramyxovirus Infections in Snakes

Etiology

Clinical signs vary from peracute death to death after a 24- to 48-hour progressive course of paresis. The snake tends to lie stretched out initially, then open-mouthed breathing occurs. Frequently, brown liquid is expelled from the mouth shortly before death. A more chronic form has been diagnosed that is characterized by a proliferative pneumonia, head tremors that can progress to seizures, mydriasis, loss of righting reflex, opisthotonos, and, many times, death.

Diagnosis

Diagnosis is based on clinical signs, necropsy, and a hemaglutination inhibition test offered by the University of Florida Veterinary Medical Teaching Hospital.

Treatment

Snakes with the chronic form may respond temporarily to supportive care and antimicrobial therapy only to relapse weeks to months later. Carriers may be common. Serology should be used to screen for this disease during quarantine of new snakes.

NUTRITIONAL DISORDERS

Secondary Nutritional Hyperparathyroidism

Etiology

The physiology of secondary nutritional hyperparathyroidism (SNHP) in reptiles is similar to that of mammals. Inadequate calcium, vitamin D_3, or UV light source in addition to excess phosphorus (usually from meats and fruits) are the main husbandry problems contributing to SNHP. Primary renal or parathyroid disease also can cause hyperparathyroidism.

Clinical Signs

- Clinical signs include pliable, thickened mandibles, folding fractures of extremities, posterior paresis due to hypocalcemia or fractured spine, kyphosis, ileus from denervation or hypocalcemia leading to impaction and/or incontinence, seizures, dystocia, anorexia, and general malaise.

Diagnosis

- The diagnosis is based on history and physical examination. Serum calcium concentration may be normal even if body stores are low. Ionized calcium may be more helpful than total calcium determination. Radiographic evidence of decreased bone density occurs only in advanced cases. Other causes of seizures include trauma, septicemia, neoplasia, or toxin.

Treatment

- Administer injectable calcium initially, followed by oral supplementation.
- An oral source of vitamin D_3 also is recommended.
- The owner *must* make appropriate environmental changes such as light cycle, UV light, and temperature gradient. Without these changes, medical therapy will fail. Many animals are chronically ill and on the verge of starvation. Tube-feed anorexic animals until their appetite returns, which may take several weeks. Most fractures heal on their own, without internal stabilization. Splinting rear legs against the tail may aid in stabilizing fractures.
- Avoid rough handling, and remove cage furniture to decrease the probability of future fractures. In mild cases, the prognosis is good if owners comply with recommended treatment. If posterior paresis is the result of a spinal fracture, the prognosis for normal ambulation is grave to guarded.

Hypocalcemia

- Reptiles with clinical hypocalcemia present with muscle tremors or seizures. A presumptive diagnosis is based on a history of inadequate diet and hus-

bandry and physical examination findings that support SNHP.

Treatment

- If the animal is having seizures, administer calcium gluconate or calcium chloride IV or IO to effect. Diazepam may be necessary to control seizures.
- If muscle tremors without seizures are present, obtain a blood sample for serum or plasma calcium concentrations, then administer an IM calcium supplement while awaiting laboratory results.
- For long-term care, see the SNHP section.

Hypervitaminosis D_3

- Metastatic calcification of soft tissues frequently is seen in herbivores, omnivores, and insectivores that are over-supplemented with calcium and vitamin D_3. The disease is seen most frequently in 4- to 6-year-old male green iguanas that were fed dog, cat, or monkey chow as a major proportion of the protein in their diet.
- Clinical signs are variable but usually include general malaise followed by anorexia. If the kidneys are mineralized, there are signs consistent with renal failure.
- Diagnosis is based on radiographic evidence of soft tissue mineralization. Diagnosis is difficult if radiographs do not reveal mineralization of soft tissues because serum concentrations of calcium and phosphorus may be within normal limits. Endoscopy or laparatomy may be necessary to make a diagnosis. Provide supportive care and eliminate the vitamin D_3 supplement from the diet.

Thiamine Deficiency

- Thiamine deficiency occurs in carnivores fed a diet high in fatty fishes such as goldfish and smelt. It also occurs in lizards fed muscle meat as a sole food source.
- Clinical signs include paralysis, paresis, pulmonary edema, dyspnea, tremor, cerebral edema, dehydration, enteritis, and blindness.
- Diagnosis is based on history and clinical signs.
- Administer thiamine at 25 mg/kg PO or SC q24h for 3 to 7 days.
- To prevent hypothiaminosis, feed a fresh, varied diet or add 1.1 mg thiamine per kg of fish fed.

Biotin Deficiency

- Biotin deficiency occurs in lizards fed a diet of raw infertile eggs.
- Clinical signs are similar to thiamine deficiency.
- Treat with injectable vitamin B complex that includes biotin.
- Prevent by feeding fertile eggs at different stages of development as well as whole-animal prey. A biotin supplement also can be offered.

URINARY SYSTEM

Gout

Etiology

Gout is the abnormal deposition of uric acid crystals into soft tissue. Gout usually occurs as one of two forms, visceral or articular. In visceral gout, the uric acid precipitates on internal organs, whereas articular gout occurs when uric acid tophi occur within and around joints and tendons. Gout occurs as a result of poor husbandry, dehydration, high-protein diets, and inappropriate use of aminoglycoside antibiotics. In many cases, however, no recognizable risk factor is apparent.

Clinical Signs

- Clinical signs are variable and range from lethargy and anorexia to sudden death. If articular gout is present, affected joints are swollen and painful. In visceral gout, clinical signs are related to failure of the organ affected by the uric acid crystals. Neurologic signs are common if there is uric acid deposition in the brain.

Diagnosis

- Diagnosis is based on physical examination and identification of the uric acid crystals via cytologic or histopathologic examination of tissue samples (do not use formalin as a fixative). Gross lesions may be visible during laparoscopy or laparotomy. Uric acid deposits are sometimes visible on ultrasound or radiographs. Serum uric acid concentrations may be elevated; however, not all reptiles with gout have elevated serum uric acid concentrations. Kidney biopsy may be helpful in cases of renal gout.

Treatment

- Administer supportive care, especially fluid therapy. Improving temperature, humidity, and access to water is critical.
- Avoid high-protein diets (especially those high in purine) and nephrotoxic drugs.
- Avoid use of furosemide because it may inhibit renal excretion of uric acid.
- Antihyperuricemic drugs such as allopurinol, probenecid, sulfinpyrazone, and colchicine can be used to control, but not cure, gout.
- The prognosis for long-term survival is grave.

Urolithiasis

Urolithiasis is seen most frequently in land turtles and lizards fed high-protein diets without adequate access to water.

- Clinical signs include anorexia, straining, or abdominal distension.

- Uroliths are palpable as caudal abdominal masses.
- If necessary, confirm the diagnosis with ultrasound. Radiographs may not be diagnostic because uric acid is often radiolucent.

Treatment

After stabilizing the patient, perform a cystotomy to remove the calculi.

- Culture the calculi, because they can be associated with bacterial cystitis.
- Decrease the protein content of the diet and encourage water consumption.
- Avoid use of nephrotoxic drugs.

DISEASES OF CHELONIANS

Chelonians can acquire most of the disorders described for snakes and lizards. See the previous section for details.

Mycoplasma Pneumonia

Etiology

Mycoplasma and secondary *Pasteurella testudinis* infections are a common cause of upper and lower respiratory tract disease in tortoises.

Clinical Signs

- Clinical signs include nasal and ocular discharge, dyspnea, anorexia, and dehydration.
- Historically, the signs are often unresponsive or only partially responsive to typical antibiotic therapy.

Diagnosis

- Diagnosis is based on clinical signs, culture for *Mycoplasma,* routine bacterial culture and sensitivity, and tracheal cytology. Anemia; elevated sodium, blood urea nitrogen (BUN); aspartate transaminase (AST), and cholesterol; and decreased phosphorus levels often are seen. Serologic testing is available from the University of Florida.
- Differential diagnosis should include bacterial, viral (such as herpes virus), or parasitic infection; aspiration or fungal pneumonia, neoplasia, or foreign body.

Treatment

- Treat with enrofloxacin or tylosin and with fluid and nutritional support.
- Survivors may always be carriers; quarantine them for life.

Herpes Virus of Tortoises

Etiology

Several strains of herpes virus are associated with severe stomatitis and rhinitis in European tortoises. Different strains are thought to have variable pathogenicity and tissue tropism.

Tortoises should be serologically screened with paired samples where possible and quarantined a minimum of 6 months (preferably 12–18 months) before introduction. Do not mix tortoise species.

Clinical Signs

- Clinical signs include nasal and ocular discharge, severe stomatitis, ptyalism, edema of the ventral neck, anorexia, and dehydration. Neurologic signs may develop later in the disease. Lymphoproliferative disease has been reported. The virus has acute, chronic, and inapparent carrier forms. Spur-tailed tortoises *(Testudo hermanni)* seem particularly susceptible, whereas spur-thighed tortoises *(T. graeca)* appear to be more resistant. An iridovirus has been identified that causes similar signs, but is less common.

Diagnosis

- Diagnosis is based on clinical signs, cytology of tongue swabs with Diff-Quik to identify inclusion bodies, paired serologic titers, virus isolation, or histopathologic examination with polymerase chain reaction on submitted tissues. Testing is available through the University of Florida College of Veterinary Medicine.
- Differential diagnosis should include iridovirus, mycoplasma, contact irritant, neoplasia, or bacterial, parasitic, or fungal stomatitis.

Treatment

- Treat with supportive care (fluids, antibiotics, nutritional support). Placement of an esophagostomy tube may be necessary if the tortoise will not eat on its own. Gentle topical cleaning of the mouth and nose with dilute iodine solution. Acyclovir at 30 to 80 mg/kg PO sid to tid may be helpful. Topical acyclovir ointments may be applied to the oral mucous membranes.
- Survivors may always be carriers; quarantine them for life.

Nutritional Disorders

Vitamin A Deficiency

Etiology

Vitamin A deficiency is seen most frequently in juvenile, semi-aquatic turtles older than 6 months of age. Before this age, the remnants of the yolk sac provide adequate levels of vitamin A. Affected animals usually have been fed high-protein, unbalanced diets such as raw hamburger. Vitamin A deficiency results in squamous metaplasia of the glandular structures of the eye, oral cavity, respiratory passages, and genitourinary tract, as well as decreased local immunity. Changes in the kidney predispose animals to gout, particularly if they are on a high-protein diet.

Clinical Signs

- Clinical signs include conjunctivitis, pneumonia, stomatitis, and hyperkeratotic eyelids.

Diagnosis

- Diagnosis is based on history, clinical signs, and biopsy samples, which demonstrate lesions compatible with epithelial squamous metaplasia.

Treatment

- In most cases, oral supplementation of vitamin A is sufficient and safe. Treat with parenteral vitamin A only in severe cases. Long-term improvements of diet and husbandry are essential.

Vitamin A Toxicity

Vitamin A toxicity is seen within 2 weeks of administration of parenteral vitamin A. Toxic levels of vitamin A cause xeroderma initially and necrotizing dermatitis with long-term toxicity.

- Clinical signs include severe sloughing of epidermis, especially in the cervical region.
- Treatment consists of supportive care. Give fluid therapy to replace fluid losses from defects in the dermis and exposed muscle. Apply dressings to open wounds as needed.

▼ ***Key Point*** Never give injectable vitamin A unless there is a history of dietary deficiency and clinical signs of hypovitaminosis A are severe.

Hypothyroidism (Iodine Deficiency)

Hypothyroidism resulting from goiter is recognized in tortoises suffering from iodine deficiency. Iodine is bound by nitrates and compounds found in cabbage, kale, brussels sprouts, and uncooked soybeans.

- Clinical signs include myxedema and goiter.
- Treat with iodine and dietary modification.

Diseases of the Shell

Shell Trauma

The most common causes of shell trauma in turtles are accidental drops, car or lawn mower collisions, and attacks by dogs.

Treatment

- Stabilize the patient and stop all hemorrhage before attempting to repair the shell.
- If possible, draw blood for baseline complete blood count (CBC) and profile.
- Lavage the peritoneum and clean all cracks.
- Bandage full-thickness cracks or openings with nonstick dressings, then wrap the shell in plastic wrap to prevent contamination and loss of peritoneal fluids.
- Administer IV, IO, or SC fluids as needed. If the turtle is in shock, administer one dose of dexamethasone (0.125–0.25 mg/kg). Oxyglobin can be used as a blood substitute if needed.
- Keep the patient warm and administer prophylactic antibiotics.
- Once the patient is stable, treat minor, relatively stable cracks by cleaning with iodine q12h, apply topical antibiotic cream, and stabilize the crack with bandages or steel wires as necessary.
- Most animals heal in 2 to 3 weeks.
- Unstable cracks or large shell defects must be repaired with fiberglass or acrylic resins or UV light-cured polymers.
- Allow ample time for underlying soft tissues to heal before attempting repair.
- Debris or microbes caught under the patch cause granulomas or abscesses.
- Once the wound is clean and has developed a healthy granulation bed, apply silver sulfadiazine cream to the wound.
- Apply Tegaderm (3M Corporation) over exposed soft tissues to provide protection from the polymers to be applied later.
- Clean the scutes adjacent to the defect with ether or acetone.
- Apply a thin layer of epoxy to the shell, then place nylon or fiberglass screening over the defect.

▼ ***Key Point*** Do not let the epoxy come in contact with bone or soft tissue. Also ensure that the epoxy or screening does not create a barrier to prevent granulation tissue from filling in the defect.

- Epoxy can be painted on top of the screen.
- Keep the animal out of water at least 24 hours to allow curing. Use only marine epoxies on aquatic turtles. Ensure adequate hydration for aquatic turtles by providing oral, SC, or IP fluids and a high relative humidity in their enclosure.
- Patches need to be removed in fast-growing animals.
- Complete healing takes 6 to 18 months.

Shell Rot

Healthy shell scutes are periodically shed in rapidly growing chelonians. Normal scute sheds should appear as translucent keratin.

- Most shell infections are secondary to poor husbandry and are caused by bacteria or fungi.
- Occasionally, algae can cause erosions.
- Clinical signs of shell rot include petechia, sloughing of discolored, soft scutes, erosions, hyperemia, and fluffy or granulomatous growths. Dermatitis and septicemia are common.

Diagnosis

- Diagnosis is based on cytologic examination of shell scrapings or biopsy and bacterial or fungal culture and

sensitivity. Differential diagnosis includes infections secondary to trauma, foreign body, or neoplasia.

Treatment

- Administer diluted topical iodine soaks for at least 1 hour daily. Dry the shell by keeping it out of water for at least 1 hour.
- Monitor for dehydration during this period.
- Use a sharp, clean knife to pare away dead sections of shell and expose the infected tissues. Use sterile technique.
- Many early cases of shell rot respond to treatment with iodine, desiccation, and improvement of husbandry.
- Turtles with deep erosions or septicemia need to be treated with systemic antimicrobials based on culture and sensitivity.
- If bone is exposed, the prognosis is guarded to grave.
- Severe erosions must be treated similar to thermal burns.

Pyramiding of Shell

Pyramiding of the scutes of the carapace or doming of the carapace are clinical signs of secondary nutritional hyperparathyroidism. The diet of affected turtles is often high in lettuce, fruit (especially melon), tomatoes, or protein. The shell also may appear to be small for the body in turtles fed too much protein. Concurrent beak deformities are often present. Recent reports indicate that this condition can also be caused by low humidity during early growth.

- Similar lesions can occur in adult chelonians with systemic disease, particularly hepatic or renal disease.
- If caught early, the defects can be minimized with proper nutrition (see above).
- More severely affected animals will be permanently disfigured.

Myiasis

Myiasis may occur in any reptile species but is most common in chelonians. Flies lay eggs into a wound.

- Maggots usually hatch in 12 to 24 hours.
- Remove the maggots and treat similar to mammals. Do not use ivermectin flushes in turtles. Provide supportive care as needed.

▼ ***Key Point*** Ivermectin is toxic to turtles and tortoises.

DISEASES OF CROCODILIANS

Hypoglycemia

Hypoglycemia is seen in stressed alligators, especially when malnutrition, cold temperatures, and high population density are present.

- Clinical signs include tremors, torpor, loss of righting reflex, generalized weakness, mydriasis, and catatonia.
- Diagnosis is based on low glucose levels on blood chemistry. To treat, administer 3 g/kg glucose PO and improve husbandry.

Vitamin K Deficiency

- Vitamin K deficiency can occur in alligators fed marginal diets and placed on long-term antibiotics. Clinical signs are similar to clotting deficiency in mammals.
- Gingival bleeding is an early sign.
- Treat with vitamin K and improve diet. Stop administration of antibiotic if possible.

Caiman Pox

Caiman pox is seen in caimans and Nile crocodiles. It is caused by a pox virus. Clinical signs include gray-white, circular, multifocal "pox-type" lesions that can be widespread on integument. Lesions may coalesce into diffuse necrotizing patches and cause digital necrosis. Proliferative oral lesions also can be seen.

- Diagnosis is made on histopathology in which large intracytoplasmic inclusions bodies are visualized in the epithelial cells.
- No treatment, other than supportive care, is available. Quarantine individuals with active lesions.

West Nile Virus

West Nile Virus was associated with acute die-offs and neurologic signs in American alligators in Florida. Signs included depression, lethargy and neurological signs. Histopathologic lesions included meningoencephalomyelitis, necrotizing hepatitis, splenitis and myocarditis. In contrast, crocodilians in Israel were serologically positive for exposure to West Nile Virus but did not show clinical signs of disease. High sero-reactivity has been noted in alligators at a farm in Idaho.

Coccidia: Eimeria species

- *Coccidia* causes necrotizing enteritis in young crocodiles.
- Diagnosis is made on routine fecal or cloacal swab. Treat with a sulfa antibiotic. Mortality can be high in dense populations.

SUPPLEMENTAL READING

Association of Reptilian and Amphibian Veterinarians (ARAV) — www.arav.org

Carpenter JW, Mashima TY, Rupiper DJ: Exotic Animal Formulary. Manhattan, KS: Graystone Publications, 1999.

Herpes virus infection in tortoises—http://sacs.vetmed.ufl.edu/wildlife/TortoiseHerpevirus

Mader DR, Reptile Medicine and Surgery. Philadelphia: WB Saunders Co., 1996.

Mycoplasmosis of tortoises—http://sacs.vetmed.ufl.edu/wildlife/urtd.html

Paramyxovirus infection in snakes—http://sacs.vetmed.ufl.edu/wildlife/Pmyx.html

Turtle and Tortoise care and conservation—www.chelonia.org/

Appendix

Drug Dosage Guidelines for Dogs and Cats

Acepromazine
0.05–0.2 mg/kg IV, 0.1–0.3 mg/kg, IM, SC (maximum 3 mg)
0.5–2.0 mg/kg q6–8h PO

Acetazolamide
Diamox
5–10 mg/kg q8–12h PO
Glaucoma: 4–8 mg/kg q8–12h PO

Acetylcysteine
Mucomyst
Antidote: 140 mg/kg (loading dose) PO, IV, then 70 mg/kg q4h for 5 doses
Eye: 2% solution topically q2h

Acetylsalicylic acid (aspirin)
Analgesic:
Dog: 10–25 mg/kg q8–12h PO
Anti-inflammatory:
Dog: 20–40 mg/kg q12h PO
Cat: 10–20 mg/kg q48h PO
Antiplatelet:
Dog: 5–10 mg/kg q24–48h PO
Cat: 80 mg q48h PO

ACTH
See Corticotropin gel (ACTH)

Actinomycin D
Cosmegen
0.7 mg/m^2 IV (consult anticancer protocol for intervals)

Activated charcoal
See Charcoal, activated

Albendazole
Valbazen
Dog: 25 mg/kg q12h PO for 2 days for giardia

Allopurinol
Zyloprim
10 mg/kg q8h then reduce to 10 mg/kg q24h

Aluminum carbonate gel
Basaljel
Phosphate binder: 10–30 mg/kg q8h PO (with meals)

Aluminum hydroxide gel
Amphojel
Phosphate binder: 10–30 mg/kg q8h PO (with meals)

Amikacin
Amiglyde-V
5–10 mg/kg q8h IV, IM, SC; or 15–20 mg/kg q24h IV, IM, SC

Aminopentamide
Centrine
Dog: 0.01–0.03 mg/kg q8–12h IM, SC, PO
Cat: 0.02 mg/kg q8–12h IM, SC, PO

Aminophylline
Dog: 10 mg/kg q8h PO, IM, IV
Cat: 6.6 mg/kg q12h PO

5-aminosalicylic Acid
See Mesalamine; Osalazine sodium

Amiodarone
Cordarone
Dog: 10–20 mg/kg q12h PO

Amitraz
Mitaban
Make a 0.025% solution (1 vial of Mitaban/2 gallons of water). Apply every 2 weeks until no viable mites are found (see Chap. 43).

Amitryptyline
Elavil
Dog: 1–2 mg/kg q12h PO
Cat: 5–10 mg/cat q12–24h PO

Amlodipine
Norvasc
Cat: 0.625–1.25 mg/cat q24h PO
Dog: 0.1–0.2 mg/kg q24h or divided q12h PO

Ammonium chloride
Dog: 100 mg/kg q12h PO
Cat: 800 mg/cat (approximately $^1/_4$ tsp) mixed with food daily

Amoxicillin
Amoxi-tabs
Amoxi-drops
11–22 mg/kg q8–12h PO

Amoxicillin plus clavulanate
Clavamox
Dog: 12.5–25 mg/kg q12h PO
Cat: 62.5 mg/cat q12h PO

Amphotericin B deoxycholate
Fungizone
0.25–0.5 mg/kg q48h IV (slow infusion), 3 times per week to a cumulative dose of 8–12 mg/kg in dogs and 4–8 mg/kg in cats

Amphotericin B lipid complex
AmBisome, Amphocil, Abelcet
1.0 mg/kg q48h IV, 3 times per week to a cumulative dose of 12 mg/kg (see Chap. 20)

Ampicillin
Omnipen

10–20 mg/kg q6–8h IV, IM, SC (ampicillin sodium)
Principen
20–40 mg/kg q8h PO

Ampicillin trihydrate
Polyflex
6.5 mg/kg q12h, IM, SC

Amprolium
Amprol
Corid
1.25 g of 20% amprolium powder added to daily feed, or 30 ml of 9.6% amprolium solution to 3.8 L of drinking water for 7 days

Amrinone lactate
Inocor
1–3 mg/kg IV (loading dose) followed by 30–100 µg/kg/min IV infusion

Antacid drugs
See Aluminum hydroxide gel; Calcium carbonate; Magnesium hydroxide

Apomorphine hydrochloride
0.02–0.04 mg/kg IV, IM; 0.1 mg/kg SC; or instill 0.25 mg in conjunctiva of eye (dissolve 6-mg tablet in 1–2 ml of saline)

Ascorbic acid (vitamin C)
Diet supplement or for copper toxicity 100–500 mg/animal qd
Acetaminophen toxicity 30 mg/kg q6h for seven treatments, PO, SC

L-Asparaginase
Elspar
10,000–30,000 IU/m^2 IM, SC, or IP as needed (pretreat with antihistamines, steroids); see Chapter 26.

Aspirin
See Acetylsalicylic acid

Atenolol
Tenormin
Dog: 6.25–25 mg/dog q12h PO or 0.25–1.0 mg/kg q12–24h PO
Cat: 6.25–12.5 mg/cat q24h PO

Atracurium besylate
Tracrium
0.2 mg/kg IV initially, then 0.15 mg/kg q30min (or IV infusion at 3–8 µg/kg/min)

Atropine
0.02–0.04 mg/kg q6–8h IV, IM, SC
Organophosphate and carbamate toxicosis: 0.2–0.5 mg/kg (as needed)

Auranofin (triethylphosphine gold)
Ridaura
0.1–0.2 mg/kg q12h PO

Aurothioglucose
Solganal
Dog <10 kg: 1 mg/dog IM first week, 2 mg/dog IM second week, 1 mg/kg/wk maintenance
Dog >10 kg: 5 mg/dog IM first week, 10 mg/dog IM second week, 1 mg/kg/wk maintenance
Cat: 0.5–1 mg/cat IM every 7 days

Azathioprine
Imuran
Dog: 2 mg/kg q24h PO initially, then 0.5–1.0 mg/kg q48h
Cat: 0.3–0.5 mg/kg PO, q24–48h (q48h is preferred)

Azithromycin
Zithromax
Dog: 10 mg/kg q24h PO × 5 days or 3.3 mg/kg q24h PO × 3 days
Cat: 5 mg/kg q48h PO

AZT (azidothymidine)
See Zidovudine

Baclofern
Lioresal
Dogs: 1–2 mg/kg q8h PO

BAL
See Dimercaprol

Benazepril
Lotensin
Dog: 0.5 mg/kg q12–24h PO

Betamethasone1
Celestone
Betasone
0.1–0.2 mg/kg q12–24h PO

Bethanechol chloride
Urecholine
Dog: 2.5–25.0 mg/dog q8h PO
Cat: 2.5–5.0 mg/cat q8h PO

Bicarbonate
See Sodium bicarbonate

Bisacodyl
Dulcolax
Dog: 5–20 mg qd PO
Cat: 5 mg qd PO

Bismuth subcarbonate
0.5–3.0 g q4h PO

Bismuth subsalicylate
Pepto-Bismol
1–3 ml/kg/d (in divided doses) PO

Bleomycin sulfate
Blenoxane
10 U/m^2 IV or SC for 3 days, then 10 U/m^2 weekly (maximum cumulative dose: 200 U/m^2)

Bromide
See Potassium bromide

Budesonide
Entocort
Dog: 1–3 mg q24h PO
Cat: 1 mg q24h PO

Bunamidine
Scolaban
20–50 mg/kg PO

Bupivacaine hydrochloride
Marcaine
0.5 mg/kg epidural
1 mg/kg total dose for local nerve block

Buprenorphine
Temgesic
0.005 mg/kg q4–8h IV, IM

Buspirone
BuSpar
Cat: 2.5–5 mg/cat q12–24h PO

Butorphanol
Torbutrol
Torbugesic
Dog: Analgesic: 0.1–0.2 mg/kg IV, 0.1–0.4 mg/kg IM or SC Antitussive: 0.55–1.1 mg/kg PO q6–12h, 0.055–0.11 mg/kg SC q6–12h
Cat: Analgesic: 0.05–0.2 mg/kg IV, 0.1–0.3 mg/kg IM, SC

Calcitonin
Calcimar
4–6 IU/kg SC initially q12h, then q8h for hypercalcemia

Calcitriol
Rocaltrol
2–3 ng/kg/d divided q12h for 3–4 days, then 1–2 ng/kg/d maintenance

Calcium carbonate
25–50 mg/kg/d PO
Camalox
60–100 mg/kg/d (in divided doses) as phosphate binder

Calcium chloride (10% solution)
Hypocalcemia: 5–15 mg/kg/h IV

Calcium citrate
Cat: 10–30 mg/kg q8h (with meals) PO

Calcium disodium EDTA
See Edetate calcium disodium ($CaNa_2$, EDTA)

Calcium gluconate (10% solution)
0.5–1.5 ml/kg IV (slowly)
Calcium gluconate tablets
25–50 mg/kg/day PO

Calcium lactate
25–50 mg/kg/d PO

Captan
0.25% solution topically, 2–3 times/wk

Captopril
Capoten
Dog: 0.5–2.0 mg/kg q8–12h PO
Cat: 3.12–6.25 mg/cat q8h PO

Carbenicillin disodium
Geopen
Pyopen
40–50 mg/kg q6–8h IV, IM, SC

Carbenicillin indanyl sodium
Geocillin
Urinary tract infections: 10 mg/kg q8h PO

Carbimazole
Neo-mercazole
Cat: 5 mg/cat q8h PO (induction), followed by 5 mg/cat q12h PO

Carboplatin
Paraplatin
Dog: 250–300 mg/m^2 q3wk IV
Cat: 150–250 mg/m^2 q4wk IV

Carnitine
See Levo-carnitine

Carprofen
Rimadyl
Dog: 2 mg/kg q12h PO

Carvedilol
Coreg
See Chapter 146

Castor oil
Dog: 8–30 ml/dog qd PO
Cat: 4–10 ml/cat qd PO

Cefadroxil
Cefa-Tabs
Cefa-Drops
Dog: 22 mg/kg q12h PO
Cat: 22 mg/kg q24h PO

Cefazolin sodium
Ancef
Kefzol
20–25 mg/kg q6–8h IV, IM

Cefepime
Maxipime
Dog: 40 mg/kg q6h IM, IV

Cefmetazole sodium
Zefazone
15 mg/kg q8h IV, IM, SC

Cefotaxime sodium
Claforan
20–80 mg/kg q6h IV, IM

Cefoxitin sodium
Mefoxin
15–30 mg/kg q6–8h IV

Ceftazidime
Fortaz
30 mg/kg q6h IV, IM

Ceftiofur
Naxcel
Dog: 2.2–4.4 mg/kg q24h SC

Cephalexin
Keflex
10–30 mg/kg q6–12h PO

Cephalothin sodium
Keflin
10–30 mg/kg q4–8h IV, IM

Cephapirin sodium
Cefadyl
10–30 mg/kg q4–8h IV, IM

Cephradine
Velosef
10–25 mg/kg q6–8h PO

Charcoal, activated
Acta-Char
SuperChar Vet/Powder or Vet/Liquid
Toxiban
1–4 g/kg PO (granules)
6–12 ml/kg PO (suspension)

Chlorambucil
Leukeran
2–4 mg/m^2 q48h PO (see Chap. 26)
Cats (FIP): 20 mg/m^2 q2–3 wk PO
Chronic lymphocytic leukemia
20 mg/m^2 q1–2wks PO or 6 mg/m^2/day

Chloramphenicol
Chloromycetin
Dog: 30–50 mg/kg q6–8h IV, IM PO
Cat: 30–50 mg/cat q12h IV, IM PO

Chlorothiazide
Diuril
20–40 mg/kg q12h PO

Chlorpheniramine maleate
Phenetron
Chlor-Trimeton
Dog: 0.4 mg/kg q8–12h PO
Cat: 2 mg/cat q12h PO

Chlorpromazine
Thorazine
0.5 mg/kg q6–8h IM, SC, PO
Prior to cancer chemotherapy: 2 mg/kg q3h SC

Chlortetracycline
25 mg/kg q6–8h PO

Cholecalciferol (vitamin D_3)
500–2000 U/kg/d PO (1 mg = 40,000 U)

Chorionic gonadotropin
See Gonadotropin, chorionic (hCG)

Cimetidine
Tagamet
5–10 mg/kg q6–8h IV, IM, PO
Renal failure: 2.5–5.0 mg/kg q12h IV, PO

Ciprofloxacin
Cipro
5–15 mg/kg q12h PO

Cisapride
Propulsid
Dog: 0.25–0.5 mg/kg q8–12h PO
Cat: 2.5–5 mg q8–12h PO

Cisplatin
Platinol
50–70 mg/m^2 q3wk IV drip (requires aggressive diuresis); do not use in cats

Clarithromycin
Biaxin
5 mg/kg q12h PO

Clavamox
See Amoxicillin plus clavulanate

Clavulanate
See Amoxicillin plus clavulanate

Clemastine
Tavist, Contac 12-Hr Allergy
Dog: 0.05–0.1 mg/kg q12h PO

Clindamycin
Antirobe
Cleocin
Dog: 5–10 mg/kg q8h PO, IV, IM
Cat: 5.5 mg/kg q12h, or 11 mg/kg q24h (staphylococcal infections) PO; 11 mg/kg q12h, or 22 mg/kg q24h PO(anaerobic infections) PO
Toxoplasmosis: 25–50 mg/kg/d PO (in divided treatments) for 2–3 weeks

Clofazimine
Lamprene
10 mg/kg q24h PO

Clomipramine
Anafranil, Clomicalm
1 mg/kg q12–24h PO up to a maximum dose of 3 mg/kg q12–24h PO

Clonazepam
Klonopin
0.5 mg/kg q12h PO

Clorazepate dipotassium
Tranxene
2 mg/kg q12h PO

Clotrimazole (1%)
Lotrimin
Topical intranasal infusion; 50–60 ml per side over 1 hour via indwelling catheter (for aspergillosis, penicilliosis)

Cloxacillin sodium
Cloxapen
Orbenin
Tegopen
20–40 mg/kg q8h PO

Cod liver oil
1 tsp/10 kg once daily PO

Codeine
Dog: Analgesic: 0.5–1.0 mg/kg q6–8h PO
Antitussive: 1–2 mg/kg q6–12h PO

Colchicine
0.025–0.03 mg/kg q24h PO

Corticotropin gel (ACTH)
Acthar
Response test: collect pre-ACTH sample and inject 2.2 IU/kg IM; collect post-ACTH sample at 2 hours in dogs and at 1 and 2 hours in cats

Cosyntropin
Cortrosyn
Response test: collect pre-ACTH sample and inject 5 µg/kg IV in dogs and 125 µg IV in cats; collect post-ACTH sample at 1 hour

Cyanocobalamin (vitamin B_{12})
Dog: 100–200 µg/dog qd PO
Cat: 50–100 µg/cat qd PO

Cyclophosphamide
Cytoxan
Anticancer therapy: 50 mg/m^2 q48h PO, or 50 mg/m^2 once daily 4 days/week PO, or 100–300 mg/m^2 IV and repeat in 21 days (see Chap. 26)
Immunosuppressive therapy: 50 mg/m^2 q48h PO (see Chap. 24)
Cat: 200 mg/m^2 q2–3wk PO (see Chap. 26)

Cyclosporine
Sandimmune, Neoral, Optimmune ointment
Dog: 10 mg/kg q12h PO
Cat: 5 mg/kg q12h PO to 15 mg/kg q24h (adjust dose via monitoring)
Perianal fistulae: 1.75–3.0 mg/kg q12h PO
Topical treatment for keratoconjunctivitis sicca: 1–2% solution in oil: instill 1 drop in eye q12hr

Cyclothiazide
Anhydron
0.5–1.0 mg/kg q24h PO

Cyproheptadine
Periactin
Antihistamine: 0.5–1.0 mg/kg q12h PO
Appetite stimulant in cat: 2 mg/cat q12h PO

Cytosine arabinoside
Cytosar
Dog: 100 mg/m^2 once daily for 4 days IV, SC (lymphoma) q3–4wk (see Chap. 26)
Cat: 100 mg/m^2 IV or SC once daily for 2 days (see Chap. 26)

Dacarbazine
DTIC
Dog: 1000 mg/m^2 IV drip for 6–8 hours, repeat q3wk (see Chap. 30)

Danazol
Danocrine
5–10 mg/kg q12h PO

Dantrolene sodium
Dantrium
Dog: 1–5 mg/kg q8h PO
Cat: 0.5–2.0 mg/kg q12h PO

Dapsone
1.1 mg/kg q8h PO

Deferoxamine mesylate
Desferal
10 mg/kg IV, IM q2h for 2 doses, then 10 mg/kg q8h for 24 hours

Delta-Albaplex (novobiocin plus prednisolone plus tetracycline hydrochloride)
Dog 3–7 kg: 1–2 tablets/d PO
Dog 7–14 kg: 2–4 tablets/d PO
Dog 14–27 kg: 4–6 tablets/d PO
Dog >27 kg: 6–8 tablets/d PO
Cat: 1 tablet q12h PO

Deprenyl (L-deprenyl, selegiline)
Anipryl
Dog: 1 mg/kg q24h PO

Deracoxib
Deramaxx
Dog: 3–4 mg/kg q24h PO for ≤7 days

Derm Caps (omega fatty acid)
1 capsule/9.1 kg daily PO

Desmopressin acetate
DDAVP
Diabetes insipidus: 2–4 drops q12–24h intranasally
von Willebrand's disease: 1.0 µg/kg SC, IV, diluted in 20 ml saline over 10 minutes

Desoxycorticosterone pivalate (DOCP)
Percorten-V
1.5–2.2 mg/kg q25d IM

Dexamethasone
Azium
Anti-inflammatory: 0.1–0.2 mg/kg q12–24h IV, IM, PO
Shock: 2.2–4.4 mg/kg IV

Dexamethasone sodium phosphate
Shock: 1–2 mg/kg IV

Dextran-70
Gentran-70
10–20 ml/kg IV q24h to effect

Dextromethorphan
Benylin DM and others
0.5–2.0 mg/kg q6–8h PO

Dextrose (5% solution)
40–50 ml/kg q24h IV

Diazepam
Valium
Preanesthetic: 0.1–0.25 mg/kg IV, IM, SC
Status epilepticus: 0.25–0.5 mg/kg IV; repeat if necessary; 1 mg/kg rectally
Appetite stimulant in cat: 0.1–0.2 mg/kg IV (q12–24h as needed)
Functional urethral obstruction in dogs: 2–10 mg/dog q8h PO
Urinary disorder in cat: 1.25–2.5 mg/cat q8–12h PO

Diazoxide
Proglycem
10 mg/kg q12h PO, do not exceed 60 mg/kg/d

Diclorophene
See Toluene

Dichlorphenamide
Daranide
2–4 mg/kg q8–12h PO

Dichlorvos
Performer
Dog: 26.4–33 mg/kg PO
Cat: 11 mg/kg PO

Dicloxacillin
Dynapen
11–55 mg/kg q8h

Dicyclomine
Bentyl
0.2 mg/kg q8–12h PO

Diethylcarbamazine
Caricide
Filaribits
Heartworm prophylaxis: 6.6 mg/kg q24h PO

Diethylstilbestrol (DES)
Urinary incontinence (dog): 0.1–1.0 mg/dog q24h PO for 3 days, then 1 mg/wk PO

Digitoxin
Crystodigin
0.02–0.03 mg/kg q8h PO

Digoxin
Lanoxin
Cardoxin
Dog: 0.22 mg/m^2 q12h PO, 0.0055–0.01 mg/kg q12h PO, (reduce dose by 10% for elixir)
Cat: 0.01 mg/kg q48h, 0.007 mg/kg q48h (with Lasix and aspirin)

Dihydrotachysterol (vitamin D)
Hytakerol
DHT
Initial: 0.02–0.03 mg/kg/day PO maintenance: 0.01–0.02 mg/kg q24–48h PO

Diltiazem hydrochloride
Cardizem
Dog: 0.5–1.5 mg/kg q8h PO
Cat: 1.75–2.4 mg/kg q8–12h PO
Dilacor XR
Cat: 30 mg/cat q12–24h PO
Cardizem CD
Cat: 10 mg/kg q24hr PO

Dimenhydrinate
Dramamine (U.S.)

Gravol (Canada)
Dog: 4–8 mg/kg q8h IV, IM, PO
Cat: 12.5 mg q8h IV, IM, PO

Dimercaprol
BAL in oil
4 mg/kg q4h IM

Dinoprost tromethamine
See Prostaglandin $F_2\alpha$

Dioctyl calcium sulfosuccinate
See Docusate calcium

Dioctyl sodium sulfosuccinate
See Docusate sodium

Diphenhydramine hydrochloride
Benadryl
2.2 mg/kg q8–12h IV, IM, PO

Diphenoxylate hydrochloride
Lomotil
Dog: 0.1–0.2 mg/kg q8–12h PO
Cat: 0.05–0.1 mg/kg q12h PO

Diphenylhydantoin
See Phenytoin

Diphosphonate disodium etidronate
See Etidronate disodium

Dipyridamole
Persantine
4–10 mg/kg q24h PO

Disopyramide phosphate
Norpace
Dog: 6–15 mg/kg q8h PO

Dithiazanine iodide
Dizan
6.6–11.0 mg/kg q24h PO for 7–10 days

Divalproex sodium
Depakote
Equivalent to valproic acid (see Valproic acid)

Dobutamine
Dobutrex
Prepare 250 mg in 1 L 5% dextrose
Dog: 2.5–20 µg/kg/min IV infusion
Cat: 2.5–5.0 µg/kg/min IV infusion

Docusate calcium
Surfak
Doxidan
Dog: 50–100 mg/dog q12–24h PO
Cat: 50 mg/cat q12–24h PO

Docusate sodium
Colace
Dog: 50–200 mg/dog q8–12h PO
Cat: 50 mg/cat q12–24h PO

Dopamine hydrochloride
Intropin
2–10 µg/kg/min IV infusion (prepare 40 mg in 500 ml lactated Ringer's solution)

Doxapram hydrochloride
Dopram
5–10 mg/kg IV
Neonate: 1–5 mg SC, sublingually, or via umbilical vein

Doxorubicin
Adriamycin
Dogs ≤ 10 kg and cats: 20–25 mg/m^2 IV q3wk
Dogs > 10 kg: 30 mg/m^2 IV q3wk (maximum cumulative dose 180–240 mg/m^2) (see Chap. 26)

Doxycycline
Vibramycin
3–5 mg/kg q12h PO
Lyme borreliosis:
10 mg/kg q12h PO

Edetate calcium disodium (CaEDTA)
Havidote
25 mg/kg q6h SC for 2–5 days

Edrophonium chloride
Tensilon
Dog: 0.11–0.22 mg/kg IV
Cat: 2.5 mg/cat IV

Enalapril maleate
Enacard
Dog: 0.5 mg/kg q12–24h PO
Cat: 0.25–0.5 mg/kg q12–24h PO

Enflurane
Ethrane
2–3% (induction); 1.5–3% (maintenance)

Enilconazole
Imaverol
Nasal aspergillosis: 10 mg/kg q12h instilled into nasal sinus for 10–14 days (10% solution diluted 50:50 with water)
Dermatophytes: solution diluted to 0.2% and lesion washed with solution 4 times at 3- to 4-day intervals

Enrofloxacin
Baytril
2.5–5.0 mg/kg q12h PO, IM, SC, or 5–10 mg/kg q24h PO, IM

Ephedrine
Urinary incontinence
Dog: 5–15 mg/dog q8h PO
Cat: 2–4 mg/cat q8h PO
Bronchodilator: 1–2 mg/kg q8h PO

Epinephrine
Adrenalin
20 µg/kg, or 0.1–0.5 ml of 1:1000 (1 mg/ml) solution; or 1–5 ml of a 1:10,000 (0.1 mg/ml) solution IV, IM, SC, IC, intratracheally

Epogen
35–100 IU/kg q48h SC until PCV rises, then weekly

Epsiprantel
Cestex
Dog: 5.5 mg/kg PO
Cat: 2.75 mg/kg PO

Epsom salt
See Magnesium sulfate

Ergocalciferol (vitamin D_2)
Calciferol
Initial: 4000–6000 U/kg/d PO
Maintenance: 1000–2000 U/kg q24h–q7d PO (see Chap. 32)

Erythromycin
Antibiotic: 10–20 mg/kg q8–12h PO
Promotility: 0.5–1.0 mg/kg q8h PO

Erythropoietin (r-HuEPO)
Epogen

75–100 U/kg SC 3 times weekly (adjust dose to reach and maintain hematocrit of 30–34%)

Esmolol
Brevibloc
Dog: 50–500 µg/kg IV bolus every 5 minutes (up to 500 µg/kg)

Essential fatty acids
(See also Omega fatty acids)
EFA-Z Plus
<6.7 kg: 3.7 ml/d PO
6.7–22.5 kg: 7 ml/d PO
>22.5 kg: 14 ml/d PO

Estradiol cypionate (ECP)
Depo-Estradiol
Dog: 0.02–0.04 mg/kg IM (total dose not to exceed 1.0 mg) within 3 days of mating
Cat: 0.25 mg/cat IM within 3 days of mating
Use of ECP for mismating is discouraged

Ethanol (20%)
For ethylene glycol toxicity:
Dogs: 5.5 ml/kg IV q4h for 5 treatments, then q6h for 4 treatments
Cats: 5.0 ml/kg IV q6h for 5 treatments, then q8h for 4 treatments

Ethoxzolamide
Cardrase
Glaucoma: 4 mg/kg q8–12h PO

Etidronate disodium
Didronel
5–10 mg/kg q12–24h PO

Etodolac
Dog: 10–15 mg/kg q24h PO

Etomidate
1–4 mg/kg IV

Etretinate
Tegison
Dog: 0.75–1 mg/kg q24h PO
Cat: 2 mg/kg q24h PO

Famotidine
Pepcid
0.5–1.0 mg/kg q12–24h IM, SC, IV, PO

Febantel
Rintal
10 mg/kg q24h for 3 days PO

Febantel plus praziquantel
RM-Parasitacide; Drontal-Plus
15 mg/kg FEB 1.5 mg/kg PRA, PO, for 3 days

Felbamate
Initially 20 mg/kg q8h PO (maximum dose: 3000 mg/d) (see Chap. 127)

Fenbendazole
Panacur
50 mg/kg/d for 3 days PO

Fentanyl
Sublimaze
0.02–0.04 mg/kg IV, IM, SC, or 0.01 mg/kg IV, IM, SC (with acetylpromazine or diazepam)
Analgesia: 0.002–0.005 mg/kg IV; 0.004–0.008 mg/kg IM, SC

Fentanyl transdermal patch
Duragesic
Dog: <10 kg, 25 µg/h, q72h 10–20 kg, 50 µg/h, q72h 20–30 kg, 75 µg/h, q72h >30 kg, 100 µg/h, q72h
Cat: 25 µg/h, q118h

Ferrous sulfate
Dog: 100–300 mg/dog q24h PO
Cat: 50–100 mg/cat q24h PO

Flavoxate
Urispas
100–200 mg q12–24h PO

Florifenicol
Nuflor
Dog: 20 mg/kg q6h PO, IM
Cat: 22 mg/kg q8h PO, IM

Fluconazole
Diflucan
2.5–5.0 mg/kg q12–24h PO or IV (double loading dose on day 1)
(for CNS Cryptococcus: 10–15 mg/kg q12–24h)

Flucytosine
Ancobon
Cryptococcosis: 50 mg/kg q8h or 75 mg/kg q12h, PO combined with Amphotericin B

Fludrocortisone acetate
Florinef Acetate
Dog: 0.2–0.8 mg/dog (0.02 mg/kg) q24h PO
Cat: 0.1 mg/cat q24h PO

Flumethasone
Flucort
Dog: 0.0625–0.25 mg/dog q24h IV, IM, SC, PO
Cat: 0.03–0.125 mg/cat q24h IV, IM, SC, PO
Anti-inflammatory: 0.15–0.3 mg/kg q12–24h IV, IM, SC, PO

Flunixin meglumine
Banamine
1.1 mg/kg once IV, IM, SC, or 1.1 mg/kg/d for 3 days/wk PO
Ophthalmic: 0.5–1.0 mg/kg once IV

Fluorouracil
5-Fluorouracil
Dog: 150–200 mg/m^2 q7d IV
Cat: do not use

Fluoxetin
Prozac
Dog: 0.5–1.0 mg/kg q24h PO
Cat: 0.5–4 mg/cat q24h PO

Folic acid
Folvite
Dog and cat: 0.004–0.01 mg/kg/d (4–10 µg/kg/d)

Follicle-stimulating hormone (FSH)
See Urofollitropin

Furazolidone
Furoxone
4 mg/kg q12h for 7–10 days PO

Furosemide
Lasix
Dog: 2–6 mg/kg q8–12h (or as needed) IV, IM, SC, PO
Cat: 1–4 mg/kg q12h IV, IM, SC, PO

Gabapentin
30–60 mg/kg/d PO (divide bid or tid)

Gentamicin sulfate
Gentocin
Dog: 2–4 mg/kg q6–8h IV, IM, SC, or 6 mg/kg q24h
Cat: 3 mg/kg q8hr IV, IM, SC

Glipizide
Glucotrol
Cat: 2.5–5 mg/cat q8–12h with food

Glucosamine chondroitin sulfate
Cosequin and others
Dog: 1–2 RS (Regular Strength) capsules/d (2–4 capsules of DS (Double Strength) for large dogs)
Cat: 1 RS capsule/d

Glyburide (Glibenclamide)
Diaβeta
Micronase
0.2 mg/kg daily PO

Glycerin
Glyrol
Osmoglyn
Glaucoma: 1–1.5 gm/kg PO initially, then 500 mg/kg q8h; or 1–2 ml of 50% solution q8h

Glycopyrrolate
Robinul-V
0.005–0.01 mg/kg IV, IM, SC q8–12h as needed

Gold sodium thiomalate
Myochrysine
Immune-mediated arthritis: 1 mg/kg once weekly IM

Gonadorelin (GnRH, LHRH)
Factrel
Dog: 50–100 µg/dog q24–48h IM
Cat: 25 µg/cat once IM

Gonadotropin, chorionic (hCG)
Follutein
Dog: 22 U/kg q24–48h IM, or 44 U/kg once IM
Cat: 250 U/cat once IM

Gonadotropin-releasing hormone
See Gonadorelin

Griseofulvin (microsize)
Fulvicin U/F powder or tablets
50 mg/kg q24h PO (maximum dose: 110–132 mg/kg/d in divided treatments)

Griseofulvin (ultramicrosize)
Fulvicin P/G
5–10 mg/kg/d PO (in divided treatments)

Growth hormone
0.1 U/kg 3 times/wk for 4–6 weeks

Halothane
Fluothane
3% (induction); 0.5–1.5% (maintenance) (see Chap. 2)

Heparin sodium
Liquaemin (U.S.)
Hepalean (Canada)
100–200 U/kg IV, loading dose; then 100–300 U/kg q6–8h SC (monitor clotting profiles)
Low-dose therapy (dog and cat): 70 U/kg q8–12h SC

Hetacillin potassium
Hetacin-K
20–40 mg/kg q8h PO

Hetastarch
See Hydroxyethyl starch

Hydralazine
Apresoline
Dog: 0.5 mg/kg (initial dose), titrated to 0.5–2.0 mg/kg q12h PO
Cat: 2.5–5 mg/cat q12–24h PO

Hydrochlorothiazide
Hydrodiuril
2–4 mg/kg q12h PO

Hydrocodone
Hycodan
Dog: 0.22 mg/kg q6–12h PO

Hydrocortisone
Cortef
Replacement therapy: 1 mg/kg q12h PO
Anti-inflammatory: 2.5–5.0 mg/kg q12h PO

Hydrocortisone sodium succinate
Solu-Cortef
Shock: 50–150 mg/kg IV

Hydromorphone
0.1–0.2 mg/kg IV, IM, SC

Hydroxyethyl starch
Hetastarch
Dog: 20 ml/kg/24h (5 ml/kg over 15 min for hypovolemia) (see Chap. 5)
Cat: 10 ml/kg/24h (2.5 ml/kg over 15 min for hypovolemia) (see Chap. 5)

Hydroxyurea
Hydrea
For polycythemia vera: 30 mg/kg/d for 1 week, then 15 mg/kg/d until remission

Hydroxyzine
Atarax
Dog: 2.2 mg/kg q8–12h PO
Cat: 10 mg/cat q12h PO

Hyoscyamine
0.003–0.006 mg/kg q8–12h PO, SC

Imidocarb
5 mg/kg IM SC once and repeated in 14 days

Imipramine
Dog: 1 mg/kg q8h PO
Cat: 2.5–5.0 mg/cat q12h PO

Insulin (NPH isophane)
Dog: 0.5–1.0 U/kg q12–24h SC (to effect)
Cat: 1–5 U/cat q12h SC (to effect) (see Chap. 34)

Insulin (PZI)
Dog: 0.5–1.0 U/kg q12–24h SC (to effect)
Cat: 1–5 units/cat (0.2–1.0 U/kg) q12–24h SC (adjust with monitoring) (see Chap. 34)

Insulin (regular crystalline)
Ketoacidosis:
See Chapter 34 for complete treatment protocol

Insulin, ultralente
Dog: 0.5–1.0 U/kg q12–24h SC (to effect)
Cat: 1–5 U/cat q12–24h SC (to effect) (see Chap. 34)

Interferon-alpha
Roferon A; Intron A (dilute to 30 U/ml)
Cat: 30 U/cat q24h for 7 days on alternating weeks

Interferon-omega (recombinant feline [rFeIFN-omega])
Virbagen
FIP: 1,000,000 u/kg SC (See Chapters 8–10 and 14 for treatment protocols)

Iodide
See Potassium iodide

Ipecac syrup
Dog: 1–2 ml/kg up to 15 ml PO
Cat: 2–6 ml/cat PO

Iron
See Ferrous sulfate

Isoflurane
3.5% (induction); 1.5–2.5% (maintenance)
(see Chap. 2)

Isoproterenol
Isuprel
0.04–0.09 µg/kg/min IV; 0.1–0.2 mg/dog q4–6h IM, SC

Isosorbide dinitrate
Isordil
Sorbitrate
2.5–5 mg/animal q12h PO

Isotretinoin
Accutane
1–3 mg/kg/d (maximum dose: 3–4 mg/kg/d) PO

Itraconazole
Sporanox
Dog: 5 mg/kg q12–24h PO
Cat: 5–10 mg/kg q12h PO, or 20 mg/kg q24h

Ivermectin
Heartgard
Ivomec
Heartworm preventive in dog: 6 µg/kg q30d PO
Cat: 24 µg/kg q30d PO
Microfilaricide in dog: 50 µg/kg PO 3–4 weeks after adulticide therapy
Ectoparasite therapy: 300–600 µg/kg q24h IM, SC, PO (do not use in collie and sheltie dogs)
Respiratory parasites: 200–400 µg/kg weekly SC, PO (do not use in collie and sheltie dogs)

Kanamycin sulfate
Kantrim
10 mg/kg q6–8h IV, IM, SC

Kaolin plus pectin
Kaopectate
1–2 ml/kg q2–6h PO

Ketamine
Ketalar
Ketaset
Cat: 4–10 mg/kg IV, 10–20 mg/kg IM, SC (see Chap 2)
Dog: 1 ml/10 kg IV of ketamine : diazepam mixture (50 : 50)

Ketoconazole
Nizoral
Dog: 10–15 mg/kg q12h PO (*Malassezia canis* infection: 10 mg/kg q24h or 5 mg/kg q12h PO)
Hyperadrenocorticism: 15 mg/kg q12h PO
Cat: 5–10 mg/kg q8–12h PO

Ketoprofen
Ketofen
Dog: 1.1 mg/kg q24h IV, PO for up to 5 days
Cat: 2 mg/kg q24h PO, SC initially, then 0.5–1.0 PO, SC

Lactated Ringer's solution
40–50 ml/kg/d IV for maintenance requirements
Shock therapy:
Dog: 90 ml/kg IV
Cat: 60 ml/kg IV

Lactulose
Cephulac; Duphalac
Constipation: 1 ml/4.5 kg q8h PO (to effect)
Hepatic encephalopathy
Dog: 0.5 ml/kg q8h PO
Cat: 2.5–5.0 ml/cat q8h PO

Leucovorin (folinic acid)
Wellcovorin
With methotrexate administration: 3 mg/m^2 IV, IM, PO
Antidote for pyrimethamine toxicosis: 1 mg/kg q24h PO

Levamisole
Levasole
Tramisol
Dog: 5–8 mg/kg PO once, up to 10 mg/kg PO for 2 days (hookworms); 10 mg/kg q24h PO for 6–10 days (microfilaricide); 0.5–2.0 mg/kg 3 times/wk PO (immunostimulant)
Cat: 4.4 mg/kg PO once

Levetiracetem
500–4000 mg/d PO (divide bid or tid)

Levo-carnitine
Dog: 50 mg/kg q8h PO
Cat: 250–500 mg/cat qd PO

Levodopa (l-dopa)
Larodopa
Hepatic encephalopathy: 6.8 mg/kg initially, then 1.4 mg/kg q6h

Levothyroxine sodium
Soloxine
Thyro-Tabs
Synthroid
Dog: 0.01–0.02 mg/kg q12h, PO
Cat: 0.01–0.02 mg/kg q24h, PO

Lidocaine
Xylocaine
Antiarrhythmia in dog: 2–4 mg/kg IV (maximum dose: 8 mg/kg over 10 min); 25–75 µg/kg/min IV infusion; 6 mg/kg q1.5h IM
Cat: 0.25–0.75 mg/kg IV, slowly

Lime sulfur (2–3% solution)
Topically once/wk for 4–6 weeks

Lincomycin
Lincocin
15–25 mg/kg q12h IV, IM, PO

Liothyronine
Cytobin or Cytomel
4.4 µg/kg q8h PO
Suppression testing: See Chapter 31 for protocol

Lisinopril
Prinivil
Dog: 0.25–0.5 mg/kg q12–24h

Lithium carbonate
Lithotabs
Dog: 10 mg/kg q12h PO
Cat: not recommended

Lomustine
60–90 mg/m^2 q21–28d PO

Loperamide
Imodium
Dog: 0.1–0.2 mg/kg q8–12h PO
Cat: 0.1–0.3 mg/kg q12–24h PO

Lufenuron
Program
Flea control
Dog: 10mg/kg q30d PO
Cat: 30mg/kg q30d PO
Coccidioidomycosis
5 mg/kg PO q24h

Luteinizing hormone
See Gonadorelin

Magnesium citrate
Citroma, Citro-Nesia (U.S.)
Citro-Mag (Canada)
2–4 ml/kg PO

Magnesium hydroxide
Milk of Magnesia
Antacid: 5–10 ml per dog or cat PO
Cathartic:
Dog: 15–50 ml/dog PO
Cat: 2–6 ml/cat q24h PO

Magnesium sulfate
Dog: 8–25 g/dog q24h PO
Cat: 2–5 g/cat q24h PO

Mannitol
Osmitrol
Diuretic: 1 g/kg of 5–25% solution IV
Glaucoma or CNS edema: 0.5–1.0 g/kg of 15–25% solution over 15–60 minutes IV (repeat in 4–6 hours if necessary)

Marbofloxacin
Marbocyl, Zeniquin
Dog: 2.75–5.55 mg/kg q24h PO

Mebendazole
Telmintic
22 mg/kg (with food) q24h for 3 days

Meclizine hydrochloride
Bonine
Dog: 25 mg/dog q24h PO (motion sickness: administer 1 hour before traveling)
Cat: 12.5 mg/cat q24h PO

Meclofenamic acid
Meclomen
Meclofen
Arquel
Dog: 1 mg/kg/d for 5 days, then 0.5 mg/kg q24h PO

Medetomidine
Domitor
Dog: 0.007–0.02 mg/kg IV; 0.01–0.04 mg/kg IM, SC
Cat: 0.01–0.03 mg/kg IV; 0.03–0.08 mg/kg IM, SC

Medium-chain triglycerides (MCTs)
MCT oil
1–2 ml/kg daily in food

Medroxyprogesterone acetate
Depo-Provera
1.1–2.2 mg/kg q7d IM

Megestrol acetate
Ovaban
Dog: Proestrus: 2.2 mg/kg q24h PO for 8 days Anestrus: 0.55 mg/kg q24h PO for 30 days Behavior problems: 2–4 mg/kg q24h for 8 days (reduce dose for maintenance)
Cat: dermatologic therapy or urine spraying: 2.5–5.0 mg/cat q24h PO for 1 week, then reduce to 2.5–5.0 mg once or twice/wk; suppress estrus: 5 mg/cat for 3 days, then 2.5–5 mg once/wk for 10 weeks

Melarsomine
Immiticide
Dog: 2.5 mg/kg, IM, q24h for 2 doses, Alternate: 2.5 mg/kg, IM once; then after 1–2 months give 2.5 mg/kg IM, q24h for 2 additional doses

Meloxicam
Metacam
Dog: 0.2 mg/kg PO, SC initially, then 0.1 mg/kg q24h for 2–3 days
Cat: 0.3 mg/kg SC, one time only

Melphalan
Alkeran
2–4 mg/m^2 q24–48h PO (see Chap. 26)

Meperidine
Demerol
Dog: 0.4–2 mg/kg IV, 1.0–4.0 mg/kg IM, SC

6-Mercaptopurine
Purinethol
50 mg/m^2 q24h PO

Mesalamine
Asacol; Pentasa
Dogs: 20 mg/kg q8–12h PO
(See also Osalazine sodium; Sulfasalazine)

Metaproterenol
Alupent
Metaprel
0.325–0.65 mg/kg q4–6h PO

Metaraminol bitartrate
Aramine
0.1 mg/kg IM, SC

Methazolamide
Neptazane
2–4 mg/kg q8–12h PO

Methenamine hippurate
Hiprex
Dog: 500 mg/dog q12h PO
Cat: 250 mg/cat q12h PO

Methenamine mandelate
Mandelamine
10–20 mg/kg q8–12h PO

Methimazole
Tapazole
Cat: 2.5 mg/cat q8–12h PO (initial), increase to 5–10 mg/cat q8–12h PO by monitoring T4

Methionine (l-methionine, dl-methionine)
Uroeze
Methio-Form
Dog: 150–300 mg/kg/d PO
Cat: 1000–1500 mg/cat PO (added to food each day) (use in adult cats only)

Methocarbamol
Robaxin-V
44 mg/kg q8h PO on the first day, then 22–44 mg/kg q8h PO

Methotrexate (MTX)
2.5 mg/m^2 q24h PO; or 2–3 times per week;
15–20 mg/m^2 IV q3wk (see Chap. 26)

Methoxamine
Vasoxyl
200–250 µg/kg IM, or 40–80 µg/kg IV

Methscopolamine bromide
Pamine
0.3–1.0 mg/kg q8h PO (use cautiously in cats)

Methylene blue (1% solution)
Dog: for pancreatic tumor identification: 3 mg/kg IV slowly, diluted in isotonic saline (can cause hemolytic anemia)
Cat: do not use

Methylprednisolone
Medrol
Dog: 0.22–0.44 mg/kg q12–24h PO

Methylprednisolone acetate
Depo-Medrol
Dog: 1 mg/kg IM q1–3wk
Cat: 10–20 mg/cat IM q1–3wk

Methylprednisolone sodium succinate
Solu-Medrol
For spinal cord trauma: 30 mg/kg IV, repeat at 15 mg/kg IV in 2–6 hours

4-Methylpyrazole (fomepizole)
Antizol-Vet
20 mg/kg initially IV, then 15 mg/kg at 12- and 24-hour intervals, then 5 mg/kg at 36h.

Methyltestosterone
Android
Fluoxymestrone
Dog: 1.0 mg/kg q48h PO
(see also Testosterone cypionate; Testosterone propionate), for sex hormone dematoses in dogs: 1 mg/kg (up to 30 mg total dose)
Cat: 1.0–2.5 mg/cat q48h PO

Metoclopramide
Reglan
Maxolon
0.2–0.5 mg/kg q6–8h IV, IM, SC, PO, or 1–2 mg/kg q24h via continuous IV infusion

Metoprolol tartrate
Lopressor
Dog: 5–50 mg/dog q8h PO
Cat: 2–15 mg/cat q8h PO
or: 0.25–1.0 mg/kg q8h PO (dog and cat)

Metronidazole
Flagyl
Dog: for giardia: 50–65 mg/kg q24h PO for 5–7 days; Antibacterial: 10–15 mg/kg q8–12h PO
Cat: for giardia: 50 mg/kg q24h PO for 5 days; Antibacterial: 10 mg/kg q8h or 15 mg/kg q12h PO

Mexiletine
Mexitil
Dog: 5–8 mg/kg q8–12h PO (use cautiously)

Mibolerone
Cheque
Dog: (2.6–5.0 µg/kg/d PO) 0.45–11.3 kg: 30 µg 11.8–22.7 kg: 60 µg 23–45.3 kg: 120 µg >45.8 kg: 180 µg
Cat: safe dose not established

Midazolam
Versed
0.1–0.25 mg/kg IV, IM, or 0.1–0.3 mg/kg/h IV infusion

Milbemycin oxime
Interceptor
Dog: 0.5 mg/kg q30d PO
For demodex: 1–2 mg/kg q24h PO
For scabies: 2 mg/kg PO twice at 14-day intervals

Milk of magnesia
See Magnesium hydroxide

Milk thistle
Marin
6–100 mg q24h PO

Minocycline
Minocin
5.0–12.5 mg/kg q12h PO

Misoprostol
Cytotec
Dog: 3–5 µg/kg q6–8h PO

Mitotane (*o,p′*-DDD)
Lysodren
For pituitary-dependent hyperadrenocorticism: 50 mg/kg/d PO (may be given in divided doses) for 5–10 days, then 50–70 mg/kg/wk PO
Adrenal tumor: 50–75 mg/kg/d for 10 days PO, then 75–100 mg/kg/wk PO (see Chap. 33)

Mitoxantrone
Novantrone
5–6 mg/m^2 IV q3wk

Morphine
Dog: 0.2–0.6 mg/kg IM, SC (as needed); 0.1 mg/kg epidural
Cat: 0.1 mg/kg IM, SC (as needed)

Nadolol
Corgard
0.25–0.5 mg/kg q12h PO

Nafcillin sodium
Unipen
10 mg/kg q6h IM, PO

Nalbuphine
Dog: 0.5–2.0 mg/kg IV, IM, SC
Cat: 0.5–1.5 mg/kg IV, IM, SC

Nalorphine
Nalline
0.44 mg/kg IV, IM, SC (1 mg for every 10 mg of morphine)

Naloxone
Narcan
0.003–0.01 mg/kg IV, IM, for opiate reversal

Naltrexone hydrochloride
Trexan
Behavior problems: 2.2 mg/kg q12h PO

Nandrolone decanoate
Deca-Durabolin
Dog: 1.0–1.5 mg/kg qwk IM
Cat: 1 mg/cat qwk IM

Neomycin
Biosol
10–20 mg/kg q6–12h PO

Neostigmine bromide
Prostigmin bromide
2 mg/kg/d PO (in divided doses, to effect)

Neostigmine methylsulfate
Prostigmin
Antimyasthenic: 10 µg/kg IM, SC, as needed (atropine may be administered to counteract side effects)
Antidote for curiform block: 40 µg/kg IM, SC (administer with atropine)
Diagnostic aid for myasthenia gravis: 40 µg/kg IM, or 20 µg/kg IV

Nitrofurantoin
Furadantin
Macrodantin
4 mg/kg q8h PO

Nitroglycerin ointment
Nitrol Ointment
Nitro-Bid Ointment
Nitrostat Ointment
(1 inch of ointment is approximately 15 mg)
Dog: 1/4–1 inch topically q12–24h
Cat: 1/4 inch topically q12–24h

Nitroprusside
Nipride
2.5–15 µg/kg/min constant IV infusion

Nizatidine
Axid
2.5–5 mg/kg q24h PO

Norfloxacin
Noroxin
22 mg/kg q12h PO

Novobiocin
See Delta-Albaplex

Olsalazine
Dipentum
Dog: 20–30 mg/kg q8–12h PO

Omega fatty acids
See also Derm Caps
1 capsule q12h PO (see also Essential fatty acids)

Omeprazole
Prilosec
Dog: 20 mg/dog or 0.7–1.0 mg/kg q24h PO
Cat: Not recommended

Ondansetron
Zofran
0.1–0.5 mg/kg q6–12h IV, SC
0.5–1.0 mg/kg q6–12h PO

***o,p'*-DDD**
See Mitotane

Ormetroprim
See Primor

Oxacillin
Prostaphlin
Bactocill
22–40 mg/kg q8h PO

Oxazepam
Serax
Appetite stimulant: 2.5 mg/cat q12h PO

Oxtriphylline
Choledyl SA
Dog: 47 mg/kg (equivalent to 30 mg/kg theophylline) q12h PO

Oxybutynin chloride
Ditropan
5.0 mg/dog q8–12h PO

Oxymetholone
Anadrol
1–5 mg/kg q24h PO

Oxymorphone hydrochloride
Numorphan
Analgesia:
Dog: 0.05–0.1 mg/kg IV 0.1–0.3 mg/kg IM, SC
Cat: 0.01–0.04 mg/kg IV 0.05–0.1 mg/kg IM, SC
For preanesthesia or sedation: see Chapter 2

Oxytetracycline
Terramycin
20 mg/kg q8h PO; 7.5–10.0 mg/kg q8h IV

Oxytocin
Dog: 5–20 units/dog IM, repeat q30min for primary inertia
Cat: 3–5 units/cat IM

2-PAM
See Pralidoxime chloride

Pamidronate
Aredia
1.3–2.0 mg/kg in 150 ml 0.9% saline in 2-hour IV infusion; can repeat in 1–3 weeks

Pancreatic enzyme (pancrelipase)
Viokase
Pancrezyme
2 tsp per 20 kg body weight, or 1–3 tsp/0.45 kg of food, mixed with food 20 minutes prior to feeding

Pancuronium bromide
Pavulon
0.1 mg/kg IV

Pantoprazole
Protonix
0.7–1.0 mg/kg q24h IV, PO

Paregoric
Corrective Mixture
0.05–0.06 mg/kg q12h PO (5 ml of paregoric corresponds to approximately 2 mg of morphine)

D-Penicillamine
Cuprimine
10–15 mg/kg q12h PO

Penicillin G potassium
20,000–40,000 U/kg q6–8h, IV, IM

Penicillin G procaine
20,000–40,000 U/kg q12–24h IM

Penicillin G sodium
20,000–40,000 U/kg q6–8h IV, IM

Penicillin V
10 mg/kg q8h PO

Pentazocine
Talwin
Dog: 1.65–3.3 mg/kg q4h IM
Cat: 2.2–3.3 mg/kg IV, IM, SC

Pentobarbital
Anesthesia: 25–30 mg/kg IV (first ½ of the dose administered rapidly, then remaining administered to effect)

Pentoxifylline
Trental
10–15 mg/kg q8h PO

Petrolatum, white (flavored)
Laxatone
Cat: 1–5 ml/cat q24h PO

Phenobarbital
Luminal
Dog: 2–8 mg/kg q12h PO
Cat: 1–2 mg/kg q12h PO
For seizures: Initially: 2.5 mg/kg q12h PO (see Chap. 127) and adjust by plasma concentration
Status epilepticus (dog or cat): 10–20 mg/kg IV (to effect) or IV loading protocol (preferred; see Chap. 127)

Phenoxybenzamine hydrochloride
Dibenzyline
Dog: 0.25–0.5 mg/kg q8h PO
Cat: 2.5 mg/cat q8–12h PO

Phentolamine mesylate
Regitine (U.S.)
Rogitine (Canada)
0.02–0.1 mg/kg IV (as needed to maintain normal blood pressure)

Phenylbutazone
Butazolidin
Dog: 10–15 mg/kg q8h PO (maximum dose: 800 mg)
Cat: not recommended

Phenylephrine hydrochloride
Neo-Synephrine
0.01 mg/kg q15min IV
0.1 mg/kg q15min IM, SC

Phenylpropanolamine hydrochloride
Propagest
Dexatrim
Dog: 1–2 mg/kg q12h PO
Cat: 1 mg/kg q12h PO

Phenytoin
Dilantin
Antiepileptic in dog: 20–35 mg/kg q8h PO
Antiarrhythmic in dog: 30 mg/kg q8h PO or 10 mg/kg IV over 5 minutes

Phytonadione
See Vitamin K_1

Phytomenadione
See Vitamin K_1

Pimobendan
Vetmedin
Dog: 0.3–0.6 mg/kg/d divided q12h PO

Piperazine
44–66 mg/kg PO once

Piroxicam
Feldene
Dog: 0.3 mg/kg q48h PO (use cautiously)
Cat: dosage not established

Polyethylene glycol electrolyte solution
GoLYTELY
25 ml/kg, then repeat in 2–4 hours PO

Polysulfated glycosaminoglycans
Adequan
1–2 mg/kg IM once every 4 days for 7 injections

Potassium bromide
Dog and cat: 30 mg/kg q24h PO (in food) (see Chap. 127)

Potassium chloride
0.5 mEq/kg/d (do not administer at a rate faster than 0.5 mEq/kg/h)
10–40 mEq/500 ml of fluids, depending on serum potassium (see Chap. 5)

Potassium citrate
Urocit-K
Dog: 50–75 mg/kg q12h PO

Potassium gluconate
Kaon elixir
Tumil-K
2.2 mEq/100 kcal of energy/day PO
Cat: 2–6 mEq/cat daily PO

Potassium iodide
30–100 mg/cat daily (in single or divided doses) for 10–14 days

Potassium (or sodium) phosphate (potassium or sodium)
0.01–0.03 mmol phosphate/kg/hr for 3–6 hours (or, 2.5 mg/kg over 6 hours) (3 mmol/ml or 93 mg/ml phosphate)

Pralidoxime chloride (2-PAM)
Protopam Chloride
Organophosphate toxicosis: 20 mg/kg q8–12h (initial dose slow IV, or IM; subsequent doses IM, SC)

Praziquantel
Droncit
Dog (PO): <6.8 kg: 7.5 mg/kg once >6.8 kg: 5 mg/kg once
Dog (IM, SC): ≤2.3 kg: 7.5 mg/kg once 2.7–4.5 kg: 6.3 mg/kg once ≥5 kg: 5 mg/kg once
Cat (PO): <1.8 kg: 6.3 mg/kg once >1.8 kg: 5 mg/kg once
Cat (IM, SC): 5 mg/kg IM, SC paragonimiasis: 25 mg/kg q8h for 2 days
Liver flukes: 20 mg/kg qd for 3 days; PO, SC

Prazosin
Minipress
0.5–2.0 mg/animal q8–12h PO

Prednisolone
Anti-inflammatory:
Dog: 0.5–1.0 mg/kg q12–24h IV, IM, PO initially then taper to q48h
Cat: 2.2 mg/kg q12–24h IV, IM, PO initially, then taper to q48h
Immunosuppressive (dog and cat): initially 2.2–6.6 mg/kg/d IV, IM, PO, then taper to 2–4 mg/kg q48h

Prednisolone sodium succinate
Solu-Delta-Cortef
Shock: 15–30 mg/kg IV, then repeat in 4–6 h
CNS trauma: 15–30 mg/kg IV, then taper to 1–2 mg/kg q12h

Prednisone
See Prednisolone

Primidone
Mylepsin
Mysoline
Initial dosage: 5–10 mg/kg q8h PO

Primor (ormetroprim plus sulfadimethoxine)
25 mg/kg on first day, followed by 12.5 mg/kg q24h PO

Procainamide
Pronestyl
Dog: 10–20 mg/kg q6h PO (maximum dose: 40 mg/kg); 8–20 mg/kg IV, IM; 25–50 µg/kg/min IV infusion
Cat: 3–8 mg/kg IM, PO q6–8h

Procainamide (extended-release tablets)
Procan-SR
Dog: 20–50 mg/kg q8h PO
Cat: 62.5 mg/cat q8h PO

Prochlorperazine
Compazine
0.25–0.5 mg/kg q6–8h IM, SC

Progesterone, repositol
See Medroxyprogesterone acetate

Promazine
Tranquazine
1–2 mg/kg q6–8h IV, IM, PO

Promethazine hydrochloride
Phenergan
0.2–0.4 mg/kg q6–8h IV, IM, PO (maximum dose: 1 mg/kg)

Propantheline bromide
For detrusor hyperreflexia and urge incontinence:
Dog: 7.5–30.0 mg/dog q8–24h PO (start low)
Cat: 7.5 mg/cat q24–72h PO
For diarrhea: 0.25 mg/kg q8–12h PO

Propofol
2–6 mg/kg IV for anesthesia (see Chap. 2)

Propranolol hydrochloride
Inderal
Dog: 20–60 µg/kg over 5–10 min q8h IV, 0.2–1.0 mg/kg q8h PO
Cat: 2.5–5.0 mg/cat (0.4–1.2 mg/kg) q8–12h PO

Prostaglandin E
See Misoprostol

Prostaglandin $F_2\alpha$
Lutalyse
Pyometra: Dog: 0.1–0.25 mg/kg, once daily for 3–5 days SC (see Chap. 90)
Abortion:
(See Chap. 90 for protocol)

Psyllium
Metamucil
Dog: 1–3 tbsp/d (added to food)
Cat: 1–3 tsp/d (added to food)

Pyrantel pamoate
Nemex, Strongid
Dog: <2.5 kg: 10 mg/kg PO >2.5 kg: 5 mg/kg PO
Cat: 20 mg/kg PO

Pyridostigmine bromide
Mestinon
Regonol
Antimyasthenic: 0.02–0.04 mg/kg q2h IV, or 0.5–3.0 mg/kg q8–12h PO
Antidote (curariform): 0.15–0.3 mg/kg IM, IV

Pyrimethamine
Daraprim
Dog: 1 mg/kg q24h PO for 14–28 days (5 days for *Neosporum caninum*)
Cat: 0.5–1.0 mg/kg q24h PO for 14–28 days

Quinacrine hydrochloride
Atabrine hydrochloride
Dog: 6.6 mg/kg q12h PO for 5 days
Cat: 11 mg/kg q24h PO for 5 days

Quinidine gluconate
Quinaglute
Duraquin
Dog: 6–20 mg/kg q6h IM; 6–20 mg/kg q6–8h PO (of base)
(324 mg quinidine gluconate = 202 mg quinidine base)

Quinidine polygalacturonate
Cardioquin
Dog: 6–20 mg/kg q6h PO (of base)
(275 mg quinidine polygalacturonate = 167 mg quinidine base)

Quinidine sulfate
Clin-Quin
Quinora
Dog: 6–20 mg/kg q6–8h PO (of base)
(300 mg quinidine sulfate = 250 mg quinidine base)

Ranitidine
Zantac
Dog: 2 mg/kg q8–12h IV, PO
Cat: 2.5 mg/kg q12h IV; 3.5 mg/kg q12h PO

Retinoids
See Isotretinoin; Retinol; Etretinate

Retinol
Aquasol-A
625–800 IU/kg q24h PO

Riboflavin (vitamin B_2)
Dog: 10–20 mg/d PO
Cat: 5–10 mg/d PO

Rifampin
Rifadin
10–20 mg/kg q24h PO

Ringer's solution
40–50 ml/kg/d IV, SC, IP for maintenance requirements

Salicylate
See Acetylsalicylic acid (aspirin)

Selegiline
See Deprenyl (Anipryl)

Senna
Senokot
Cat: 5 ml/cat q24h (syrup); $^1/_2$ tsp/cat q24h with food (granules)

SMS 201-995
Octreotide
10–20 µg q8–12h SC

Sodium bicarbonate ($NaHCO_3$)
Acidosis: 0.5–1.0 mEq/kg IV, monitor blood gases (8.5% solution = 1 mEq/ml of $NaHCO_3$)
Renal failure: 10 mg/kg q8–12h PO (adjust as necessary)
Alkalinization of urine: 50 mg/kg q8–12h PO (1 tsp is approximately 2 g)

Sodium chloride (0.9%)
40–50 ml/kg/d IV, SC, IP

Sodium chloride 7% (hypertonic saline)
2–8 ml/kg/ IV for shock therapy

Sodium iodide (20%)
20–40 mg/kg q8–12h PO

Sodium nitroprusside
See Nitroprusside sodium

Sodium thiomalate
See Gold sodium thiomalate

Sotalol
Betapace
Dog: 1–3.5 mg/kg q12h PO
Cat: $^1/_8$ of 80 mg tab q12h PO

Spironolactone
Aldactone
1–2 mg/kg q12h PO

Stanozolol
Winstrol-V
Dog: 1–4 mg/dog q12h PO; 25–50 mg/dog/wk IM
Cat: 1 mg/cat q12h PO; 25 mg/cat/wk IM

Streptozotocin
(See Chapter 35 for administration protocol)

Sucralfate
Carafate
Dog: 0.5–1.0 g/dog q8–12h PO
Cat: 0.25 g/cat q8–12h PO

Sufentanil
Sufenta
2 µg/kg IV, up to a maximum dose of 5 µg/kg (premedicate with acepromazine)

Sulfadiazine
100 mg/kg IV, PO (loading dose), followed by 50 mg/kg q12h IV, PO (see also Trimethoprim)

Sulfadimethoxine
Albon, Bactrovet
55 mg/kg PO (loading dose), followed by 27.5 mg/kg q12h PO (see also Primor)

Sulfaguanidine
100–200 mg/kg q8h PO for 5 days

Sulfamethazine
100 mg/kg PO (loading dose), followed by 50 mg/kg q12h PO

Sulfamethoxazole
Gantanol
100 mg/kg PO (loading dose), followed by 50 mg/kg q12h PO

Sulfamethoxazole plus trimethoprim
Bactrim
Septra
See Trimethoprim plus sulfadiazine

Sulfasalazine (Sulfapyridine plus mesalamine)
Azulfidine (U.S.)
Salazopyrin (Canada)
Dog: 10–30 mg/kg q8–12h PO
Cat: 10–20 mg/kg q12–24h PO
(See also Mesalamine, Olsalazine)

Sulfisoxazole
Gantrisin
50 mg/kg q8h PO (urinary tract infections)

Tacrolimus
Prototopic (ointment)
Apply topically q24h

Taurine
Dog: 250–500 mg/dog q12h PO
Cat: 250 mg/cat q12h PO

Tegaserod
Zelnorm
Dog: 0.05–0.1 mg/kg q12h PO

Telezol
See Tiletamine plus zolazepam

Temaril-P (Trimeprazine plus prednisolone)
0.7–1.1 mg/kg (of trimeprazine) q12–24h PO

Tepoxalin
Zubrin
Dog: 10–20 mg/kg q24h PO then 10 mg/kg q24h PO

Terbinafine
Lamasil
Dog: 30 mg/kg q24h PO for 21–28 days
Cat: 30–40 mg/kg q24h PO for 21–28 days

Terbutaline
Brethine, Bricanyl
Dog: 2.5–5.0 mg/dog q8h SC, PO
Cat: 0.625 mg/cat q12h SC, PO

Testosterone cypionate
Andro-Cyp
1–2 mg/kg q2–4wk IM (see also Methyltestosterone)

Testosterone propionate
Testex
Malogen
0.5–1.0 mg/kg 2–3 times/wk IM (see also Methyltestosterone)

Tetanus toxoid (equine antitoxin)
100–500 U/kg (maximum 20,000 U); IV slowly over 5–10 minutes

Tetracycline
Panmycin
Achromycin
15–22 mg/kg q6–8h PO
4.4–11.0 mg/kg q8–12h IV, IM
(See also Oxytetracycline, Doxycycline, Minocycline)

Theophylline
Dog: 9 mg/kg q6–8h PO
Cat: 4 mg/kg q8–12h PO
(See also Aminophylline)

Theophylline (long-acting)
Theo-Dur
Slo-bid Gyrocaps
Dog: 20 mg/kg q12h PO (Theo-Dur) 30 mg/kg q12h PO (Slo-bid)
Cat: 25 mg/kg q24h PO at night

Thiabendazole
Omnizole

Equizole
Dog: 50 mg/kg q24h for 3 days, repeat 1 month
Cat *(Strongyloides):* 125 mg/kg q24h for 3 days

Thiacetarsamine sodium
Caparsolate
2.2 mg/kg IV twice daily for 2 days

Thiamine (vitamin B_1)
Dog: 10–100 mg/dog/d PO
Cat: 5–30 mg/cat/d PO (up to a maximum dose of 50 mg/cat/d)

Thiomalate sodium
See Gold sodium thiomalate

Thiopental sodium
Pentothal
Dog: 6–10 mg/kg IV (to effect)

Thiotepa
0.2–0.5 mg/m^2 intracavitary or IV

Thyroid hormone
See Levothyroxine, Liothyronine

Thyrotropin (TSH)
Thytropar
Dog: collect baseline sample, followed by 0.1 IU/kg IV (maximum dose is 5 IU); collect post-TSH sample at 6 hours
Cat: collect baseline sample, followed by 2.5 IU/cat IM and collect post-TSH sample at 8–12 hours

Ticarcillin
Ticar
33–50 mg/kg q4–6h IV, IM

Tiletamine plus zolazepam
Telezol
0.5–4.0 mg/kg IV, 4–10 mg/kg IM, SC

Tobramycin
Nebcin
2 mg/kg q8hr IV, IM, SC

Tocainide
Tonocard
Dog: 10–20 mg/kg q8h PO

Toluene
267 mg/kg PO (of Toluene), repeat in 2–4 weeks

Topiramate
2–10 mg/kg q12h PO

Tramadol
Dog: 1 mg/kg q12h PO

Triamcinolone
Vetalog
Aristocort
Anti-inflammatory: 0.5–1.0 mg/kg q12–24h PO, taper dose to 0.5–1.0 mg/kg q48h PO

Triamcinolone acetonide
Vetalog
0.1–0.2 mg/kg IM, SC, repeat in 7–10 days
Intralesional: 1.2–1.8 mg, or 1 mg for every cm diameter of tumor q2wk

Tribrissen: see Trimethoprim sulfadiazine

Trientine hydrochloride
Syprine
10–15 mg/kg q12h, PO (1 hr before meals, do not give concurrently with other medications).

Triflupromazine
Vesprin
0.1–0.3 mg/kg IM, PO q8–12h

Tri-iodothyronine
See Liothyronine

Trimeprazine
Panectyl
0.5 mg/kg q12hr PO (also see Temaril-P)

Trimethobenzamide
Tigan, Trimazide
Dog: 3 mg/kg q8h IM, PO
Cat: not recommended

Trimethoprim plus sulfadiazine
Tribrissen
15 mg/kg q12hr IM, PO, or 30 mg/kg q12–24h SC, PO (for Toxoplasma: 30 mg/kg q12h PO)

Tripelennamine
Pelamine
1 mg/kg q12h PO

TSH (thyroid-stimulating hormone)
See Thyrotropin

Tylosin
Tylocine, Tylan
20–40 mg/kg q12h PO

Urofollitropin
Metrodin
Cat: 2 mg/cat q24h IM

Ursodiol (ursodeoxycholate)
Actigall
10–15 mg/kg q24h PO

Valproic acid
Depakene
Dog: 60–200 mg/kg q8h PO; or 25–105 mg/kg q24h PO when administered with phenobarbital

Vancomycin
Vancocin
Dog: 15 mg/kg q6–8h IV
Cat: 12–15 mg/kg q8h IV

Vasopressin (ADH)
Pitressin
Aqueous (20 U/ml): 10 U IV, IM (see also Desmopressin acetate)

Verapamil
Calan
Isoptin
Dog: 0.05 mg/kg q10–30 min IV (maximum cumulative dose is 0.15 mg/kg); oral dose is not established
Cat: 1.1–2.9 mg/kg q8h PO

Vermiplex
See Toluene

Vinblastine
Velban
2 mg/m^2 q7–14d IV

Vincristine
Oncovin
Antitumor: 0.5–0.75 mg/m^2 q7d IV
Thrombocytopenia: 0.025 mg/kg once/wk IV

Viokase (See Pancreatic enzyme)

Vitamin A (Retinoids)
See Isotretinoin (Accutane), Retinol (Aquasol A), or Etretinate (Tegison)

Vitamin B complex
Dog: 0.5–2.0 ml q24hr IV, IM, SC
Cat: 0.5–1.0 ml q24hr IV, IM, SC

Vitamin B_1
See Thiamine

Vitamin B_2
See Riboflavin

Vitamin B_{12}
See Cyanocobalamin

Vitamin C
See Ascorbic acid

Vitamin D
See Dihydrotachysterol; Ergocalciferol

Vitamin E (Alpha tocopherol)
Aquasol E
100–400 IU q12h PO (or 400–600 IU q12h PO for immune-mediated skin disease, hepatitis, and copper-associated liver disease)

Vitamin K_1
AquaMEPHYTON
Mephyton
Short-acting rodenticide toxicity: 1 mg/kg/d SC, PO for 10–14 days; long-acting rodenticide toxicity: 3–5 mg/kg/d SC, PO for 3–4 weeks; birds: 2.5–5.0 mg/kg q24h
Severe cholestatic liver disease: 1 mg/kg q12hr SC or IM

Warfarin
Dog: 0.1–0.2 mg/kg q24h PO (adjust dose by monitoring clotting time)
Cat: 0.06–0.1 mg/kg (monitor clotting time)

Xylazine
Rompun
Dog: 0.3–0.8 mg/kg IV, 0.5 –1.5 mg/kg IM, SC
Cat: 0.4–1.0 mg/kg IV, 0.8–1.8 mg/kg IM, SC

Yohimbine
Yobine
For xylazine reversal: 0.1–0.4 mg/kg IV

Zinc
Liver copper chelation: 5–10 mg/kg q12hr PO (1–2 hr separate from meals)

Zidovudine (AZT)
Retrovir
Cat: 15 mg q12h to 20 mg/kg q8h PO

Zolazepam
See Tiletamine plus zolazepam

Zonisamide
5–10 mg/kg/d PO (divide bid or tid)

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